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Message from the Chairman of Board of Trustees

On behalf of the Trust Board and Management, I extend a warm welcome to all participants involved in the publication of the 11th Volume of NSHM Journal of Pharmacy and Healthcare Management. The journal emphasizes the high quality of original research articles while also encouraging reviews and short communications. It focuses on innovative research and development in health sciences, making it a remarkable event in the Healthcare field.

The journal aims to provide a platform for leading experts, researchers, practitioners, and policymakers to share their opinions and explore the innovative transformations occurring in the field of Pharmacy and Healthcare. As technology rapidly advances, it is crucial for us to adapt and seize the opportunities presented by the digital era.

I would like to express my sincere gratitude to all the participants, sponsors, and organizers who have contributed to making this journal a reality.

Your support and dedication are invaluable in ensuring the success of this event.

Regards,

Dr. Utpal Naresh Patel

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Message from the Chief Mentor

It gives me immense pleasure & honour to celebrate the launch of the 11th issue of the NSHM Journal of Pharmacy & Healthcare Management. This momentous occasion marks another significant milestone in our relentless pursuit of knowledge and innovation in the fields of pharmacy and healthcare management.

Over the years, the NSHM Journal has evolved into a platform that not only disseminates research but also fosters intellectual exchange and collaboration among scholars, researchers, and practitioners. Each issue is a testament to the dedication and hard work put in by our editorial team, reviewers, and authors who contribute their valuable insights and findings.

In today's rapidly changing world, the domains of pharmacy and healthcare management are facing unprecedented challenges and opportunities. The ongoing global health crisis has underscored the critical importance of healthcare systems and pharmaceutical research in safeguarding the well-being of our communities. This journal plays a pivotal role, serving as a beacon of knowledge that illuminates the path forward.

The research papers, reviews, and articles have been carefully curated to provide an overview of the latest trends, innovations, and breakthroughs in health sciences. They represent the collective wisdom of experts from around the world, and I believe you will find them both insightful and inspiring.

I would like to take this opportunity to express my gratitude to the authors and the reviewers, whose expertise and insights have been invaluable in maintaining the journal's reputation for excellence.

Wishing all of you an enriching and insightful experience with this latest edition of our journal.

With Best Regards

Cecil Antony

Chief Mentor, NSHM Knowledge Campus

Message from the Desk of Chief Editor

This is the eleventh consecutive year that we celebrate the launch of 11th volume of the NSHM Journal of Pharmacy and Healthcare management the official journal of NSHM Institute of Health Sciences, NSHM Knowledge campus Kolkata.

First and foremost, I would like to extend my heartfelt thanks to all the authors who have submitted their valuable research and manuscripts to our journal. Your commitment to pushing the boundaries of knowledge in your specific areas of expertise is truly admirable. The institute acknowledges the significance of research in technical education and is dedicated to fostering a research-oriented mind-set among both students and faculty.

I would also like to extend my appreciation to our reviewers and members of the editorial board and members of the journal publication committee, who have invested a substantial amount of their time and expertise in reviewing the manuscripts that have been submitted. Your critical evaluation, constructive feedback, and commitment to ensuring the integrity and rigor of the published articles are vital to maintaining the credibility of our journal.

As we move forward, we remain committed to quality and integrity in the publication of research. We will persist in our pursuit of excellence, offering researchers a platform to present their pioneering work. We will continue to strive for excellence and provide a platform for researchers to showcase their ground-breaking work. we look forward to your continued support and collaboration in the future.

Finally, I congratulate the members of the Advisory board and Chief patron for their continued support.

Prof. (Dr.) Subhasis Maity

Chief Editor

Director, NSHM Institute of Health Sciences

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BIOMARKER IN PUBLIC HEALTH RESEARCH WITH A SPECIAL FOCUS ON CONTROL OF SILICOSIS AND SILICO-TUBERCULOSIS BY THEIR EARLY DETECTION AND NECESSARY INTERVENTION

Prof. (Dr.) Kamalesh Sarkar, Department of Public Health, NSHM Knowledge Campus

Abstract:

Biomarker is often proved to be an essential component for public health activities such as control of diseases of public health importance. In this article, club cell protein 16 or CC-16 has been described as a biomarker to evaluate silicotic lung damage by using it as a screening tool for early detection of silicosis and silicotuberculosis. Research carried out by the Indian Council of Medical Research – National Institute of Occupational Health (ICMR-NIOH) had conclusively evidenced that CC-16 (a lung protein) is inversely related with the extent of lung damage among the occupational-inhalational silica dust exposed workers; higher the exposure with higher silicotic lung damage, more is the decline of serum CC-16 level. Public health scientists have suggested to use it as a proxy biomarker and screening tool for early detection of silicosis and silicotuberculosis through a suitably designed and initiating a national silicosis control programme. They have also evidenced that unless silicosis is controlled, elimination of tuberculosis is not possible from our country (which is mandated by the Government of India by 2025) as India has a huge burden of silicosis and silicotic subjects are highly vulnerable to lung tuberculosis due to progressive decline of their lung immunity. So, early detection of silicosis and silicotuberculosis along with required intervention are absolutely necessary to achieve the elimination of tuberculosis in our country. The biomarker, CC-16 might play an important role towards that if a point-of-care and user friendly device is made for detection of serum CC-16 level.

Introduction:

A biomarker or biological marker is an objective measure that signals what is happening in a cell or an organ or its related system at a given point of time. Biomarkers can serve as an early warning system for our health. On the other hand, silicosis is a neglected occupational respiratory disease caused by continuous or intermittent inhalational exposure to dust containing crystalline silica particles with a size of 3 micron or less (figure-1). Workers working in mines, stone cutting, quarrying, road and building construction, glass manufacturing, steel industry, ramming mass industry, thermal power industry, sandblasting, some *hobbies* can involve exposure to silica e.g. sculptor, and working with artificial stone, etc., are vulnerable to silicosis. India has a huge burden of silicosis. An article published in the Lancet indicated that an estimated 11.5 million people are at risk of silicosis in India (1). However, this appears to be grossly underestimated as silicosis is often diagnosed at a late or advanced stage by a chest x-ray or CT scan. Before it is detectable by chest x-ray, a lag period of 10 to 15 years is passed during which the disease is not detectable radiologically but by lung biopsy or pathologically. This is known as sub-radiological silicosis, which was not included in the above estimation. It appears the number of sub-radiological silicosis cases would be more than the estimated number of radiological silicosis cases in India due to huge population growth, massive industrialization, and rapid urbanization since the last few decades. A similar observation was observed in a study in South Africa that showed sub-radiological cases were more compared to radiologically confirmed silicosis cases (2).

Silicosis is a progressive, irreversible, incurable disease. Once exposure has occurred, the disease progresses even after the stoppage of silica dust exposure. There is no treatment available to cure the disease except by providing symptomatic and supportive treatment. As a result, often silicotic workers die prematurely due to progressive destruction of both lungs between the ages of 30 and 50 years. Other outcomes of silicosis are pulmonary tuberculosis,

kidney disease, lung cancer, etc. Silicosis declines lung immunity progressively, thus facilitating the development of pulmonary tuberculosis, known as silico-tuberculosis. Sub-radiological silicosis also facilitates the development of pulmonary tuberculosis. The adverse outcomes of silico-tuberculosis are the development of multidrug-resistant tuberculosis (MDR-TB), the uncertainty of treatment outcomes, and difficulty in the detection of TB bacilli in silicotic subjects. Considering the above, it appears unless silicosis is controlled, the elimination of tuberculosis from India is difficult to achieve by the year 2025 (3), which is mandated by the Ministry of Health & Family Welfare, Govt. of India.

Methodology:

With the above background, the ICMR-National Institute of Occupational Health (ICMR-NIOH) has already identified, a lung protein for assessing its role in evaluating the existence and magnitude of silicotic lung damage among the occupational silica dust-exposed workers (4,5). The said biomarker is club cell protein 16, in short, known as CC16. Earlier, it was known as the Clara cell. It is a protein, secreted from the non-cilliated distal bronchial epithelial cells. It is anti-inflammatory in nature and protects the lung tissue against any lung injury by the offending agents. At least 22% (6) of the lung epithelial cells constitute CC16-secreting cells. There is a progressive destruction of CC16-secreting cells and serum CC16 value in silicotic lung damage. In acute silicotic lung injury, there is a temporary increase in serum CC16 value, which usually declines within the next 24 hours. However, in chronic silicosis, serum CC16 remains declined persistently due to the permanent destruction of lung tissue caused by silica dust-induced inflammation leading to fibrosis. Since most silicosis cases belong to chronic silicosis, serum CC16 proves to be an effective biomarker for assessing silica-induced lung damage. ICMR-NIOH conducted a number of studies with silicosis and serum CC16 (4,5). Three groups of x-ray confirmed silicosis patients were subjected (mild, moderate and severe or high) for this study. Their blood samples were drawn for testing CC-16 level, which was test

by ELISA. The values were compared with serum CC-16 level of unexposed or healthy control subjects.

Results:

Initially, an study showed progressive decline of serum CC16 values in cases with short-duration silica exposure but without having x-ray evidence of silicosis and cases with x-ray-confirmed silicosis from the serum CC16 values of healthy subjects. But the second study showed progressively declined values of serum CC16 in mild, moderate, and severe x-ray-confirmed silicotic subjects. The categorization of X-ray-confirmed silicosis was done by using International Labor Organization (ILO) radiography guidelines for assessing silicosis. Both the studies conclusively evidenced in favor of use of CC-16 as a biomarker for assessing silicotic lung damage including assessing its sub-radiological component too.

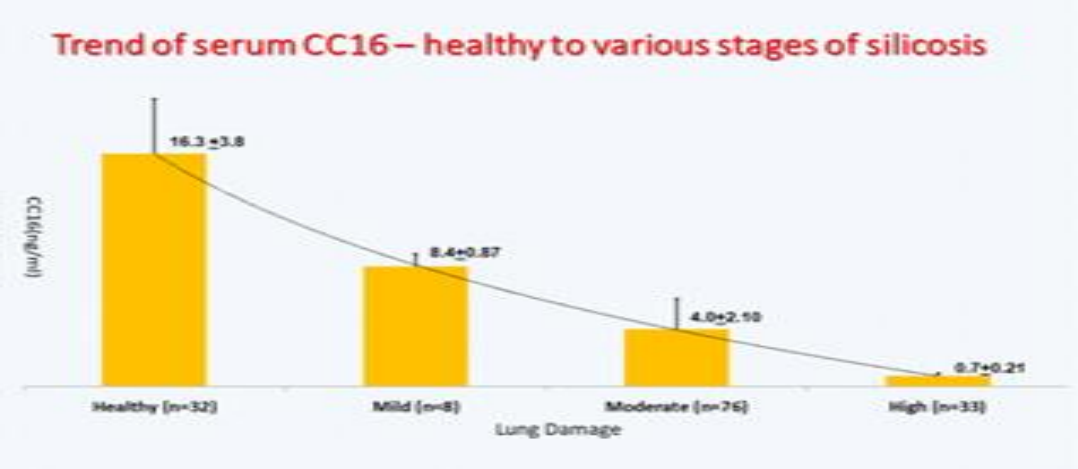

Fig-1: Serum CC-16 level & its declining trend in mild, moderate & severe silicosis

Discussion:

It may be noted that CC-16 is not a specific marker for assessing silicotic lung damage (7). Serum CC-16 levels will change in other lung-damaging conditions too such as lung cancer, Covid-pneumonia, etc. But when a selective group of occupational silica dust-exposed workers is assessed, it would provide a reasonably reliable indication of silicotic lung damage. Hence,

it is better viewed as a proxy marker and a screening tool for early detection of silicosis among silica dust-exposed workers for early and effective intervention. If required intervention is done, it will prolong the life of the affected workers. Since silicosis is a neglected public health and occupational disease and workers are under the Ministries of Labor, Mines, Industries, etc.,

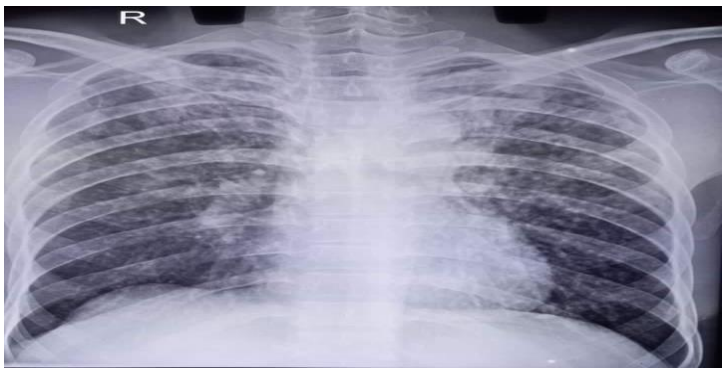

Fig-2: Chest X-ray of a silicosis affected worker showing bilateral patchy white opacities

there are hardly any initiatives taken by the Ministries of Health. But control of tuberculosis is strongly linked with control of silicosis as already mentioned. Ministry of Health is committed to eliminating tuberculosis by the year 2025. Hence, the integration of both control activities needs to be done together for dual control of both silicosis as well as tuberculosis. Effective coordination among all the relevant departments as mentioned above, is urgently required to achieve this. It may be noted that healthy workers are a precious asset of any country as they maintain the productivity of the country and thereby economy of the country. Therefore, the Government of India needs to initiate a national silicosis control program on an urgent basis to achieve as mentioned above.

Scientists have been working on the development of a rapid serum CC16 detection kit so that it could be utilized in the national silicosis control program. If we train all our designated peripheral health care workers in all states to detect serum CC16 levels periodically (annually) among the silica dust-exposed workers residing in nearby areas along with maintaining a national/regional digital register linking unique identifier (Adhar no.) of detected subjects,

perhaps it would work. There should be a system of tracking a subject longitudinally using Adhar no., as many of them are migrant workers. Once early suspicion of silicosis is done, intervention should be initiated. There is no need to wait for X-ray confirmation. It may be noted that repeated screening promotes healthy behavior. So, the periodic screening will definitely help him to avoid and/or minimize further silica dust exposure by various means, using protective devices, and creating pressure to their managers for providing a healthy workplace with dust-sucking and mechanized facilities. Once silicotic lung damage is detected by estimating the serum CC16 level, sputum of the same needs to be tested for CB-NAAT or True-NAAT diagnostic mechanism to explore presence of tubercle bacilli if any. Suitable legislation is necessary for the support of vulnerable workers. Silicosis is a compensable disease in India but it needs to be confirmed radiologically. Sub-radiological silicosis and sub-radiological silico-tuberculosis cases must be brought under the umbrella of compensation by the appropriate authorities.

Conclusion:

With above background, it is hoped that the elimination of both silicosis as well as silicotuberculosis will show its momentum using advanced technology for making a suitable point-of-care device and using CC-16 as an effective biomarker under an effective and targeted diseases control programme.

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MEDICINAL USE OF MICROBIAL SIDEROPHORES

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Abstract

Siderophores are chemical substances that sequester iron from the environment. Mammalian cells use some iron-binding proteins to limit the growth of bacteria. Bacteria, on the other hand, secrete siderophores to fetch iron in iron-restricted environments. Siderophores can be used to deliver antibiotics into the bacterial cells and also to bind and remove iron in the clinical management of iron-overload diseases. Some other potential applications of siderophores are highlighted.

Keywords: siderophoresis, iron,bacteria, clinical importance.

Introduction

Iron is essential to various forms of life. In humans, it is required for the synthesis of the oxygen-carrying proteins viz hemoglobin and myoglobin, deoxyribonucleic acid and some hormones. In microorganisms also, it is needed for the reduction of oxygen and formation of ATP. A number of enzymes require iron as cofactor in various biological systems. Iron is one of the most widely available elements in earth. It constitutes more than 30% of the mass of the earth. However, despite being ubiquitous, it is not widely available to the living organisms since in the aerobic environment of this planet, naturally-occurring iron exists mostly in the ferric state (Fe^{3+}) that forms an insoluble rust-like solid. Free iron is cytotoxic. Some highly specialized networks of proteins regulate concentration of free iron in our body. Majority of iron in our body is present as heme.

The growth of pathogenic bacteria is inhibited or retarded in the tightly-regulated iron concentration prevailing in the host system. That is why use of iron supplements during a

bacterial infection may have a counter-productive effect on the management of the infection. When bacteria are challenged with an iron-deficient condition, some genes are turned on, leading to the synthesis and secretion of a group of organic compounds called siderophores. These low molecular weight (500-1500 daltons) chemical substances synthesized and secreted by bacteria yeasts fungi and plants, detect iron (Fe^{3+}) even when it is present in low concentration and form complex with it. Following receptor-mediated transport of the ferric iron-siderophore complex into the cytoplasm, the ferric ion is reduced to the ferrous state, which is utilizable to the organism. Pathogenic bacteria prevent competing microorganisms from taking iron. But they have to compete also with the hosts for supply of iron. The host cells use iron-chelating compounds to deprive invading pathogens of iron. Lactoferrin, for example, is a protein secreted by the neutrophil granules at the site of inflammation. It inhibits bacterial growth by sequestering iron. A bacterium *Borrelia burgdorferi*, the causative agent of Lyme disease, overcomes the challenge by directly acquiring iron from the iron-carrying proteins present in the host (heme, transferrin or lactoferrin). But other bacteria bypass the crisis by secreting the siderophores, the iron-specific chemical chelators.

Bacterial siderophores

Synthesis and secretion of siderophores are found to occur in many bacteria (e.g *Pseudomonas, Azotobacter, Bacillus, Enterobacter, Serratia, Azospirillum, Rhizobium, Actinomycetes*). Gram-positive and gram-negative bacteria use different mechanisms involved in siderophore-mediated transport of iron. Fungi utilize multiple mechanisms of iron transport using siderophores.

Varieties of siderophores

More More than 500 different types of siderophores are known. Out of them, 270 have been structurally characterized. They belong to different categories viz hydroxamates, catecholates

and carboxylates. Hydoxamates, the most common group of siderophores, are made up of C(= O) N-(OH)R, where R is an amino acid and its derivatives. They are formed by bacteria and fungi. The prototype of catecholate siderophores is enterochelin (enterobactin). It is a cyclic catecholate siderophore produced primarily by gram-negative bacteria e.g *E. coli*, *S. typhimurium* and *K. pneumoniae*. Production of a mixed catecholate-hydroxamate siderophore was reported earlier. Some species are known to produce linear catecholate siderophores also. Rhizobactin, produced by *Rhizobium meliloti* strain DM4, is an example of carboxylate siderophore. It is an amino poly(carboxylic acid) with ethylenediaminedicarboxyl and hydroxycarboxyl moieties as iron-chelating groups. Under conditions of iron deficiency, graminaceous plants (e.g. barley and wheat) also secrete Fe^{3+}-chelating compounds. The most common and the first identified phytosiderophore is Mugineic acid.

Medicinal importance of siderophores

The dependence of bacteria on iron forms the basis of a therapeutic approach called “Trojan horse” strategy. Some naturally occurring siderophore-antibiotic conjugates (Albomycins, Ferrymicins, Salimycins) are transported into the microbial cells utilizing the iron-transport ability of the siderophores. Taking cues from the nature, attempts have been made to design some siderophore-antibiotic conjugates that are taken up by pathogenic bacteria. Like the proverbial “Trojan horse” these conjugates release the antibiotic within the cell, ultimately leading to the death or growth inhibition of the bacteria. A typical example of this strategy is a catechol/ hydroxamate siderophore analog conjugated with a β-lactam antibiotic. Promising results were obtained in an investigation performed some time back involving BAL30072, a siderophore-monosulfactam.

The potential of iron-chelators in the treatment of cancer is beginning to be understood. The iron-chelators deprive cancer cells of iron, an essential nutrient, and thus restrict growth of the

tumors. In addition to this, they may form redox-active metal complex, causing a cytotoxic effect within the cancer cells by producing reactive-oxygen species.

Some siderophores are known to enter the cells of the malarial parasite *Plasmodium falciparum* leading to depletion of intracellular iron. Potential of the siderophores in the clinical management of malaria is under investigation.

Patients who undergo prolonged hemodialysis, may develop aluminium overload and consequent dialysis encephalopathy because of the use of untreated tap water in the preparation of the dialysis fluid. Besides electroencephalographic abnormalities, dialysis encephalopathy is characterized by disturbances of speech, cognition, movement or behavior. Death was also reported in some cases. The aluminium-chelating siderophore Desferrioxamine B was claimed to have a definitive therapeutic effect on the clinical and EEG manifestations of dialysis encephalopathy, when used in conjunction with deionized or reverse osmosis water.

Iron overload or hemochromatosis is a serious problem that damages various organs including the heart, liver and pancreas. The problem is hereditary in nature. Transfusion, hemolysis and excessive dietary consumption of iron are believed to be some of the secondary causes behind accumulation of excess iron in the body. Some siderophore-based drugs appear to be promising candidates in the clinical management of such conditions.

Concluding remarks

The multifaceted potential of siderophores in therapeutics remains by and large, an unexplored area of research. Extensive studies are required to ascertain their efficacy and also safety.

The ability of siderophores to act as biosensor and also as agents for biocontrol, bioremediation and chelation has been reported, besides their important role in weathering soil minerals and

enhancing plant growth. Rapid progress in these areas of investigation is expected during the years to come.

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COLON-TARGETED DELIVERY OF BUDESONIDE FOR THE TREATMENT OF INFLAMMATORY BOWEL DISEASE

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Abstract

In the case of inflammatory bowel disease (IBD), the target of delivery at the site of action is a major challenge for formulators. Oral budesonide (BUD) has been recommended by the European Crohn's and Colitis Society (ECCO) as the preferred medication for the treatment of IBD. BUD is a corticosteroid that acts locally and has a strong affinity for glucocorticoid receptors. BUD has a limited ability to dissolve and exert therapeutic effects due to its weak solubility and bioavailability. Colonic administration of BUD must be enhanced for IBD patients by a more dependable colon-specific formulation with extended residence time and regulated release at the location of inflammation. In the treatment of IBD, the administration of BUD via hydrogel matrices and nanocarrierhas proven to be an advantageous method that can specifically target and localize the drug at the inflamed colon tissues with low side effects and better therapeutic efficacy. The development of functionalized nanocarriers that selectively absorb into inflammatory cells and specifically release within target cells would provide a new challenge. This review discusses the hydrogel matrices and nanocarrier for colon targeted delivery of budesonide.

Keywords

Inflammatory bowel disease, colon targeting, Budesonide, hydrogel, nanocarrier, natural polysaccharides.

1. Introduction

IBD is a group of inflammatory diseases that includes Crohn's disease **(**CD) and Ulcerative colitis (UC)[1]. Although the colon is the primary area of the gastrointestinal (GI) tract affected by CD, it can also spread to other areas of the GI tract, frequently leading to transmural inflammation. CD patients experience the development of lesions in Peyer's patches [2]. The aggregation of many macrophages frequently results in the formation of non-necrotizing granulomas. In contrast, UC only affects the colon and is characterized by a significant inflammatory response, the creation of complex inflammatory mediators, and the emergence of mucosal ulcers. It is discovered that a prominent histological characteristic of UC is neutrophilic excess in the lamina propria that results in crypt abscesses. The goblet cells' ability to produce mucin also declines. Abdominal discomfort and diarrhea are the primary clinical signs of IBD. Additionally, CD has higher rates of weight loss and perianal illnesses while UC has higher rates of rectal hemorrhage.Although the exact cause of IBD is unknown, genetic, immunological, and environmental factors have all been proposed as potential contributors. The use of steroids, antibiotics, aminosalicylates, and even immunosuppressive medications are some of the standard treatments for IBD, even though there is currently no treatment available. The primary goals of medication are to treat active disease, provide and maintain remission following a reduction in symptoms [3]. Treatment for CD and UC is based on the patient's drug tolerance, the subtype of the disease, how severe the IBD is, and other factors. Anti-inflammatory medications are the most often utilized pharmacological classes to treat IBD's acute inflammation.

The European Crohn's and Colitis Organization (ECCO) claims that oral budesonide (BUD) is the drug of choice for the treatment of inflammatory bowel disease (IBD) [3]. BUD is a potent glucocorticosteroid with broad anti-inflammatory effects. BUD is locally efficacious in the GIS with much less systemic adverse effects than traditional corticosteroids due to its extensive first-pass liver metabolism. BUD release from oral formulations needs to be managed for local medication administration in GIS inflammation to be successful. In addition, drug release should reach the entire affected area rather than just one site because intestinal inflammation is typical in IBD. Only a regulated medication release that targets the inflammatory region during the GI transit can do this.

Different strategies are used by commercially available oral BUD formulations to target the site of the inflammation. Enteric-coated tablets, pellets, granules, and capsules coated with a pH-sensitive polymer are some of the colon delivery methods currently available for this type of disease [4]. However, diarrhea, a typical IBD symptom, typically shortens the residence period of these delivery systems. The effectiveness of the single unit and large particle delivery methods may be hampered by the observed incidence of diarrhea associated with IBD, which ranges from 66 to 92%. Another issue with pH-dependent systems is early drug release in the small intestine due to inter- and intra-individual variations in gut pH, which leads to a reduction in therapeutic efficacy. The creation of a medicine delivery system that can target the colon's inflammatory tissue specifically is therefore still urgently needed. A method like this could increase therapeutic effectiveness while minimizing systemic adverse effects related to anti-inflammatory medication.

Extended-release or sustained-release medication has recently been utilized to treat chronic illnesses. The advantages of controlled-release dosage forms include their potential to provide locational or time-based release control due to the use of the proper polymer. The targeting of the colon is crucial for preventing medication release in the entire stomach region and the

intestines. The delivery mechanism should be created for the site-specific release taking into account the environmental variations between the small and large intestine, including microbial content, pH of digestive fluids, and transit duration. To address issues with conventional formulations advances in nanotechnology have been used in the creation of various conventional dosage forms. The systemic toxicity levels of the incorporated medications inside the patient's body are reduced as a result of the nanoparticles' ability to increase drug stability. As demonstrated in situations of experimental colitis, they can easily get into dendritic cells or macrophages in the inflammatory zone. They can adhere to the mucosa more effectively due to their low mass and ease of penetration. This selective absorption is also hypothesized to be influenced by pathophysiological alterations brought on by mucosal layer inflammation: (i) crypt deformities, changes in the mucosal surface, and ulcers may disrupt the intestinal barrier; (ii) an invasion of dendritic cells, macrophages, or lymphocytes; and (iii) an increase in mucus production. The increased distribution of entrapped drugs to the areas of inflammation is made possible by the higher concentration of nano-sized drug carriers, improving therapeutic effectiveness and reducing side effects. Nakase et al. recently presented a novel therapeutic strategy that uses a micro-particulate drug delivery technology to target the immune regulatory cells in IBD [5]. It has been demonstrated that macrophages and M cells present at the site of inflammation can effectively absorb small-size particle drug delivery systems. Additionally, a breakdown in the intestinal barrier's ability to function would allow the accumulation of the particle delivery system at the site of inflammation [6]. According to Lamprecht et al., the efficacy of this accumulation increases with decreasing particle size and is the highest for nanoparticles of about 100 nm [7].

The medicine is protected from the stomach's low pH and digestive enzymes by a colon-targeting drug delivery system, and it should release when it enters the colonic environment [8]. The dosage form's mucoadhesive capabilities should be sufficient to deliver the medication

to the colon. The contact time of the formulation at the target site is extended by the sticky interaction. Because of its hydrophilicity and loose, porous 3D network structure, hydrogel is one of the most competitive ones [9]. Over the past few decades, research into hydrogel materials for IBD has grown. Natural polymers like chitosan, alginate, hyaluronic acid, and dextran, as well as proteins like chondroitin sulfate and gelatin, have been used to create hydrogels for IBD. Since its inception as a single medicinal carrier, hydrogels' functions have evolved and become increasingly multifaceted. The effectiveness of treating IBD can be increased by using enteral drug delivery that is effective and manageable. Fourth-generation polyamide dendrimers conjugated to 5-ASA nanoparticles (G4-ASA) were created by Wang and colleagues [10]. To create the injectable and sticky 5-ASA hydrogel, the surface amino groups of G4 were further utilized to cross-link with oxidized dextran via the Schiff base reaction. 5-ASA was progressively delivered into the colon through rectal injection, where it chemically linked with the intestinal mucosal epithelium and became permanently attached to the intestinal wall. Additionally, G4 made 5-ASA more soluble in water, which improved its ability to treat intestinal disorders.The colon is the primary target of the conventional IBD drug delivery techniques discussed earlier, not the actual location of inflammation. It can be difficult to target the inflamed intestinal tissue itself, especially if it is not in the expected target area. This is particularly true with CD, in which the sites of inflammation are dispersed throughout the GI tract in a typically discontinuous fashion. The GI tract has different physiological conditions;therefore, traditional targeted medication delivery devices don't work well. Additionally, the pattern of inflammation is typically discontinuous even when patches of inflammation are present in the targeted intestinal region. Because of this, only a small portion of the medication may reach the sites of inflammation; the remainder may instead cause serious side effects by being absorbed into the bloodstream through the gut's healthy regions (as is the case with CD). Therefore, two significant problems when adopting drug delivery systems in

the management of IBD are targeting medications selectively to the sites of inflammation and avoiding absorption from the healthy intestinal regions.

2. Inflammatory bowel disease(IBD)

IBD, also known as inflammatory bowel disease, is a chronic, multifactorial, recurrent illness marked by immune system disorders and intestinal inflammation [11]. The epidemiology of IBD, a condition prevalent in developed countries, is evolving globally at the start of the 21st century. Gradual changes in eating habits, lifestyles, and living situations, such as the switch from high-fiber diets to fried or frozen foods, the industrialization of agriculture, and the transition from rural to urban regions, may have a significant impact on the occurrence of inflammatory bowel disease (IBD). IBD has only begun to be recognized as a disease that affects the entire world, with a high and stable incidence in Western nations and a fast-rising incidence in newly industrialized nations. In regions like North America, Oceania, and Europe, the prevalence of IBD has been estimated to be around 0.3% since 1990, whereas IBD cases have been rising each year in Asia, Africa, and South America. As a result, it is evolving into one of the major problems the world is currently confronting. IBD, or inflammatory bowel disease, is a group of inflammatory diseases that includes CDand UC. Although the colon is the primary area of the GI tract affected by CD, it can also spread to other areas of the GI tract, frequently leading to transmural inflammation. CD patients experience the development of lesions in Peyer's patches [2]. The aggregation of many macrophages frequently results in the formation of non-necrotizing granulomas. In contrast, UC only affects the colon and is characterized by a significant inflammatory response, the creation of complex inflammatory mediators, and the emergence of mucosal ulcers. It is discovered that a prominent histological characteristic of UC is neutrophilic excess in the lamina propria that results in crypt abscesses. The goblet cells' ability to produce mucin also declines. Abdominal discomfort and diarrhea

are the primary clinical signs of IBD. Additionally, CD has higher rates of weight loss and perianal illnesses while UC has higher rates of rectal hemorrhage.

Cause of IBD: Although the exact cause of IBD is unknown, genetic, immunological, and environmental factors have all been proposed as potential contributors. Although the precise cause of this illness has not been determined, it is widely believed that several factors, including the microbiome, genetics, environmental stress, and immunological dysfunction, play significant roles. Clinically immunocompetent individuals are typically affected by IBDs, which are brought on by a protracted, cytokine-driven GI tract inflammation. Granulomas are usually seen in CD, which is characterized by an excessive production of IL-17 and IL-12/IL-23 in the small intestine and colon, as well as intermittent ulceration and intestinal wall inflammation. In addition to GI problems, patients also report rectal bleeding, abdominal pain, weight loss, and fatigue. In people with CD, fistulae and bowel strictures are frequent. Contrarily, UC is associated with an overproduction of Interleukin-13 and has an impact on the colon. While there is no fistula formation in the case of UC, these symptoms are comparable to CD. While UC can be treated by surgically removing the colon, both conditions are typically chronic and recurrent. Traditional anti-inflammatory and immunosuppressive medications are utilized in medical treatment, including corticosteroids, mesalamine compounds, azathioprine, and its derivatives. IBD therapy aims to change the course of the illness while encouraging good lifestyle choices and weighing the potential dangers of the regimen.

Variations of gastrointestinal tract physiology during inflammatory bowel disease: Pathophysiological abnormalities brought on by mucous membrane inflammation include (a) excessive mucus production (b) a deformed intestinal wall as a result of mucosal surface variations, crypt abnormalities, and lesions (c) immune cell infiltration (e.g., dendritic cells, neutrophils, lymphocytes, and macrophages). In addition to experiencing reduced GI function and diarrhea during an IBD relapse, patients with chronic mucosal inflammation may also have

changes in pH, intestinal volume, and mucosal health. The inflammatory response at the mucosal membrane hinders the local microbiota, potentially changing the metabolism of bacteria in the GI tract. Active inflammation thus has an impact on the fundamental physiology of the GI tract, potentially lowering the effectiveness of medicine delivery to the colon.

3. Budesonide for the treatment of IBD

Treatment options for remission in CD vary depending on the location, severity, and behavior of the disease. The first-line treatment for nonsurgical colitis remains in various forms of 5-aminosalicylic acid (5-ASA; sulfasalazine or mesalazine), available in oral and rectal formulations. Rectal formulations may be more effective than oral formulations in the treatment of proctitis or left-sided colitis. For patients with mild-to-moderate CD affecting the ileum or ileum and proximal colon, first-line therapy would include oral conventional corticosteroids [12].

While conventional corticosteroids are often effective in achieving remission, they do so with a burden of medication-related effects that preclude their usefulness as maintenance therapy. Using data derived from a population-based cohort of IBD patients in the USA, steroid dependence has been shown to occur in 28% of patients and 22% of UC patients who were started on conventional corticosteroids within the first year of diagnosis [13]. The side effect profile of conventional corticosteroids has prompted the development of the synthetic corticosteroid BUD as an alternative to systemically active conventional corticosteroids.

BUD is a synthetic corticosteroid with potent local anti-inflammatory effects due to location-specific delivery along with limited systemic bioavailability due to extensive first-pass metabolism. BUD achieves its anti-inflammatory effects by regulating the production of NF-kB, IL-1, IL-6, and TNF-a [14]. BUD has a strong local effect due to its high affinity for

glucocorticoid receptors. The affinity of BUD for the glucocorticoid receptor is about 15 times greater than that of prednisolone, and greater than that of dexamethasone or triamcinolone, two potent corticosteroids [15-16]. The latest European Crohn's and Colitis Organization (ECCO) IBD treatment guidelines recommend BUD as a "first line" treatment for mild to moderately active localized CD [17].

An oral, controlled-release formulation of BUD for targeted use in the distal ileum and ascending colon for the treatment of CD was first reported in the early 1990s. BUD is available in three oral formulations: pH-dependent with a temporary drug release mechanism (Entocort®, AstraZeneca [Wedel, Germany] or Astra Draco [Lund, Sweden]; Entocir, SofarSpA [Trezzano Rosa, Milan, Italy]), pH-dependent BUD (Budenofalk® or Budeson®, Dr. Falk Pharma GmbH [Freiburg, Germany]) and multimatrix formulation (BUD). MMX®, Cosmo Technologies, Santarus [CA, USA]).

Various controlled-release formulations of BUD have been developed to protect against gastric damage and allow placement in clinically relevant sites such as the distal ileum, proximal colon, or entire colon.

The first-line treatment for nonsurgical colitis remains in various forms of 5-ASA, available in oral and rectal formulations. Rectal formulations may be more effective than oral formulations in the treatment of proctitis or left-sided colitis. Corticosteroids available such as hydrocortisone, BUD, and beclomethasone are effective when administered topically. The remission rate in patients with active proctitis or proctosigmoiditis treated with BUD as a liquid enema or foam is 60-66% after 4 weeks of treatment [18]. Although topical corticosteroids are effective in the treatment of UC, 5-ASA remains the first-line treatment because of its proven efficacy. Recent studies have shown the superiority of BUD for the induction of remission in

UC, and endoscopic and histological improvement, as well as improving the quality of life. These results are consistent with those reported in previous meta-analyses.

4. Why colon targeted delivery of BUD required?

Targeted drug administration into the GI tract, typically the colon or large intestine, is referred to as colon-specific drug delivery systems (CSDDS). There are multiple barriers to medicine distribution to the GI tract. The local management of ileocecal and intestinal illnesses is thought to be successful when using CSDDS. These include the management of inflammatory bowel disease (IBD) as well as intestinal conditions such as diverticulum, amebiasis, malignancy, and irritable bowel syndrome (IBS). Additionally, it can be utilized to administer proteins and peptides orally. The colon is rich in lymphoid tissue, and antigen uptake by colonic mucosal mast cells causes rapid local antibodies, resulting in negative antibodies [19]. Various methods are used with commercially available BUD formulations to target inflamed areas. Tablets or tablets coated with pH-sensitive polymers are often used in these formulations. This method is designed to interact with various GIT components.

Recently, extended-release or sustained-release drugs have been used to treat chronic diseases. Due to the proper use of polymers, controlled-release dosage forms can provide temporal or local control of release. Intestinal targeting is important to prevent drug spread throughout the digestive tract and intestines. Coupling mechanisms must be designed taking into account environmental changes between the small and large intestine, such as microbial composition, pH of the digestive fluid, and duration of transit [20].

Several approaches have been used in an attempt to achieve the targeting of drugs in the colonic region. This system is designed to meet the following requirements: to protect the drug or the system itself during intestinal transit, to regulate the time of entry into the intestine, and to

ensure the specific release of the drug. To achieve this specific intestinal delivery, three main mechanisms of action can be directed to the intestine after oral administration: pH-dependent coating, time-dependent coating, and biodegradation by colonic bacterial enzymes [21].

BUD is a locally acting corticosteroid with a high affinity for glucocorticoid receptors. It offers several therapeutic advantages such as negligible oral bioavailability, rapid clearance, and no formation of active metabolites and is therefore preferred over older steroids such as hydrocortisone, prednisolone, and dexamethasone for topical treatment of inflammatory bowel diseases. However, BUD has poor solubility and bioavailability, which limits its dissolution and therapeutic potential. However, the solubility of BUD needs further improvement, and a structure is needed for effective drug targeting [22].

The currently marketed oral controlled-release formulations release most of the BUD in the small intestine and proximal colon which is desirable in the case of CD [23-24]. However, their efficiency is limited in treating colonic inflammatory bowel disease that affects the lower parts of the colon [25]. For the benefit of IBD patients, colonic delivery of BUD needs to be optimized by a more reliable colon-specific formulation with prolonged residence time and controlled release at the site of inflammation. For the benefit of IBD patients, colonic delivery of BUD needs to be optimized by a more reliable colon-specific formulation with prolonged residence time and controlled release at the site of inflammation. The applicability of naturally available polysaccharides, such as starch, chitosan, and pectin have been tried as polymers in control release drug delivery applications [26].

5. Colon-targeted drug delivery system for budesonide

Colon-specific drug targeting is appropriate for both local and systemic effects. Several disorders, including UC, Crohn's disease, colon cancer, and irritable bowel syndrome, can be

treated with colon targeting [27-28]. Furthermore, the colon also serves as a target area for the delivery of enzyme-sensitive proteins and therapeutic peptides. The various enzymes in the stomach and small intestine can hydrolyze these proteins and peptides [29]. The ascending portion of the colon is thought to be the most appropriate location to administer colon-targeted drugs. Successful delivery of drugs to the colon needs several specific colonic environment features such as colonic pH, transit time through the colon, and enzymes produced by colonic microorganisms [30-32]. In colon-specific delivery of drugs, the active pharmaceutical component is targeted to the colon, and the delivery system should not release the drug in any other region in the GI tract instead of the colon.

As a result, acid-labile drugs can be effectively administered to the colon via colon-specific strategies [33]. Colon-specific drug targeting has various benefits, including colonic mucosa having reduced proteolytic activity and being the best site for peptide and protein absorption [34]. The colon-specific dosage forms have a longer retention time (up to 5 days), allowing for higher doses to be delivered. This extended transit time and increased targeting capabilities finally resulted in an enhanced therapeutic effect. Furthermore, colon targeting provides limited systemic absorption, resulting in a lower frequency of adverse effects.

5.1 Budesonide-loaded hydrogel matrix for colon targeting

Hydrogels comprise three-dimensional networks composed of hydrophilic polymers that can absorb a huge quantity of water without being dissolved in them [35]. They are soft and elastic, similar to normal tissue, and serve to minimize irritation and immunological reaction [36-38]. Water absorption inside the matrix and swelling of the hydrogel is facilitated by a large number of hydrophilic groups (COOH, NH_2, SO_3H, and OH), osmotic pressure, and capillary action [39].

Hydrogel is now recognized as a promising biomedical technology for the treatment of IBD. The role of hydrogels has evolved from a single drug delivery vehicle to an intelligent platform with the constant depth and refining of therapeutic needs. Although several research has been conducted using hydrogels to treat IBD, there are still significant challenges to overcome in clinical applications. The direct administration of drugs using hydrogel as a carrier has become the focus of IBD therapy.

Pandey et al. created a pH-sensitive and enzymatically triggered hydrogel of pectinand polyacrylamide for colon-targeted administration of BUD for the treatment of UC [40]. SEM revealed that the hydrogels had a highly porous shape, which is ideal for drug loading, as well as a pH-responsive swelling behavior, with less swelling in an acidic medium. The burst release of BUD from the hydrogel was followed by a sustained release behavior via a non-fickian diffusion mechanism. The Higuchi kinetic model was the greatest fit for the BUD released. It was determined that enzyme/pH dual-sensitive hydrogels are an efficient colon-targeted UC delivery strategy.

Kumar et al. created an enzyme-responsive injectable hydrogel (ER-hydrogel) to address the limitations of therapeutic enemas [41]. The hydrogels have two significant benefits for therapeutic drug delivery in UC: extended retention and enzyme responsiveness. For therapeutic objectives, BUD was encapsulated into the ER-hydrogel and investigated for its varied physicochemical and therapeutic potentials in dextran sodium sulfate-induced mice. In vitro and ex vivo adhesion investigations showed that the ER-hydrogel's retention or mucoadhesive nature, and the increase in Bud release from the Bud-loaded ER-hydrogel following the addition of esterase enzyme validated the ER-hydrogel's enzyme-mediated drug release. Furthermore, Bud-loaded ER-hydrogel has shown promising outcomes in reducing UC disease activity index and restoring colon length, which is a key feature of UC. The Bud-loaded ER-hydrogel healed colonic tissue damage, as demonstrated in H&E-stained, AB-NR-stained,

and HID-AB-stained colon sections. Ultimately, the Bud-loaded ER-hydrogel significantly reduced the levels of IL-1β, TNF- α, MPO, and nitrite in blood and colon tissues. Thus, the synthesized Bud-loaded ER-hydrogel has substantial translational potential due to its capacity to considerably reduce inflammatory changes in acute experimental colitis in mice when compared to a naïve or water-based therapeutic enema.

Crcarevska et al. created a novel hydrogel-based dosage form made of chitosan and alginate loaded with BUD which exhibited bioadhesive and controlled release capabilities in the GI tract [42]. The hydrophilic (chitosan-Ca-alginate) matrix of the microparticulate hydrogel system had been coated with the pH-sensitive (Eudragit® S 100) polymer. The physical characterization of produced microparticles confirmed their localization and prolonged release in the colon. The Eudragit coating had effectively maintained BDS release in the upper GIT (pH 2.0 and 6.8) while additionally permitting efficient BDS release in the colon (pH 7.4). The prepared formulations were stable for 12 months at regulated room temperature. Based on the results, Eudragit-coated chitosan-Ca-alginate microparticles loaded with BDS could be suitable candidates for controlled release oral delivery of BDS, opening up a new therapeutic potential for these carriers for local treatment of inflammatory bowel disease.

5.2. Budesonide loaded nanocarrier for colon targeting

Conventional oral drug delivery system such as tablets, granules, and capsules does not achieve expected success in IBD due to some obstacles such as enzymatic degradation, decreased stability, first-pass metabolism, and earlier systemic absorption from the stomach or small intestine. These problems reduced the concentration of the drug before reaching the inflamed location of the colon. Although, rapid clearance and short residence time of drug delivery systems were observed due to heavy diarrhea which is more visible in IBD. Repeated administration of drugs and higher dosages may cause severe adverse effects and also increase

patient compliance [43]. Moreover, BUD gets extensively metabolized by cytochrome P-450 enzyme because it has a strong affinity for glucocorticoid receptors. For that reason, a very low amount of the drug reaches into the systemic circulation [44]. BUD exhibits extensive hepatic first-pass metabolism (approx 85%) to the extent that imposes frequent administration of this drug or high doses by the oral route [45]. Hence, nanoparticulate-based drug delivery of BUD has shown an auspicious approach in IBD therapy which may specifically target and localize the drug at the inflamed colon tissues with minimal adverse effects, and improved therapeutic efficacy.

Ali et al, designed BUD-loaded poly(lactic-co-glycolic) acid (PLGA) nanoparticles by oil-in-water (O/W) emulsion technique which is further coated with pH-sensitive methyl-methacrylate-copolymer with particle size 200 ± 10.1 nm and 240 ± 14.7 nm, respectively [44]. They investigated that coated PLGA nanoparticles alleviated the delivery of the drug into the induced colitis significantly better than normal drug-loaded PLGA nanoparticles and more effective than conventional treatment with the same dose of the free drug. A drug release kinetics study exhibited that, PLGA nanoparticles and coated PLGA nanoparticles diminished the initial burst release at acidic pH and released the drug at neutral to slightly alkaline pH.

In another study, Vafaei et al prepared BUD-loaded self-assembled amphiphilic hyaluronic acid nanoparticles for targeted delivery to inflamed colonic tissue and to determine the targeting efficacy of the system [46]. Self-assembly of nanoparticles in an aqueous environment was obtained through chemical conjugation or amidation of an amine-terminated alkyl chain such as decyl amine onto the backbone of HA using carbodiimide chemistry. The prepared nanoparticles have a size range of between 177 to 293 nm with negative surface charge and confirmed higher anti-inflammatory effect on IL-8 and TNF-α secretion in inflamed cell models compared to the same dose of free drug.

Some researchers encapsulated BUD into nanostructured lipid carriers (NLCs) as nanoparticulate drug delivery systems by high-pressure homogenization with size of 200 nm and a negative zeta potential for the treatment of dextran sulfate-induced colitis in a murine model [47]. These nanocarriers exhibited their activity through decreased neutrophil infiltration and the levels of the pro-inflammatory cytokines IL-1β and TNF-α in the colon and improved the histological scores of the colons.

Ali et al focused on the in-depth pharmaceutical characterization of BUD-loaded PLGA nanoparticles and proved the accumulation of nanocarriers at the site of inflammation by in-vivo fluorescence imaging in a relevant mouse model [48]. Prepared nanoparticles have size within 200 ± 05 nm and $85 \pm 3.5\%$ encapsulation efficiency. They revealed the drug in the polymer matrix existed in the crystalline state by XPRD study. BUD release from the nanoparticles showed a biphasic release profile with an initial burst followed by sustained release due to the diffusion of drug molecules across the polymer matrix.

Some researchers synthesized BUD-encapsulated pH-triggered surface charge-reversal lipid nanoparticles (LNPs) by hot homogenization techniques, for exactly deliver the drug to inflamed colon segments for the treatment of UC [49]. Researchers used polyethyleneimine to render LNPs cationic and Eudragit® S100 was used to coat on polyethyleneimine-LNPs to obtain pH-triggered charge-reversal LNPs which could switch the surface charge of LNPs from negative to positive under colonic conditions. Eudragit coating avoided a burst release of the drug under acidic conditions into the stomach and early release in small intestine environments, exhibited a sustained release in the colon. Bioimaging results of the mouse GI tract and confocal analysis of colon tissues exposed that the lipid nanoparticles selectively accumulated in an inflamed colon.

In another research, BUD-loaded nanosized micelles were prepared for the treatment of dextran sulfate sodium (DSS)-induced UC [50]. They developed self-assembled micelles (an amphiphilic compound) where stearic acid, a hydrophobic core, and caffeic acid, hydrophilic tails are linked to each other with ethylenediamine and sufficiently encapsulate BUD. The micelles were self-assembled in aqueous media for convenient rectal administration in a mouse model of ulcer colitis. These micelles show cytocompatiblebehavior and sustained release behavior with downregulation of various related cytokines (myeloperoxidase enzyme, NO, and TNF-α) and inflammatory enzymes such as Cyclooxygenase 2 and inducible nitric oxide synthase. Therefore, they concluded that the smart nanocarrier drug delivery systems of BUD had a promising potential for targeted drug delivery of IBD.

6. Conclusion

A novel target-specific colonic drug delivery system can overcome some problems associated with conventional dosage forms for IBD treatment. Colon-targeted NDDS has made advancements by adjusting their size, shape, surface ligands, and drug release behaviour to promote safe and effective therapy of colon-specific illnesses. An ideal colon-targeted drug delivery system should be able to overcome all the physiological barriers in the GI tract, differentiate disease sites from healthy tissues and target specific cells, and on-demand release of BUD at specific doses. Surfaced charged smart nanocarriers can improve the therapeutic efficacy of BUD by avoiding the burst initial release of the drug, degrading in acids or by enzymes, and drug entrapment in the mucosal layer. More research is needed to understand the molecular causes of IBD to develop specialized therapies and site-specific systems that enable complete health recovery by re-establishing the immune system and the gut microbiota, improving treatment effectiveness and IBD patients' quality of life. Furthermore, a new challenge would be to create functionalized nanocarriers that selectively absorb into

inflammatory cells and specifically release within target cells, to increase medication levels at the site of injured tissues at lower doses.

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ASSESSMENT OF COVERAGE AND QUALITY OF ANTE-NATAL CHECK-UP AMONG PREGNANT WOMEN RESIDING IN BOROUGH VI and VII OF KMC

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Abstract

Diagnosis of pregnancy as soon as possible has always been desired by planners of maternal and child care providers. The gamut of services under antenatal care (ANC) includes a thorough examination of pregnant women (examination of physical parameters like blood pressure, height, weight pallor for anaemia, pedal oedema). Urine also can be examined for the presence of proteinuria- an important feature of eclampsia. Until optimum conditions, there should be four antenatal visits and the inclusion of iron and folic acid (IFA) intake for every pregnant woman. Nowadays calcium tablets have been included in the ANC package. The role of frontline workers which include ANM and ASHA (in urban areas of Kolkata they are called honorary health care) is to facilitate registration of pregnancy, facilitate ANC and provide health care messages on danger signs of pregnancy. The present study is an observational study on 150 mothers who had recently delivered or had a child below five years of age and visited the selected urban primary health centre for a postnatal examination or child immunization. These women belonged to low socio-economic status and dwelt in the project area of the voluntary health organization of Child in Need Institute and their health workers had facilitated the visits. Over 93.3% had taken 100 IFA tablets before delivery. Those who did not consume them, cited physical complaints as the major problem. All women delivered at government health care facilities with zero out-of-pocket expenses. This study shows advocacy efforts can bring a change among the socioeconomically deprived sections of the society.

Key words- NHM, Iron Folic Acid, SBA trained staff, institutional deliveries, antenatal care

Introduction

Antenatal care (ANC) is the systematic observation of pregnant women to track the development of the foetus and ensure both the mother's and the child's well-being. ANC is the systematic monitoring of pregnant women in order to track the development of the foetus and ensure both the mother's and the foetus' well-being (1, 2). There should be a minimum of four prenatal visits for every pregnant woman. It should be made clear that this is merely a minimal need and that further visits could be required based on the woman's demands and health. (2). The availability and use of healthcare during pregnancy is shown by ANC coverage. Pregnant women may get interventions throughout the prenatal period that may be crucial to both their health and that of their unborn children. Effective maternal health treatments during the antenatal period are more likely to be provided if prenatal care is received at least four times (3).

Childbirth and pregnancy are common occurrences in a woman's life. most of the of pregnancies end in a normal delivery, it's thought that 15% of them might have unexpected difficulties (4). Some of these might endanger the mother's life or the life of her child. Therefore, the presence of trained attendants is essential for the early diagnosis of such issues as well as for the proper and prompt care of them. Under the Janani SurkashaYojana and RMNCH+A program, the Government of India has made a commitment to guarantee universal coverage of all births with skilled attendance. Government would be promoting institutional deliveries. Maternal death is defined as the death of woman within 42 days of the pregnancy's termination (delivery or abortion), from any cause connected to or aggravated by pregnancy, or its management, but not from trauma, accidents, or incidental causes. In India, there are an extremely high number of maternal deaths. Sample Registration Services released in 2020 based on reports of 2016-18 has shown that MMR is 113 per 100000 live births. Haemorrhage,

puerperal sepsis, hypertensive disorders of pregnancy and obstructed labour are the top five direct obstetric causes of maternal death in India (3,4, 5)

In India, there are an extremely high number of maternal fatalities per 100,000 live births or the MMR. The most recent information provided by the RGI for the years 2004–2006 indicated that the MMR was 254 per 100,000 live births (7). Haemorrhage, puerperal sepsis, hypertensive disorders of pregnancy, obstructed labour, and unsafe abortions are the five main direct obstetric causes of maternal mortality in India, which account for roughly 70% of all maternal fatalities in the nation (6). One of the main 'indirect' obstetric reasons is maternal anaemia. Early identification and treatment can prevent complications and death (7)

Pregnancy-related problems are more likely to occur in women under the age of 18 or over the age of 40. Grand multiparas and prime gravida (those with four or more pregnancies) are more likely to have problems during pregnancy and labour. According to research, mothers who have spaced their children fewer than 36 months apart are more likely to have preterm births and child birth with low birth weights, which increases the risk of infant death. The likelihood that a woman would develop anaemia rises if there has been less than two years since her last pregnancy or less than three months after her last abortion (3, 4, 7). Every pregnancy has to be cared for by an SBA throughout pregnancy, labour, and the post-partum period since every pregnancy might develop difficulties at any point. SBA has been defined as a person having the skills capable of managing common obstetric and neonatal emergencies, has the ability to quickly identify when a situation is beyond his or her scope of practice, and can refer the woman or newborn to the appropriate facility without delay or unsafe abortions. As a result, prompt obstetric care services delivery is crucial for managing such instances. Age below 20 (young prim gravida) and elderly primary or grand multigravida (having more than 4 childbirths) are considered risk factors for maternal mortality.

ANC registration

As soon as pregnancy is suspected, a pregnant woman should make her first appointment or register for ANC. If a woman in the reproductive age range thinks she could be pregnant, she should be urged to see her health service provider which could be a front like worker or a doctor. The first appointment should ideally occur within 12 weeks; the second visit should occur between 14 and 26 weeks; the third visit should occur between 28 and 34 weeks; and the fourth visit should occur between 36 weeks and term.

During the 1st trimester visit it is essential a detailed physical examination is done along with all detailed past and current medical history Any history of repeated abortion or loss of pregnancy at term is considered a bad obstetric history and a cause for concern. It is essential that a proper ANC check ensures that blood pressure is checked accurately, and oedema is monitored so as to prevent pregnancy-induced hypertension and eclampsia. Optimum check-ups during pregnancy can also prevent open neural tube defects (prevented by administration of folic acid during conception and continued with folic acid. Providing iron tablets from 2nd trimester onwards ensures that iron deficiency anaemia is prevented and hence complication associated with it is prevented. WHO recommends an intake of 1.5–2.0 g elemental calcium/day with the total daily dosage divided into three doses (preferably taken at mealtimes) from 20 weeks gestation until the end of pregnancy. The Target group includes all pregnant women, particularly those at higher risk of gestational hypertension and in areas with low calcium intake (8).

Some of the positive reinforcing factors considered to have positive pregnancy outcomes is socioeconomic status. Migration, declining family income is considered a negative factor. Continuing to do heavy manual work is considered a negative risk factor. Age may have a positive impact on availing and use of ANC services. The higher age of women ensures better ANC coverage (9). Higher education of women ensures better ANC coverage. There is an

inverse relationship between the utilization of ANC services and parity. It is assumed that women with higher parity utilize previous experiences in less availing of antenatal care services (3). Women with a bad obstetric history has a positive impact on pregnancy outcome. Assessment of economic status has been done on Modified BG Prasad Socioeconomic scale:2022 update India. Staying in mostly in kuccha pucca house and family income in the range of rupees 10,000 to 20,000, most of them are best described as Middle and Lower Middle Class, hence classified as lower socioeconomic status (10).

Objectives of the study: The study aims to assess the adequacy of antenatal coverage among women of low social and economic status. Here, adequacy being measured by having the quantum of availing ANC at a government health care facility and having completed all components of ANC services. They must have obtained Iron Folic Acid and Calcium with zero out-of-pocket expenses

Study Methodology: This was an observational and descriptive type of study. The sample included 150 mothers who had recently delivered or had a child below five years of age and visited the selected urban primary health centre for a postnatal examination or child immunization. All were residents of Borough VI and VII of KMC. Most of the variables assessed in this study were categorical and hence, summarized by percentages. Continuous variables were summarized by their means. The primary researcher conducted interviews with the respondents using a mobile form created on the KOBO platform. Finally, the dataset was exported to MS Excel and SPSS. Descriptive statistical analysis of the dataset was done using SPSS version 20. Charts were made in MS Excel.

Results and findings

For their age distribution, the percentage of respondents between ages 21-30 years was majority (64%), followed by 31- 40 years which constituted 20.67% of the sample population (Refer Table 1.1).

Those below age 20 years constituted only 15.33% of the study population. In the present study, more than 90% of the mothers had received schooling (either completed primary or high school).54.67% of the women had completed primary level of school,36.67% of them completed high school and 8.67% of them had done their graduation degree. 62% of the families had a household monthly income of less than 10,000 Indian rupees and 26% of the families had a family income of more than Rs. 20,000 Indian rupees. 22% of the respondents in the study were Hindus, 76.6% were Muslims and 2% were Christian. The dwelling was mostly in Semi- pucca House (71.3%), followed by Pucca (25.3%) and Kuccha houses 5 (3.33%). The source of water supply in most of the homes was from the municipality (94%), and the remaining was from tube well (4.67%) or packed drinking water (1.33%).

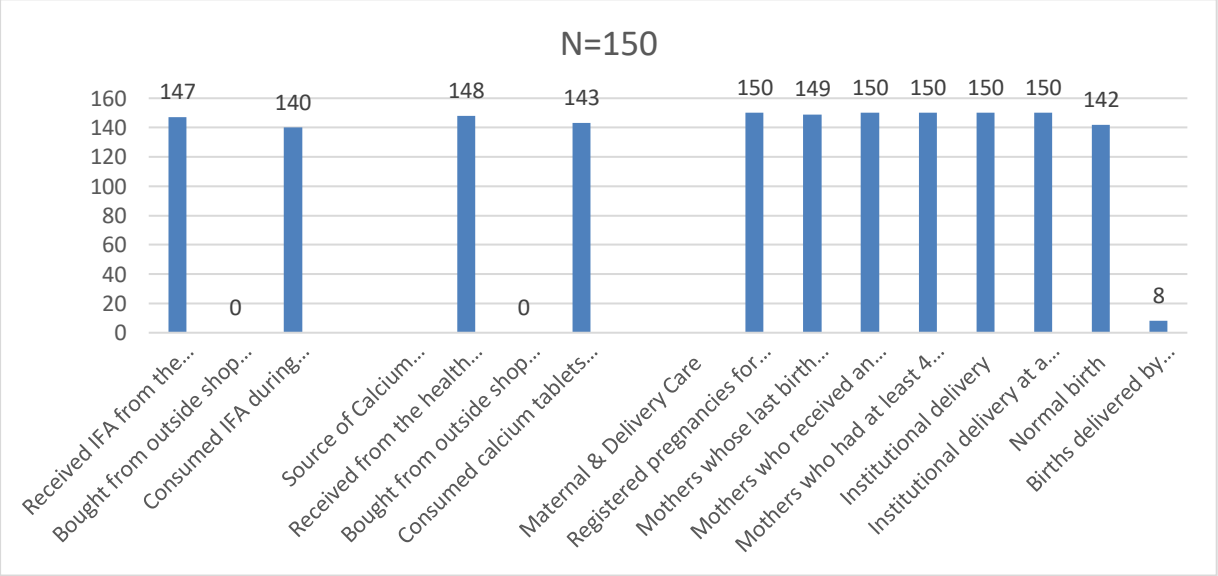

Fig. 1.1. Chart showing Compliance with ANC and Maternal Care

Source: Researchers Compilation of Field Survey

Among the respondents,93.3% (140) reported that they consumed all the IFA tablets given to them. The reasons for not taking the IFA tablets were physical complaints mainly like vomiting, passing of black stool, etc. Out of 150 respondents, 148 (98.6%) had received calcium tablets during the ANC visits. Respondents who didn't receive the tablets didn't purchase it from outside shops (Refer to Table 1.2). Compliance to the intake of calcium was

satisfactory (96.6%). The women who did not consume the calcium tablets said that they did not consume them because they did not like the taste of the calcium tablets, forgot to consume them, nausea and vomiting. The source of the calcium tablet was mostly from government supply (98%).

In many states of India, there is a lack of communication, education, and information throughout antenatal care. Women struggle to make wise decisions, particularly when they are in danger. Ability of women to take positive decision has a key impact on their health status. Empowerment indicators has been found to be one of the determinants of maternal mortality in almost all Low and Middle Countries (11, 12, 13). In this study, it was found that the husband was the major decision-maker in almost all the families (96.67%).146 out of the 150 respondents, in this study had visited the Anganwadi Centre (AWC) and these visits were guided by the front-line health workers. Frontline staff members and medical officials are taught about the need to educate women about prenatal care and impart knowledge about danger signs during complications. In an effort to raise awareness, they speak to women at centres and during home visits about the warning indicators of pregnancy, such as swelling in the hands and feet, high blood pressure, fits, and heavy bleeding. 100% of respondents had institutional delivery in the neighborhood government tertiary-level health facility. 142 of them had normal delivery and the researcher during the conversation found that they had good knowledge regarding complications following delivery. The rest had a C-Section delivery.

Discussion

Frontline employees have a critical role in closing the maternal health care utilization gap. They gave advice on antenatal care, which included measurements of haemoglobin levels, the use of iron supplements, the determination of urine protein levels, thyroid exams, blood pressure checks, weight monitoring, and tests for Hepatitis B and HIV. The physicians and front-line staff did talk about the effects of anaemia and how to manage it, a healthy diet, the

value of iron-folic acid supplements, and tetanus dangerous shots. In addition to immunizing moms and children, frontline staff members seemed to conduct prenatal clinics twice a week. Workers on the front lines provide advice to women on family planning options, nursing, and baby care (13, 14). From the viewpoints of health professionals, the current qualitative research emphasized the obstacles to and facilitators of access to maternity or adolescent health care in the communities. The results highlight the efforts and contribution of frontline staff to ensure that all women, regardless of caste or economic status, had access to services.

In this research, it was identified that frontline workers have been giving pregnant or nursing women quality treatment and counseling via routine clinics and outreach programs. Frontline staff believed that women had little knowledge about and access to prenatal or postnatal care services. ASHA workers have played a key role in improving the nutrition and maternity and child health conditions in the nation by linking mothers and adolescents with resources, giving care, and connecting them with counselling. The local maternal health services were improved thanks to effective communication and collaboration between ASHA and ANM staff. This research has shown that a critical factor in the use of ANC services is having enough awareness about the advantages of ANC and the problems that might arise during pregnancy. Findings therefore highlight the significance of designing interventions that build on the institutional practice of offering a tried-and-true set of ANC standards that are strictly adhered to by healthcare professionals.

Table 1.1. Socio demographic profile of Respondents

Source: Researchers Compilation of Field Survey

Respondent Characteristics	No. of Respondents (N= 150)	Frequency (%)
Age (years)		
≤ 20	23	15.33
21-30	96	64
31-40	31	20.67
41-50	0	0
Religion		
Hindu	33	22
Muslim	115	76.67
Sikh	0	0
Christian	2	1.33
Education		
Illiterate	0	0
Primary school	82	54.67
High school	55	36.67
Graduate/postgraduate	13	8.66
Type of House		
Kutcha	5	3.33
Semi-pucca	107	71.34
Pucca	38	25.33
Source of drinking water		
Municipal tap	141	94
Tube well	7	4.67
Packed Filter water	2	1.33
Household Monthly Income		
< 10000	93	62
10001- 20000	18	12
>20,000	39	26
No. of dependents in family		
0-2	31	20.67
3-5	114	76
6-8	5	3.33
> 9 members	0	0

Table 1.2. Information about Maternal Care and ANC

Respondent Characteristics	No. of Respondents (N= 150)	Frequency (%)
Gravida		
One child	65	43.33
Two child	63	42
Three	16	10.67
Four	6	4
Source of IFA		
Received IFA from the health centre	147	98
Bought from outside shop (OPE)	0	0
Consumed IFA during pregnancy	140	93.33
Source of Calcium supplement		
Received from the health centre	148	98.6
Bought from outside shop (OPE)	0	0
Consumed calcium tablets during pregnancy	143	96.6
Maternal and Delivery Care		
Registered pregnancies for which mothers received a MCP card	150	100
Mothers whose last birth was protected against neonatal tetanus*	149	99.33
Mothers whose last birth was protected against neonatal tetanus (received only one dose of TT)	1	0.67
Mothers who received an ANC in the 1st Trimester	150	100
Mothers who had at least 4 ANC visits	150	100
Institutional delivery	150	100
Institutional delivery at a public facility	150	100
Normal Birth	142	94.67
Births delivered by Caesarean Section	8	5.33
Decision maker of the family		
Husband	145	96.67
Self	2	1.33
Mother or father-in-law	3	2
*includes mothers with two injections during the pregnancy for their last childbirth, or two or more injections (the last within 3 years of the last live birth) or three or more injections (the last within 5 years of the last birth)		

Source: Researchers Compilation of Field Survey

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NANOPARTICLES AS DRUG DELIVERY SYSTEM

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Abstract

Site-specific drug delivery is possibly the most difficult challenge of modern drug therapy. A group of colloidal drug carriers like microemulsions, liposomes, niosomes and nanoparticles have evolved to answer this challenge. However, most of them specially microemulsions and liposomes, suffer from to low thermal stability. Nanoparticles free of this limitation have stood out as an alternative drug carrier. This articles gives an overview of the prospect of nanoparticles as a carrier for site specific delivery of different drugs.

Keywords: nanoparticles, polymers, cancer drugs, vaccine, oral delivery.

Introduction

In pharmaceutical research, design and development of new drug delivery systems with a view to enhance the efficacy of existing drugs is an ongoing process. The challenge of modern drug therapy is to deliver the drug to the target site and improve the pharmacological action of drugs along with the reduction of their toxic side effects *in-vivo*. Colloidal drug carriers including microemulsions, liposomes, niosomes and nanoparticles can provide site- specific targeted drug delivery combined with optimum drug release profile. But due to low thermal stability of microemulsions and liposomes, nanoparticles are proposed to be the alternative drug carrier. Nanoparticles in pharmaceutical application has gained a lot of attention during last few decades, particularly anti-cancer drugs are widely studied because the formulation might reduce toxicity of the drugs while improving efficacy of the treatment. However, very few

polymeric nanoparticulate products have reached to the market. AbraxaneTM prepared from albumin bound with paclitaxel, an anti-cancer drug is a nanoparticulate formulation possessing particle size of 130 nm and intended for intravenous application. Another anti-cancer drug, doxorubicin loaded in poly (isohexylcyanoacrylate) polymer has gained clinical importance. Other candidates to be encapsulated in nanoparticles include macromolecules like proteins and genes (nucleic acids), which tend to be inactivated in the body by enzymatic degradation. In terms of controlled release, nanoparticles provide protection against the body conditions, resulting in sustained release and maintenance of bioactivity before the drug reaches the site of action (Bender et al., 1996; Florence 1997).

Nanoparticles

Nanoparticles can be defined as colloidal particles ranging in size from 10-1000 nm. They are usually made up of macromolecular materials from natural or synthetic origin. Depending on their method of preparation two types of nanoparticles are formed namely nanospheres where drug may be adsorbed in polymeric surface or dispersed in polymeric matrix and nanocapsule where polymer forms a membrane wall and drug is present in the core. In drug delivery systems nanoparticles are usually dispersed in a liquid (preferably in water). Such a system can be applied through oral, parenteral or ocular route. Nanoparticles can also be dried to a powder and can be further processed to solid dosage form like tablets or capsules. For pharmaceutical application, nanoparticles must be biocompatible and biodegradable in nature. The characteristics including biocompatibility, biodegradability as well as targeting and controlled release of drug are dependent upon the selection of materials for the preparation of nanoparticles. A wide variety of materials including synthetic polymers, proteins, natural macromolecules and solid lipids are used for the preparation of nanoparticles. A variety of fabrication methods exist for the processing of the above mentioned materials into nanoparticles (Gupta and Kompella, 2006).

Materials used as Nanocarriers

The materials used for preparation of drug-loaded nanoparticles include natural hydrophilic polymers, synthetic hydrophobic polymers and solid lipids. Among the natural macromolecules, proteins such as albumin, gelatin, legumin or vicilin as well as polysaccharides such as alginates or agarose have been extensively studied for the preparation of nanoparticles. These natural polymers have the advantages including inherent biodegradability and biocompatibility. The natural polymers possess some disadvantages like batch-to-batch variation, conditional biodegradability and antigenicity, etc.

Synthetic polymers which are used for nanoparticles preparations are mainly those, which are conceivably employed in preparation of microparticles. The polymers are either preformed or synthesized during the process of nanoparticles preparation. Among preformed polymers, poly (lactic acid), and its co-polymer with glycolic acid have already been approved for human use. Poly (alkyl-cyanoacrylates) represent the group concerned with polymerization during nanoparticles preparation. However, cyanoacrylates gathered number of controversies due to the toxicity of the corresponding alkyl cyanoacrylate monomer.

Use of solid lipids as nanocarriers is also a very attractive idea to achieve controlled drug release. Solid lipids have been used for several years in the form of pellets to achieve retarded drug release after per oral administration. The lipids used for preparation of nanoparticles include triglycerides (eg, tristearin), partial glycerides (eg. Imwitor), fatty acids (eg. Stearic acid), steroids (eg. cholesterol) and waxes (eg. Cetyl palmitate).

The development of nanoparticulate carriers with suitable size along with protein resistant surface (minimized opsonization) is of great interest in current research. During the last decade, several approaches have been proposed to obtain long circulating nanoparticles. The

approaches are (a) Sterically stabilized nanoparticles; (b) Biomimetic nanoparticles; (c) Antibody coated nanoparticles and (d) Magnetically guided nanoparticles (Leroux et al., 1996).

Drug Delivery Potential of Nanoparticles

Nanoparticles prepared from different materials and possessing different characteristics have been investigated for various therapeutic applications.

Delivery of Anticancer Drugs

One of the most promising applications of nanoparticles is the parenteral application of anticancer drugs. Nanoparticles were found to have tendency to accumulate in different tumors after i.v. injections. This phenomenon is related to high endocytic activity of cancer cells. Moreover, some tumors possess increased vascular permeability favoring the accessibility of nanoparticles to tumor cells. A reduction in general toxicity was also found. This may be due to the modification of the drug pharmacokinetic parameters which alter the distribution profile of drug. In nanoparticulate system, drugs mainly concentrate in liver and spleen and are precluded to exert acute toxicity in other organs. Therefore, one of the most suitable applications of drug loaded nanoparticles may be their use in hepatic metastases. Passive targeting by incorporating of magnetic particles into nanocarriers and subsequent electromagnetic guidance was found to improve the activity of the anticancer drug due to the increased access to extravascular tumor. MAb coated nanoparticles was also studied for tumor-specific targeting. These particles should be able to recognize specific cell determinants belonging to tumor cells. But very poor accumulation of particles at tumor site was observed from the particles showed promising results *in-vitro*. Recently PEO-coated surface modified nanoparticles were found to be a promising nanocarrier to cancer therapy. Coating of PLA nanoparticles with PEO 20,000 by adsorption was shown to significantly increase the circulation time in blood and tumor accumulation in mice (Mondal et al., 1996).

Delivery of Anti-infective Drugs

Another field of interest to use nanoparticles is in intracellular infections. Infectious diseases usually are bacterial, parasitic, fungal or viral in nature. Most of the anti-infective agents have some limitations in treating intracellular infections including, antibiotics have poor ability to penetrate the infected cells or a decreased activity in intracellular compartments. Antiparasitic agents possess a poor therapeutic index due to their limited efficacy resulted from their lack of selectivity for the infected cells. Antiviral drugs usually show short half-lives. Polyalkylcyanoacrylate (PACA) nanoparticles with ampicillin as a model drug was investigated both in cell culture and in mouse model. In the field of viral infections, a very important challenge is the targeting of human immunodeficiency virus (HIV)- infected macrophages. Nanoparticles may represent an interesting system for the specific transport of antiviral agents displaying poor selectivity. Recent studies on macrophage targeting by using PACA nanoparticles were found to be effective in HIV infected human macrophage culture.

Delivery of Poorly Absorbed Drugs

Nanoparticles was found to be a potential delivery system to improve the oral bioavailability of peptide or protein drugs because nanoparticles can protect the labile drugs from enzymatic degradation and enhance their absorption by optimizing their interaction with the absorption site or by directly transporting them through intestinal mucosa to systemic circulation. Although, in many studies, the passage of nanoparticles across the gastrointestinal mucosa was found to be very less (2-3% of the injected dose), leading to the conclusion that only very potent drugs would be able to exert their activity through oral route. The improvement of bioavailability of those specific drugs was due to the protective effect of polymer from enzymatic degradation. In a more recent study, it was reported that pH sensitive nanoparticles could significantly increase the bioavailability of poorly water-soluble HIV-protease inhibitors in mice and dogs. Those formulations were prepared from polymethacrylic copolymers which

rapidly dissolve and release the poorly water soluble drug at a specific part of GIT. The rapid and specific release was suggested to be combined with the very high level of dispersion provided by the nanoparticulate formulation, favoured the solubilization of the drug in intestinal fluid.

Delivery of Vaccines

The very slow degradation rate of polymers like PACA, Polymethyl methacrylate (PMM) may make the nanoparticles made from those polymers appropriate for vaccine delivery. Prolonged contact between the antigen and the immunocomponent cells favours the persistence of immunity. The important factors to affect the performance of immunonanoparticles include particle size, hydrophobicity and presence or absence of surface ligands. By associating targeting agents like MAb specific from M cells, it may be possible to increase the level of absorption of nanoparticles vaccine and therefore the immune response. With the advancement of molecular biology, immunology, virology and controlled delivery nanoparticulate systems may be an effective and potential delivery system of vaccine in oral immunization (Mondal et al., 2008).

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EFFECTIVENESS OF LOW VISION AIDS IN PATIENTS VISITING THE LOW VISION CLINIC IN A TERTIARY EYE CENTRE.

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ABSTRACT

Low Vision is a conformation of visual impairment, which remains unavenged with regular medical, surgical, or refractive means and the number of people with impaired sight that cannot be improved with the usage of spectacles or treatment is growing. Globally, an estimated 253 million people live with vision impairment, out of which 36 million are blind, and 217 million have moderate to severe vision impairment.The burden of visual impairment in India is estimated at 62 million, of these, 54 million persons have low vision, and 8 million are blind.Low Vision Devices play a major role in low vision rehabilitation.This is a prospective type of study, conducted at Dr Shroff CharityEye Hospital, New Delhi.A total of 60 patients fulfilling the criteria of low vision as per WHO definitions. As the study was conducted during the time of pandemic (Covid-19), the reviews as per the questionnaire were carried out over telephonic call to the patients.Among the 60 study patients the effectiveness of low vision devices for near in males & females were 47.67% and 63.30% respectively.The effectiveness of LVA for near in age group below 20 was 70.52%, 21-40 was 78.57%, 41-60 was 73.18% and 61 and above was 67.43%.The most effective device for near was Dome magnifier with a score of 69.95% and Prismatic spectacle magnifier 68.29%.

Key words: low vision, impairment, pandemic, optical devices

Introduction

“A person with Low Vision is one who has impairment of visual functioning even after treatment and/or standard refractive correction, and has a visual acuity of less than 6/18 to light

perception, or a visual field of less than 10 degrees from point of fixation, but who uses, or is potentially able to use, vision for planning and/or execution of a task." Low Vision is a conformation of visual impairment, which remains unavenged with regular medical, surgical, or refractive means and the number of people with impairedsight that cannot be improved with the usage of spectacles or treatment is growing.

Globally, an estimated 253 million people live with vision impairment, out of which 36 million are blind, and 217 million have moderate to severe vision impairment [1]. The burden of visual impairment in India is estimated at 62 million, of these, 54 million persons have low vision, and 8 million are blind [2]. The prevalence of visual impairment in this study was estimated to be 24.5 %.[3] The common causes of low vision are retinal diseases, optic atrophy, glaucoma, corneal diseases [4].

Low Vision Devices play a major role in low vision rehabilitation. The ranges include Optical Devices, Non-Optical Devices and also various adaptive techniques. Optical devices maximize the efficiency of surplus vision for distance using Telescopes, near using magnifiers[5] and non optical devices maximize the usage of residual vision in a better way. Devices range from simple magnifying lenses, telescopes to high power video magnifiers.

In India, tertiary eye care units dispense Low Vision Devices and provide complete rehabilitation whereas the primary clinics do not. Also, only about half of the ophthalmologists were aware, and one- third had knowledge about low vision services in an Indian study [6].The acceptance rate of low vision devices in India is a big challenge as it requires adequate counselling and understanding. Low Vision devices play a major role in the life of visually challenged person as it provides them a different aspect to see this world and be a part of this world. To maximize the rehabilitation of visually impaired individuals. The present study aims

to explore the clinical profile of patients requiring Low Vision Devices (LVD) and assess the effectiveness of Low Vision devices among patients with low vision.

Methodology

This is a prospective type of study. This study is conducted at Dr. Shroff Charity Eye Hospital, New Delhi.A total of 60 patients fulfilling the criteria of low vision as per WHO definitionswere included after obtaining detailed ocular evaluation to detect low vision.

Participants were recruited after administering an informed written consent.The sample size was calculated as 60, using the formula, $S= Z \times p(1-p)/ m2$ considering 90% confidence interval and 5% allowable error.

After a detailed ocular examination was done and patients were given trial of various low vision devices (Hand held magnifiers, stand magnifiers, telescopes,portable video magnifiers, prismatic spectacle magnifiers, dome magnifiers) according to their need.

The review of patients were taken after 2 months of usage of a low vision device. The outcome measures included visual ability domains (reading, mobility, visual information processing, and visual motor skills) and overall visual ability estimated from difficulty ratings using the 48-item Veterans Affairs Low-Vision Visual Functioning Questionnaire.

As the study was conducted during the time of pandemic (Covid-19), the reviews as per the questionnaire were carried out over telephonic call to the patients.

Inclusion criteria:

• Visual acuity of less than 6/18 to light perception or visual field of less than 10 degrees from the point of fixation.

• Age group between 8 to 80 years.

• Patient should be first time LVD user.

• Patient should have comprehensive eye check-up along with retinal evaluation before visiting low vision clinic.

Exclusion criteria:

• No access to telephone.

• Unable to speak Hindi or English

• Previously received comprehensive low vision services

• Severe hearing impairment that would interfere with participation in telephone questionnaires.

• Cataract extraction planned within the next month.

• Those cases of corneal opacities, dense posterior sub-capsular cataract, and diabetic maculopathy for which potential treatment /surgical options were possible and planned were not included in the study.

Results & Discussion

A total of 60 patients fulfilling the criteria of low vision as per WHO definitions were included after obtaining detailed ocular evaluation to detect low vision. None of them were using LVD previously.

In this study the questionnaire was divided into four categories- Distance, Near, Mobility and Daily living skills.The effectiveness of low vision devices in respect of gender was:

Table 1. Effectiveness of low vision devices in respect of gender

Gender	Distance	Near	Mobility	DLS
Male	72.86%	47.67%	43.01%	81.17%
Female	67.19	63.30	-21.99	62.06
Total	71.44	56.35	30.01	76.39

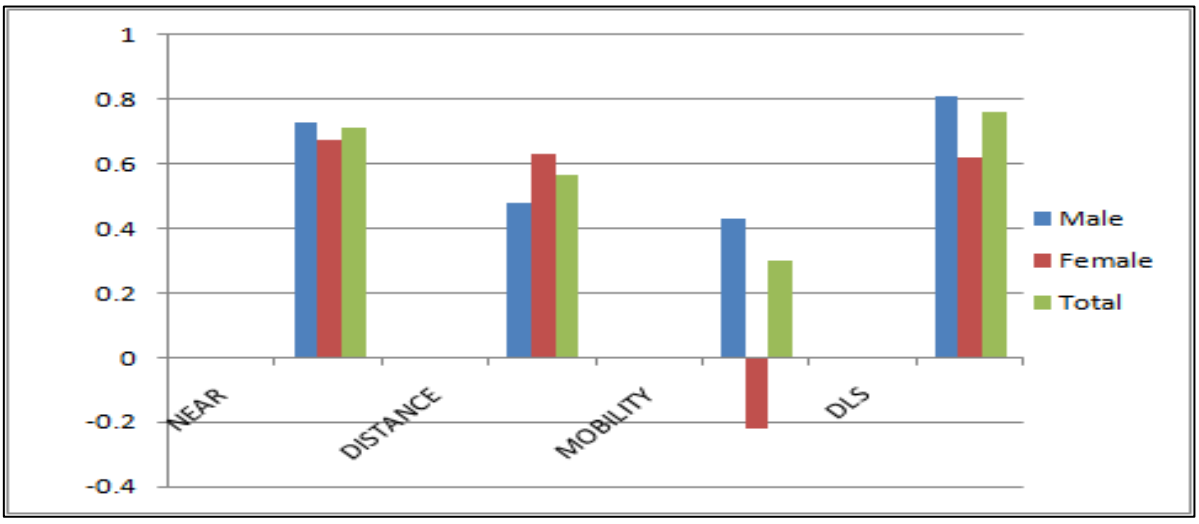

Fig 1. Effectiveness of low vision devices in respect of gender

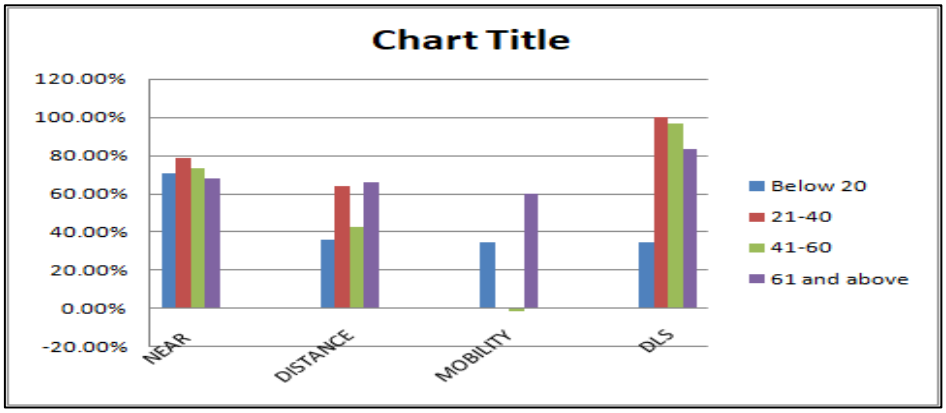

Fig 2. Effectiveness of low vision devices on basis of age

Table 2. Effectiveness of low vision devices on basis of age

Age	Near	Distance	Mobility	DLS
Below 20	70.52	63.44	34.48	34.07
21-40	78.57	63.44	00	100
41-60	73.18	42.61	-2.12	96.41
61 and above	67.43	65.91	59.92	83.39
Total	71.44	56.35	30.01	76.39

Devices	Near	Distance	Mobility	DLS	Total
DOME MAGNIFIER	69.59%		21.99%	92.82%	68.51%
PRISMATIC SPECTACLE MAGNIFIER	68.29%		45.86%	87.54%	67.15%
TV VIEWING GLASSES		61.37%			61.37%
PORTABLE VIDEO MAGNIFIER	84.36%			100.00%	84.36%
DOME MAGNIFIER, HAND HELD TELESCOPE	26.03%	6.33%	34.48%	36.84%	24.77%
HAND HELD MAGNIFIER, PORTABLE VIDEO MAGNIFIER	94.67%				94.67%
PORTABLE VIDEO MAGNIFIER, BOLD LINE	89.13%				89.13%

NOTEBOOKS				
DOME MAGNIFIER, READING GUIDE	69.75%			69.75%
PRISMATIC SPECTACLE MAGNIFIER, TV VIEWING GLASSES	78.05%	64.36%		71.21%
DOME MAGNIFIER, READING STAND	62.19%			62.19%
PORTABLE VIDEO MAGNIFIER, POCKET LED MAGNIFIER	100.00%			100.00%
DOME MAGNIFIER, BOLD LINE NOTEBOOK	69.53%			69.53%
NOIR FILTER, DOME MAGNIFIER	50.12%		31.31%	42.11%
PRISMATIC SPECTACLE MAGNIFIER, DOME MAGNIFIER	74.12%			74.12%
	71.44%	56.35%	30.01%	76.39%	69.49%

Findings:

The study was conducted on 60 Low vision patients to study the effectiveness of low vision devices.

1. Gender Distribution:

Among the 60 study patients the effectiveness of low vision devices for near in males & females were 47.67% and 63.30% respectively. Therefore, whole effectiveness of LVDs for near in both the gender was 56.35%. The basis behind this was the female patients that visited to Low

Vision clinic, had near task more compare to distance due to the involvement various household work. The effectiveness of distance vision devices was 72.86% for males and 67.19% for females, therefore whole effectiveness being 71.44%. The result significantly depicts that male patients visited clinic had more occupation related issues for distance.

The overall effectiveness towards mobility was 30.01% & for Daily living skills was 76.39%.

2. Age distribution:

We divided the age group in 4 categories i.e. below 20, 21-40, 41-60, 61 and above. So the effectiveness of LVA for near in age group below 20 was 70.52%, 21-40 was 78.57%, 41-60 was 73.18% and 61 and above was 67.43%. So the total effectiveness in different age groups for near devices was 71.44%. For distance it was 35.81% for below 20, 63.44% for 21-40, 42.61% for 41-60 and 65.91% for 61 and above. Therefore total effectiveness for distance was 56.35% . For mobility below 20 it was 34.48%, 21-40 was 0, 41-60 was -2.12% and 61 and above 59.92%. Overall came out to be 30.01% for mobility. In DLS below 20 the effectiveness was 34.07%, 21-40 was 100%, 41-60 its 96.41 and for 61 and above 83.39% and total effectiveness was 76.39%

3. Low vision Devices:

Different low vision devices were given to patients for both distance and near as per patient's visual requirements. The response was noted after patient used the device for 2 months. Some patients were given devices both for distance and near together so the effectiveness as per the devices were calculated. So the most effective device for near was Dome magnifier with a score of 69.95% and Prismatic spectacle magnifier 68.29%. And the most effective device for distance was TV viewing glasses with effectiveness of 61.37%.

Conclusion

Low vision is a problem of significant dimension among Community. The proportion is generally higher in the lower socio-economic class due to unawareness & affordability. The proportion of inherited conditions like Retinitis Pigmentosa, Macular dystrophy, Optic atrophy as a cause of low vision was high and could relate with increased consanguinity. Almost many of those with low vision showed improvement in vision with LVDs. The most effective device for near was dome magnifier with a score of 69.95% and prismatic spectacle magnifier 68.29% Whereas the most effective device for distance was TV viewing glasses with effectiveness of 61.37%.Use of LVDs would emphatically persuade daily activities like reading, stitching, mobility etc. thereby improving the overall quality of life. However, there is a need to raise the availability of low vision centers and boosting their activities to make the LVDs accessible and affordable to all patients suffering with low vision.The most appropriate platform for implementing this change would be strengthening the overall pyramid of ophthalmic eye care to cater to the needs of the low vision patients across the community .The responsibility of rehabilitating patients with residual vision by prescribing suitable and affordable LVDs should also be taken up by practicing optometrist/ Low Vision Therapist/ Rehabilitation specialist along with contributions fromgovernmental, INGOs and NGOs. The planning should be made to increase the availability of low vision centers which can serve these needy individuals. To conclude, all treating Eye Care Practitioners must regard these “individuals” and not merely as ‘two eyes’.The Limitations of the study are less sample size, short term review taken, lack of pre questionnaire evaluation and majority of data collected over telephonic call in regard of Pandemic situation.

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FORMULATION AND EVALUATION OF LIPSTCIK USING NATURAL COLORING AGENTS

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Abstract

Natural and organic cosmetics are greatly influencing and changing the cosmetics panorama. More and more consumers are expecting to find sustainable, environmentally friendly and ethical qualities in the cosmetics that they purchase. Synthetic coloring agents produce various side effects compared to natural agents. Under this context, an attempt was made to formulate lipstick prepared from natural coloring agents to overcome the problem associated with synthetic agents. The ideal characteristics of lipsticks should be non-irritating and non-toxic, both physically and chemically stable, free from gritty particles, and maintain lip color for a prolonged period after its application. The main objective of this work is to formulate and evaluate lipstick containing coloring matter from natural beet root, carrot and pomegranate juice. The prepared lipstick formulations were evaluated for pH, breaking point, melting point and color uniformity. Results were obtained in acceptable range hence formulation of lipstick containing natural coloring agents were successfully developed.

Keywords: Herbal lipstick, beet root, natural coloring agents.

Introduction

Natural and organic cosmetics represent a safe way to make oneself attractive and also contributes to the wearers psychological wellbeing. The constituents of these cosmetics are antioxidant, anti-inflammatory, antiseptic, and antibacterial properties. Herbal constituents are

preferred these products claim to have no side effects that are commonly seen with products containing synthetic agents. The literature in Ayurveda, especially Charaka, Samitha, stated numerous medicinal plants. Among the popular functional natural ingredients, several antioxidants used in cosmetics are scientifically proven to offer additional benefits in supporting appearance, skin texture and tone.

Coloring lips is an ancient practice that dates to the prehistoric period. In present days' use of cosmetic products has increased, and choice of color shades, textures, luster have been changed and become more extensive. This can be observed from the fact that lipstick is being marketed in hundreds of shades of colors to satisfy the increasing demand.

However, in recent times lipstick has been under the scanner of health watchers. Lipsticks are often eaten away by the user, and hence are imperative that health regulators have a microscopic look at the ingredients that go into the lipstick. To overcome the adverse effects of synthetic preparation, the present work was conceived by us to formulate an herbal lipstick having minimal or no side effects, which will be extensively used by the women without bothering about safety. Lipsticks are the cosmetic product containing pigments, oils, waxes, and emollients that apply color, texture, and protection to the lips. Many colors and types of lipsticks exist. As with most other types of makeup, lipsticks are typically but not exclusively worn by women. Some lipsticks are also used as lip balms, to add color along with hydration properties.

Formulation of Herbal Lipstick:

Freshly chosen beetroots were cut into pieces and juice was extracted. Beetroot juice was concentrated by leaving at moderate temperature for a period of 10 hrs and this concentrate is used for further preparation. To the concentrated extract, carrot juice and pomegranate juice was added. Required quantity of waxes and oils were heated in china dish and completely

melted. To this, Sapindusmukorossi (shikakai) powder was added and mixed well. To this, concentrated mixture of juices was added and mixed well. Upon reduction of volume, lipstick formation was observed due to proper emulsion formation.

Table No .1: Formulation chart of herbal lipstick

Name of ingredient	Qty	Uses	Make
Castor oil	16gm	Blending agent	SD Fine
Paraffin wax	28gm	Stiffening agent	SD Fine
Beeswax	36gm	Stiffening agent	SD Fine
Ripe fruit powder of *Sapindusmukorossi*	12gm	Emulsifying agent	Local market
Juice of beet betavulgaris	1gm	Coloring agent	Local market
Juice of Daucus carota subsp. sativus	1gm	Coloring agent	Local market
Juice of *Punica granatum*	1gm	Coloring agent	Local market

Evaluation

The prepared lipstick formulations were evaluated for following parameters

Color and Texture: Formulated lipsticks were checked for color, glossiness and smooth texture.

pH: The pH of formulated herbal lipsticks was determined using digital pH meter.

Determination of Melting Point: The melting point of formulated lipstick was determined by capillary tube method. Approximately 50 mg of lipstick sample was taken and melted and filled

into glass capillary tube opened at both ends. Capillary was cooled with ice for 2h and fastened with thermometer. Thermometer with capillary was inserted in the beaker containing water which was placed on heating plate with magnetic stirrer. Heating and stirring was started slowly at fixed speed. The temperature at which material moved along the capillary tube was considered as melting point.

Breaking Point: This test was carried out to find out the value of maximum load that lipstick could withstand before it broke. Prepared herbal lipstick was held horizontally in a socket an inch away from the edge of support. The weight was gradually increased by a specific value (10 gm) at specific interval of 30 second and weight at which the lipstick broke was considered as its breaking point. This test showed strength of lipstick.

Results and Discussion

All the parameters were evaluated and results are tabulated below.The color was found to be light pink. Melting point obtained was 62°C indicating stability of prepared lipstick at the temperatures recorded in India. Breaking point indicated the tensile strength of lipstick which was found to be 32 gm. Prepared lipstick is smooth in texture.

Table No. 2: Different evaluation parameters

Evaluation parameter	Inference
pH	6.8 ±0.2
Solubility	Soluble in ethanol and methanol
Color	Light pink
Breaking point	32gm
Melting point	62°C
Color uniformity	Uniform color was observed

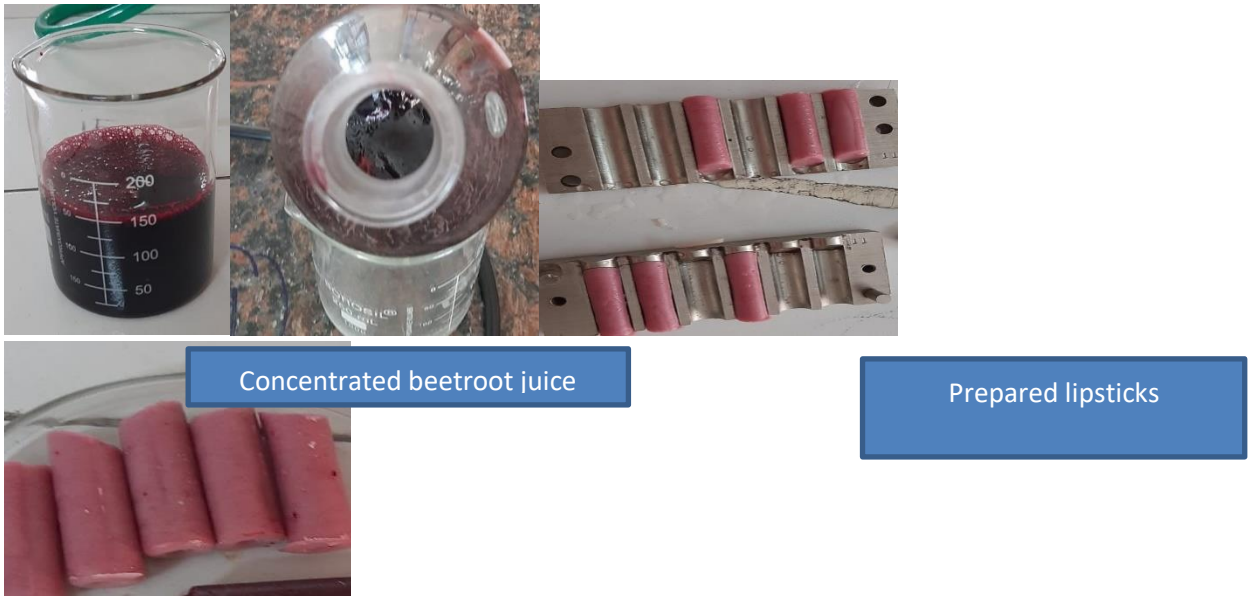

Fig. 1: Prepared concentrated beetroot juice and prepared lipsticks

Conclusion

Lipstick using natural coloring agent's beetroot, carrot and pomegranate juice was successfully prepared using an oily base --beeswax, castor oil and paraffin wax. Ripe fruit powder of Sapindusmukorossi was used as emulsifying agent. On evaluation the product was found to be acceptable.

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A COMPARATIVE STUDY ON DIET, NUTRITIONAL SUPPLEMENTATION DURING PERINATAL DEPRESSION

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ABSTRACT

This review article represents on whether dietary intake or nutritional supplementation influences the risk for perinatal depression. Perinatal depression which means depression during pregnancy or post partum. The study is designed to evaluate whether perinatal depression is related to dietary intake, which was defined as adherence to certain diets, food-derived intake essential nutrients or supplements. The study was conducted for the analysis of dietary intake, adherence to dietary patterns, essential nutrients, specific nutrients that includes B vitamins, Vitamin D, calcium, and zinc, along with intake of fish or polyunsaturated fatty acids. The pregnant women with higher depression score tends to have undesirable life pattern which might affect negative pregnancy outcomes. The factor inducing stress includes anxiety of the baby, anxiety for health, depressive feeling. In addition, higher intakes of energy, fat, phosphorus, potassium and cholesterol increased the risk for incidence of pregnancy stress while intake of proteins, carbohydrates, dietary fibre, and vitamin B2 decreased the risk for stress. Women with low body weight and poor nutritional status prior to pregnancy have more low birth weight infants, premature spontaneous rupture of membranes. Pregnant women have been exposed to depression during pregnancy not only because of physical changes but also because of changes of roles, emotions, and psycho-social characteristics. Age of the pregnant women is another high risk factor for depression. A better understanding of

how depression and intake of nutrients work together can be known from the nutritional research.

Keywords: Perinatal depression, nutrients, diet, maternal health, pregnancy outcome, nutritional supplements.

INTRODUCTION

Perinatal depression, also referred to as maternal depression is defined as depression during pregnancy and up to 1 year post-partum. It is a common morbidity during pregnancy and lactation and can have severe and long- long consequences for women and their children. In low-income and middle-income countries, perinatal depression is thought to be more common because of concomitant stress, anxiety, family and political instability and poverty. Studies shows that maternal depression is associated with poor self-care and caregiving, poor child growth and cognitive development, child malnutrition and increased incidence of child illness. Nutrition could play a biological role in depression.[1] Various nutrients are needed for synthesis and modulation in the neurotransmission system and may therefore be involved in mood regulation.[1] The biochemistry of each nutrient and its role in mood regulation are also related to each other. During lactation and pregnancy, nutritional demands increases, and deficiencies thus arise more easily. It is also possible that hormonal and life changes post-partum increases the risk for depression. There is appositive correlation between BMI and depression during pregnancy, along with pre-pregnancy over weight has been reprted to have strong correlation with possibility for depression. Adequate nutrition is needed for countless aspects of brain functioning. Poor diet quality is risk factor for depression. Poor omega-3 fatty acid status increases the risk of depression. Fish oil and folic acid supplements each have been used to treat depression successfully.Deficiencies of folate,

vitamin B12, iron, zinc, and selenium tend to be more common among depressed than non-depressed persons.[1] Childbearing- aged women are particularly vulnerable to the adverse effects of poor nutrition on mood because pregnancy and lactation are major nutritional stressors to the body. The depletion of nutrient reserves throughout pregnancy and a lack of recovery postpartum may increase a woman's risk of depression.[1] Women as expectant mother are at high risk for major depressive disorder (MDD) and peak prevalence between age group of 25-44years of age. During the perinatal period, MDD increases the risk of adverse birth outcomes, insecure mother-infant attachment, and cognitive, emotional, social, and behavioral developmental problems of the offspring. Severe vitamin B12 deficiency causes loss of memory, mental dysfunction, and depression. Similarly, fatigue, confusion, dementia, and irritability are common clinical signs of folate deficiency.[1,2] These numerous dietary constituents are needed for countless aspects of normal brain functioning, include enzymatic activity, cellular and oxidative processes, receptor function, signal transmission, maintenance of neuronal tissue, and synthesis and function of neurotransmitters and catechol amines. Only 23%, 43% and 5% of women aged 20-39 met the Dietary Guidelines for Americans recommended servings of fruit, vegetables and whole grains. As per the overall study on perinatal depression, the mental health is mainly found among the women belonging to low and low-middle income countries.

NUTRITIONAL BENEFITS ON MENTAL HEALTH

Three mechanisms can be followed by which nutrition could be effective in improving mental health. First, modifying dietary intake or supplementing diets with single or multiple vitamins and minerals may correct nutrient deficiencies that contribute to poor mental health. Pregnant and lactating women are mostly vulnerable to nutrient deficiencies because their needs are elevated compared to non-pregnant women.

Depression appears to be virtually absent when there is large intake of seafood, compared to low intake which is associated with increased prevalence of depression.[2]

Secondly, pharmacologic doses of one or more dietary supplements may improve mental health among psychiatric patients who have a metabolic abnormality that dramatically raises nutrient requirements, such as individuals with alterations in nutrient absorption, transport, and storage. Depressed patients are more likely than non depressed people to have a point mutation in a gene coding for a key enzyme in folic acid metabolism. Person with such a mutation have previously been shown to have higher folic acid needs than the general population. Certain dietary supplements could be used to safely and effectively improve mood or even prevent mood disorders in this at risk-population.[2]

Third, improving the brain's nutritional milieu the antidepressant medication is known to have varying degrees of effectiveness among depressed individuals, with the extreme being resistance to treatment, which occurs in to 30%-40% of patients.[2] Nutritional deficiencies are common among individuals with MDD and nutrients are essential substrates for brain function, an individual's nutritional status can be partially determined. Medication may be unable to overcome nutritional deficit(s) in a "poorly nourished" brain, and therefore would be rendered as less effective.[2]

Perinatal depression is a serious mental health problem. It has negative effects on women and poses risks for delivery and infant development. Reducing perinatal depression may therefore be critical to ending the growing rates of depression and meeting goals of the WHO initiative on depression in public health. Women's risk of developing major depressive disorder during childbearing years may be high as 20 percent.[3] Post-partum depression ranges from maternity blues to psychosis. Women with perinatal depression have increased risk of pregnancy complications including preeclampsia, birth difficulties for mother and child, post- partum depression. Infants of

mothers with major depressive disorder are at risk for below average physical growth, malnutrition, and chronic illness. Beyond these physical ailments perinatal depression can have negative effects on care giving, which in turn affects cognitive and social development, including language development.[3]

Nutritional interventions have the potential to serve both for preventive measures and treatment measure for depression. Since depression awareness is on the rise, prophylactic use of nutritional measures may reduce the incidence of perinatal depression. It is important to find a way to treat depression in pregnant and lactating women without harming infants. Nutritional interventions are cost effective, safe, and the best way to alleviate depression during pregnancy.[3]

KEY ELEMENTS ESSENTIAL TO PREVENT PERINATAL DEPRESSION

Nutrition is essential for normal brain function including proper functioning of neurotransmitters, which is the key element to connect between nutrition and depression.. Nutritional status, particularly fatty acids, folate, and B12 have been shown to affect depression. Low omega-3 fatty acids status has been linked to an increased incidence of depression. Membranes phospholipids mediate the entrance of neurotransmitters into the cell. Several studies shows that providing folic acid supplements in conjunction with selective serotonin reuptake inhibitors led to a 50 percent decrease in depression score.[4]

POLYUNSATURATED FATTY ACIDS AND DEPRESSION

Polyunsaturated fatty acids are classified into two group- n-3, in which the parent essential fatty acid is alphalinolenic acid (ALA), and n-6, in which the parent essential fatty acid is linoleic acid (LA). N-3 and n-6 fatty acids must be obtained through diet. Major sources of ALA are fish, canola oil, soybean oil, and walnuts, major sources of LA are vegetable oil, margarine, lean meats, organ meats, and eggs.[4]

n-3 fatty acids may influence depression through their effects on membrane fluidity. Deficiency of n-3 fatty acids alters the fatty acid composition of brain. Change in membrane viscosity influences metabolism of serotonin 5-hydroxytryptamine neurotransmitter which is associated with the pathophysiology of depression.[4] Depressed patients have reduced concentrations of n-3 fatty acids, especially DHA, in red blood cell membranes and an increased AA:EPA ratio. This alteration is generally attributed to low dietary intake of n-3 fatty acids. Post-partum depression is associated with alterations in fatty acid composition of serum lipids. A study of patients with postpartum depression found that postpartum depression patients had reduced n-3 fatty acids and a shift in the balance of fatty acids from n-3 towards n-6. Maternal concentrations of both EPA and DHA decreases during pregnancy. It may take up to 1 year for DHA concentrations to normalize. DHA is particularly important during pregnancy because it accumulates rapidly in the neural tissue of the fetus from gestation through the first year of life. Fatty acid supplementation also demonstrates relationship between essential fatty acids and depression.[4]

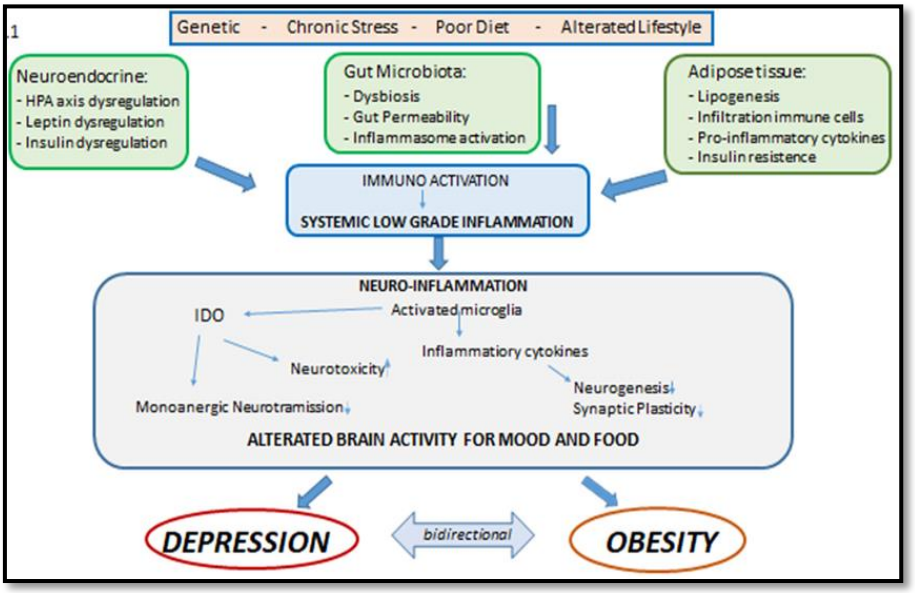

Figure 1: Depression and Obesity: interaction between genetic factors, chronic stress, unhealthy dietand lifestyles, Source:Milano et al., 2020 (Researchgate.net)

NUTRITIONAL REQUIREMENTS FOR PERINATAL DEPRESSION

- Essential fatty acids
- Folate and Vitamin B12
- Antioxidants
- Selenium
- Iron
- Zinc[5]

1. ESSENTIAL FATTY ACIDS (EFAs)

Linoleic acid and alpha linolenic acid are the parent fatty acids of the n-6 and n-3 families of EFAs. The fatty acids termed as essential because they cannot be endogenously synthesized and must be consumed through diet. Eicosapentanoic acid (EPA) and decosehexaenoic acid (DHA)[10] are the n-3 PUFAs that are most biologically relevant for mental health and are predominant in the brain. Both EPA and DHA are derived almost exclusively from fish and seafood, whereas vegetable oils for example canola oil are primary source of n-6 PUFAs.[5]

Corn, cotton seed, safflower and soyabean oils are god sources of linoleic acid. Alpha-linolenic acid is present not only in fish oils but also found in green leafy vegetables, flax seeds, rape seeds, soyabean and walnuts.

2. FOLATE AND VITAMIN B12

Folate and vitamin B12 are essential for normal central nervous system function through several mechanism. Folate and vitamin B12 are needed for single carbon metabolism involved in the synthesis and metabolism of serotonin and other monoamine neurotransmitters and catecholamines. Folate helps to maintain normal brain concentrations of tetrahydrobiopterin, a cofactor in the synthesis of serotonin and catecholamines. Additionally, a deficiency of either folate or vitamin B12 causes elevated

homocysteine concentration, which may contribute to the pathogenesis of MDD by mediating a vascular response.[5]

Patients with perinatal depression tends to have lower concentrations of serum or red cell folate than healthy control subjects. Poor folate status has been associated with severity of depression and prolonged episodes of MDD. ICMR recommended during pregnancy are 480ug/day. Folate deficiency at the time of conception can cause spina bifida, the greatest significance of folic acid and its potential influence on pregnancy outcomes is to prevent neural tube defects. Folic acid deficiency can lead to anencephaly which means *"absence of brain"*. Folate deficiency has also been implicated in pregnancy induced hypertension.[5]

Studies have shown that red cell folate levels exceeding 400ng/ml are best for prevention of perinatal depression and neural tube defects. This can be achieved by folic acid supplementation. Women should be encouraged to include generous amount of folic acid. Foods such as dark green leafy vegetables, legumes, orange juice, soya, wheat germ, almonds and peanuts contain folic acid. In addition women planning pregnancy should begin periconceptional supplementation with folic acid at levels of 400 to 800ug per day. It is difficult to provide 300ug of additional amount of folic acid during pregnancy through food and can be met through supplements of medicinal folate.[5]

SUGGESTED FOOD GROUPS FOR BALANCED DIET FOR PREGNANT WOMAN

CITATION: (REVISED SHORT SUMMARY REPORT RDA – 2023)

ICMR – NIN, HYDERABAD

Nutrients from the above suggested balanced diet for a pregnant woman (sedentary)				
Nutrient	**Vegetarian diet**	**Non-vegetarian diet**	**EAR**	**RDA**
Energy (kcal)	1994	1973	2010	-
Protein (g)	72.9	74.4	59	68
Visible fat (g)	20	20	30	30
Calcium (mg)	1263	1325	800	1000
Iron (mg)	31.0	29.6	21	27
Zinc (mg)	9.2	8.8	12.0	14.5
Magnesium (mg)	662	614	370	440
Vitamin A (µg) #	799	928	406	900
B-carotene (µg)	2845	2824	-	-
Thiamine (mg)	1.6	1.5	1.6	2.0
Riboflavin (mg)	1.0	1.0	2.3	2.7
Niacin (mg)	11.3	11.5	14	16
Vitamin B_6 (mg)	1.24	1.2	1.9	2.3
Vitamin C (mg)	190.0	191.0	65	80
Total Folates (µg)	346.0	347.0	480	570
Vitamin B_{12} (µg)	2.0	2.4	2.2	2.5

Deficiency of vitamin B12 leads to pernicious anemia of the mother thus giving birth to premature baby. For non-pregnant women requirement of vitamin B12 is 1ug and this requirement may exceed to 2ug-2.4ug during pregnancy. The foetus has priority over the mother in B12 and foetal blood had twice the amount of B12 than does maternal blood, even when maternal levels are depleted. Low maternal levels are associated with prematurity, and the capacity of abosorbing vitamin B12 increases during pregnancy and large amount is transferred to the foetus.[5]

3. ANTIOXIDANTS

The brain is a major consumer of oxygen. Therefore, it is an important substrate for oxidation by reactive oxygen species. In particular, neuronal membranes are extremely susceptible to lipids peroxidation due to their high polyunsaturated fatty acid content. Peroxidation of nerve endings alters neurotransmitter transport and subsequently affects

central nervous system functioning. In addition to causing neural damage, reactive oxygen species can cause oxidative stress and vascular changes, all of which have been observed in MDD. Antioxidants serve as the body's defense mechanism against oxidative stress, but interestingly, the antioxidant concentration of the brain is low which may favor pro-oxidant environment.[6] High dosage may lead to neural damage and vascular disease and helpful in preventing or treating perinatal depression.

Vitamin C (ascorbic acid) is a potent antioxidant required for prevention of oxidative stress in foetus, and no other antioxidants are reduced until ascorbic acid is depleted. High dose of ascorbic acid of 3g/day shows reduction in severity of MDD. Low maternal intake of vitamin C is associated with premature rupture of foetal membranes and increased neonatal death rates.[6]

Vitamin E refers to tocopherols that are the major lipid soluble antioxidants that protects membranes from peroxidation. It is studied that women with perinatal depression have lower concentrations of serum vitamin E and there is a positive correlation between serum vitamin E and duration of perinatal depression. Very little vitamin E crosses the placenta so infant has low tissue concentration that persists up to at least 6years. Requirement of vitamin E increases intake of PUFA.[6]

4. SELENIUM

Selenium is thought to play an important role in brain function because its metabolism in the brain is vastly different than other organs. Specifically, during times of deficiency, the brain retains selenium at the expenses of tissues such as muscle, kidney, and liver. Indeed, selenium is an important modulator of mood. Supplementation of 100-150ug selenium/day for 5 to 6 weeks significantly improved mood scores.[7] Selenium is a trace element that takes part in biological process like neural development. In randomized trial researchers found that 200u/day selenium caused 20-fold reduction of depressed-

dejected mood state and a trend towards improvement in quality of life scores. Selenium is also required for synthesis and metabolism of thyroid hormones. A deficiency is thought to compromise thyroid-hormone metabolism and may mediate the effects of altered selenium status and depression. Selenium deficiency reduces immune function in the individuals with MDD. Finally, selenium is an essential component of the antioxidant enzyme glutathione peroxidase, which scavenges hydrogen peroxide, thereby protecting nerves from lipoperoxidation and tissue damage.[7]

5. IRON

Iron deficiency alters myelination, neurotransmitter metabolism, and function, cellular and oxidative process, and thyroid hormone metabolism. Decreased brain iron stores may impair activity of iron dependent enzymes that are necessary for the synthesis, function, and degradation of dopamine, serotonin, and noradrenaline.[6] It is seen that among women of childbearing age, iron deficiency causes deficits in cognitive function such as memory, learning, and concentration. Iron deficiency with anemia is associated with higher depressive scores among young women taking oral contraceptives. A recent study showed that significantly higher depressive symptoms at postpartum day 28 among women who were anemic on postpartum day 7 compared with nonanemic women and a negatie correlation between hemoglobin concentrations and depressive symptoms. Iron improves depressives symptoms.[4,6]

6. ZINC

Zinc has the second highest concentration of all transition metals in the brain. Most zinc is localized within synaptic vesicles of specific neuron where it is thought to modulate synaptic transmission and may itself act as a neurotransmitter.[6,7] Zinc deficiency causes immunosuppression, which is also a common occurrence in MDD. Clinical manifestation of zinc deficiency include behavioral disturbances such as

depression and dysphoria. Blood zinc concentrations are lower in individuals with MDD. Zinc deficiency during antenatal period leads to adverse effects on the newborn including foetal mortality, foetal malformations including CNS teratogenicity and reduced intra uterine growth rate. Low zinc during pregnancy doubles the risk of low birth weight and trebles the risk of preterm delivery.[6,7]

INVESTIGATING THE CAUSE BEHIND PERINATAL DEPRESSION

Two studies are included in this review that suggests protective measures against perinatal depression from eating healthy diet and finding that may encourage further investigations. Other studies have examined the role of specific dietary patterns on the depression outside of the perinatal period and it was found that "healthy diet" is protective.[8]

The current interest in the relationship between dietary intake and perinatal depression focuses mostly on treatment of depression with non-pharmacological interventions, such as PUFAs.[8]Exsisting interventions for perinatal depression are often inaccessible or ineffective for women who are exposed to numerous risk factors, so a shift of focus to prevention is warranted.

There are series of articles published that highlighted the risk for perinatal depression such as low socioeconomic status, trauma, domestic violence, lack of support, migration status, history of psychopathology, and chronic illness and medical problems. Some of the complex interventions suggested comprise health and economic components that are also designed to improve nutrition.[9]

CONCLUSION

This review shows the nutritional requirement for prevention of perinatal depression and improving of dietary pattern. Further studies in populations that have a wider variation in nutrient intake and compromised nutrition needed to better elucidate this relationship.

Also future studies should incorporate baseline levels of nutrition and depression, as well as measuring dietary intake and depression at several time points throughout the perinatal period. High quality longitudinal studies could also overcome the problem of reverse casualty between dietary intake and perinatal depression.

Nutritional status plays important role in mental health and poor nutrition contributes towards of pathogenesis of MDD. Data support a relationship between MDD and poor EFA and folic acid status, with a strong likelihood that nutrients can be used effectively to treat MDD.[10]

Nutritional interventions for improving mental health may be particularly salient among women of childbearing age. Women of childbearing age are particularly vulnerable to nutritional deficiencies because pregnancy and lactation are major nutritional stressors to the body.[10]

Finally if we want to advance our understanding of the role of nutrition in MDD prevention among childbearing age women, we must fill the important gaps in our knowledge.

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DRUG TARGETING TOWARDS COLON USING CHITOSAN: RESEARCH TRENDS IN THE LAST DECADE

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Abstract:

Colon targeting has been a subject of interest since quite few decades. Drugs are targeted to the colon intending local action for the management of colonic diseases like inflammatory bowel diseases or colon cancer as well as for systemic action and can assure major benefits to the patients including reduced side effects or better therapeutic activity. However major challenges for drug targeting to the colon may limit its use. Several approaches are thus devised to target drugs to the colon successfully. One of them is the use of natural polysaccharides which utilize the huge population of microbiota present in the colonic tract. In this present review we would throw a light on one of the most popular natural polysaccharides used by researchers - chitosan and the novel techniques and devices used for this purpose, especially in the last decade. Recent works have been discussed thoroughly which surely throws a light on the present scenario of colonic targeting and future directions of research.

Keywords: Chitosan; Colon targeting; Recent research works

Introduction:

Local diseases of the colon like chron's disease, ulcerative colitis or colon cancer require local targeted release at the site to bypass the systemic action of the drugs used for their treatment. Targeted delivery of the drugs in the colon may further help to reduce the dosage

and frequency of drug administration. Drugs administered through colon-specific module is found out to be released in the colon and acts locally to treat the diseases, the systemic absorption is low and thus the adverse effects associated with the drugs are also minimized (Das and Ghosh 2013).

However, targeted delivery to the colon may be challenging owing to the varied characteristics of the gastrointestinal tract pertaining to pH, retention time, motility, fluid content and microbial content and enzymes (Fig.1) (Das, M et al. 2019). The colon is a part of the large intestine in the terminal part of the gastrointestinal tract. In case of oral delivery, a particular dosage form has to cross the upper parts of the gastrointestinal tract including the stomach and the small intestine to reach the colon. The stomach is acidic with a pH within the range of 1-3 whereas the small intestine has an acidic to neutral pH ranging from 5-6 in duodenum, 6-7 in jejunum and greater than 6.5-7.5 in ileum. A dosage form may require around 2 hours to cross the stomach and 3 hours to pass the small intestine, which again may be subjected to intra-subject variations. The lumen fluid is also higher in content in these parts. During this time, unintended drug release may occur in the stomach or parts of the small intestine which may lead to wastage of drug, cause systemic absorption and give rise to adverse effects (Das et al, 2019).

Therefore, several approaches have been tried and evaluated with the formulations intended for colon targeting (Fig.2). One among those is the pH dependent approach. While the pH of the stomach is acidic and that of the small intestine is from acidic to neutral, the pH of the colon is within 5 and 7. Thus protective coating based on the pH responsive polymers may cause delayed release while avoiding unintended drug release in the upper region of gastrointestinal tract and releasing major amount of drug in the large intestine due to the dissolution of the coating polymer at higher pH. Examples of such polymers include acrylate polymers like Eudragit, shellac or cellulose acetate phthalate. Another approach of colon

specific delivery is based on time. The retention times of a dosage form in the upper parts of the gastrointestinal tract is around 5-6 hr and 24-36 hr in the colon. Thus if the release can be sustained or controlled with rate controlling polymers, minimal release would take place in stomach or small intestine and major amount of drug release would occur in the large intestine. Formulations may be prepared as matrix or coated systems with the polymers applied in matrix or in the coating resulting in slower drug release. Examples include ethyl cellulose, hydroxyl propyl methylcellulose, pectin, guar gum, etc. Lastly, the microbial triggered systems is hugely dependant on the diverse microbial population in the colon and their high concentrations releasing chores of metabolizing enzymes compared to the stomach or small intestine where the microbial growth can't occur due to extreme conditions of pH. The microorganisms are capable of acting on certain natural polysaccharides causing their breakdown. Thus, formulations prepared with such natural polysaccharides like sodium alginate, chitosan, xanthan gum, pectin, etc would pass through the upper parts of the gastrointestinal tract and would be broken down releasing the drug in the colon. Often a combination of the approaches is used to achieve minimal drug release in the upper gastrointestinal tract and maximum release in the colon (Philip and Philip 2010).

Natural polysaccharides as one of the most popular carriers for colon targeted delivery. Natural polysachharides have been used since decades due to their several beneficial properties like their safety, biocompatibility, biodegradability or potential of mucoadhesion. Polysaccharides such as sodium alginate, chitosan, pectin, guar gum, xanthan gum, inulin have been especially utilized in colon targeting as they are easily digested in the colon by the action of residing microorganisms. Their chemical structures with active functional groups are responsible for their beneficial properties (Fig.3) (Tasdighi, Elahe et al. 2012, Mudgil, Deepak et al. 2014, Hassan, Bilal et al. 2018). Crosslinked polysaccharides can entrap small drugs in their structure and sustain their release. Thus, they are especially suitable for use in colonic

delivery. When coated with pH sensitive materials, they can avoid release in the upper gastrointestinal tract and selectively release drug in the colon. (Chourasia and Jain, 2004)

Some of the recent research studies based on one of the natural polysaccharides used by researchers most frequently used for colon targeting and the practical challenges of colonic delivery have been discussed in the next section.

Chitosan is an "attractive biomaterial": What makes it attractive?

Despite having immense potential to be applied in diverse scientific areas, use of chitin is limited by its water insolubility owing to the formation of intra- and inter-molecular hydrogen bonding with neighboring amino or hydroxyl groups and also due to N-acetylation which further limits its extent of swelling in presence of aqueous environment (Hoffmann, Daum et al. 2010). That prompted researchers to develop small molecular weight oligosaccharides with the property of aqueous solubility as well as viscosity by means of structural modification. The resultant polymer chitosan refers to the modified chitin obtained after deacetylation to varying degrees irrespective of chemical or enzymatic deacetylation. The degree of acetylation differentiates chitin from chitosan. Deproteination by proteases and subsequent demineralization by acidic treatment to extract chitosan is performed similarly to the extraction of chitin but further process of deacetylation to yield chitosan additionally leads to the change in the molecular weight (Younes and Rinaudo 2015). Chitin deacetylase isolated from the organism *Mucor rouxii* and other sources has been observed to be able to deacetylate the chitosan even up to 97% in selected condition (Gao, Katsumoto et al. 1995, Tsigos and Bouriotis 1995). Partially deacetylated chitin, in this case, may act as the more suitable substrate to the enzyme as it was found to be inactive in insoluble chitins (with a high degree of N-acetylation) (Martinou, Bouriotis et al. 1998). The process of deacetylation, although leads to the solubility of chitosan in water but the varying solubility in aqueous environment at

varying pH mostly depends on the distribution of the remaining acetyl groups in the structure as characterized by solid-state ^{13}C-NMR and liquid-state ^{1}H-NMR spectroscopy etc. (Heux, Brugnerotto et al. 2000, Brugnerotto, Lizardi et al. 2001).

Delivering drugs orally directly to colon: An overview of literature

High level of patient compliance, no needle-stick injury and ease of self-administration make the drug administration through oral route much more popular compared to invasive routes. Low cost associated with such treatment in case of chronic therapies lead to further reduction in economic burden due to less requirement of hospitalization for long duration. Treatment of various colon-specific diseases such as ulcerative colitis, Crohn's disease, amoebiosis, colonic cancer often need targeted delivery to colon which can increase the local concentration of drug into colon, improved bioavailability resulting in requirement of less amount of drug (Philip, Dabas et al. 2009). Protecting the drugs into colon specific drug delivery systems not only prevents the hydrolysis of protein/ peptide drugs in gastrointestinal tract but also carries them to the suitable absorption site in colon (Chourasia and Jain 2003). The pH varies greatly throughout the gastrointestinal tract which starts from stomach where pH ranges between 1 and 2 while fasting. The pH starts to increase in small intestine at proximal region at about 6.5 which further increases to slightly basic at the distal region of small intestine. Then the pH declines in the ascending colon to slightly acidic and reaches up to pH 7 at descending colon (Rubinstein 1995). Development of pH sensitive polymer coating as well as time-controlled drug delivery systems are usually considered suitable for targeting drugs to colon. Z. Cong et al designed a colon specific drug delivery system where drug loaded unilamellar micelles were developed by crosslinking chitosan by Ca^{++} ions and beta glycoprotein and the composite was further formed by combining the micelles with alginate hydrogel at ratio of 1:3 especially for hydrophobic drug delivery (Cong, Shi et al. 2018). Presence of hydrogel was found to reduce swelling and degradation of the chitosan micelles in

the simulated gastric fluid significantly leading to negligible percentage of drug release in stomach as studied *in vitro*. The problem arises in working with pH sensitive polymeric system while reaching the lower small intestine which harbors basic pH with a risk of solubilizing the polymer before reaching the colon (Fukui, Miyamura et al. 2001). X. Sun et al. modified this pH sensitive drug release technique by developing 5-Fluorouracil and zinc oxide nanoparticle loaded carboxy methyl cellulose (CMC) beads which were further coated with chitosan (Sun, Liu et al. 2019). The ionic interaction between cationic regions of CMC and anionic regions of chitosan were observed to restrict the release of drug in colonic region as evident from *in vitro* high swelling index in simulated intestinal fluid (pH 6.8) and simulated colonic fluid (pH 7.4). Chitosan thus protects the drug molecules from such pre-mature chemical and enzymatic degradation. Owing to the mucoadhesive property due to molecular attraction between positive charged amino groups present in chitosan and negatively charged mucin layer present in mucous also enhances the permeability of drug molecules through intestinal epithelial membrane which further increases with the degree of deacetylation (Kotzé, Luessen et al. 1998, Kumar, Vimal et al. 2016).

This specific problem has been anticipated to be overcome by developing a double layer coating around the drug containing core in form of a tablet. Min Soo Kim et al. designed the double layer in such a way that the outermost enteric coating did not only impede the drug release in stomach but also inner chitosan-dispersed subcoating inhibits drug release in small intestine (Kim, Yeom et al. 2016). On reaching the colon, water penetrates to the core containing drug accompanying citric acid, which was dissolved to initiate microclimate acidification as claimed by the group. The resulting pore formation was found to be enhanced in the latter part of colon due to the activity of chitosan digesting microflora leading to the creation of more microporous channels aiding in colon specific drug release. Simpler approaches also have been tried by crosslinking chitosan with genipin around the core which

was found to retard the release of drug at acidic pH up to the extent of 50% when drug release pattern was compared between coated and uncoated samples at different gastrointestinal pH. This approach has been successfully evaluated in live probiotic microorganism containing micro-carriers to target the release specifically in colon and in some other cases as well (Kumar, Su et al. 2016, Kamguyan, Torp et al. 2021). Patel et al. reported the target specificity of meloxicam loaded chitosan microspheres when compressed into enteric coated tablets (Patel 2017). Enteric coating by Eudragit S on the tablet was reported to protect the microspheres until colon where the drug gets released owing to the microbial degradation of chitosan by colonic microflora. Optimization of drug to polymer ratio is essential in developing such micro/ nano-particulate systems as the increase in polymer content results in formation of thick gel around drug core which needs a long path to be traversed for diffusion with the intestinal fluid. This often results in premature burst release of drug in acidic pH of upper gastrointestinal tract. Increased chemical crosslinking of the polymer was not only found to increase drug encapsulation but also observed to regulate the drug release making the permeation difficult. The *in vitro* release of 5-Flurouracil from chitosan nanoparticles further encapsulated in retrograded starch and pectin micro-particulate system also ensured specific release in colon bypassing the non-specific drug absorption in bloodstream (dos Santos, Meneguin et al. 2021). Chitosan possessing the profound colon targeting properties also has a tendency to get solubilized in lower pH, which necessitates its encapsulation inside a protective carrier. Retrograded starch is often found to have resistance to enzymatic degradation in upper region of gastrointestinal tract (Dimantov, Kesselman et al. 2004) which was used to further protect the chitosan nanoparticles in this study to ensure the colonic release of drug. Targeting the drug release to colon followed by the enzyme-assisted degradation of drug delivery modules may also be considered as a preferred alternative. In lieu of this, a recent work published by Nalinbenjapun et al. showed that 5-aminosalicylic acid was transformed to a prodrug by linking

with chitosan carrier via 4-aminobenzyl spacer by diazotization reaction (Nalinbenjapun and Ovatlarnporn 2020). Formation of the azoconjugate made the prodrug more sensitive to the azoreductase in the colonic region to be released through digestion of the linkage by the mentioned enzyme. Similar strategy had also been applied in another study where hollow mesoporous silica spheres were linked with chitosan through azo bond formation as a linkage (Cai, Han et al. 2020). Chitosan grafting aided towards improved biocompatibility as well as stability of the system acting as a capping agent to block drug release while azo bond helped in further protecting the premature drug release until it reached colon. All the *in vitro* experiments namely cellular uptake studies, cell viability assays indicated towards specific activity in colon as desired.

Conclusion:

Colon targeted delivery has been the topic of interest since the last few decades due to several advantages like site specific delivery for better management of colonic diseases like inflammatory bowel diseases, colon cancer or delivery of proteins and peptides which may degrade in the upper gastrointestinal tract. Colonic delivery would help in reduced adverse effects and frequency of dosing. Natural polysaccharides like chitosan has been utilized extensively for the development of colon targeted delivery systems as they are non toxic, biodegradable and metabolized specifically by the microbial population present in the colonic lumen. However, there are several challenges which should be met to deliver a drug successfully in the colon in significant amount so that the therapeutic objectives are met. The review focuses on the recent studies focusing on colonic drug delivery through few of such natural polysaccharides which would help to generate the ideas for future research.

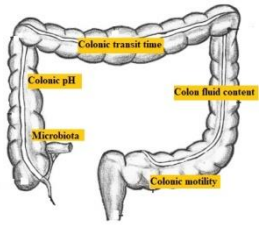

Figure 1: Factors affecting targeting of drugs to the colon

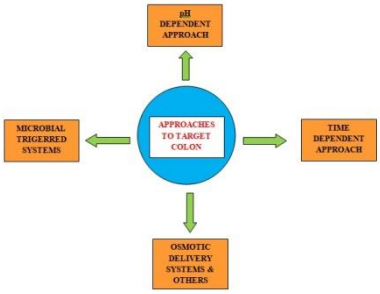

Figure 2: Approaches for targeting drugs to the colon

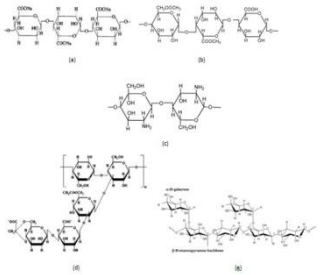

Figure 3: Chemical structure of a) sodium alginate; b) pectin; c) chitosan; d) xanthan gum; e) guar gum

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THE INVISIBLE SCARS: A STUDY ON THE RELATIONSHIP AMONG ADVERSE CHILDHOOD EXPERIENCES, TRAUMA AND INTERPERSONAL RELATIONSHIP AMONG ADULTS.

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ABSTRACT

Childhood experiences play a significant role in shaping one's own personality as well as have significant impact on interpersonal relationship. This quantitative study investigates the relationship between negative life experiences and intimate romantic relationships. The research sample consists of 40 adults engaged in relationships lasting over one year. The study explores the domains of negative life experiences, perception of self, perception of others, and intimate romantic relationships. The tools used include the Adverse Childhood Experiences Questionnaire, Trauma Symptom Checklist, and Functional Idiographic Assessment Template. Findings reveal that trauma symptoms have a significant relationship with intimate romantic relationships, as indicated by positive Pearson correlations across all domains. The study highlights the importance of addressing trauma symptoms within couple therapy and intervention programs to enhance relationship functioning and satisfaction. Overall, this study contributes to understanding of the complex dynamics between negative life experiences and intimate romantic relationships, providing valuable insights for supporting individuals and couples affected by trauma.

Keywords: Adverse childhood experiences, trauma, trauma symptoms, perception of self, perception of others, and intimate romantic relationship.

Introduction

Sigmund Freud, an Austrian neurologist, and the father of psychoanalysis, believed that the past has a significant impact on how we behave, think, and feel now. Freud believed that our past experiences, especially those that occurred in childhood, are stored in our unconscious mind, which is a reservoir of thoughts, feelings, memories, and impulses that we are not aware of.

Trauma is an emotional reaction to a traumatic event that overwhelms a person's capacity for coping and daily functioning. Numerous things, including accidents, violence, abuse, natural catastrophes, war, or racism, can result in trauma. Trauma can have lasting effects on the individual's mental and physical health. One of the most influential psychologists who studied trauma was Pierre Janet, a French psychodynamic theorist who defined psychological trauma as "one or more events that, due to their characteristics, can alter the subject's psychic system, threatening to fragment mental cohesion". (1)

Romantic relationships are close and meaningful connections that involve mutual attraction, affection, and intimacy. They can bring joy, satisfaction, and growth to people's lives, but they can also pose challenges and difficulties that can affect their quality and longevity. One of the most influential psychologists who studied romantic relationships was Robert Sternberg, an American cognitive psychologist who developed the triangular theory of love. Sternberg defined love as "a feeling of strong personal attachment and emotional dependence on another person". (2) He proposed that love consists of three components: passion, intimacy, and commitment. Passion is the physical and sexual attraction, intimacy is the emotional closeness and sharing, and commitment is the decision to stay together and maintain the relationship. Different combinations of these components result in different types of love, such as infatuation, friendship, or consummate love. (2) Romantic relationships can bring joy,

satisfaction, and growth to people's lives, but they can also be affected by past trauma that can interfere with their quality and longevity. Trauma, if left unresolved, can also hamper the passion, intimacy, and commitment between two individuals in a romantic relationship. A lot of the behaviour and cognitive changes (such as defense mechanisms, inner conflicts, etc.,) that trauma can cause in an individual can be reflected in various different ways which are harmful to the relationship.

Some of the common problems that can arise in romantic relationships include:

Communication problems: It can be difficult to feel intimacy when partners have trouble communicating their thoughts, feelings, and needs.

Trust issues: Past trauma can make it hard to trust others or oneself. People who have been betrayed, lied to, cheated on, or abused by their previous partners may have difficulty trusting their current partners or opening up to them.

Fear of intimacy: Past trauma can make it difficult to feel safe or comfortable with intimacy. They may also fear losing their identity or autonomy in a relationship.

Hyper arousal or hypo arousal: Past trauma can trigger a fight/flight/freeze response that can affect one's emotional regulation and arousal levels.

Method

Aim of the study:

To explore the relationship among adverse childhood experiences, trauma, and the quality of adult intimate relationships.

Objectives of the study:

1. To explore the relationship between adverse childhood experiences and adult intimate relationships.

2. To explore the relationship between presence of trauma and adult intimate relationships.

3. To explore the relationship between adverse childhood experiences and presence of trauma in adults.

Hypothesis:

H01: - There will be no significant relationship between adverse childhood experiences and intimate relationships among adults.

1.1: No significant relationship between adverse childhood experiences and Negative life experience in intimate relationships among adults.

1.2: No significant relationship between adverse childhood experiences and perception of self in intimate relationships among adults.

1.3 No significant relationship between adverse childhood experiences and perception of others in intimate relationships among adults.

1.4: No significant relationship between adverse childhood experiences and intimate partner relationships among adults.

H02: - There will be no significant relationship between trauma and intimate relationships among adults.

2.1: No significant relationship between trauma and Negative life experience in intimate relationships among adults.

2.2: No significant relationship between trauma and perception of self in intimate relationships among adults.

2.3 No significant relationship between trauma and perception of others in intimate relationships among adults.

2.4: No significant relationship between trauma and intimate partner relationships among adults.

H03: - There will be no significant relationship between adverse childhood experiences and presence of trauma among adults.

Research Design

This study utilized a quantitative research design to analyse the data.

Materials and Study Design

Study Design - The present study is a cross-sectional, correlational study.

SAMPLING TECHNIQUE: Sample was chosen using the purposive sampling technique

Sample: The Sample was composed of 40 adults, both male and female.

INCLUSION CRITERIA:

1. Adults can be of either sex.

2. Adults falling in the age range of 18-35 years.

3. Adults who are currently in an intimate relationship for at least 1 year.

EXCLUSION CRITERIA

1. Participants should not have chronic physical illness as a reason for negative life experience

2. Current relationship issues should not be attributed to past negative life experiences.

Tools used for the study:

- Adverse Childhood Experience (ACE) Questionnaire - The Adverse Childhood Experiences (ACEs) Questionnaire is a self-report measure that identifies childhood experiences of abuse and neglect founded by Felitti and his colleagues in 1998. ACEs are potentially traumatic events that occur in childhood and can include violence, abuse, and growing up in a family with mental health or substance use problems. The ACE questionnaire is not designed to measure a single underlying construct. Instead, it assesses various categories of adverse childhood experiences. As such, internal consistency reliability (e.g., Cronbach's alpha) may not be as applicable as it would be for a scale measuring a single construct.

- Trauma Symptom Checklist - The TSC-40 is a 40-item self-report measure developed by Briere&Runtz in 1940. It assesses symptomatic distress in adults resulting from childhood or adult traumatic experiences. The TSC-40 generates a total score ranging from 0 to 120, as well as six subscales: Anxiety, Depression, Dissociation, Sexual Abuse Trauma Index, Sexual Problems, and Sleep Disturbances. The TSC demonstrates reasonable construct validity in capturing trauma-related symptomatology.

- The Functional Idiographic Assessment Template-Questionnaire (FIAT-Q) - The FIAT-Q is a 117-item self-report measure designed for therapists to quickly assess client interpersonal performance. It is based on the five FIAT Classes A-E (Assertion of Needs,

Bidirectional Communication, Conflict, Disclosure and Interpersonal Closeness, and Emotional Experience and Expression).

Procedure

Participants in the sample were pre-informed about the potential for re-traumatization and given the choice to opt out if they felt uncomfortable. After obtaining consent, they received a Google Forms link containing a clear study description and instructions. The form consisted of 9 subsections, beginning with demographic information and relationship tenure. It was followed by sections for the ACE Questionnaire, TSC-40 checklist, and FIAT-Q, each with accompanying instructions. The form link was sent to the 40 eligible participants, with assistance provided when needed.

Results

The study aimed to explore the relationships among adverse childhood experiences, negative life experiences, and intimate interpersonal relationships. It specifically examined domains such as negative life experiences, self-perception, perception of others, and intimate romantic relationships.

Table 1: represents the summary of calculated Pearson product-moment correlation to assess the relationship between variables like Adverse Childhood Experiences, Trauma and Interpersonal Romantic Relationships

	ACEQ	**TSC**	**FIATQ A**	**FIATQ B**	**FIATQ C**	**FIATQ D**	**FIATQ E**
ACEQ Pearson Correlation		0.549**	0.378*	0.310	0.226	0.317*	0.127
TSC Pearson Correlation	0.549**		0.562**	0.416**	0.358*	0.329*	0.422**
FIATQA Pearson Correlation	0.378*	0.562**		0.592**	0.489**	0.571**	0.525**
FIATQB Pearson Correlation	0.310	0.416**	0.592**		0.639**	0.400*	0.444**

FIATQC Pearson Correlation	0.226	0.358*	0.489**	0.639**		0.360*	0.429**
FIATQD Pearson Correlation	0.317*	0.329*	0.571**	0.400*	0.360*		0.268
FIATQE Pearson Correlation	0.127	0.422**	0.525**	0.444**	0.429**	0.268	

**Significant at p<0.01, *Significant at p<0.05

[ACEQ- Adverse childhood experience Questionnaire, **TSC** - Trauma Symptom Checklist, **FIATQA** - The Functional Idiographic Assessment Template-Questionnaire: Assertion of Needs,**FIATQB**-The Functional Idiographic Assessment Template-Questionnaire: Bidirectional Communication , **FIATQC** - The Functional Idiographic Assessment Template-Questionnaire:Conflict, **FIATQD** - The Functional Idiographic Assessment Template-Questionnaire: Disclosure and Interpersonal Closeness, **FIATQE** -The Functional Idiographic Assessment Template-Questionnaire: Emotional Experience and Expression]

Findings suggest that ACEQ and TSC has a significant positive correlation (r=0.549, p<0.01), indicating that more adverse childhood experiences are associated with a higher presence of traumatic symptoms in later life. Furthermore, ACEQ has significant positive correlation with FIATQA (r=0.317, p<0.05) and FIATQD (r=0.562, p<0.01), suggesting that increased

adverse childhood experiences are linked to greater problem in assertion of needs, disclosure and maintaining closeness in interpersonal relationship.

TSC has a significant positive correlation with every domain of FIATQ, that is FIATQA ($r=0.562$, $p<0.01$), FIATQB ($r=0.416$, $p<0.01$), FIATQC ($r=0.358$, $p<0.05$), FIATQD ($r=0.329$, $p<0.05$), FIATQE ($r=0.422$, $p<0.01$). Thus findings indicate that increased levels of trauma are linked to increased problems in assertion of needs, including identification and expression, problems in bidirectional communication, including impact and feedback, increased level of conflict, problem in disclosure and maintenance of interpersonal closeness along with problems in emotional experience as well as expression.

Various domains of FIATQ have significant positive correlation with each other which indicate that increased problem in assertion of need is associated with greater problem in bidirectional communication along with increased conflict, problem with maintenance of emotional closeness, emotional experience as well as emotional expression. So, all these factors are interlinked with each other.

Discussion

Through the collection and analysis of data from a diverse sample, this study aimed to shed light on the relationship dynamics influenced by negative life experiences. The results of the analysis revealed a significant positive correlation between negative life experiences and the quality of intimate romantic relationships.

● Negative life experiences and Trauma symptoms

According to the study conducted, a positive correlation was found between the Adverse Childhood Experiences Questionnaire (ACEQ) and the Trauma Symptom Checklist (TSC). This positive correlation suggests that as the number of adverse childhood experiences

increases, there is a corresponding increase in the presence of traumatic symptoms. Individuals who have encountered a higher number of adverse childhood experiences are more likely to exhibit a greater occurrence of traumatic symptoms.

An earlier study in line with present findings found that the connection between cumulative exposure to various traumatic experiences (cumulative trauma) in childhood and the overall number of distinct symptomatology reported (symptom complexity) in adulthood was related. (3)

● Relation between Adverse childhood experiences and assertion of needs

The study conducted also revealed a positive correlation between the Adverse Childhood Experiences Questionnaire (ACEQ) and the FIAT-Q Class A: Assertion of Needs. The results suggest that an increase in adverse childhood experiences are correlated with an increased problem in an individual's assertion of needs, including the identification and expression of those needs. In other words, individuals who have experienced more adverse childhood trauma are more likely to have problems in identifying and expressing their needs.

In an earlier study justifying the findings of the present study that childhood trauma can affect an individual’s interpersonal functioning. Findings showed that there was a greater incidence of the need to be consoled among those who reported physical neglect. The findings also indicated that people who had access to a carer or confidant needed love less. (4)

● Relation between Adverse Childhood Experiences and Disclosure and Interpersonal Closeness

The study also revealed a positive correlation between the Adverse Childhood Experiences Questionnaire (ACEQ) and the FIAT-Q Class D. The results suggest that adverse childhood experiences are correlated with an increased problem in an individual's disclosure and

closeness with other people. This implies that individuals who have experienced more adverse childhood experiences tend to exhibit an inclination not to disclose personal information and it is hard for them to develop a sense of closeness in relationships. They mostly remain isolated and lack social connection.

A study in line with the findings of the present study stated that Ideal conditions for healthy child and adolescent development occur during secure attachment in childhood. It lays the groundwork for higher levels of self-worth, justice, trust, empathy, and gratifying interpersonal connections. Secure attachment can be negatively impacted by childhood trauma, which could lead to the maintenance of mistrust of other people throughout childhood and into adult relationships (5).

● Relation between Trauma symptoms and domains of Interpersonal Relationship

The study conducted found positive correlations between the Trauma Symptom Checklist (TSC) and three components of the Functional Idiographic Assessment Template - Questionnaire (FIAT-Q): Class A, Class B, and Class E. Specifically, the positive correlation with FIAT-Q Class A suggests that trauma symptoms are correlated with an increased problem in an individual's assertion of needs. Victims of abuse go through situations where they are dominated by another individual, which in turn causes them to have problems with assertion of needs. The positive correlation with FIAT-Q Class B suggests a relationship between trauma symptoms and an increased problem in bidirectional communication. Lastly, the positive correlation with FIAT-Q Class E indicates a connection between trauma symptoms and an increase in emotional experience and expression. Abuse causes victims who experience trauma symptoms are more emotionally vulnerable to various situations which might cause problems in expressing their emotions. Furthermore, the study revealed a positive correlation between Trauma Symptom Checklist (TSC) and two components of the Functional Idiographic

Assessment Template - Questionnaire (FIAT-Q): Class C and Class D. Specifically, the positive correlation with FIAT-Q Class C suggests that trauma symptoms are correlated with an increase in an individual's experience of conflict. On the other hand, the positive correlation with FIAT-Q Class D indicates a relationship between trauma symptoms and an increase in an individual's disclosure and interpersonal closeness. Increase in trauma symptoms therefore, can have a detrimental effect on an individual's experience of conflict as well as their disclosure and interpersonal closeness. These findings demonstrate that trauma symptoms can negatively affect an individual's assertion of needs, bidirectional communication, and emotional experience and expression.

A study conducted by Huh supports the findings of the present study where they found that childhood experiences of emotional abuse, emotional neglect, and sexual abuse were strongly linked to overall interpersonal discomfort as well as a number of particular interpersonal issues as adults. These findings offer some preliminary evidence that interpersonal issues in adulthood may be significantly influenced by childhood trauma. (6)

- Relationship among various domains of Interpersonal Relationship such as Assertion of Needs, Bidirectional Communication, Conflict, Disclosure and Interpersonal Closeness and Emotional Experience and Expression

The study conducted uncovered multiple positive correlations among various components of the Functional Idiographic Assessment Template - Questionnaire (FIAT-Q). These correlations provide valuable insights into the connections between an individual's expressions of their needs and other dimensions of their experiences and expressions. Firstly, there was a positive correlation between FIAT-Q Class A (assertion of needs) and FIAT-Q Class B (bidirectional communication) suggests that individuals who have problems in asserting their needs more frequently are more likely to have problems in effective bidirectional communication.

Individuals with problems in assertion of needs have second thoughts when providing feedback or a reply to another individual's choice or decision which causes them to have problems in bidirectional communication as they cannot speak out against the other individual. Secondly, there was a positive correlation between FIAT-Q Class A (assertion of needs) and FIAT-Q Class C (conflict) indicates that individuals who have problems asserting their needs more strongly may also experience higher levels of conflict. Without properly asserting one's needs, it is not possible for other people to understand our needs which can lead to conflict due to misunderstandings. Thirdly, there was a positive correlation between FIAT-Q Class A (assertion of needs) and FIAT-Q Class D (disclosure and interpersonal closeness) which implies that individuals who are unable to express their needs more confidently and openly tend to have problem in disclosure of personal information and experience greater interpersonal closeness. Lastly, there was a positive correlation between FIAT-Q Class A (assertion of needs) and FIAT-Q Class E (emotional experience and expression) which suggests that individuals who are not able to assert their needs more frequently show problems in experiencing and expressing emotions more strongly.

Overall, these findings highlight the interconnections between an individual's assertion of needs and various aspects of their communication, conflict, disclosure, interpersonal closeness, and emotional experience and expression. Understanding these correlations can provide valuable insights into the complex dynamics of human interactions and the importance of assertiveness in interpersonal relationships. If there is deficiency in assertion of needs, it's likely that there will be deficiency in communication, conflict, disclosure, interpersonal closeness, emotional experience and closeness.

A study presenting contradictory results stating that interpersonal relationships and assertiveness are not significantly correlated. The findings also show that those with high interpersonal liking are more likely to have an avoidance-focused approach of conflict

management, while people with low interpersonal liking are more likely to choose an accommodating strategy. (7)

Conclusion

In conclusion, this quantitative dissertation examined the influence of negative life experiences on intimate romantic relationships among a sample of 40 adults in established partnerships lasting over a year. The study explored the domains of negative life experiences, perception of self, perception of others, and intimate romantic relationships, utilizing three tools: The Adverse Childhood Experiences Questionnaire, the Trauma Symptom Checklist, and the Functional Idiographic Assessment Template.

Through meticulous analysis, the findings of this study have unequivocally demonstrated that trauma symptoms significantly contribute to difficulties within intimate romantic relationships. The positive Pearson correlations across all domains indicate that the presence of trauma has a significant relationship with the dynamics and overall functioning of these relationships.

This study has shed light on the intricate relationship between negative life experiences, trauma symptoms, and intimate romantic relationships, emphasizing the need for continued exploration and support for individuals and couples affected by such challenges.

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UNDERSTANDING IMMUNIZATION COVERAGE IN CHILDREN 0-2 YEARS IN BOROUGH VI OF KMC

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ABSTRACT

Routine Immunization remains a cost effective intervention to prevent some common disease of childhood which cause mortality and morbidity which are termed vaccine preventable diseases. Vaccine preventable now encompasses 12 diseases. Outbreak of Covid 19 had denting effect on gains of immunization. This was observed by development partners Forced lockdown in March 2020, resulted in large scale migration of migrant with families, mass gathering for immunization was restricted, health workers remained busy in preventing Covid 19 related health promotion and community mobilization for Covid 19 vaccination, so Routine Immunization was affected. This study assesses the immunization coverage in slums of Borough VI covering UPHC 62,UPHC 65, UPHC 66 using a structured questionnaire among children born between 2020-21. Timely vaccination has been taken as a quality indicator for vaccination. The data analyzed a good coverage specifically among all the social milieu, no specific difference in religion was observed. Literacy state of both parents have a positive impact on Immunization. All most all cases have been institutional deliveries. In an average there has been 98% coverage of Hepatitis B, BCG and 0 dose OPV. There has been a good coverage of Pentavalent vaccines, Measles Rubella Vaccines. PCV which was introduced in late 2021 in West Bengal so coverage was considerable lower.

Key Words: Health Promotion, Development partners, Borough VI, Birth dose vaccine, Pentavalent, parents' literacy.

Introduction:

Immunization and Vaccine Preventable Disease are synonymous terms. These vaccines are effective against 12 childhood diseases. Advocacy, promotion and encouraging vaccination uptake is considered one of the Sustainable Development Goals and also in the newly introduced Immunization Agenda 2030. Health workers being involved in awareness promotion in breaking the chain of transmission of Covid 19 and Covid vaccination. Routine immunization had taken a back seat and there was an increased number of children who has been called as "Zero Dose Children" (1, 2, 3).

The aim of this study is to assess immunization status of children living in borough VI ward-62, UPHC 65 and UPHC 66 of Kolkata Municipal Corporation, to find out reasons for immunization delays and dropout. also, to classify factors promoting immunization update (positive factors) such as who is the decision maker of the family. This was the survey which was conducted at borough VI ward-62, 65 and 66 Mothers having at least one child below the age of 5 years were included. Data were collected by interviews using a self-structured questionnaire. A total of 250 children were included. Educating mothers about immunization, increasing the days of immunization, and proving facilities to them are important interventions to increase the immunization coverage.

The World Health Organization (WHO) launched the expanded program on immunization (EPI) in 1974 with the aim of immunizing children globally, ever since Immunization is the most effective intervention in preventing Under 5 Child mortality globally. The program uses innovative approaches like use of drones and helicopters to reach the unreached. Using this strategies, it has been possible to save 2-3 million lives worldwide every year. WHO has prescribed the vaccination in the following schedule including the prescribed upper age limit for all vaccination. All these vaccines are now included in the national program schedule.

Taking vaccines within the prescribed upper limit has now being introduced as one of the quality markers of immunization

	Name of vaccines	Maximum age limit for which vaccination is allowed
1	BCG (Bacillus Chalmette Guerin)	1 year
2	Hepatitis B	24 hours
3	Zero dose bOPV (bivalent Oral Polio Vaccine)	15 days after birth
4	**bOPV**: Upto 5 years	5 years
5	Pentavalent	1 year
6	**RVV (Rotavirus vaccine)**	1 year
7	PCV (Pneumococcal conjugate vaccine)	1 year
8	MR (Measles Rubella Vaccine)	5 years
9	DPT vaccine (Diphtheria Polio Vaccine)	7 years
10	Japanese Encephalitis	2 years

Pentavalent, Inactivated Polio Virus vaccine (IPV), PCV and Rotavirus vaccines, if at least one dose is given before one year of age, then remaining doses can be administered, and the schedule must be completed by two years of age of the child.

If the first dose is not administered before one year of age, Pentavalent vaccine IPV, PCV, RVV cannot be administered to the child under UIP (4).

Some of the major challenges are maintaining the quality in vaccination process are as follows:

- Inadequate supplies, particularly of vaccines, vaccination cards, registration materials, and other drugs
- Inability of ANM or vaccinator to provide 4 key message- what vaccines are given, when to come for next vaccine, there may be pain and fever for which paracetamol has to be given and keep the MCP card safely

Immunization has been found to be influenced by parents' perceptions regarding the difficulty to access health services, health beliefs and attitudes toward childhood vaccination, it has been identified these are risk factors for decreased vaccination coverage, whereas others suggest that socioeconomic factors play a more important role, parents' beliefs Religion and socioeconomic status of a household, mother's education and employment status, and sex of the child have found to be determinants of immunization (2).

In India, over 50% of deaths in post-neonatal period in children are attributable to pneumonia, diarrhea, or meningitis, which can be prevented through vaccination. The Government of India initiated the Expanded Program on Immunization (EPI) and gradually introduced all requisite antigens, WHO recommends immunization coverage of 90% at the national level and at least 80% for every district. India's immunization indicators have improved since the program's inception; however, recent data from 2015 to 2016 recorded merely 62% full immunization coverage for children aged 12–23 months.

Barriers to immunization has been found in African countries specifically in the Covid 19 pandemic times in countries like Ghana, Uganda and also in Malwai. This was in the post covid 19 pandemic. Education of the mother had a positive impact on immunization status of the mother. The role of development partners like UNICEF has found to be a positive role on immunization promotion through SBCC activities (4). In India during the early stages of Covid 19 pandemic various DO by the central and state government have been issued from time to time ensure that routine immunization is unaffected. It has been estimated by various development partners that Covid 19 pandemic has dented routine immunization gains substantially and worst affected areas are urban slums specifically with migratory population (2,3).

Objective of the study: This study aims to assess immunization status of children living in borough VI ward 62, 65 and 66.During the period of lockdown and duringfirst 3 waves of

Covid 19 betweenJune 2020 to April 2021 did it have any impact on routine immunization in the cohort of children born 2020-21. Find out Reasons for immunization delay and dropout which programmatically called the left and drop out. Finally, classify factors promoting immunization update (positive factors).

Study Methodology: This cross sectional assessment was undertaken by visiting individual child home and askingthe mother about the immunization status and MCP cards. The study areas were at borough VI covering ward 62, 65 and 66. Mothers of children were randomly selected to find out what are the factors affecting immunization delay and dropout children of age group 0 to 2 years. Those who could not show MCP cards questionnaire was not administered. Field researcher also asked the mothers about the factors which could affect their child's immunization, as has anyone told you not to vaccinate your child or do you follow any religious rituals which stops you from vaccinating your child. These questions were part of qualitative assessment.

Questions were also asked if any of the caregivers had notion of not vaccinating the child for other than illness of child which would require hospitalization. Questions were asked about reasons for immunization delay and dropout Researchers asked if caregivers could correctly identify the vaccine and disease these vaccines were preventing. The participants who scored 0 to 2 were categorized as having a negative attitude for the question regarding not vaccinating the children for whatever reasons apart from medical reasons. The tool used was KOBO Collect which is based on the open source ODK collect app and is used for primary data collection in humanitarian emergencies and other challenging field environments. Through headcount by the field workers it has been possible to enumerate number of children as 7479 in the age group of 1-2 years. The total coverage of mothers having at least one child below 2 years of age who were residing in borough VI ward 62, 65and 66was done of 250 children.Data collected was

socio demographic profile of parents, mother educational status, family income and mother's working status.

Results and findings: Over 90% of the respondent had taken vaccines from the government health care facility. There has been 100% institutional deliveries and coverage of the birth dose vaccine as per MCP card record was BCG 100%, 98% for Hepatitis B and 98% for 0 dose of OPV. Among the respondents interviewed 90% had their vaccination done at a government health care facility. Over 90% families belonged to low -middle class economic families as per 2022 released BG Prasad Scale for urban population (6).

When researcher did analysis of children who were 1.5 months old, we got that 71.21% children have received PCV1, 100% children have received Penta1, 94% children have received Rotavirus vaccine 1, 98% of them have received IPV and 100% of them have received OPV1. When researchers started assessing the vaccine coverage of children of 3.5 months, the results were asfollows that 72.4% of children received PCV, 100% children have received. Pentavalent 3, 93.2%children have received Rota 3 and 96.8% of children have received IPV. This no. shows that people are aware about their children's vaccination.

Coming to the 9 months and above children, it was observed 71.6% of children have received PCV-booster, 99.6% of children have received MR1, 95.61% of children have received Vit-A oil and 98.4% of children have received JR1.

Lastly, the researchers came to know that children from 16 to 24 months have received 95.6% vitamin-A oil, 99.6% of children have received MR2, 95.6 % of children have received DPT-Booster, 92.4% of children have received JE 2 and 95.6% of children have received OPV-Booster.Mothers were predominant respondents 211 out of 250, and mostly in the age group 18 years to 30 years 179 respondents out of 211 which amounts to 71.2 % of the respondents When education of the respondents was evaluated it was found indicating literacy status of the parents are high.

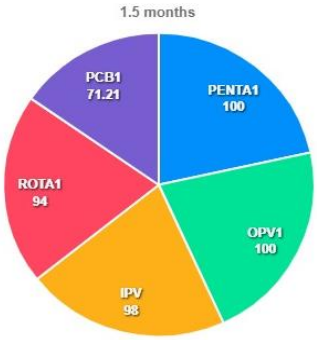
Table 1: Education of mothers among respondents		
Level of Education	Numbers	Percentage
Illiterate	26	10.4%
Primary	92	36.8%
Secondary	54	21.6%
Higher Secondary	48	19.2%
Graduate	27	10.8%
Post Graduate	3	1.2%

Table 2: Income of families among respondents		
Income (monthly in Rupees)	**Number of families**	**Percentage**
5000-10000	81	32.4%
11,000-20,000	153	65.6%
21,000-30,000	9	3.6%
31,000-40,000	3	1.2%
41,000-50,000	2	0.8%

Table 3: Education of fathers among respondents		
Level of Education	**Number**	**Percentage**
Illiterate	42	16.8%
Primary	94	37.6%
Secondary	55	22%
Higher Secondary	31	12.4%
Graduate	28	11.24%
Post Graduate	0	0

Among the people who were Muslims are 78.8% respondents and 75.6 respondents lived in kuchha-pucca houses and 84.4% families had 1-2 children

Fig 1. Immunization status of children of 1.5 months

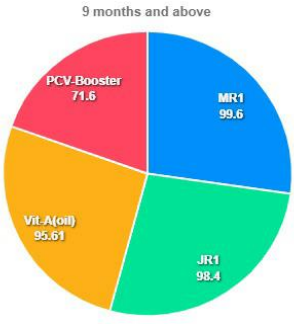


71.21% of children have received PCV, 100% of them have received Penta 1 and OPV 1, 98% of them have received IPV and 94% of them have received Rota 1.

Fig 2. Immunization status of children of 3.5 months

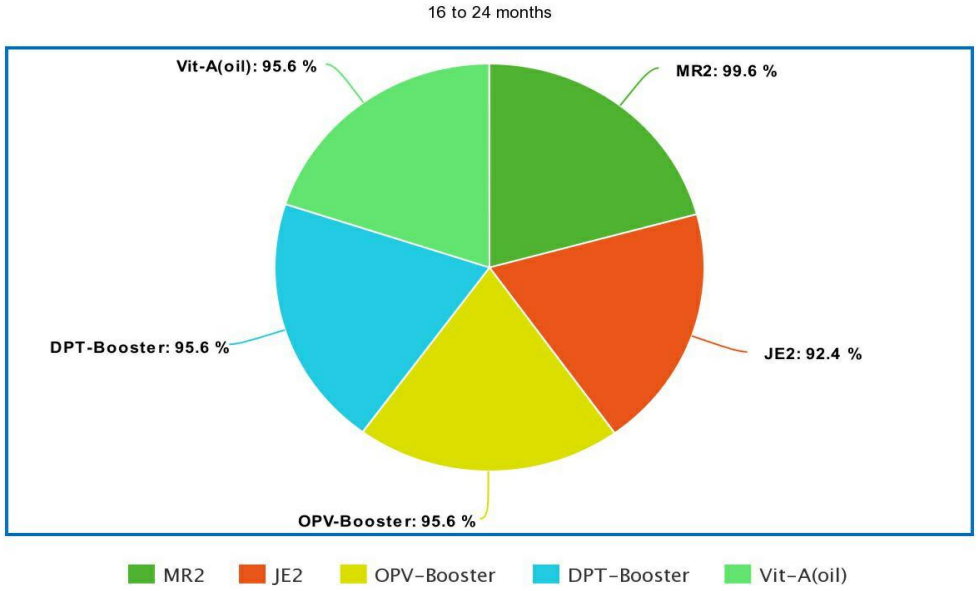
72.4% of children have received PCV, 100% of them have received Penta 3, 99.6% of them have received OPV 3, 96.8% have received IPV 3 and 93.2% of them have received Rota 3.

Fig 3. Immunization status of children of 9 months



71.6% of them have received PCV-booster, 99.6% of them have received MR 1, 98.4% of them have received JR1 and 95.61% of them have received Vit-A (oil).

Fig 4. Immunization status of children of 16-24 months



95.6% of children have received DPT-Booster, 95.6% of children have received OPV-Booster, 92.4% of children have received JE 2, 99.6% of children have received MR 2 and 95.6% of children have received Vit-A oil.Results of qualitative study shows no evidence of difference in religion as a determinant in immunization. There was no evidence apart from medical reasons parents never felt not to immunize the child or no social cultural barriers for taking immunization. Out of pocket expenses for immunization has been zero as parents have availed immunization either in medical college hospital or KMC run UPHCs. None from private health care facility.

Discussion

The findings of this study suggest that increasing vaccination days in vaccination units and providing outreach immunization services for newborns are important interventions to be considered. They will increase immunization coverage for children from 0 to 5 years. Training healthcare workers on delivering a high- quality vaccination, health education for mothers on health promotion is also an important intervention that will help clarify and combat the wrong belief and taboos surrounding immunization which increases mother's compliance and, hence, immunization coverage. In this studyover 90% of children are vaccinated and people are aware

about the benefits of vaccination. The respondents replied they were aware how to manage minor side effects like pain and fever. Mother having education at least up to primary level are better empowered to take decision on the children health needs including immunization. Their response is positive towards immunization it as evident from the present study. Contrary to other studies done elsewhere the impact of immunization had little or no impact on routine immunization

Societal and cultural factors can also play a significant role in the immunization of children. Religious or cultural beliefs that discourage immunization can lead parents to avoid vaccinating their children. Fear or mistrust of government or healthcare systems can also contribute to this problem, as some parents may be hesitant to trust the safety and efficacy of vaccines. Poverty and social inequality can also limit access to healthcare and immunization services, making it difficult for some parents to vaccinate their children. For example, a study conducted in Pakistan found that poverty and lack of education were significant barriers to immunization. The study found that children from poorer households were less likely to be vaccinated than those from wealthier households. Additionally, the study found that lack of education among mothers was associated with lower rates of immunization. In conclusion, the immunization of children is affected by a range of factors, including lack of awareness and education, inadequate healthcare infrastructure and resources, and societal and cultural factors.

Lack of information among parents was the main reason for non-immunization in this study and elsewhere. Finally, the literacy level of mother and the children of urban areas have important role for better immunization coverage of the children in this study (1, 6, 7). The reported immunization coverage might be the cause for regularly occurrence of the vaccine preventable diseases in the study area. So, this indicates that the UIP of Government of India has not achieved so far in the study area (8).

Observation from the present study point towards a pressing need to accelerate efforts in improving the immunization coverage in the area. Efforts should be made to increase information, education, and communication (IEC) to educate mothers especially in rural areas. Improvement in female literacy coupled with the reduction in the dropout rate would add to achieve a higher target of immunization among children.The role of development partner in this case CINI Urban unit the role played need to promote immunization even in the pandemic period needs to be mentioned which ensured a good coverage among the cohort of children in this period. Giving the vaccines within the stipulated tine constitutes the quality service for immunization a newly introduced concept of Immunization Agenda 20230.

Limitations of the study

Duration of the study was too short and small sample size compared to calculated sample size. The study did not capture immunization status of Under 5 Children due to lack of time.

However, in this study some positive findings are evident as children born during the Covid 19 1st wave, 2nd wave and 3rd wave (March 2020 to February 2022) have normal immunization status bellowing expected findings of zero dose children in the area. This can be hypothesized for many reasons. Though the respondents are of low socio economic status and slum dwellers. They belong non migratory population as evident from their history, role of health worker of voluntary health organization CINI is also needs to be highlighted.

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THERAPEUTIC BENEFITS OF ROSEMARY (*SALVIA ROSMARINUS*) HERB

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Abstract

Rosemary (*Salvia rosmarinus*) is an aromatic herb with a long history of food and medicinal uses. It is recognized for its characteristic fragrance and flavor, which comes from the essential oils existing in its leaves. It contains bioactive compounds such as rosmarinic acid, carnosic acid, and essential oils, which contribute to its antioxidant, anti-inflammatory, and antimicrobial properties. These compounds have been studied for their potential therapeutic effects on digestion, cognitive function, pain relief, hair and scalp health, and skin conditions. In conclusion, rosemary is a versatile herb with a range of culinary and potential medicinal uses.

Keywords: Rosmarinic acid, Carnosic acid, Antimicrobial, Antioxidant, Cognitive function.

Introduction

Rosemary(Salvia rosmarinus), an aromatic herb that belongs to the mint family, Lamiaceae,is native to the Mediterranean region, and commonly used in Mediterranean cuisine. With its distinct fragrance and versatile nature, rosemary has been valued for centuries for its culinary flavor, aromatic qualities, and potential health benefits(1). The herb is characterized by its needle-like, evergreen leaves, which are dark green on top and silver-gray on the underside. The leaves grow on woody stems and can be harvested fresh or dried for various uses.

Rosemary plants can reach a height of around 1 to 3 feet (30 to 90 cm) and produce small, paleblue or purple flowers that add beauty to gardens and landscapes (Figure 1). It is believed that rosemary haspotential health benefits, such as being rich in antioxidants, possessing anti-inflammatory properties, and supporting digestion. Its essential oil is also used in aromatherapy for its invigorating scent and potential therapeutic effects.

Figure 1: **Rosemary (Salvia rosmarinus) herb**

PHYTOCHEMICALS

Rosemary (Salvia rosmarinus), known for its medicinal properties, contains various phytochemicals, which are natural bioactive compounds found in plants. The prominent phytochemicals present in rosemary are Rosmarinic acid, Carnosic acid, Carnosol, Ursolic acid, Flavonoids, and Essential oils(1).Rosmarinic acid has been studied for its potential benefits viz. antioxidant, anti-inflammatory, antimicrobial properties, improving digestion, and protecting against certain chronic diseases. Carnosic acid is known for its antioxidant and neuroprotective properties(2). It has been investigated for its potential role in protecting against neurological disorders, e.g., Alzheimer's disease and stroke. Carnosol, a diterpene, exhibits antioxidant, anti-inflammatory, and anticancer activities. Studies have suggested that carnosol

may help in inhibiting the growth of cancer cells and reducing inflammation in the body. Ursolic acid, a pentacyclic triterpenoid, has been associated with various health benefits, including anti-inflammatory, antioxidant, and anticancer effects. Ursolic acid has also shown potential in promoting muscle growth and improving metabolic health. Rosemary contains several flavonoids, including apigenin, luteolin, and diosmetin. Flavonoids have antioxidant and anti-inflammatory properties and have been studied for their potential role in reducing the risk of chronic diseases, such as cardiovascular disease and certain types of cancer (3). Rosemary essential oil, obtained from the plant's leaves through steam distillation, contains several volatile compounds such as camphor, cineole, and pinene (Figure 2) (1, 4).

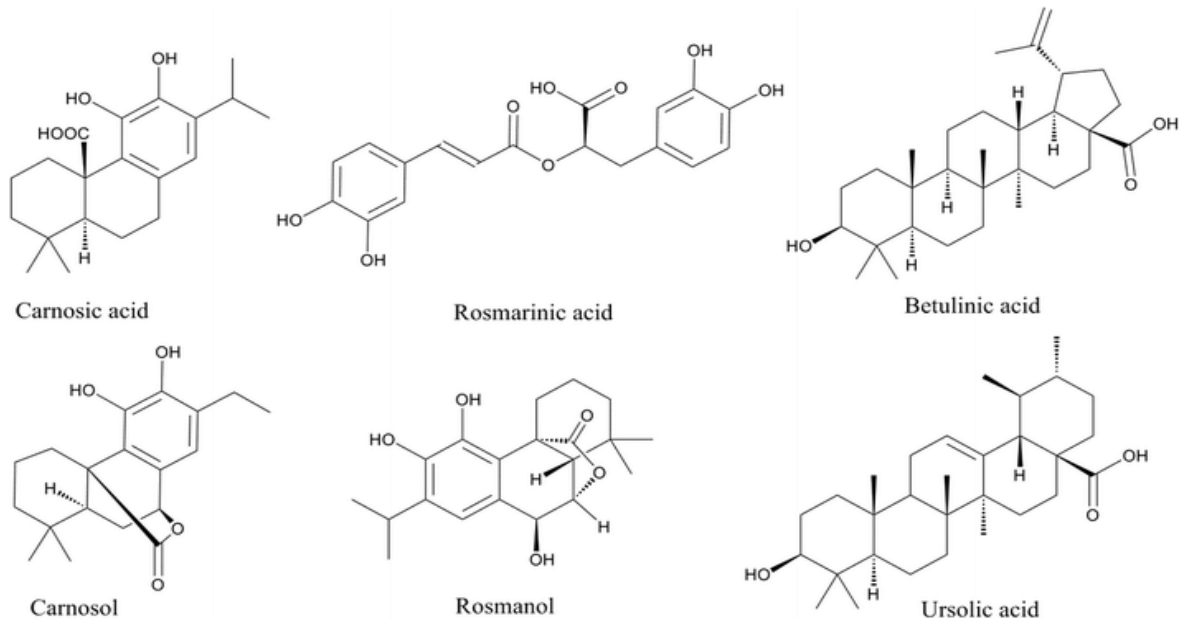


Figure2: Phytochemicals of Rosemary.

HEALTH BENEFITS

Rosemary has been associated with several potential health benefits, shown in a pictorial form in Figure 3(1). While it's important to note that further research is needed to fully understand its effects and mechanisms of action, here are some of the commonly mentioned health benefits of rosemary:

Antioxidant Properties:

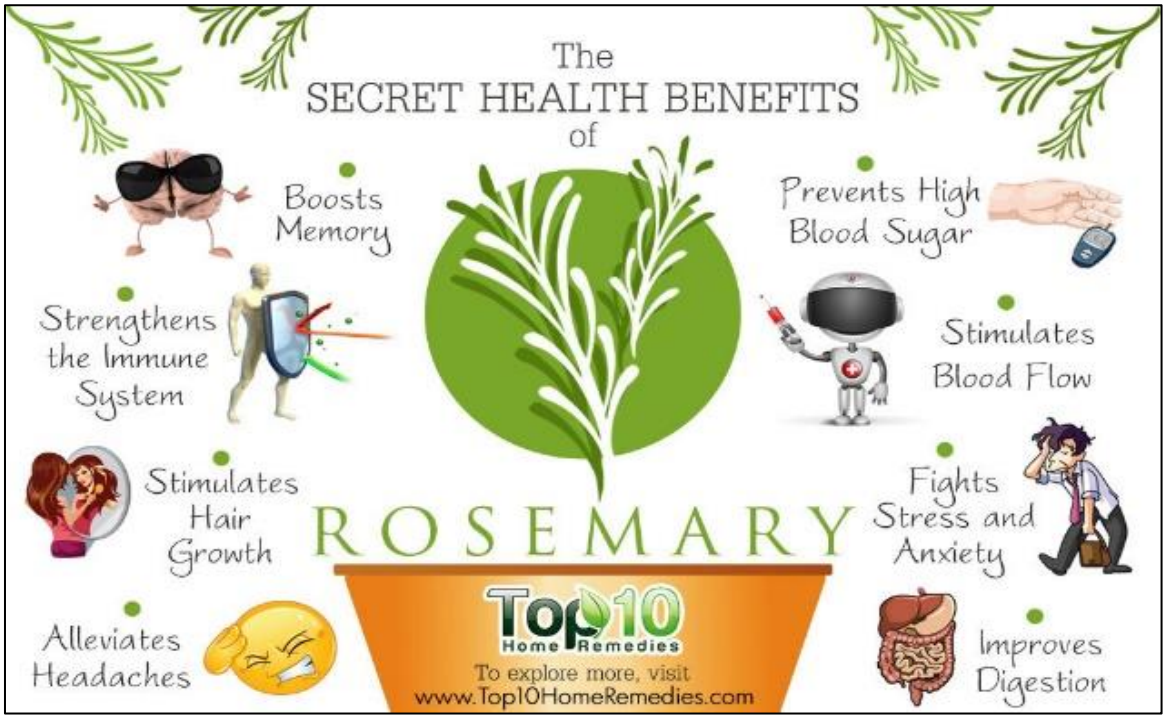
Rosemary contains various compounds, e.g., rosmarinic acid, carnosol, and carnosic acid, that have potent antioxidant properties. Ithelpsto protect cells from damage caused by free radicals, potentially reducing the risk of chronic diseases and promoting overall health.By donating electrons to free radicals, rosemary antioxidants can stabilize them and prevent them from causing oxidative damage to cells(4).Lipid peroxidation inhibition is a process in which free radicals attack and damage fats in cell membranes, leading to cell dysfunction and tissue damage. Rosemary's antioxidant compounds have been shown to inhibit lipid peroxidation, thus protecting cellular membranes from oxidative stress.DNA protection of Rosemary extracts has been found to exhibit protective effects against DNA damage caused by oxidative stress. By reducing DNA damage, rosemary antioxidants help maintain the integrity of genetic material and prevent mutations.Neuroprotective effects ofthe antioxidants in rosemary may have neuroprotective properties. They can help combat oxidative stress in the brain, which is associated with neurodegenerative diseases such as Alzheimer's and Parkinson's (5). Some studies suggest that rosemary extract may improve cognitive function and protect against age-related brain decline.Food preservation of Rosemary extracts has been used as natural antioxidants in food preservation to extend the shelf life of perishable products. The antioxidant properties of rosemary can help inhibit the oxidation of fats and prevent spoilage.

Anti-Inflammatory Effects

Rosemary's anti-inflammatory compounds may help reduce inflammation in the body.

Figure 3: Health benefits of Rosemary.

Anti-inflammatory compounds of rosemary contain various bioactive compounds, such as



rosmarinic acid, carnosol, and carnosic acid, which possess anti-inflammatory properties(3). These compounds can help inhibit the activity of inflammatory enzymes and modulate inflammatory pathways in the body. Modulation of inflammatory pathways studies has shown that rosemary extracts can modulate the production of pro-inflammatory molecules, such as cytokines and chemokines. By downregulating the expression of these molecules, rosemary may help suppress the inflammatory response. Pain relief in traditional medicine, rosemary has been used topically for pain relief. The analgesic properties of rosemary may be attributed, at least in part, to its anti-inflammatory effects. By reducing inflammation, rosemary may help alleviate pain associated with inflammatory conditions. Inhalation of rosemary essential oil has

been reported to have anti-inflammatory effects on the respiratory system (6). It may help reduce inflammation in the airways and alleviate symptoms of respiratory conditions, such as asthma.

Cognitive Function

Rosemary has been traditionally associated with cognitive enhancement. Some studies indicate that the aroma of rosemary may improve cognitive performance, memory, and alertness. However, further research is needed to fully understand its effects on cognitive function.Inhalation of rosemary essential oil has been associated with improved memory and cognitive performance in tasks related to memory retrieval and attention. The aroma of rosemary may stimulate certain brain areas and neurotransmitter systems involved in memory processes.Inhaling rosemary essential oil or using rosemary-infused products may help increase mental alertness and improve focus, which can enhance cognitive performance.Rosemary is rich in antioxidants, which help protect the brain from oxidative stress. Oxidative stress can lead to the accumulation of free radicals and damage to brain cells, contributing to cognitive decline(5). Chronic inflammation in the brain has been linked to cognitive impairment and neurodegenerative diseases. Rosemary possesses anti-inflammatory properties, which may help reduce inflammation in the brain and potentially protect against cognitive decline.Some studies suggest that rosemary may have neuroprotective effects, protecting the brain from damage and degeneration. The antioxidants and bioactive compounds in rosemary may help prevent or slow down the progression of neurodegenerative conditions such as Alzheimer's disease and Parkinson's disease (5).

Digestive Health

Rosemary has been historically used as a digestive stimulant, helping to improve digestion and relieve symptoms such as bloating, gas, and indigestion. It is believed to stimulate the

production of digestive enzymes, which aid in the breakdown of food and facilitate nutrient absorption.Rosemary contains compounds with anti-inflammatory properties, such as rosmarinic acid. Inflammation in the digestive system can lead to discomfort and contribute to conditions like irritable bowel syndrome (IBS) or inflammatory bowel disease (IBD)(7). The anti-inflammatory effects of rosemary may help reduce inflammation in the gut and potentially alleviate related symptoms.Rosemary has antimicrobial properties and may help combat certain bacteria, fungi, and parasites that can cause digestive infections. However, more research is needed to determine the specific effects of rosemary against gastrointestinal pathogens.Some studies suggest that rosemary may have a regulatory effect on gut motility. It may help normalize the movement of the digestive tract, which can be beneficial for individuals with conditions like constipation or diarrhea.By neutralizing free radicals, rosemary's antioxidants may help protect the digestive system from oxidative damage.

Antimicrobial Properties

Rosemary extracts, including essential oil, have shown antibacterial effects against various strains of bacteria. Research indicates that rosemary's antimicrobial action is primarily due to its bioactive compounds, such as rosmarinic acid, carnosic acid, and carnosol. These compounds can disrupt the cell membranes of bacteria, interfere with their metabolism, and inhibit their growth(6).Rosemary has demonstrated antifungal effects against a range of fungal species. Studies have shown that rosemary extracts can inhibit the growth of fungi like *Candida albicans*, which can cause infections such as thrush and yeast overgrowth. The antifungal properties of rosemary are attributed to its active components, including phenolic compounds and essential oils. Rosemary has also exhibited antiparasitic effects against certain parasites (8). For instance, it has been reported to have activity against the protozoan parasite responsible for giardiasis, a common intestinal infection. Rosemary's antiparasitic activity may be

attributed to its bioactive compounds, which can disrupt the survival and replication of parasites.The antimicrobial properties of rosemary have been utilized in food preservation. Rosemary extracts and essential oil have shown effectiveness in inhibiting the growth of foodborne pathogens and spoilage microorganisms, thus extending the shelf life of perishable foods.

Hair and Scalp Health

Rosemary oil is commonly used in hair care products due to its potential benefits for the scalp and hair. It may help stimulate hair growth, improve hair thickness, and alleviate scalp conditions like dandruff. Some research suggests that rosemary oil when applied to the scalp, may help promote hair growth by improving circulation and stimulating hair follicles(1).Rosemary has antimicrobial properties that may help combat scalp conditions caused by certain bacteria or fungi. It may help maintain a healthy scalp environment and potentially reduce issues like dandruff or scalp itchiness. The anti-inflammatory properties of rosemary may also contribute to scalp health by reducing inflammation and irritation. Rosemary-infused products or rinses are believed to provide conditioning benefits to the hair, making it soft, smooth, and shiny. Rosemary extracts contain compounds that can coat and protect the hair shaft, providing a lustrous appearance. The antioxidants present in rosemary, such as phenolic compounds, can help protect the hair and scalp from oxidative stress (1). This may help prevent damage to the hair follicles and maintain overall hair health. Rosemary may have a stimulating effect on the scalp, which can help improve blood circulation to the hair follicles. Adequate blood flow to the hair follicles is essential for delivering nutrients and oxygen, supporting healthy hair growth.

Mood and Stress Management

The aroma of rosemary has been linked to mood enhancement and stress reduction. Inhalation or diffusion of rosemary essential oil may promote relaxation and improve mood. Inhalation of rosemary essential oil has been linked to improved mood and mental well-being. The aroma of rosemary is believed to have stimulating and uplifting effects on mood, helping to increase alertness, reduce mental fatigue, and enhance cognitive performance (9). It may provide a sense of clarity and promote a positive emotional state. Rosemary may have stress-reducing properties. Some studies indicate that rosemary essential oil may help lower cortisol levels, a hormone associated with stress. By modulating the stress response, rosemary may contribute to a more balanced emotional state and improved stress management. Rosemary contains antioxidants that help reduce oxidative stress in the body. High levels of oxidative stress can contribute to mood disorders and mental health issues. Some individuals report feeling relaxed and experiencing reduced anxiety after using rosemary. However, responses to rosemary can vary, and it may have different effects on different individuals. In traditional medicine, rosemary has been used for centuries as a natural remedy for various mood-related conditions, including depression, nervousness, and fatigue. While traditional uses provide insights into its historical use, scientific validation is needed to fully understand the mechanisms and efficacy of rosemary for mood management (10). Individual responses to rosemary may vary, and its effects may depend on factors such as dosage, preparation, and personal health conditions. It's always advisable to consult with a healthcare professional before using rosemary for any specific health concerns or if you are considering using it in concentrated forms such as essential oils.

PRECAUTIONS

While rosemary is generally safe for most people when used in culinary amounts, there are a few precautions to keep in mind, especially when using it in medicinal or concentrated forms (9). Here are some precautions and considerations:

Allergic Reactions:

Some individuals may be allergic to rosemary. If you have known allergies to other plants in the Lamiaceae family (such as mint, basil, or oregano), it's advisable to exercise caution and do a patch test before using rosemary topically or consuming it in large amounts.

Pregnancy and Breastfeeding:

Rosemary in culinary amounts is generally considered safe during pregnancy and breastfeeding. However, consuming rosemary in large amounts or using concentrated rosemary supplements or essential oil is not recommended, as it may stimulate the uterus and potentially cause complications (11).

Seizure Disorders:

Rosemary contains a compound called camphor, which can potentially trigger seizures in individuals with epilepsy or other seizure disorders. It's advised to avoid high doses of rosemary or concentrated forms in such cases. Rosemary may affect blood sugar levels and blood clotting.

Drug interaction

Rosemary may interact with certain medications (Figure 4). It may interfere with the metabolism of certain drugs, such as blood thinners (e.g., warfarin) or antiplatelet medications. Rosemary may have mild sedative properties and may enhance the effects of medications that

cause drowsiness or central nervous system (CNS) depression, such as benzodiazepines, opioids, or barbiturates. Using rosemary in conjunction with these medications may increase the risk of excessive sedation or drowsiness.

These are not exhaustive lists, and other medications not mentioned here may also interact with rosemary. It's crucial to consult with your healthcare provider or a qualified pharmacist if you have any concerns about potential drug interactions with rosemary, especially if you are taking medications for any specific health condition (11).

Essential Oil Precautions:

When using rosemary essential oil, it should be diluted properly before application on the skin to avoid skin irritation or allergic reactions. Internal consumption of essential oils should be done under the guidance of a qualified healthcare professional, as they are highly concentrated and can be toxic if used improperly (10).

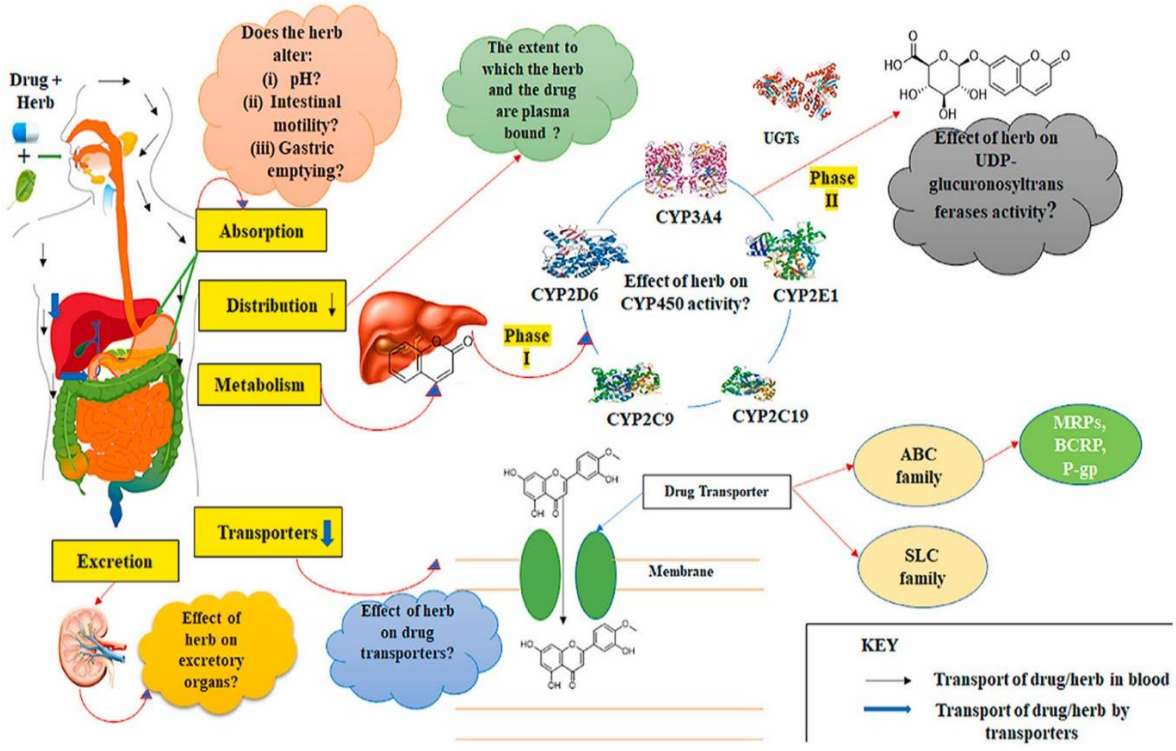


Figure 4: Rosemary plant drug interaction

Clinical Uses

Rosemary (*Salvia rosmarinus*) has a long history of traditional use in various cultures for its potential medicinal properties. While further research is needed to fully understand its clinical uses, here are some of the potential therapeutic applications of rosemary, such as digestive aid, pain relief, antioxidant and anti-inflammatory, improvement of memory and cognitive function,hair, scalp, andskin health (12).

Side Effects

While rosemary is generally considered safe for most people when used in culinary amounts, there are some potential side effects and considerations to be aware of:

Allergic Reactions: Some individuals may be allergic to rosemary or other plants in the Lamiaceae family. Allergic reactions to rosemary can manifest as skin rashes, itching, hives, or respiratory symptoms such as wheezing or difficulty breathing. If you have known allergies to related plants, it's advisable to exercise caution and do a patch test before using rosemary topically or consuming it in large amounts.

Gastrointestinal Disturbances: In some cases, consuming large amounts of rosemary or using concentrated rosemary supplements may cause gastrointestinal issues such as stomach upset, heartburn, or diarrhea. If you experience any digestive discomfort after consuming rosemary, it's best to reduce the amount or discontinue use.

Seizure Disorders: Rosemary contains a compound called camphor, which has the potential to trigger seizures in individuals with epilepsy or other seizure disorders. It's advised to avoid high doses of rosemary or concentrated forms if you have a history of seizures.

Drug Interactions: Rosemary may interact with certain medications. It may interfere with the metabolism of certain drugs, particularly anticoagulants (blood thinners) and antiplatelet

medications, which could affect blood clotting. It's important to consult with your healthcare provider if you are taking any medications to ensure there are no potential interactions.

Pregnancy and Breastfeeding: While the culinary use of rosemary is generally considered safe during pregnancy and breastfeeding, using rosemary in medicinal amounts, particularly in concentrated forms or high doses, is not recommended. It may stimulate the uterus and potentially cause complications. It's best to consult with a healthcare professional before using rosemary medicinally during pregnancy or while breastfeeding.

Essential Oil Precautions: Rosemary essential oil is highly concentrated and should be used with caution. Undiluted or excessive use of essential oils can cause skin irritation, allergic reactions, or even chemical burns. It's important to dilute essential oils properly before topical application and perform a patch test on a small area of the skin to check for any adverse reactions.As with any herbal remedy, it's important to use rosemary in moderation and be aware of your sensitivities and health conditions (11). If you have any concerns or pre-existing medical conditions, it's always best to consult with a healthcare professional before using rosemary medicinally or in concentrated forms.

Future prospective

Rosemary (*Salvia rosmarinus*) has been traditionally used to improve memory and concentration. Some studies suggest that rosemary may have cognitive-enhancing effects, potentially improving alertness, cognitive performance, and mental clarity.While more research is needed, preliminary studies suggest that rosemary may have anti-inflammatory effects.Some studies have suggested that certain compounds found in rosemary, such as carnosol and rosmarinic acid, may possess anticancer properties. However, further research is needed to fully understand the mechanisms and potential clinical applications.

Conclusion

Rosemary (*Salvia rosmarinus*) is an herb that has been used for both culinary and medicinal purposes. It contains compounds with antioxidant properties, which can help protect against oxidative stress and damage. Rosemary also possesses anti-inflammatory effects, although further research is needed to fully understand its potential. Additionally, rosemary has been used to support digestive health, with anecdotal evidence of its effectiveness in relieving indigestion and stomach discomfort. It has also been used topically for skin and hair health, with potential antimicrobial properties and potential benefits for conditions like acne and dandruff. There is preliminary evidence suggesting that certain compounds in rosemary may have anticancer properties, but more research is needed to confirm and understand their mechanisms. While rosemary is generally considered safe when used in culinary amounts, concentrated supplements or essential oils should be used with caution and under the guidance of a healthcare professional. As always, it's important to consult with a healthcare provider before using rosemary for medicinal purposes, especially if you have any underlying health conditions or are taking medications.

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PARENTING STYLES ACROSS GENERATIONS: A LITERATURE REVIEW

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Abstract

Parenting styles play an important role in the development of a child, be it a child's personality, behavior, self-esteem, academic achievement or any other factor. The review focuses on how parenting styles affect child development and the changing parenting styles across generations. Although it is said that authoritative parenting style is the most effective parenting style among the traditional parenting styles, it is highly debatable. Differential findings are there regarding the best parenting styles. Also, culture, socio-economic status as well as gender plays a huge mediating role as evidenced that parenting styles vary across culture. Additionally, with the need for income in the family, majority of the parents are working outside home which is making them emotionally unavailable for the child as well as the technological development increases the involvement of the child in internet addiction, drug abuse and increase in mental health issues. However, though with the change of generations, a permissive parenting approach is seen among parents, it is very difficult to conclude which parenting style is best for a child in a particular culture coming from a particular socio-economic status. However, it can be said whichever parenting style a parent adopts, the degree of responsiveness and control must vary from one to another depending on the child's needs and for the purpose of giving the child an appropriate environment to grow and flourish into a self-sufficient successful human being.

Keywords : Parenting styles, child development, culture, socio-economic status, authoritative, generation.

Introduction

Humans are a product of nature and nurture. While some characteristics or traits are inherited from birth genetically, or inborn in the child (nature), a lot also depends on the environment in which the child grows up. A child's environment has the power to influence their behaviour, personality, way of life, and other aspects of their development. The parenting styles are one of the most important aspects of a child's environment. In future, whether a child will grow up having a strong sense of self or high self-esteem is greatly influenced by how they are reared up by their parents. From infancy through adulthood, parenting and child rearing foster and support a child's physical, emotional, social, spiritual, and intellectual growth. (1)

Parenting style is a determinant factor in child development. It affects the psychological and social functioning of the children. Parenting style is largely affected by the experience of their own parenting. A parent’s age, personality, temperament, gender-identity, developmental history, educational achievement, culture, socioeconomic status, beliefs and the influence of their spouse are few important factors that affect parenting styles as well. Based on responsiveness or parental warmth and demandingness, there are three parenting styles given by Baumrind – authoritarian , authoritative , permissive. Later, in 1983, Maccoby and Martin added the neglectful parenting style. These four parenting styles are taken into account in this review.

Authoritarian parenting styles involve high demandingness and low acceptance while permissive or indulgent parenting style involves high responsiveness and low demandingness. Thus, authoritarian parents are highly strict and one-way communication is seen among them. The parents have high expectations of their children and disobedience leads to punishment. Though these make a child obedient, these children lack in social competence, self-esteem as well as happiness. On the other hand, permissive parents are extremely accepting and all the child’s needs are met. Thus, these children with permissive parenting style score high in self-

esteem, confidence as well as have good social skills but they are more prone to problem behaviour due to lack of control from parents. Accepting responsibilities is difficult for them when they grow up.

Authoritative parenting style is high on both demandingness as well as responsiveness. Though the parents set clear standards for the children, they accept a reciprocal responsibility to be as responsive as possible to their children's demands and point of views. Since both responsiveness as well as personal autonomy is also there, these children score high on self-esteem, social skills, self-confidence as well as academic achievement. Researches suggest that authoritative parenting style is the most appropriate parenting style for the development of a child. The neglectful or uninvolved parenting style scores low both on responsiveness as well as demandingness. These children tend to score low in all developmental areas of life be it social skills, happiness, academic achievement or self-esteem. Thus, this review discusses different aspects of child development that can be impacted by parenting styles while keeping culture, socio-economic issues as well as generational changes in mind.

Parenting styles and self-esteem

Self-esteem, the degree to which people think of themselves as competent, successful, deserving and important, is one of the fundamental components of personality. Those who have high self-esteem tend to have high creative skills as well. Studies show that parental autonomy and psychological control affect self-esteem of a child. The research done by Dong and others in 2022 reflected the effect of parenting styles on a child's creativity and self-esteem keeping socio-economic status in mind. The study has shown that families with high SES were more involved with their child's performance in activities as well as academic achievement providing them with better educational methods. (2) Thus, studies suggest that a positive parenting style is linked with a high level of self-esteem of the child. Additionally, studies have shown that children with permissive parenting styles have the highest level of self-esteem while

authoritarian ones have the lowest degree of self-esteem. Authoritative parenting style also scores a high level of self-esteem but in most research, permissive parenting style scores the highest. An interesting insight offered by Driscoll was that the parenting styles evolved across the course of individual's development, with authoritative parenting taking precedence in the early years and permissive parenting emerging as the predominant style between the age of 18 to 23 years.(3) However , the limitations of the review lies in the narrow range of studies , as well as inclusion of other variables like attachment styles or mediating impact of culture would have given a better overview. Lastly, the inclusion of directives on how to modify parenting styles to foster development of healthy self-esteem would have been a beneficial addition to these studies.

Parenting styles and behaviour

Just like self-esteem, emotional intelligence, attachment styles, academic achievement, parenting styles inevitably affect a child's behaviour. While a healthy parenting style leads to a good and healthy behaviour of a child, excessive psychological or behavioural control can lead to the problem behaviours of the child. However, research regarding the same offers different outcomes. While external problem behaviours include offending behaviours and even anti-social behaviours, internalizing behaviours include social withdrawal and negative emotions towards oneself. All the three parenting style dimensions – affection, psychological control like love withdrawal, guilt induction as well as behavioural withdrawal like strictness, increased demandingness, limit setting etc are said to have an effect on child's problem behaviours. Studies suggest that a high level of behavioural control can lead to low externalizing behaviours while parental affection helps in child's adjustment in the society. However, research done by Galambos and few other researchers in 2003 showed that a combination of both psychological and behavioural control behaviours was associated with externalizing problem behaviours of adolescents. But the study done by Aunola and

Nurmishowed contrasting results saying that a mother's high level of psychological control can increase a child's externalizing behaviour while a high level of behavioural control can decrease the external problem behaviour. Additionally, it has been seen that the problem behaviours of the children tend to decrease with age. Also, no correlation between a father's parenting style and problem behaviours were found.(4) Though little is known about the relation between the delinquent behaviours of the child and parenting styles, findings from a research indicate high demandingness can increase the likelihood of crime among adults when they grow up. In the same way, parenting approaches that were less demanding but more responsive are likely to increase the rate of adult crime as well.(5) However, very limited research has been done focusing on the internalizing behaviours of the child. Effect of the peers, school environment, genetic predispositions, culture and socio-economic status definitely contributes to a child's behaviour, but it can be said that a certain balanced level of demandingness as well as responsiveness can contribute to a healthy behaviour of the child.

Parenting styles and academic achievement

It is needless to say that parenting styles have a significant impact on the academic achievement of a child. Compared to other areas of child development, extensive research has been done on the same. According to studies, students who experience authoritative parenting style tend to perform well academically. In a research conducted by Dornbusch and colleagues in 1987, findings showed that while authoritarian and permissive parenting style was negatively correlated with school grades, authoritative parenting style was positively correlated with the student's academic performance. Additionally, another study showed that students were more confident and persistent academically when they were offered more autonomy, demand and support by parents. The study conducted by Gary and his colleagues in 2005 also showed the same results. But the best part of the study was different variations of cultural background. While almost the same percentage of East Indian and Canadian groups practised authoritative

parenting style, only 19% of East Indian groups and 35% of Canadians practised authoritarian approaches. Studies conducted by Tay and Tam in 2011, Cramer's study in 2002, Hickman's study in 2000 supported the same hypothesis. Thus, it can be concluded that authoritative parenting style is best for a child's academic achievement irrespective of age, gender and culture. Not only does it help the child in academic achievement, better self-efficacy, coping skills and adjustment skills are also noticed among the child.

Parenting styles and personality

Self-esteem, coping skills, behaviour , academic achievement, attachment styles, emotional intelligence ultimately contributes to the personality of an individual. The parenting style that an individual experiences as they grow up has a significant impact on who they are as an adult, as well as on their qualities, social skills and habits. In order to affect their children's cognitive, emotional and social development, parents have a responsibility to take on the duty of socialisation for their offspring. Not only is a child's personality important, but also, to have a good parenting style, the parent's personality traits should also be taken into account. According to studies, conscientiousness is related to high responsiveness and low demandingness, while extraversion is related to parenting styles associated with authoritative parenting. Also, emotional stability is associated with authoritative parenting, whereas agreeableness is linked to authoritarian parenting. The more the supportiveness and responsiveness, the more the openness of the individual will be there. Results from a study in 2009 suggest that dimensions of extraversion and agreeableness were related to high levels of supportiveness, while emotional stability was associated with strict control which is exactly needed for authoritative parenting style.(6)

Just like the parent's personality, it has been said earlier as well that parenting styles have a significant impact on the child's overall personality. Furthermore, authoritative parenting style has been proven to be the best parenting style for a child's development. A study was done by

Mensah and others in 2013 which focused on the social development and personality of the children as well as to find out the widely practised parenting style in that area. Result suggest that authoritative parenting style is the highest practised parenting style in that areas, the number being 330 among 480 individuals.(7) From this, it can be said that not only authoritative parenting style is mostly practised in that area, but since it has a balance between strictness and demandingness, it should be followed in general as well. As seen in the previous study as well, that authoritative parenting style is associated with good qualities like agreeableness, extraversion, openness which showed a positive correlation with social development and personality in the children. One of the limitations of the studies were other factors like age, educational background, culture, SES, self-esteem which are important for a holistic view of personality were not taken into account in this study. Also, since the research was conducted in a particular area, it cannot be generalized that authoritative parenting style is the widely practised parenting style among all areas in the world leading to the conclusion that further research in this particular area is needed.

Parenting styles across generations

While parenting styles can have a wide range of effects on a child's wellbeing, it is also expected that parenting styles can change over time and across generations. This may or may not result in different parenting styles in the same family over time. Since parenting styles vary across cultures, it is possible that a family migrating to a new country from their native land will exhibit their child more or less warmth than they did growing up. Moreover, there have been researches focusing on cross-generational parenting practices and how they impact the children.

The most remarkable study done by Garcia and colleagues published in 2020 which focused on the four parenting styles and their relationship with psychosocial adjustment of children in adulthood , took cross-generational parenting styles into account.(8) All the three generations

– G1- the first generation, G2 -the second generation and G3- the most young generation i.e. college students of Spain indicated that the permissive parenting style has the most positive outcomes for psychosocial adjustment of a child .The findings also indicated that families across generations have increasingly adopted parenting practices with more warmth.While the G3 generation received most affection from the parents and highest educational qualification as well, the G1 generation reported getting least affection as well as least educational qualification. The most striking factor in this study was though G3 generation received most resources and warmth, they scored lowest in life satisfaction, while on the contrary, G1 generation , though grown up with most strictness scored higher life satisfaction.G3 scoring highest in happiness can be well predicted as they are mostly getting more warmth and less strictness than other generations. Along with age-related differences, some sex-related differences were also seen in this study. Males scored higher in emotional and physical self-concept than females. Females from G1 reported highest in emotional self-concept as well as family self-concept.

Talking about the relationship between type of parenting style and psychosocial adjustment of an individual, it was seen that permissive or indulgent parenting style was equal or more effective in psychosocial adjustment than the authoritative parenting style. Adult children from permissive parenting families scored highest, while authoritative parenting styles scored second highest. Apart from these, a mediating effect between parenting style and children's generation was found on social and family self-concept and here permissive and authoritative parenting styles was better than other parenting styles across generations as well. While neglectful parenting style showed mixed results on some domains, authoritarian parenting style was worst among all. Thus, the belief that authoritative parenting style is the best or most appropriate parenting style does not hold true in all cases as from studies it can be seen that permissive parenting style is better than the former one. One limitation of the study was that

very limited data samples were taken, no diverse population samples were people from different SES or people belonging to any other culture or any other settings. However, from this study, it can be concluded that parents are becoming more lenient with their children across generations.

Parenting styles and culture

It is a well known fact that culture has a huge impact on parenting styles leading to an impact on child development. While Baumrind's studies have consistently linked authoritative parenting to the best psychosocial adjustment of a child, those researches were largely carried out in Anglo-Saxon contexts with European-American samples. But there are doubts over the same. For instance, research conducted in the U.S. with ethnic minority groups such as African Americans, Chinese Americans, Hispanic Americans, multiethnic Americans as well as Arab families indicated that authoritarian parenting was superior for a child. However, certain studies based on Latin American and European Nations discovered that permissive parenting was beneficial for the wellbeing of the children.

When it comes to parenting styles and practices, culture along with generational gap and changes play a huge role especially in the case of immigrants. According to research , immigrant children typically conform to the values of host culture for their own children but there has been research for first and second generation immigrant parents. According to certain theories, it is normally believed that families may not fully acculturate to the host culture until the third or fourth generation. It is said that collectivism, linked with authoritarian parenting, predominates in Eastern and less industrialized countries while individualism, linked with authoritative parenting style, predominates mainly in Western culture.(9) Fathers are more likely to adopt a more authoritarian approach towards their children, however results on the same have been contradictory. Along with culture, educational level also plays a mediating

factor. It is often believed that the less educated mothers are, the more authoritarian approach she is likely to adopt.

In a study conducted by Zervides and Knowles in 2007 to evaluate the generational change between samples of immigrants and non-immigrants and the role of culture in parenting styles, Greeks and Australians were taken into study. While Greeks are well known for their collectivistic culture, holding on to their values and practising an authoritarian parenting style, Australians tend to have an individualistic culture and want their children to be self-sufficient. The findings demonstrated that Greek-Australian respondents viewed their parents as more authoritarian than Anglo-Australian samples. The most striking factor in the results was that the Anglo-Australian group showed remarkably identical findings in the authoritative approach in the second-generation samples, which raises an interesting possibility of significant generational variations in parenting approaches. Furthermore, it was also seen that mothers adopted a more authoritative approach than the fathers. One reason behind this could have been that mothers spend more time with their children than fathers do and are aware of their child's needs. Also, there was minimal difference in permissiveness between both the genders.

Several other studies have shown the impact of culture on parenting styles. Cultural differences can not only impact parenting styles, but can also indirectly affect a child's self-esteem. A research done by Mimi Chang focuses on how cultural values mediate parenting practices and the impact of cross-cultural practices on the development of the child. In particular, Caucasian and Asian American parents were taken into study. It is well known that the idea of independence versus interdependence is the main cultural difference among Caucasian Americans and Asian Americans. While Asian societies put a greater emphasis on interdependence, unity among individuals to feel connected to their families, Caucasian American society believes in independence, building a strong sense of self and individuality. Adolescence, probably being the most crucial point in one's life may affect an individual while

they are acculturation to a new culture, especially when they see completely two different cultures- one at their home and different one among the peers. Thus, adolescent Asian Americans may experience some difficulty in balancing the both cultures which may result in a person's dual identity leading to an internal conflict about the person's true identity, especially when adolescence is the key time when an individual faces identity crisis. According to studies, Asian Americans youths may experience higher degrees of social isolation, be rejected by their American peers and have interpersonal skills. The results of the study, as predicted, showed that Asian Americans practise a more authoritarian approach than the Caucasian American parents which resulted in higher self-esteem among Caucasian individuals. (10) The findings also suggest that authoritarian parenting was positively correlated with adolescent rebellion and negatively correlated with self-esteem. One reason behind social isolation and lack of self-esteem can be that Asian Americans witness how their non-Asian peers are treated and question why they are not treated the same way.This may even lead to adolescent rebellion behaviours. But perhaps since Asian American parents are more controlling in nature , Asian American scored higher academic achievement than the Caucasian Americans.

Thus, to sum up, definitely culture along with generation, educational background , socio-economic status, gender plays a huge role in parenting styles. It can be said that parenting with some level of parental guidance is best for a child's well-being. This restrictiveness and a little bit of discipline may make the child feel a sense of belongingness among their families, peers and relatives. On the other hand, permissive parenting style can be too lenient for a child in some cases which can have a negative impact on the child like disobeying the parents or taking wrong decisions without parental supervision.

Parenting styles and socio-economic status

Similar to culture, socio-economic status has a significant impact on parenting practices and how they affect the environment of the children. Simply said, a child growing up in a high SES will experience a completely different environment than a child growing up in a low SES. Nowadays, due to increase in economic needs and urbanization issues, most parents work on a part-time or full-time basis. When working conditions are involved, a lot of factors like role satisfaction in employment and parenting, issues associated with work, work-life balance, job flexibility, work plans are involved in the parental involvement with a child.

The study done by Talib and his other colleagues in 2011 focused on socio-economic status and the impact of the same on parenting styles. Malaysia, being a developing nation has witnessed women driven to work in the industrial sector due to rising living costs and a labour shortage. Currently, 60% of Malaysians reside in urban areas , among which 64% of mothers work a full-time job outside their home.Along with that, due to Malaysia's examination-focused culture and the aspiration of many parents for their children's academic performance , demands from the children are also high. (11)

The best part of the particular study was that families were chosen from low and middle-class backgrounds and the data collected was appropriate because the place represented Malaysian society properly where people ethnicities were mostly Chinese, Malay and Indian. According to the studies, both parents were more authoritarian with their son than their daughters. So the results of the authoritative style were greater in females. Thus, the child's gender played a role on the authoritarianism level of the mothers. Additionally, employment circumstances and lower SES among mothers were positively correlated with stronger authoritarian styles. Overall, the relationship between a mother's working environment and her children's behaviour showed that better working conditions are associated with better child behaviour. The authoritative approach also has a strong relationship with children's behaviour, suggesting that it helps children develop better behaviour as well as academic success. On the contrary,

authoritarian parenting style is negatively correlated with children's good behaviour and overall development of the child. Three key factors seemed to be significant predictors for a child's behaviour – mother's authoritative parenting style, SES background and working conditions. Though very few research has been done on the neglectful parenting style, it is expected that a full-time working mother or father won't be able to engage themselves in a manner a parent from a better socio-economic status will be able to do. However, few limitations in few studies have been seen like immediate environment of the family as well as personality of the parents were not taken into account and the studies solely focused on the SES and child's development or particularly academic achievement.

Conclusion

Parenting styles are one of the important aspects of a child's environment. It has the ability to modify a child's environment, influencing their behaviour, personality, self-esteem, academic achievement and overall psychosocial aspects of the child. Baumrind states that the authoritative parenting style is the best one for the development of a child. Few studies' findings were in contradiction to the statement, despite the fact that the majority did so. While a longitudinal study found that permissive parenting during adolescence is most beneficial for a child, a couple of studies have shown that authoritative parenting is more useful for a child's self-esteem. However, in that specific study, parenting styles changed over time. High academic achievement of children & authoritative parenting style was positively correlated, while academic achievement and permissive as well as authoritarian parenting were negatively correlated. It goes without saying that, depending on the situation , some form of psychological, behavioural or emotional control is needed to promote the advancement of the child be it development of self-efficacy or healthy behaviours. However, studies showed a child's externalizing problem behaviour is linked to a high level of psychological or behavioural control. Though internalizing behaviour were also subjects of research, no connection was

found, hence more research is required on the same. Also, there is limited research when the overall personality of children as well as parents are involved in parenting styles. According to a study that looked at the relationship between a child's personality and parenting methods, authoritative parenting style was widely used there and was considered as the most effective parenting style for the growth of the child. However, results have been contradictory on a research which focused on the cross-generational changes and psychological adjustment of the child. This happens because parenting styles across the world are highly culture-specific.

Though Diana Baumrind has consistently considered authoritative parenting style the most effective, it is highly contradictory in many areas. Not only did few research show different results , but also, when the role of culture, socio-economic status and changing parenting styles across generations come into play, one parenting style cannot be generalized as the best parenting style. Though Diana Baumrind was the first one to give the different types of parenting styles based on responsiveness and demandingness, the researches were largely carried out in Anglo-Saxon contexts with European-American samples. In that culture, at that particular time, authoritative parenting style proved to be most effective but, parenting styles, the strictness of the parents are changing over time. Additionally, due to migration of people and globalization, acculturation and mixture of different cultures are taking place which may lead us to say that a particular culture cannot be completely collectivistic or individualistic, thus making co-existence of individualism and collectivism. When a person is migrating to a new culture, he/she will leave a tinge of one's own culture and imbibe new values from that particular society which will be reflected in their parenting styles as well. Thus, definitely, with time, not only culture, but with changing generations, parents are becoming more lenient with their children, while gender as well as educational qualification also play a mediating factor in parenting styles. Also, parents, especially mothers coming from a lower SES show a more authoritarian approach towards their children. One striking factor among few researches was

that when both parents were studied, either fathers showed more strictness or authoritarian approach towards their children or no effect at all.

Thus, keeping culture, gender, socio-economic status as well as generational changes in mind, though studies have proved yet and again that authoritative parenting style is most effective for a child, it is difficult to conclude which parenting style works best for a child in a particular culture. Though it is a well-known fact that with time, parents are becoming more lenient towards their children because they feel that their parents were more strict with them, still it cannot be generalized globally. Also, more research needs to be done on the socio-economic status, cross-generational changes, culture holistically to come to a conclusion for the best parenting approach for a child, especially in these crucial times where in the most advanced generation least life satisfaction as well as increase in mental health issues can be seen. But from the researches studied, it is advisable to give a child an appropriate environment to grow and flourish into a self-sufficient human being, parents should adopt a certain level of demandingness so that the child becomes disciplined and does not engage oneself in wrong activities or mix with wrong peers as well as some level of warmth is required so that the child can also feel heard, get enough and required emotional support and feel loved and secured.

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CANCER IMMUNOTHERAPY: HALLMARKS OF CANCER PERSPECTIVE

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Abstract

Cancer immunotherapy is a newer trend in cancer therapeutic arsenal by promising outcomes over past decades research. In immunotherapy, the immune cells are invaded into the cancer cells to abrogate the cancer cell survival, growth, differentiation and invasion due to the inauguration of immunogenic cell death (ICD).The immune system plays a crucial role to regulate the tumor microenvironment from tumor manifestation to differentiation and metastasis. Programmed cell death 1 (PD-1) and cytotoxic T-lymphocytes antigen 4 (CTLA-4)are two important immune checkpoint molecules expressed in naïve T cells. While programmed cell death ligand 1/2 (PD-L1/2) and B7-1 / B7-2 are ligands more expressed in tumor cells and binds with PD-1 and CTLA-4 respectively which attenuatesT cell amplification and hyperactivation in host cells to facilitate malignant cellular propagation. Immune checkpoint blocker is comprehensively attributed the blockade of PD-1 and CTLA-4 interactions with its ligands, thereby consequently causes the induction of apoptosis in

neoplastic cells thru the immunogenic cell death (ICD) mechanistic pathway. Adoptive T cell (ATC) therapy is subject to the infusion of the tumor fighting immune cells into the bodyto activate host immune system. Moreover, cancer vaccine can participate toencourage the immune system against tumorigenesis by either therapeutically or prophylactically. In this review, summarize the biological and clinical significance of Immune checkpoint blocker (ICB), Adoptive T cell therapy (ATC) and cancer vaccine in cancer immunotherapy with an emphasis on T cell regulation.

Keywords: Cancer, Immunotherapy, Immune checkpoint blockade, Adoptive T cell therapy, Cancer vaccine.

Introduction

Cancer immunotherapy is an advancement therapy of tumor bearing cells. The concept of immunotherapy is considered to be the activation of immune system for combating against cancer cells to protect the body from neoplastic antigen. Recently the immunotherapy was accomplished to be the “fifth pillar” in cancer treatment arsenal as assembly the ranks of surgery, chemotherapy, photodynamic therapy and targeted therapy.[1]William B. Coley, now often known as the father of immunotherapy, firstly investigated the strength of immune systems to treat various malignancy in late 19th century.[2]Paul Ehrlich in 1909, was first hypothesized the concept of immunotherapy as well as reported that the antibodies might have the strength with combating tumor cells by the activation of host immune system.[3]In 1950s, Burnet and Thomas suggested that the idea of immune surveillance can directly recognize the primary tumor sites by the stimulation of immune system resulting as the destruction of malignant cells.[4]Later, Robert D Schreiber et al, 2001, revealed that the theory of immunoediting, the light of advancement of cancer investigation. They devised that the

immune system can significantly prevented the manifestation of carcinoma induced sarcomas and extemporaneous epithelial cancers.[5]

The immune system plays an important role to develop a mechanism for detecting and eradication of tumor cells proliferation. The development of cancer due to the poor prognosis of host's immune response to invade into the tumor microenvironment.[6]Interestingly, the recent investigation is endorsed accompanying with targeted cytokines to alter the immune cell function. For instance, the high dose of interferon α-2b (IFN α-2b) and interleukin 2 (IL-2) caused the downregulation of several carcinogenic pathway for the treatment of renal cell cancer (RCC) and advanced melanoma.[7]

Programmed cell death 1 (PD-1) and cytotoxic T-lymphocytes antigen 4 (CTLA-4) are two immune checkpoint molecules to play a crucial role in the development of cancer via the downstream of host's immune system.[8]Allison and Honjo first discovered the T cell immune checkpoint molecules including PD-1 and CTLA-4 and were awarded the Nobel prize from Physiology or Medicine in 2018.[9] The ligands of immune checkpoint molecule are programmed death ligand 1/2 (PD-L1/2) and B7-1/2 which consequently binds with PD-1 and CTLA-4 in malignant cells. Interestingly, the inhibitory effect of immune checkpoint blockade therapy in cancer associated with promoting immunogenic cell death (ICD).[8]Adoptive T cell therapy, in other hand, tumor infiltrating cytotoxic T lymphocytes are infused into host bodies to recognize, target and destruction of cancer cells. Tumor infiltrating lymphocytes can obstacle the antigenic activation to eradicate the distant metastases.[10]Moreover, cancer vaccine can be accomplished the stimulating the immune system to destroy the cancer cell that acting prophylactically or therapeutically. The prophylactic vaccine is used to protect body from attacking the carcinogenic viruses. By contrast, the therapeutic vaccine causes the harness of immune system to abrogate the tumor cell proliferation.[11]

In decades, several monoclonal antibodies and combination have been widely used in cancer immunotherapy through different preclinical and clinical approaches. As such, pembrolizumab and nivolumab are the first FDA approved anti-PD-1 mAbs for the management of refractory and unresectable melanoma in 2014.[12, 13]From this perspective, ipilimumab can significantly target the cytotoxic T-lymphocyte antigen 4 (CTLA-4)to block the interaction of CTLA-4 and B7-1/2 in non-resectable stage III/IVmelanoma which was approved by FDA in 2011.[14]

This review has highlighted the holistic insight on the role of immune system in connection with the cancer progression and initiation of apoptotic events in tumor cells. Additionally, this study portrayed the different approaches of immunotherapy in the treatment of cancer with the activation of immune system.

The role of immune cells in cancer immunotherapy

Immunotherapy in cancer treatment is helping to eliminate the malignant cells via the stimulating of body's natural defense mechanism through invading the immune cells into the malignant cells (Figure 1). The immune system is a crucial aspect for the development of tumorigenesis. The both innate and adoptive immune system can participate for provoking the carcinogenic proliferation as well as repression of cancerous stimulation. The immune cells consisting with neutrophils, eosinophils, basophils, monocytes, natural killer cells, macrophages, dendritic cells and lymphocytes including T and B lymphocytes which subsequently controls the tumor microenvironment.[15]

In 1960s, two major subtypes of lymphocytes in the field of immunology were identified namely B lymphocytes and T lymphocytes. B lymphocytes distinguish the antigen in its native form and respond through release the protecting antibodies.[16]T lymphocytes, on the other hands, identify the peptide-based antigens which is derived from intracellularly degradation of proteins and loaded onto the surface of MHC molecules, this phenomenon known as antigen

presentation.[17]CD8+ T lymphocytes identifying the antigen in MHC class I molecules which exerts the cytotoxic effects to killing the malignant cells. CD4+ T lymphocytes recognize the antigen in MHC Class II molecules which demonstrated the activation of immune system via the releasing of cytokines with pro-inflammatory, chemotactic and immune-protective characteristics. By contrast, the subtypes of CD4+ T lymphocytes, CD4+CD25+ regulatory T lymphocytes diminishes the immune response to contest against cancer.[18]The unique clone specific cell surface protein is T cell receptor (TCR), which identifies the antigen and responsible for orchestrating the T cells activity. The amplification and hyperactivation of T cells followed by the antigenic stimulation of TCR is named as co-stimulation that engrossed the phosphorylation process for early signal transduction. Moreover, the non-polymorphic surface protein on naïve T cells is CD28, a potent co-stimulatory receptor which enhance the immune system thru the synergy of anti-CD28 stimulatory antibodies and the interaction of TCR with MHC molecules on malignant cells.[19]

Dendritic cells are the archetypal antigen presenting cells (APCs) in the immune system, which can participate to control innate and adaptive immune response with the activation of T cells to kill neoplastic cells. Dendritic cells can be originated from the bone marrow progenitors termed common myeloid progenitors (CMPs). CMPs can be differentiated into common dendritic cell progenitor (CDP) that further characterized into plasmacytoid dendritic cells (pDCs) and conventional dendritic cells (cDCs). Initially, the differentiated dendritic cells are immature which can be matured by the stimuli from damage or pathogen associated molecular patterns (DAMPs / PAMPs) or inflammatory cytokines and consequently causes the activation of immune system.[20, 21]Due to the maturation of dendritic cellscauses the increment of MHC and co-stimulatory molecule mutation, downregulation of phagocytosis, increases cytokine release and enhance the migration into lymph nodes. The mature dendritic cells are responsible to prime the naïve T cells and inaugurate the adaptive immune stimuli.[22, 23]

Cancerous cells can develop the defense pathway to counter immune response facilitated by the natural killer cells (NK) against malignancy. Natural killer cells are large molecules, granular lymphocytes which demonstrate the natural cytotoxicity activity counter to neoplastic cells.[24, 25] NK cells induce apoptotic events via caspase dependent and independent pathways due to the release of cytoplastic cytotoxic mediators like perforins and granzymes in calcium dependent fashion into intracellular space. The cytoplasmic cytotoxic mediator perforin facilitates the perforations in the cell membrane for allowance the entry of granzymes into the tumor cells, consequently initiates apoptotic events thru mitochondrial death receptor pathway.[26]Due to the activation of cytokine release like IL-2, IL-12, IL-15 and IL-18 causes the IFN production which further facilitated the cytotoxic action by natural killer (NK) cells.[27, 28]

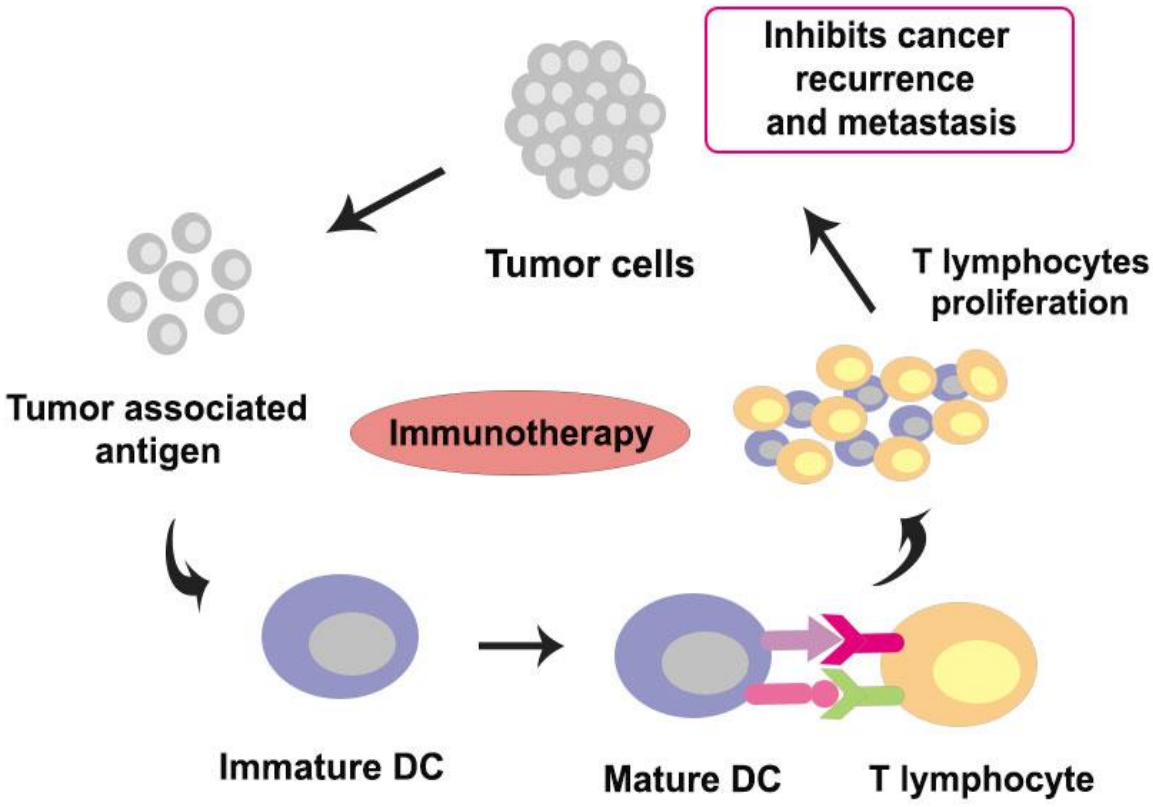

Figure 1: The role of immune cells in cancer immunotherapy

Different approaches of immunotherapy in cancer:

Immune checkpoint blockade in cancer

Different downstream mediators of T cell activation are considered as 'checkpoint molecules'to alter the immune responsiveness in host cells. Programed cell death 1 (PD-1) and cytotoxic T lymphocyte antigen 4 (CTLA-4) are two utmost effective immune checkpoint molecules to regulate the T cells function. They showed their biological activity after binding with distinct sites and times throughout the T cell lifespan.[8] In 2018,Allison and Honjo were awarded the Nobel Prize in Physiology or Medicine for the successful targeting the checkpoint molecules including CTLA-4 and PD-1in the treatment of wide variety of recalcitrant cancers.[29]

Biology and function of CTLA-4 in cancer

Cytotoxic T lymphocytes antigen 4 (CTLA-4) is an immune checkpoint molecule which belongs in immunoglobulin superfamily as structurally and functionally similarities with CD28 genes.[30] CD28 and CTLA-4 genes are basically obtained in same area of chromosome 2 (2q33.2) which are particularly articulated in haematopoietic section. Moreover, the upregulation of the expression of basal CD28 gene that recognized on conventional T lymphocytes after antigenic stimulation where the expression of CTLA-4 is significantly lower.[31]By contrast, CD4+CD25+ regulatory T (Treg) cells exerts an immunosuppressive activity via the superior of CTLA-4 expression constitutively.[32]While, CD28 and CTLA-4 structurally both are membrane bound homodimers which comprised with an extracellular immunoglobulin domain like a transmembrane zone and a cytoplasmic tail that enabling for associating with signaling proteins and regulating the surface expression. Interestingly, both CTLA-4 and CD-28 are binding with same ligands namely B7-1 (CD80) and B7-2 (CD86) which are extensively expressed in infectious cells (APC). CTLA-4 has higher avidity and

affinity towards the binding with B7 ligands than CD28 demonstrating a key modification in their function and biology. The proliferation and hyperactivation of T cells are downregulated due to the CTLA-4 binding with B7 ligands by involving with obstruction of CD28-B7 interaction(Figure2).[33, 34]T cell receptor signaling after antigenic stimulation is explicitly representing that CTLA-4 impedes the T cell amplification and activation to facilitates the development of anergy. CTLA-4 may also be identified the cytoskeleton with initiate the disturbance into APC-T cell conjugate formation. CTLA-4 can arbitrate the internalization of its ligands to prevent the binding with CD28 as a resulting of decreases the IL-2 releases and T cell amplification.[35]The inhibitory signals of CTLA-4 caused the reduction of the stimulationof several transcription factors including nuclear factor κβ(NF- κβ), activator protein 1 (AP-1) and nuclear factor activated T cells (NFAT) which reprogramming the T lymphocytes towards the antigenic fates.[36]Besides that, the regulatory T cells also release the CTLA-4 can participate directly and indirectly immunosuppressive actions of these cells. From this perspective, the in-vitro investigation suggested that the anti-inflammatory effects of CTLA-4 was induced via the releasing of cytokine mediators from Treg cells which involving with the reduction of polyclonal activation and explosion of naïve T lymphocytes.[37]

CTLA-4 blockade in cancer

CTLA-4 can act as an inhibitory regulator of T cell hyperactivation which provides the knowledge to block its activity could release the therapeutic responses of T cells counter to malignant cells.[38]James Allison et al were first examined that the neutralization of CTLA-4 interaction with B7 ligands by anti-CTLA-4 antibodies therapy to enhance the antitumoral immune responses in mice against fibrosarcoma and colon carcinoma. Additionally, the experimental animals treated with anti-CTLA-4 antibodies have been enabled to frequently

kills the malignant cells via the activation of immune systems and suggested the blockade of CTLA-4 interactions with long lasting immunological memory.[39, 40]

Apart from the preclinical studies, monoclonal antibodies targeting CTLA-4 also provides the efficiency in clinical research of melanoma.[38]Ipilimumab, a human IgG1κ anti CTLA-4 mAb which have been approved thru FDA in 2011 to treat non-resectable stage III/IV melanoma. Long term survival information reported that 22% of patients of advanced melanoma treated by Ipilimumab which supplemented with three or more of life, indicating the endurance of anticancer immunity by blockade of CTLA-4 -B7 interactions.[41, 42]Tremelimumab, an IgG2 isotype of anti-CTLA-4 antibody, has yet to gain FDA endorsement while it was not increased the lifespan in advanced melanoma.[43]The efficiency diverges in ipilimumab and tremelimumab due to the variation in binding kinetics as well as the ability to induce antibody-dependent cellular cytotoxicity. Anti CTLA-4 antibodies therapy causes the depletion of intratumoral Treg cells responses by antibody dependent cellular cytotoxicity in mice model which maintain the tumor microenvironment away from the immunosuppressive activity. The overall findings revealed that the most critical features to predict the results in association with effector T cells to Treg cells infiltrating into tumor cells.[44]

Biology and function of PD-1 axis in cancer

PD-1, also denoted as CD279, which was first pioneered in 1992 by the In-vitro assessment on interleukin-3 (IL-3)-deprived LyD9 (murine hematopoietic progenitor) and 2B4-11 (murine T lymphocyte hybridoma) cell lines.[45]PD-1 and its ligand including PD-L1 and PD-L2 are the participates of CD28/B7/CTLA-4 family receptors, which refers to as PD-1 axis. PD-1 axis is 55-kDa type 1 transmembrane glycoproteins, comprising of 288 amino acids with an immunoglobulin variable type (IgV) extracellular N-terminal domain, a transmembrane area and a cytoplasmic tail positioned at the N and C terminal region, correspondingly, with two

tyrosine residues that enables to facilitate the downstream signalling pathways in cancer.[46, 47]PD-1 represents the 20% resemblance with CTLA-4 amino acid sequence, 15% with CD28 and 13% likeness with the co-stimulator of T lymphocyte.[48]

In tumour microenvironment, PD-1 axis performs as an important checkpoint regulator in association with malignant cellular survival, growth, and proliferation due to the evading of tumour neutralizing immune surveillance. Earlier revision has been suggested that the PD-1 is expressed on the variety of immune cells, such as dendritic cells, T cells, B cells, and tumor-infiltrating lymphocytes (TILs).[15]As consequences of the antigenic activation of T cell receptor (TCR) causes significantly upregulation of the expression of PD-1 receptors on the T lymphocytes and thereby binds with its ligand PD-L1 (B7-H1) and PD-L2 (B7-DC), which are existing constitutively on the surface of the tumor cells (Figure2). Followed by the engagement of PD-1 with PD-L1 or PD-L2 ligands, as resulting of T cell dysfunction, including T lymphocytes exhaustion, anergy, and interleukin-10 production and neutralization which subsequently promoting the immunosuppressive effects.[49]Dueto the T lymphocytes exhaustion, the malignant cells become highly aggressive and unleashes the various pro-inflammatory cytokines like interleukin-2, tumor necrosis factor-α, and interferon-γ which endorsing the malignant cell survival, proliferation and invasion.[50, 51]

PD-1 constrains immune responses predominantly by the repressing intracellular signalling pathway in the effector T lymphocytes and regulatory T lymphocytes (T_{reg} cells).[52]The immune-receptor tyrosine-based switch motif and immune-receptor tyrosine-based inhibitory motif of PD-1 are phosphorylated and thereby recruit SPH1 and SPH2 phosphatases to fostering the inactivation of downstream effectors CD3 and ZAP70 which is chief regulators of T lymphocytes hyperactivation.[53, 54]Checkpoint molecules can significantly obstruct the expression of Akt/ PI3K signalling pathway. Another subclass of T lymphocytes, CD4+CD25+

regulatory T lymphocytes (T_{reg} cells) inventing an immunosuppressive action in tumour milieu via regulating the mutation of PD-1 on its surface. In the presence of TGF-β and CD3 (non-polymorphic signalling chains of TCR), the PD-1 receptor of T_{reg} cells attenuating the de novo conversion of naïve CD4+ T cells to regulatory T cells.[55]Consequently, this mechanism may accompany to restrain PI3K/Akt/mTOR mediated transduction scheme.[56]

PD-1 axis blockade in cancer

Recently, PD-1 axis mediated apoptosis is an active area of research in onco-immunotherapy. In preclinical investigation suggested that the inhibitory signaling pathway of PD-1 axis can applicableto treat cancer and biomarker discovery. Primarily it has beendetected the overexpression of PD-L1/2 in malignant cells to restrain the $CD8^+$ T cell mediated anticancer effect. Secondly, the confinement of PD-1 expression through PD-L1 blockade fascinates the repression of the expression of transplanted myeloma cells in mice.[57]Neutralizing the PD-1 axis by mAbs or PD-1 extracellular domains inverted the actions that improved T cell mediated cytotoxicity towards cancer cell proliferation. Restoration of T lymphocytes cytotoxicity via interrupting PD-1 axis which is involving with losses the appearance of CD28 as PD-1 depended immunomodulation in subject to B7 blockade or CD28 knockout mouse model.[58]Furthermore, it was showed that rejuvenated the exhausted T lymphocytes with CD28 expression followed by PD-1 inhibition in peripheral blood of patients with lung carcinoma.[59]The deactivation of PD-1 expression may also be represented the possible mechanistic pathway to treat haematogenous spreading in several recalcitrant cancer model.[60]Numerous studies have been revealed that an adverse relationship between PD-1 axis mediated tumor expression and prognosis, emphasising the clinical benefits of these protein as a potential biomarker.[61, 62]

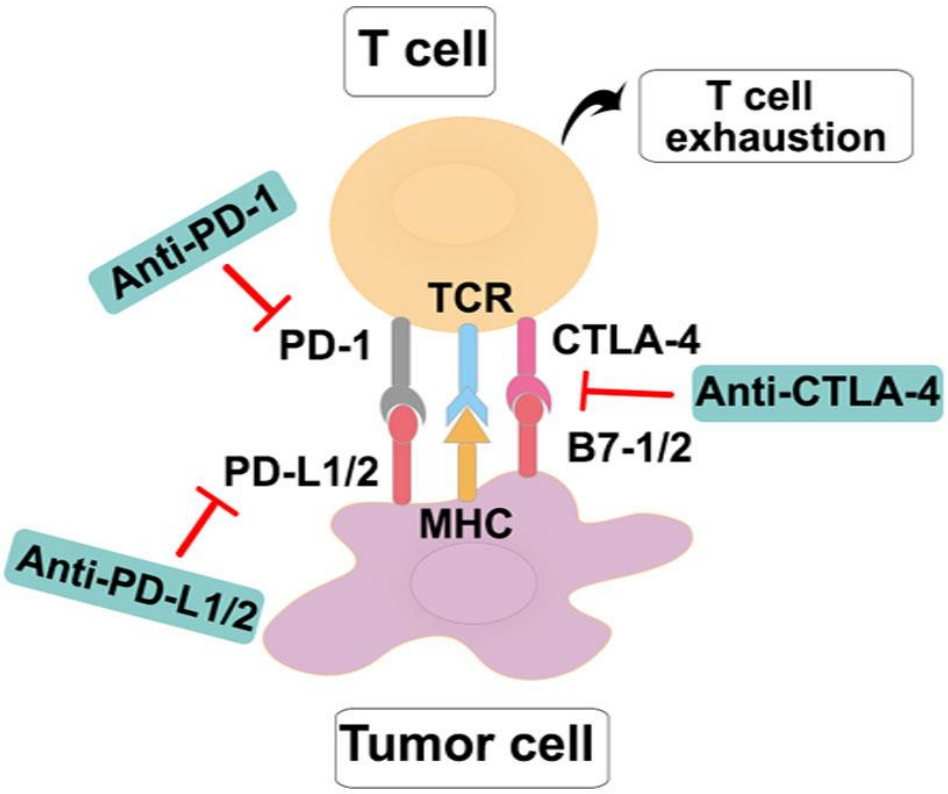

Figure2: Immune checkpoint blockade in cancer

Adoptive T cell therapy

Adoptive T cell (ATC) therapy is a type of immunotherapy in which T cells are genetically altered to express a chimeric antigen receptor (CAR) or T cell receptor (TCR). ATCtherapy is accompanying to activate the immune response as a therapeutic approach to combat cancer cells. Busch and Fehleisen have been first described an epidemiological link between immunological state and cancerous state.[63]The tumor cells can alter its phenotype in order to evade a cytotoxicity or pro-inflammatory immune system. The particular identification of cancer cell by T lymphocytes, which resulting of the generation of immune-activating cytokines to activate adaptive immune system.[64]

In adoptive T cell therapy, allogenic or autologous T lymphocytes have been infused into the patients with malignancy. Allogenic haematopoietic stem cell transplantation has been demonstrated in leukaemia, the first adoptive T cells transplants strategy depicted that T cells grafting in contrast to cancer.[65]Tumor-infiltrating lymphocytes (TIL) therapy and CAR T-cell therapy are the two main approaches of T-cell transfer therapy. This strategy assembles the naturally occurring T cells which already colonised tumors in patients, which can be further activated and infused into patients (Figure3).In late 1980s, the National Cancer institute was first inaugurated the adoptive T cell therapy by tumor infiltrating lymphocytes for the management of metastatic melanoma. T lymphocytes harvested from the patients with cancer have been significantly expanded along with IL-2 which is further reinfused into the same patients with larger bolus of IL-2 (Figure3). Chimeric antigenic receptors (CAR) T cell therapy, in other hand can bypasses the MHC restraints and initiates the cytotoxic effect to target molecules on the surface of cancer cells.[66]Followed by the isolation of T cells, the lymphocytes were modified and stimulated the expression of CARs which is further expanded and reinfused into patients.CAR comprises with an antigenic binding domain, mostly accompanying through the TCR signaling domains and several co-stimulatory molecules.[67]The hyperactivation of T lymphocytes resulting of the production of toxic substances that harm cancer cells and draw in additional helper cells to the location when the receptor connects with an antigen. The reprogrammed T cells can target the antigens gets attached with CAR on release of certain soluble factors upon activation of CAR-T cells. These soluble factors can aid to represent the anti-tumor effect, or they could stimulate the bystander myeloid cell. Stimulated myeloid cell can secrete inflammatory cytokines including IL-6 and IL-1β which subsequently attributed the inflammatory toxicities.[68]

The recent investigation has been improved utilising TCR-transgenic animal models to initiate the study on identifying the transferred T cell properties that affected therapy efficacy. In many

models, CD8+ T lymphocytes have been discovered to be an essential for the antitumor effects. These ATC therapy-based experiments gave the first proof that the activation of immune system to encourage the therapeutic effect against recalcitrant malignancies.[69]The examination of systemic medications that might enhance ATC therapy in mice models has been added to the characterization of the transplanted T cells. For instance, interleukin-2 (IL-2) has significantly increased the longevity and potency of transplanted cells. From this perspective, clinical study reported that CAR T cell therapy was successfully treated the B-ALL that diffuses the large B lymphocytes to target CD19 antigen, a perfect approach due to upregulate the certain B lymphocytes expression in carcinoma. CD22, is other type of antigen frequently expressed in B-ALL tumor cells that can participate to phase I trial of CAR T cell therapy. Recently, the CAR T lymphocytes engineered to release IL-12 for avoiding immunosuppressive action mediated by Treg cells and myeloid cells in tumor milieu, to initiate CD8+ T lymphocytes facilitated cytolytic effects and stimulate the recruitment of myeloid cell as well as antigenic presentation.[70, 71]

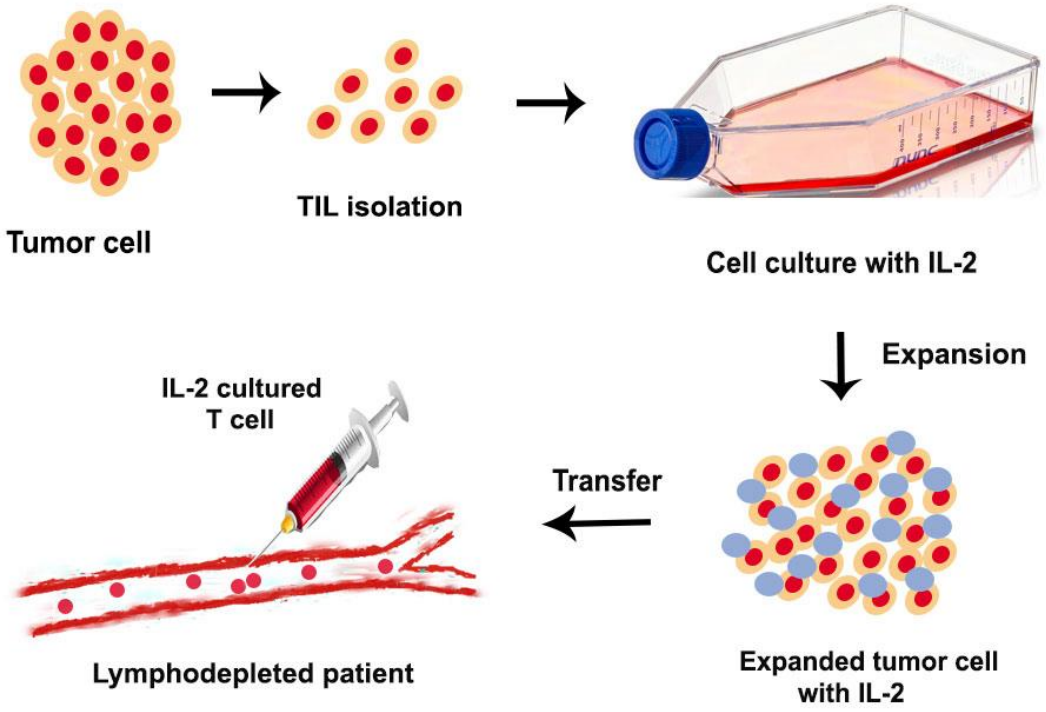

Figure3: Adoptive T cell therapy in cancer

Cancer vaccine

Cancer vaccines are a kind of immunotherapy intended to activate the body's immune response to identify and target malignant cell. Apart from the traditional vaccines that primarily avert the infectious diseases.Cancer vaccines is focused to treat or prevent cancer by training the immune system to recognize and destroy malignant cells. The cancer vaccines often contain specific molecules, known as antigens, derived from cancer cells, which prompt an immune response. The goal of cancer vaccines is to enhance the body's ability to recognize cancer as foreign and mount an effective immune attack against malignancies, ultimately leading to the destruction of cancerous cells while minimizing damage to healthy tissue.[72, 73]The cancer immunotherapy is accompanying with the stimulation of immune system thru cytokines release

like interleukin-2(IL-2) and interferon-α in renal cancer and melanoma to modulating antibodies against cytotoxic T cell lymphocyte antigen 4 (CTLA-4) and programmed death 1 (PD-1) checkpoint molecules as well. The advancement of cancer vaccine accomplished to disabling the immune suppressive factors of tumor cells and translating from "cold" tumors into "hot" tumors and consequently persuading the robust cancer specific immune systemwhich are able to kill malignant cell.The cancer vaccines employ diverse strategies in cancer immunotherapy, including personalized approaches, cellular immunotherapies, and targeting specific cancer markers.[74, 75]

Initially, cancer vaccine is a type of an autologous and allogeneic cancer cell vaccine. Cancer vaccine consists of all the relevant tumor antigens accompanied by the immune system to establish an effective antitumor effect.[76]Moreover, the tumor-APC hybrids, a fusion technology in the field of cancer vaccines where the tumor cells and APCs are produced by exposing to polyethylene glycol (PEG) or electrical fields, resulting in the formation of a tumor - APC hybridoma. This Strategy is already associated with major clinical responses in patients with metastatic renal cancer. In some cases, cancer vaccines are associated with the immune checkpoint inhibitors like PD-1 or PD-L1/2 inhibitors which aim to enhance the immune system thru blocking the proliferation of cancer cells.[77]

Onyvax, a monoclonal antibody 104AD7, anti-idiotype vaccine which is used for treatment of advanced colorectal adenocarcinoma. This vaccine is managed together with BCG vaccine or intramuscularly through the alum adjuvant.[75]Cancer VAX, a polyvalent melanoma vaccine is being used for the treatment of melanoma stage three.[78]NY-ESO-1 Peptide vaccine is used endermic to treat the stage 2 to stage 4 sarcoma of soft tissues which expresses NY-ESO-1, LAGE antigen NY-ESO-1 or LAGE antigen.[79]Monoclonal Antibody 11D10 Anti-idiotype vaccine and monoclonal Antibody 3h1 Anti-idiotype vaccine are being used in the treatment

of the patients with stage 2 or 3A non-small cell lung cancer.[80]Oncophage (Vitespen) which is approved by Russia in 2008 which is used for treatment of kidney cancer. This is a personalised cancer vaccine which uses heat shock protein (HSP) technology to activate an immune system against cancer cells.[81]Furthermore, Sipuleucel-T (Provenge) which is approved by FDA in the year 2010 and used for metastatic hormone-refractory prostate cancer. This vaccine uses the Autologous cellular immunotherapy technique which is designed to activate the patient's immune system.[75]In 2011, CimaVax-EGF was approved in Cuba which are used for the management of lung cancer to targeting the epidermal growth factor receptor (EGFR). This vaccine is currently undergoing phase 2 trials for potential U.S. approval.[82]Bacillus Calmette-Guérin (BCG) approved by FDA in the year 1990, is used for bladder cancer. The vaccine contains live attenuated *Mycobacterium bovis* strain which is used to activate an immune response against bladder cancer cells.[83]

Concluding remarks

Cancer immunotherapy is attentive on the activation of immune system by which emphasizing a powerful tool for the treatment of recalcitrant carcinoma. However, the several studies associated with basic science discoveries and clinical studies evaluated the power of the alteration of immune system to treating malignancy. From this perspective, the modulation of immune system can allow to directly correlated with cancer immunotherapy. The immunotherapeutic approaches such as immune checkpoint blockade, adoptive T cell therapy and cancer vaccine have also been far advanced treatment strategies as comparison with the mostly effective chemotherapeutic approach. The innovative immune targeting therapies have been continuously grown up to emerging as an indicator for currently approved treatment to evaluate the newer druggable targets.

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IMPACT OF CLIMATE CHANGE ON OCULAR AILMENTS AND ASSOCIATED ECONOMICAL COSTS: A REVIEW ON CURRENT TRENDS IN INDO-ASIAN REGIME

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Abstract

Numerous Ocular diseases, including cataract, conjunctivitis, glaucoma, and dry eye, are brought on by environmental factors such as pollutants, toxic gases and chemicals, bacteria, smoking, various drugs, variable humidity, temperature variations, ultraviolet radiations, and cosmetics. The eye is the organ that is most susceptible to contamination from the air and the environment at large. [1]Climate change generates negative impacts on human health. But little is understood about the precise effects on eye ailments, particularly in dry and semi-arid regions where rising air temperatures are anticipated. [2]Therefore, the key goals is to highlight the correlation between environmental factors and common diseases of the eye, and to review, using the literature that is at present accessible, the costs associated with treating these diseases, in addition to the savings from mitigating the environmental factors that aggravate them. The cross-variables (environmental factors, eye disorders, and health costs) were evaluated using mixed methods. [21]In particular when it comes to pollutants other than carbon dioxide, air quality affects human health. In particular, tropospheric ozone has to be highlighted as a typical urban contaminant that heatwaves may amplify.

Keywords: Ocular Ailments, Cost Analysis, Climate Change, Vision Impairment

Introduction

Widespread and significant effects on many facets of life, including health, sustainable development, and the economy, can be attributed to eye health and vision. Numerous studies have indicated that 43 million individuals will be blind worldwide in 2020, out of the estimated 596 million people who have distance vision impairment. But fortunately, more than 90% of those who suffer from vision impairment can be prevented or treated with already available, quite affordable therapies. All ages are affected by eye diseases, although young children and the elderly are most vulnerable. Significantly, women, people who live in rural areas, and people who belong to ethnic minorities are more likely to have vision impairment, and this pervasive disparity needs to be addressed. Climate change generates negative impacts on human health.

Air Pollutant Distribution and its impact on Ocular Diseases

Air pollution is the top environmental health concern, according to the WHO. A particulate-polluted environment may contribute to the development of several eye conditions (1). Ozone [O3] is a secondary pollutant that is produced by primary pollutants like NO and NO2, which are known to travel great distances and have serious negative long-term impacts on human health. According to a study by Bourcier et al., there is a high correlation between air NO and NO2 concentrations and conjunctivitis. The increased air pollution in Paris caused an ophthalmological emergency for residents. According to Schwela et al. in accordance with Lal et al. these pollutants can alter the [6]pH of the lacrimal fluid and may irritate the ocular surface. In addition to destroying the ozone layer, air pollutants, particularly CFC or chlorofluorocarbons, released by air conditioners, refrigerators, and aerosol sprays can also cause eye injury (2). Due to the constant contact of the pre-ocular tear film with the surrounding

air, toxins have direct access to these ocular structures and can abnormally affect the cornea, causing very high levels of subclinical ocular surface changes in people travelling in highly polluted areas (3). Thornton et al.'s study suggested that the quality of environmental air can cause premature break-up of the pre-ocular tear film and corneal epithelial damage (4-7). Exposure to environmental smoke from cigarettes raises the risk of ophthalmopathy in those with Grave's disease. Strabismus is one of the eye conditions and diseases linked to exposure to tobacco smoke in children, and maternal smoking during pregnancy is linked to a 6.55 times higher risk of strabismus in children. There is a direct correlation between thyroid eye disease and amount of smoking. Age-related macular degeneration, acute uveitis, and inflammatory responses are all brought on by endotoxins created by cigarette smoke.

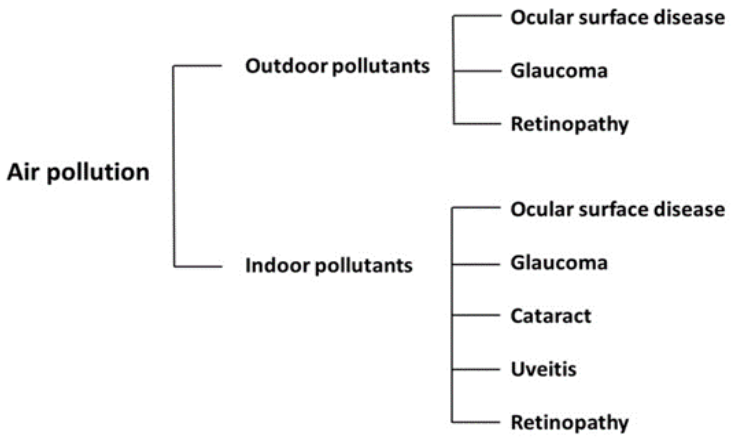

Fig. 1: Air pollution and different ocular diseases

The ocular surface is affected by smoking, which causes symptoms like itching, redness, and irritation of the eyes (8-10). Smoking's effects on the ocular surface also include changes to the lipid layer of the tear film, decreased tear secretion, decreased corneal and conjunctival sensitivity, and disorders like atopic kerato-conjunctivitis and allergic conjunctivitis. The amount of environmental pollution is growing exponentially as a result of growing industrialization and global warming (11-16). The air, waterways, and soil all contain chemicals that are dumped as industrial waste. The ocular surface is constantly exposed to the

atmosphere and appears to be negatively impacted by the current environmental circumstances (17-18). The prevalence of subclinical and acute ocular illnesses was extremely high in people, birds, and aquatic creatures. The various parts of the eyes, such as the cornea, conjunctiva, etc. are affected in a variety of ways by environmental factors, including particulate materials, toxic gases, smoke and chemicals, biomaterials, such as bacteria and viruses, and climatic and natural changes, such as variable humidity, temperature variations, and ultraviolet radiations. This results in serious eye disorders like cataract conjunctivitis, glaucoma and dry eye (19-20).

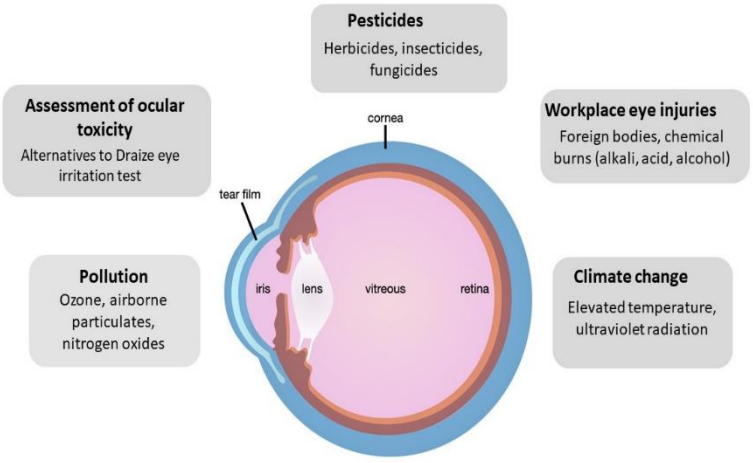

Fig 2: Ocular disease contaminants

Conclusion

We found that treatment costs for all causes of visual impairments varied considerably between and within countries, reflecting variation in methodological and reporting approaches, and differences in health care systems including therapeutic options and regimens, organizational systems, clinical pathways and resources. Treatment options forserious eye disorders like cataract conjunctivitis, glaucoma and dry eye, trachoma and cataract tended to be less expensive than those for AMD, diabetic retinopathy and glaucoma. The cost of treating serious eye disorders like cataract conjunctivitis, glaucoma and dry eye has tended to reduce over time in low-, middle- and high-income countries.

In contrast, the introduction of anti-VEGF treatment for AMD has increased costs of AMD treatment, though the range of anti-VEGF medication regimens resulted in many different costs estimates.

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A COMPREHENSIVE OVERVIEW OF DRY SYRUP

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Abstract:

The simplicity of administration, patient compliance, and formulation stability of oral dosage forms make them so popular. The most common oral dosage forms are tablets and capsules, but these have a significant drawback in that they can be difficult to swallow, particularly when they are designed for juvenile and geriatric patients. In the past year, interest in reconstitutable oral suspension dosage form has increased due to modern scientific and technological advancements in the pharmaceutical industry. The reconstituted system is the preferred formulation when medication stability is a top priority. Reconstitutable oral systems demonstrate the drug's acceptable chemical stability over the course of its shelf life and also lessen the end product's weight. In terms of bioavailability, the dry syrup form of the medication is also helpful because it has a higher bioavailability than tablets and capsules because it dissolves in water outside of the oral cavity and the suspension travels directly through the gastrointestinal tract. In the GIT, the suspension thus absorbs with ease. The excipients employed are described in the current review.

Keywords: Dry syrup, reconstitutable suspension, ICH guideline, packaging, storage.

Introduction:

The most preferred method of administration is oral. Since a single large dose of an active pharmaceutical ingredient (API) is difficult to swallow or necessitates the administration of multiple tablets or capsules at once, it is not appropriate to administer high doses of API using tablets or capsules, which also reduces patient compliance. Chewable pills are not recommended for elderly or pediatric patients due to the requirement for chewing, poor taste masking, and lack of control release possibility. Oral liquid suspensions are primarily designed for those who have trouble swallowing. However, controlled release liquid suspension is challenging because of the possibility of early API release during storage in the suspending media. Therefore, creating a reconstitutable suspension dosage form is crucial.

Dry Syrups: "Dry pharmaceutical syrup may be defined as a finely divided insoluble particle ranging from 0.5-5 μ, which is to be distributed in the suitable vechicle". Dry syrups are the solid dosage form that can be reconstituted by the addition of water to administer by the oral route. Mostly antibiotics, some moisture sensitive and pediatric drugs are available in the form of dry syrup

Reasons for formulation of such suspensions: [1,2]

Reconstitute suspension is formulated due to many reasons such as for patient which have difficulty in swallowing, drug stability etc. Some reasons are discussed below.

1. The main reason for the formulation of suspensions for reconstitution is inadequate chemicalstability of the drug in an aqueous vehicle.

2. Another reason for the formulating suspensions for reconstitution is to avoid the physical stabilityproblems. These problems include possible increased drug solubility due to pH

changes fromchemical degradation, incompatibility of ingredients, viscosity changes, conversion of polymorphicform and crystal growth and caking.

3. Formulation for reconstitution reduces the weight of the final product because the aqueous vehicleis absent and consequently, transportation expenses may be reduced.

4. Suspension for reconstitution is convenient dosage form for large doses.

5. Safe and compliant for pediatric and geriatric patient. 6. Suitable for insoluble or poorly soluble API.

Advantages: [1-3]

1. Enhanced Stability: By removing water from the formulation, the risk of microbial contamination and chemical degradation is significantly reduced.

2. Enhanced bioavailability: Dry syrup form of drug showsn improved bioavailability as compared to tablets and capsules as it is in the dispersed state at the time of administration

3. Ease of Storage and Transportation: Dry syrups are inherently lightweight and compact. This characteristic makes them exceptionally convenient for both storage and transportation.

4. Precise Dosage Control: Accurate dosing is crucial in healthcare to ensure that patients receive the appropriate treatment. Dry syrups facilitate precise dosage control.

5. Cost-Effectiveness: The manufacturing and packaging of dry syrups are often more cost-effective than their liquid counterparts.

6. Reduced Preservatives: Liquid medications often require the addition of preservatives to inhibit microbial growth and maintain stability over time. With dry syrups, these preservatives can be minimized or eliminated altogether.

7. Customization: Healthcare providers have the flexibility to customize the concentration of the reconstituted solution when using dry syrups This customization aspect is particularly valuable in pediatrics, where dosages often need to be adjusted based on a child's age and weight.

8. Suitability for Warm Climates: Dry syrups are less susceptible to temperature-related degradation compared to their liquid counterparts.

Disadvantages: [1-3]

1. Reconstitution process: Need for reconstitution before administration. It requires careful measurement and can be challenging for patients.

2. Inconvenience: For patients and caregivers, the need to mix a dry syrup before each dose can be inconvenient, particularly when compared to the simplicity of ready-to-use liquid formulations

3. Stability after reconstitution: Once a dry syrup is mixed with water, its stability can be limited. Reconstituted solutions may be more susceptible to microbial growth and chemical degradation.

4. Limited range of medications: Not all medications can be formulated as dry syrups. Some drugs are inherently unstable in powder form or require complex excipients for reconstitution.

5. Hydration requirement: Patients taking dry syrups must have access to clean water for reconstitution.

Method of Preparation: [3,5,6,7]

Excipients:

Excipients are selected based on both suitability for reconstitution and on the physical type of powder mixture desire.

Frequent	**Infrequent**
Suspending agent	Anticaking agent
Wetting agent	Flocculating agent
Sweetener	Granule disintegrant
Preservative	Granule binder
Colour	Lubricant
Flavour	Solid diluents
Buffer	Antioxidant

Preparation of dry mixture:

- Direct mixing
- Granulated products
- Combination products

Direct mixing:

Fig no 1: Direct mixing

Powder mixtures are prepared by mixing the excipients of the dry mixture in powder form. Excipients present in small quantities may require a two stage mixing operation. Such excipients can be mixed with a portion of a major excipient to aid in their dispersion. The second stage comprises the mixing of the remaining excipients. The selection of the appropriate mixer involves several considerations, the most significant of which is that the mixer should rapidly and reliably produce a homogenous mixture.

Advantages:

- Least capital equipment and energy.
- Least likely to have chemical and physical stability problems because no heat or solvents are used.
- Low moisture content can be achieved in dry mixture.

Disadvantages:

- Prone to homogeneity problems.
- Loss of the active ingredient during mixing.
- The loss during mixing is significant if potent drug which is used in very low concentrations is lost.

The equipment used is mixers. Few types of mixers are listed below.

1. Dry mixer
2. Paddle mixer
3. Vertical screw mixer
4. Double cone mixer
5. V blender

Granulated products: [8]

Fig no 2: Dry Granulation Process

Fig no 3: Wet granulation process

All the excipients in granulated products are processed by granulation. Wet granulation is the usual process and the granulating fluid is water or an aqueous binder solution. There are two methods of incorporating the drug. The drug can be dry blended with the other excipients or it can be dissolved or suspended in the granulating fluid.

Advantages:

- Improved appearance
- Improved flow characteristics
- Less segregation problem
- Less generation of dust during filling operation

Disadvantages:

- Requires more capital investment and energy
- It is difficult to remove the last traces of granulating fluid from the interior of granules
- The excipients and drug must be stable to the granulation process

- Uniform granulation is necessary because an excess of very small particles will result in rapid segregation

The equipment used in this process are --

1. Planetary mixers
2. Rotating sieve
3. Fluid bed dryer

Combination product: [3,8,9]

Powdered and granulated excipients can be combined to overcome some disadvantages of granulated products. Less energy and equipment for granulation may be required if the majority of the diluents can be added after granulation. Also, heat sensitive excipients such as flavours can be added after drying of the granulation to avoid exposure to elevated temperatures. The general method is first to granulate some of the excipients, then blend the remaining excipients with the dried granules before filling the container. The presence of the diluents helps to improve flow and reduces both segregation and dust formation.

Condition for manufacturing Dry Syrup: [6]

For manufacturing of dry syrup following conditions should be maintained.

- Relative humidity: Not more than 60%.
- Temperature: Below 25°C
- All relevant materials are removed
- Equipment is cleaned
- Balanced is calibrate
- Relative humidity: Not more than 60%.
- Temperature: Below 25°C
- All relevant materials are removed

- Equipment is cleaned
- Balanced is calibrate

Evaluation parameter of dry syrup: [9-14]

1. Colour, odour and appearance:

All the developed batches of syrup were evaluated for organoleptic properties such as colour, odour and appearance.

2. Drug content:

Dry syrup equivalent to 100 mg of linezolid was taken in 100 ml volumetric flask and dissolved in 10 ml methanol and volume was made up to 100 ml by adding sufficient 0.1 N HCl. The solution was analysed at 243.6 nm to found out drug content

3. Bulk density:

The powder (2 gm) filled in measuring cylinder called as bulk volume of powder and measure mass of that powder. Bulk density is ratio of mass of powder to bulk volume of powder. It is a measure used to describe a packing of powder. The equation for determining bulk density is

ρb = m/ vb-

Where, ρb= Bulk density m = Mass of powder vb= Volume of powder

4. Tapped density:

The pre-weighed powder (2gm) was filled in measuring cylinder. Then it was tapped in bulk density test apparatus. After 50 taps the volume is measured and the tapped density was measured using following formula.

ρt = m/ vt-

Where, ρt= Tapped density m = Mass of powder vt= Tapped volume

5. Carr's index (CI):

Compressibility is indirectly related to the relative flow rate, cohesiveness and particle size distribution of the powder. Powders with compressibility values lesser than about 20%, has been found to exhibit good flow properties. Tapped (ρt) and Apparent (ρb) Bulk density measurements can be used to estimate the compressibility of a material.

Carr's index (%) = (ρt - ρb) / ρt * 100 --

Where, ρb= Bulk density ρt= Tapped density.

6. In vitro drug release:

The in vitro dissolution studies were carried out using USP apparatus Type II at 100 rpm. The dissolution medium consisted of 900 ml distilled water maintained at 37°C ± 0.50 C. The drug release at different time intervals was measured for two hours using UV spectrophotometer.

7. Particle size:

The oral reconstitutable suspension is evaluated, the average particle size of the formulation is examined using standard microscopy method average and standard deviations of 100 particles are estimated.

8. Viscosity:

The rheological behaviour of the suspension is determined by using Brookfield viscometer (Model - LVDI).

9. Zeta potential measurement: Suspension is diluted with distilled water and the measurements are taken in triplicate.

10. Stability study: The reconstitutable suspension is stored in air tight amber coloured glass bottles for 36 days at 45°C and then reconstituted with distilled water to make up the volume

to 60 ml with gentle shaking. The reconstituted suspension is stored at 4°C, 25°C and 45°C for 15 days.

11. pH values: The pH of suspensions was measured with the aid of a pH meter

ICH guidelines (q6a) for re-considerable oral suspensions: [2,15]

International conference on harmonization (ICH) provides some guidelines for reconstitutable oral suspension. One or more of the following specific tests will normally be applicable to oral liquids and to powders intended for reconstitution as oral liquids.

1. Uniformity of dosage units
2. pH
3. Microbial limits
4. Antimicrobial preservative content
5. Antioxidant preservative content
6. Extractables
7. Alcohol content
8. Dissolution
9. Particle size distribution
10. Redispersibility
11. Rheological properties
12. Reconstitution time
13. Water content

Packaging of Dry Syrup: [16,17]

1. Primary Container Material: Dry syrup powders are typically packaged in primary containers made of high-density polyethylene (HDPE), glass, or sometimes aluminum foil sachets. The choice of material depends on factors like the medication's compatibility, protection from light and moisture, and cost considerations.

2. Airtight Seals: The primary containers must feature airtight seals to prevent moisture and air from entering, which can compromise the stability of the dry syrup. This seal ensures that the product remains intact from manufacturing to consumption.

3. Tamper-Evident Features: To safeguard the integrity of the product, dry syrup packaging should incorporate tamper-evident features. These features include induction seals, shrink bands, or breakable caps, which indicate if the package has been tampered with.

4. Dosage Measurement Tools: To assist patients and caregivers in accurate dosing, the packaging should include a dosage measurement tool. This is often a scoop or spoon, which is provided in an appropriate size for the recommended dose. Instructions on how to use this tool should be clear and easily understandable.

5. Child-resistant Packaging: When applicable, dry syrup containers should meet child-resistant packaging standards. This is especially important for medications that may be harmful if ingested accidentally by children. Child-resistant caps or closures should be designed to be challenging for young children to open.

6. UV protection: If the medication is photosensitive, the primary container may incorporate UV-blocking features to protect the powder from light exposure, which can lead to degradation.

Storage of dry syrup: [16,17]

1. Temperature Control: Proper temperature control during storage is crucial. Dry syrups are typically stored at controlled room temperature.

2. Protection from Moisture: Dry syrup containers should be stored in a dry environment to prevent moisture absorption. Moisture can cause clumping of the powder and chemical degradation, rendering the medication ineffective or unsafe.

3. Protection from Light: In addition to moisture, exposure to light, especially direct sunlight, can have detrimental effects on the stability of the dry syrup.

4. Separation of Components: Manufacturers often recommend storing the dry powder and the reconstituted solution separately.

5. Humidity Control: In areas with high humidity levels, additional precautions may be necessary.

Labelling of dry syrup: [16,17]

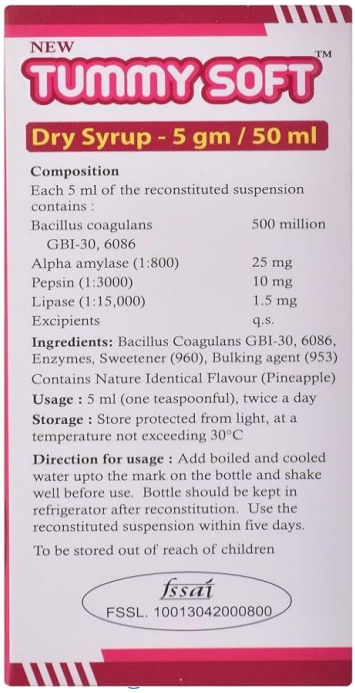
1. Product Information: The label must prominently display the product's name, including both the generic and brand names, if applicable.

2. Active Ingredients: The label should clearly list the active ingredients, including their names and concentrations per dose. This information is crucial for patient safety and proper medication administration.

3. Usage Instructions: Detailed instructions on how to reconstitute the dry syrup should be provided on the label. This includes the recommended volume of water or other suitable liquid, along with specific mixing instructions.

4. Storage Conditions: Include storage instructions on the label, specifying the recommended temperature range, humidity level, and protection from light and moisture.

5. Expiry Date: Every dry syrup container must display an expiration date. This date is determined through rigorous stability testing and ensures that the product remains safe and effective up to that point



6. Batch Number and Manufacturer Information: Each dry syrup product should have a unique batch or lot number for traceability.

7. Warnings and Precautions: Any potential side effects, warnings, and precautions associated with the medication should be prominently displayed on the label.

8. Barcodes: In modern pharmaceutical distribution, barcodes are often included on the label for accurate tracking, inventory management, and data recording during dispensing and administration.

9. Tamper-Evident Seal: The label should clearly indicate if the packaging has a tamper-evident seal. It should also provide guidance on what to do if the seal is broken

Direction of reconstitution: [[16,17]]

The process of reconstituting dry syrup is a critical step in ensuring the proper administration of medications in this dosage form. It typically begins with the thorough reading of the instructions provided on the medication label or as prescribed by a healthcare provider. Cleanliness is paramount, so washing hands before handling the dry syrup and reconstitution materials is essential.

The next step involves measuring a precise quantity of clean drinking water or the specified reconstitution liquid, often using a clean measuring tool if provided. This liquid is then combined with the dry syrup powder, and the mixture is vigorously stirred, shaken, or swirled, as directed, to dissolve the powder completely and evenly. Accurate dosing is imperative, and the reconstituted solution should be administered according to the prescribed dosage and schedule. If there are uncertainties or questions about the reconstitution process, consulting with a healthcare provider or pharmacist is advisable to ensure safe and effective medication administration.

Marketed formulation:

Drug	Manufacturers
Amoxicillin trihydrate	SmithklineBeecham
Ampicillin &probencid	Biocraft
Ampicillin	Biocraft
Dicloxacillin sodium	Apothecan
Erythromycin ethylsuccinate	Abbott
Cefalexin	Dista

Conclusion:

When compared to conventional oral suspensions, the reconstituted oral suspension exhibits excellent levels of acceptance in terms of simplicity of administration, patient compliance, and physical stability. The absence of the aqueous vehicle also reduces the weight of the finished product, which could save transportation costs. The dry mixture can be delivered regardless of the time of year. So long as it is prepared in accordance with the instructions, this formulation is perfect for administering medications to children, particularly antibiotics.

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BEAUTY IN THE EYE OF THE BEHOLDER

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ABSTRACT

The claim that beauty lies in the eye of the beholder has been researched by psychologists across several domains of the discipline. However, in this article, there is an attempt to discover and explain the connections between the implications of the results in these large bodies of research. There have been several studies conducted throughout the decades, in an attempt to uncover the relationships between the factors that contribute towards formation of beauty ideals, which in turn shape what the beholder regards as beauty. This paper intends to serve as an initial point of inquiry into all of these factors.

Keywords: Beauty, Looking glass, Perception, Impression formation.

INTRODUCTION

There is a question that society has continued to ponder over for a while now. The question is regarding beauty and whether it lies in the eyes of the beholder or not. Due to the evolving presence of culture and media in everyone's daily lives, its impact on beauty hasn't gone unnoticed. Beauty plays an unknowingly pervasive role in people's lives, and we are influenced by it through a varied number of factors, including culture, gender, attention, perception, motivation, sexuality, age, race and not to mention the physical nature of the human body itself. A lot of the research conducted about this topic has shown that the attractiveness of someone's face has the ability to control and determine the degree of attention being aimed towards them. Studies have shown that people tend to linger on attractive faces more than unattractive faces,

which signifies the advantage of facial beauty in situations in which multiple parties are demanding spatial attention (1).

It has been established that the topic of beauty can be explored through various domains of understanding, and in order to contextualize the question of whether it lies in the eyes of the beholder or not, we should be focusing on multiple perspectives of this question. The impact of beauty standards and what is deemed as attractive, has determined patterns of social behavior in many ways. Therefore, one of the various topics that will be discussed in this paper are the several components of this social behavior that seem to inform and shape how we perceive beauty in our society. One of the overarching themes that play a role in the perception of beauty is the role of the gaze. Research studies have shown that eye-gaze direction has been known to shape our perception of people who are conventionally attractive. This heavily socialized ability of people to process and interpret the nonverbal language of the eyes as a means to facilitate social interaction and communication has been demonstrated consistently in such studies (2). The gaze direction plays such an important part in the process of coming to conclusions about someone's level of physical attractiveness, owing to the fact that humans process vast amounts of initially-acquired information and facial cues while trying to make a decision about whether they deem a person to be attractive or not. Some of these factors could be the level of confidence they exude, their state of mental health or even the skills they appear to be in possession of. This makes an effective case for the argument that beauty does reside in the eye of the beholder. Due to one's ideographic experiences with society, every person will have their own set of criteria for measuring attractiveness in general. These experiences could possibly be shaped by not only the identities they possess within themselves within the framework of society, but also by the ways in which others have judged their own physical appearances. There exists an extensive body of research that is filled with evidence against the argument that the concept of beauty is a monolith, and that the conventionality of physical

attractiveness is static in nature. Hence, it would be quite ineffective to argue for a reality with a foundation of truth that's based on consistent beauty standards. Since the dawn of time, history and culture have evolved in a multitude of ways that has made it very nearly impossible for the world's population to establish and come to terms with a singular identity of beauty. Therefore, the stance which is reflected in this review paper is one in favor of the argument that beauty in fact lies in the eye of the beholder.

One of the questions I have that has been raised while considering the role of beauty in society is: how is one seen as an attractive individual in a society where the social standards for beauty keep changing? The dynamic nature of what beauty can be defined as, makes it a fascinating site of inquiry about the varying components of society that influence each other and the people that comprise it, in the process of creating these societal ideas of what beauty is. From the outset, these ideas and definitions might seem conceptually tedious and impractical. But from the research perspectives, it is even more impractical to paint a picture of our diverse world in fossilized definitions of beauty, with rigid concepts that fail to encapsulate the changing nature of what it means to be beautiful in 21st century society. Some of the main emphasizing factors in this paper are perception and culture, and how they both contribute together and individually to cement these societal ideas of who is regarded as beautiful and how such beauty has the power to shape and impact interactions between people. Another important factor that beauty plays is its capacity to shape the cognitive processes of individuals. The ideas we come to develop about physical attractiveness have the ability to change the way we process cognitive information about any encounter that involves the judgement of someone's facial attractiveness. Some research has indicated that the differences in facial preference are the result of experience and a flexible information processing mechanism (3). This implies that people cognitively modify their preferences for these attractive faces as they continue to process facial appearances as visual stimuli. So technically

speaking, people show tendencies of updating their prototype or their model for how a beautiful individual should look like. One of the aims of this review literature is to identify a broad body of research that conceptualizes and summarizes the many reasons why beauty originated in the eye of the beholder. Some of the factors that are discussed in this process are attention, perception, biology, sex & gender and not to mention personality and cross-cultural narratives.

ASSESSMENT AND EVALUATION

Attention

When it comes to making judgments about a person's level of attractiveness, attention plays a principal role in the process. The amount of time we allocate to a person in order to regard and observe their facial features says a lot about our opinions of their physical appearance in itself. A lot of studies have tried to find out whether these cognitive processes are influenced by externally sourced ideologies of what beauty looks like, or whether we are primarily guided by our personal perceptions of what a beautiful person should look like. Some studies have shown evidence that the speed at which people try to observe someone's face can be instrumental in our judgement of their level of attractiveness. Perceiving and processing beauty appear to require little attention and to bias subsequent cognitive processes (4). This relationship between the rapid amounts of attention people use to engage with visual stimuli and the act of labelling people as attractive or not, shows how much they rely on our preconceived notions of what beauty is. By extension, it also highlights how reliant we are on these rapid cognitive processes to make almost instantaneous social evaluations of people we meet. While taking the research into consideration, there is no doubt about the fact that there are conventionally attractive individuals that reap many positive benefits from the biases we have about their appearances via these rapid cognitive processes. In other words, this beauty bias may result from a host of low-level visual and emotional effects (4). This has not been done purposefully. But as human beings, we have cognitive tendencies of building mental

schemas about certain ideas and concepts regarding society and we tend to heavily rely on those in order to process large amounts of perceptual information in a short amount of time without having to focus on our awareness and intentionality of our perceptions every single time.

Besides our self-perceived notions and beliefs of what a beautiful individual should be like, there are other factors that determine how our attention is captured when it comes to judging beauty. Some research studies have indicated that certain natural biological processes like ovulation can shape women's degree of attention with which they deem the physical attractiveness of another individual. These studies have attempted to explore how ovulating women are more susceptible to their menstrual cycle's effect on early-stage cognitive processing (5). This research implies that due to women experiencing their menstrual cycle, they are biologically more fertile during this state and as a result they tend to pay attention to and seek out individuals who are not only attractive but who are also attractive potential candidates to become their future mate. During the time of ovulation, women are not only paying more attention to more attractive individuals, but they are also rendering this increase in attention towards visual stimuli into increased memory (5). Thus, the natural next step after forming these increased memory levels is using them as a basis to make future decisions about who is regarded as beautiful and who isn't.

Perception

Our sense of perception of other people and of society in general plays a salient role in shaping the ideas and notions that we have about beauty and attraction. Hence, it is understandable why a lot of research has been conducted to find out how perception guides and changes our comprehension of the standards of beauty that we have come to possess over time. Some studies have shown evidence for the argument that our tastes in physical attraction have been shaped by contributions from both private and shared judgments regarding the standards

of facial attractiveness. The current research has made claims about how standards of beauty are widely shared and that is one of the possible reasons why attractiveness can appear to be homogenous because multiple individuals can come to possess the standards through socialization (6).

Other bodies of research have tried to explore other reasons for why people perceive certain faces to be attractive over others. There is a branch of psychology known as evolutionary psychology that has made claims about facial symmetry and how it has played an instrumental role in shaping our ideals of beauty and how we judge a person's face to be attractive by conventional standards of society. The role of facial symmetry in determining standards of beauty has been replicated across a lot of studies, and the results have generally shown that the more symmetrical a face is, the more attractive it is generally perceived. One can't help but wonder why this happens and how this has gradually shaped individuals' perception of beauty in society. Many evolutionary biologists have proposed that a preference for symmetry would also be adaptive because symmetry is a signal of health and genetic quality (7). This implies that even when people are casually determining the facial attractiveness of an individual, they are looking out for factors that put them at an evolutionary advantage over others when it comes to picking potential mates. Researchers have attributed this tendency to seek out symmetrical faces to a theory known as the symmetry hypothesis. It can be defined as the theory that explains why symmetry of human faces can explain the attractiveness of averaged composites or of average facial attractiveness in general (8). The research regarding the attractiveness of average faces has several insights into how individuals have the tendency to group certain facial characteristics into societal expectations of beauty ideals. Studies have talked about how there are empirical reasons to believe that very attractive faces are somewhat atypical rather than average (9). Hence, this can be used as evidence towards the tendency of human beings to determine someone's beauty on the basis of their personalized and atypical

ideas about beauty. This reiterates a point about societal perceptions of beauty, and also reflects that the standards of beauty have the capacity to be personalized based on the experiences we have as individuals. The atypical nature of our perception of human faces is something that should be noted, but this does not mean that shared meanings of beauty should not be valued in society. On the contrary, personal perceptions of beauty that are found to be common across communities help people to reinforce their own individual perceptions of physically attractive faces.

The brain

Another aspect of research that digs deeper into our understanding of beauty ideals is from the perspective of biology. The research that has been conducted in this academic discipline has mostly kept itself busy by attempting to zone in on the regions of the brain that are responsible for human beings to distinguish between faces and deem them to be attractive, unattractive, or just average. In a lot of these studies, researchers used fMRI scans to measure the brain activity of test subjects trying to complete tasks that would involve the judgement of faces in terms of their perceived attractiveness. A lot of the research results have indicated that the right amygdala showed greater responses to highly attractive and unattractive faces, in comparison to middle ranked faces, independent of the task given to them at hand (10). As shown in the research regarding the perception of individuals when it comes to considering the attractiveness of someone's face, there exists a pursuit of biological advantages in this process. People seek out handsome faces because they want to potentially mate with someone that would be beneficial to them from a genetic perspective. The biological research regarding this topic has demonstrated that the brain has a reward system that enables them to seek out faces that activate certain parts of the brain like the amygdala and the orbitofrontal cortex (10). These studies have basically connected the need to have these regions activated via the process of purposefully seeking out faces that an individual think is attractive. This shows that even from

a biological standpoint, people are looking towards their own ideas of beauty while they're trying to seek out attractive faces in order to activate certain regions of their brain.

Sex and gender

The relationships between sex, gender and the social constructions of beauty ideals have been explored in the field of research, and it has revealed some interesting connections between these factors. Some researchers have tried to find out more about this connection between gender and beauty by using behavioral techniques to activate certain regions of the brain that are responsible for motivational processing and record the results of heterosexual subjects in tasks that ask them to judge between presented faces for degrees of attractiveness. The overarching theme in the results of the studies in this domain indicated that healthy men and women displayed similar perception of heterosexual facial attractiveness, with men providing lower ratings for beautiful males, but they showed substantial greater motivational effort for beautiful female images than women for beautiful males (11). Researchers have made some interesting inferences from this body of research, one of them being that women have demonstrated a tendency towards having a more primary motivation towards male visual stimuli, as opposed to men who seem to be more drawn towards the encouragement or incentive behind the visual stimuli of women. Some researchers have tried to further explain what these incentives are and how they drive individuals to make decisions regarding their own mate preferences. Some research studies have shown that different mating-related motives may guide the selective processing of attractive men and women (12). The evidence in these studies have implied that individuals tend to be selectively attentive to physically attractive people with respect to the stage of cognitive processing they are in and what kinds of immediate and long-term factors are influencing these processes.

Culture

One of the more prominent perspectives through which research has been conducted about the role of beauty ideals and how it has shaped society, has been of culture. Culture plays an instrumental role in influencing the ideas and perceptions of beauty in terms of race and ethnicity. There have been studies that have had test subjects composed of over a dozen different racial and ethnic identities that have contributed to this body of research. Some studies have indicated that White people and Black people display similar standards of beauty for the face but varying standards for the rest of the body (13). One of the possible explanations for such results could be due to the existence of cultural diffusion and sometimes it's also due to cultural socialization that individuals tend to be primed more with Westernized ideals of beauty which is an integral part of the dominant cultural narrative in the West. Another source of explanation for why culture might play a role in the shaping of one's beauty ideals is the narrative that is woven into a person's understanding of the world through the identities of the people one is exposed to. Certain research has shown that when judging the relative beauty of a human face, the sex and race of the person judging, and the age, sex, and race of the face being judged may influence the response, but the subject's age probably will not have an effect (14). One could infer from this that the traits of someone's sexual and racial identities might have a more pervasive effect on the formation of beauty ideals over a person's age.

Research studies about the relationship of cross-cultural narratives in the formation of beauty ideals have tried to examine why certain aspects of identities across the board are highlighted and then come together to form an amalgamation of traits that a person prefers to find in their potential mate. The research regarding this topic has had some issues in terms of representation and it has been seen in evidence in studies that there is a growing disparity between beauty ideals held by Caucasians and for Caucasians and the same goes for African American individuals. However, the imposition of the former on the latter is quite evident. In

culturally sensitive body image studies between African American and Caucasian women, the examination of attractiveness has largely been confined to body image studies that may overlook the multi-component views of beauty held by some African American women (15). The beauty standard measures of one culture are being imposed on other cultural standards in research studies, which is a concerning indication for what is happening in society in general. Sometimes the beauty that is in the eye of the beholder might not reflect the ideals of the cultural communities they are a part of, but as a consequence of cultural diffusion. Interestingly, some of these cross-cultural studies have indicated how a person's notion of an average face depends on the faces they have been exposed to during their lifetime (16). This implies when someone is considered conventionally beautiful in a culture, it means that their facial features are close to that of the average person who is originating from that culture.

Personality

There has been a recurring theme in society when it comes to making judgments about a conventionally attractive person's personality. Most people tend to place their bets on the more positive nature of attractive individuals during or as a consequence of initial encounters with them. The reason behind this has been extensively researched in the field of psychology and these inquiries have led to some interesting discoveries. One of the most consistent findings within the area of person perception is that there exists a physical attractiveness stereotype, also known as the what-is-good phenomenon which indicates that highly attractive persons are perceived as possessive positive traits while those who score low with regards to this stereotype are perceived less positively (17). This natural tendency for people to stereotype individuals in terms of their personality can have lasting impact on our perception of beauty in general. Generally speaking, people gravitate towards those who appear to possess positive traits over negative ones. Researchers have claimed that if casual acquaintances invariably assume that attractive individuals are sincerer, noble, and honest than unattractive persons, then attractive

individuals should be habitually regarded with more respect than unattractive persons (18). Results like this, gives people considerable insight into the connection between beauty ideals and how they are formed as a result of the personality traits we are looking for in a potential significant other. Some research studies have discussed how possessing personality traits that are attractive may be causal in making a face attractive (19). This means that as people, when we are actively seeking out certain personality traits in people, by extension we are also trying to seek out the attraction we will form upon the imminent acknowledgement of these positive traits in the person we like.

CONCLUSION

In this process of inquiry to try and answer the question of why beauty lies in the eye of the beholder, this research comes across many different factors that contribute to the process of the creation of our personal beauty ideals. The studies regarding the influences of human perception and attention are important in terms of explaining how our mind plays an integral role in shaping the experiences we have with the construction of beauty ideals. Culture and personality also shape our experience with beauty ideals in ways that aren't immediately apparent to us. However, the similarities in all these studies have shown that the study of physical beauty always flourishes when one is studying multiple factors and their influence on each other. Some researchers have alluded to the fact that it might be preferable to cease the study of physical attractiveness in isolation and instead focus on the joint effects of physical attractiveness and other status characteristics, both on personal perception and on social success, academic achievement, and life satisfaction (20). Unlike this vision, if there is more research conducted regarding this topic from a multi-dimensional perspective, the answers to questions of how and why beauty lies in the eye of the beholder would gradually expand. Certain researchers have also stressed the importance of the kinds of research data that should

be kept an eye out for. Historical and cross-cultural data may provide further insight into consistency and variability in the facial features associated with attractiveness (21).

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MANIPULATION OF GENE EXPRESSION THROUGH ELECTRO-STIMULATION: A POSSIBLE CURE FOR GENETIC DISEASES.

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Abstract

Electronic devices that can be worn on the body for medical purposes have become one of the features of the 21st century. However, most of the devices are diagnostic in nature. The electronic devices developed for therapeutic purpose is few and far between. But recently there is a breakthrough research that claims mammalian gene function can be manipulated through electricity to serve therapeutic purposes. The possibility brings hope for a non-invasive solution for a group of diseases characterized by over/under-expression of some vital genes. Researchers at the Department of Biosystems Science and Engineering at ETH Jurich Switzerland have developed a new technology that is able to control transgene expression in human cells using direct current from batteries. The new technology has been named, direct current actuated regulation technology (DART). In a proof of concept study performed on a diabetic mouse model, the researchers could stimulate the implanted insulin-producing human cells using electrically energized acupuncture needles.

Introduction:

The role of human genes in the initiation and progression of some incurable diseases is well established. For example, over-expression of HER2/ErbB2 oncogene is related to breast cancer (1) while under-expression of FoxP3 gene is related to certain autoimmune diseases (2). Hence controlling gene expression through both physical or chemical stimulus is an important area of

drug research. As a result, a number of chemical mediators have been identified and developed as a medicine to control gene expression (3). Similarly, effort is on to use physical techniques, like optogenetics, heat stimulation, magnetic fields and electrical stimulation are being attempted to control transgene expression (4). However, the attempts have met with limited success. Specially the electronic devices developed for the production of therapeutic purpose is few and far between (5).

The human body with its reserve ions is a very good conductor but this great potential was rarely utilized for disease prevention and treatment, because of the fundamentally different ways the two systems work. The communication of the biological system is through ions which flow through the lipophilic barrier membranes whereas electronic systems are controlled by the flow of electrons through insulated wires. There is a need for an interface that would be able to directly relay the electrical signal to the effector cells which contained the gene / transgenic material. Delivering the electrical energy directly to the gene without causing much collateral damage is a difficult job. A recent paper published in Nature Metabolism seems to have overcome the difficulty (6).

It was known that electrodes delivering direct current can generate free electrons which can lead to the formation of free radical species or reactive oxygen species (7,6) When operated at low voltage, the concentration of this generated ROS remains below the cytotoxic levels 3. Based on this observation, Researchers at ETH Sweden created an electro-genetic interface where external electrical inputs will be able to adjust the gene expression. They strived to manipulate transgene expression through DC-triggered electrostimulation.

The concept

When the mammalian system is exposed to DC, reactive oxygen species ROS like superoxide anion (O2•-), hydrogen peroxide (H2O2), and hydroxyl radical (OH•). These ROS can act as biosensors. ROS has both constructive and destructive effects on the body (8). Over

production, of ROS can damage cellular structure but at low concentrations, they play an essential role as a signalling molecule. If the intensity of the voltage is low, the level of ROS produced remains at a nontoxic level. Researchers hypothesized as ROS could be produced by electrical stimulation, it will serve as a signalling molecule for gene expression.

Human embryonic kidney cells (HEK293) co-transfected with constitutive KEAP1 - and NRF2 expression vectors, as well as the reporter, construct pJH1005 which encodes the human model glycoprotein SEAP (human placental secreted alkaline phosphatase) was used. KEAP1 (and NRF2 are two important proteins in the regulation of the respiratory pathway that controls cellular defence against oxidative stress. The Kelch-like ECH-associated protein 1 (KEAP1) is an important tumor and metastasis suppressor that also acts as a native ROS biosensor (6) NRF2, on the other hand, is a transcription factor that regulates the expression of genes involved in cellular defence mechanisms against oxidative stress (9). Under normoxia, KEAP1 binds to NRF2 and promotes its degradation through the ubiquitin-proteasome system (10)., preventing its accumulation in the nucleus. When cells are exposed to oxidative stress KEAP1 undergoes a conformational change. This prevents KEAP1 from binding to NRF2, allowing NRF2 to escape degradation and translocate into the nucleus to trigger the expression of SEAP.

The experiment

For conducting electricity, protons and chlorine ions were produced in the culture medium through platinum electrodes. The culture media containing engineered cells were subjected to electrical stimulation through 0.5-mm platinum electrodes. The distance between the electrodes was 6 mm. A significant increase in SEAP expression was noted upon electrostimulation. Intracellular ROS levels were measured through a fluorescence assay and it was found that SEAP expression increased over two-fold after DC electrostimulation (5 V, 20 s) which returned to normal levels within 6 h, suggesting that production of ROS was the causative factor behind the enhanced SEAP expression.

In vivo experiment for treatment of diabetes

To prove the concept, the authors used a type 1 diabetic mouse as a model. Their objective was to produce insulin in this model by electrically stimulating the subcutaneously implanted cells which were engineered to produce insulin. Direct current was applied (4.5 volts,10secs) to this site by using WHO-approved acupuncture needles. The once-daily application was able to restore normoglycemia in the diabetic mouse.

Significance

The energy to control the expression of the target gene can be provided by readily available low-voltage batteries. It was estimated, that 0.06 W of DC power can produce ROS that can produce insulin enough for a day's requirement. Moreover, DART requires only a simple manual electrical ON/OFF switch.

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