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Nanoscience Enhanced Synbiotics - An Approach to Augment Human Health

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ABSTRACT

Recent metagenomic scrutiny of the human gut microbiota has led to the discovery of nearly 3.3 million microbial genes present in the tissues in the entire human body with a rapid expansion in the various evidences revealing their numerous beneficial roles in human health and disease. Perturbation of the intestinal microbiota may lead to chronic diseases. The food supplements: prebiotics, probiotics and synbiotics termed as functional foods have been verified to alter, transform and reinstate the pre-existing intestinal flora. They also facilitate smooth functions of the intestinal environment. Probiotics are live microorganisms that promote health benefits upon consumption, while prebiotics are non digestible food ingredients that selectively fuel the growth of favourable microorganisms in the gastrointestinal tract. Amalgamation of prebiotics and probiotics with a synergy between them is referred to as synbiotics. Encapsulation of probiotic bacteria within prebiotics helps to protect them and enhance their survival rate while passing the gastrointestinal tract. Present study has focused on functions and roles of probiotics, prebiotics and synbiotics in human health. It is the advent of nanomedicine that confers it to be appropriate to forge a union with the known practices of these supplements for creating an optimal environment within the gastrointestinal tract and thus is considered to be the most valuable approach.

Keywords: - Microbiota, prebiotics, probiotics, synbiotics, human health, diseases, nanomedicine.

INTRODUCTION

In the contemporary world, many infectious diseases are being treated. Even so, diseases associated with microbes are yet ambivalent by numerous current discoveries that justify the search for new strategies to control them [1]. This is aggravated by the continuous emergence of novel variants of established pathogens. The human gut is a relatively under-explored ecosystem and yet affords the best opportunity for developing interventions to cope with a variety of alimentary canal and genitor-urinary tract diseases through dietary intervention strategies. An advantageous approach to maintain health and control disease can be the

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use of dietary bacterial and carbohydrate supplements that facilitate the host's indigenous bacterial communities form a barrier against infesting pathogens. This comprises use of probiotics Live microorganisms, which when administered in adequate amounts confer a health benefit on the host [2] and prebiotics A non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria that can improve the host health [3]. Recent strides made in the study of probiotics and prebiotics have been made possible with improved understanding of the diversity and function of the human microbiota, including the genomic sequencing of some probiotic organisms. The oral, nasopharyngeal, stomach, intestinal and vaginal ecosystems are clearly very complex. Many currently non-culturable organisms could form an important part of the host's defense [4], while others may be responsible for chronic diseases [5]. The synbiotic concept was first pioneered as "concoction of probiotics and prebiotics that favors the health of the host by improving the endurance, implantation and encouragement of living microbial dietary complements in the gastrointestinal tract." They selectively incite the growth by activating the embolism of health enhancing bacteria and therefore are profitable in enriching host welfare.

Nanotechnology is a field that has become increasingly of interest to medical researchers because of the particle size, which has evolved and involved every facet of science, engineering, and technology. For this reason, the field has become a central focus in providing medical treatment advancement, through creating medicine with a unique perspective conducted at scales less than 100 nanometers [6]. Nanotechnology significantly relies on the nanometer scale to perform manipulation of molecules for influencing the desired effects of both a compound and its cellular target. It is this validation that the subject has the intrinsic value in the attempts to develop nano-treatments in gastroenterology [7]. It is the introduction of nanomedicine that presents it to be apt to create an amalgamation with the acknowledged practices of prebiotics, probiotics and synbiotics in creating the most favorable environment within the gastrointestinal tract; thus became the most valuable approach.

PREBIOTICS PHENOMENON The term 'Prebiotic' was defined in 1995 by Gibson and Roberfroid. Prebiotics thus can be defined as non-digestible food ingredients that beneficially affect the body by selectively stimulating the growth and/or activity of a limited number of bacteria in the colon [8]. For having prebiotic action, the compound must reach the colon without alteration and must be a food substrate

that stimulates the existing saprophytic bacterial flora. Food constituents with prebiotic uniqueness generally exhibit certain exclusive characteristics, such as restricted hydrolysis and absorption in the upper gastrointestinal tract, selective stimulation of the multiplication of beneficial bacteria in the colon, potential to suppress pathogens and limit virulence by processes such as immunostimulation and the stimulation of the beneficial microflora, which promote resistance to colonization by pathogens [9].

To be called and worked upon as prebiotic, a food supplement should be non-digestible, resistant to gastric acidity, easily absorbed gastro intestinally, fermentable and should be in a selectively stimulated for intestinal bacteria that are associated with health and wellbeing.

Significance of Prebiotics in Functional Foods and Medical Practice

Prebiotics are substances that can promote the growth of beneficial microorganisms, mainly in the intestinal tract, by modifying the colonic microbiota. Prebiotics help to get relief from poor lactose digestion, increases bacterial infection resistance, develops a better immune response, provides the host with possible protection against cancer, and reduces the risk of diseases related to intestine, cardiovascular disease, non-insulin dependent diabetes, obesity and osteoporosis. Prebiotic fibres like oligosaccharides can help ease gut 'dysbiosis' common among the obese and overweight, said Belgian Researchers [10]. Prebiotics have nutrition which can modify gene expression & gut microbiota metabolism. Prebiotics (Fermentable carbohydrates) can counteract many alterations of metabolism linked to obesity which includes hyperglycaemia, inflammation and hepatic steatosis [11]. Dietary substances metabolised by the microbiota in the colon are the polyphenols that have to be hydrolyzed by intestinal enzymes or by the colonic microflora before absorption can occur [12-16].

PROBIOTICS PHENOMENON

At the start of the 20th century, Russian noble prize winner and father of modern immunology, Elie Metchnikoff, a scientist at the Pasteur institute, was the first one to conceptualize "probiotics". Probiotic term was coined in 1965 by Lilly and Stillwell. In 1907, Metchnokoff projected that the acid producing bacteria in fermented milk products could prevent "stinking" in the large intestine if consumed on a daily basis can lead to a longer and healthier life. In early 1930's, in Japan, Minoru Shirota developed a fermented milk product called Yakult (probiotic yogurt by fermenting a mixture of skimmed milk with a special strain of *Lactobacillus casei shirota*) [17-20].

Probiotics are bacterial microbes that help in maintaining the natural balance of organisms

(microflora) in the intestine. Human digestive tract on an average contains about 400 types of probiotic bacteria that reduce the growth of harmful microbes and promote a healthy digestive system. The largest group of probiotic bacteria in the intestine is lactic acid bacteria, *Lactobacillus acidophilus*. The strains, *Lactobacillus* and *Bifidobacterium* are the most common probiotic bacteria. The Lactobacillus genus has 18 different bacteria strains, while the *Bifidobacterium* genus consists of eight strains [21].

Probiotics firstly modify the microbial population, then they aggregate with the pathogenic bacteria followed by the competition with epithelial receptors for adhesion and finally they produce specific substances like organic acids, bacteriocins and dipicolonic acids. However, they compete for the nutrients and modifications of the structure and function of the intestinal epithelium [22-23].

Probiotics are capable of exerting a beneficial effect on the host by being anti-inflammatory, anti-mutagenic and immune-stimulatory. They are also able to survive the passage through the digestive system, adhere to the intestinal epithelia and colonise. They can also maintain good viability, utilise the nutrients and substrates in a normal diet and are totally non pathogenic and non toxic [24-26].

Significance of Probiotics in Functional Foods and Clinical Practice

People use probiotics nowadays, to prevent diarrhoea, gas, and cramping caused by antibiotics as antibiotics harm the favorable microbes too along with the illness causing ones that leads to digestive problems. Probiotics may also be used to help prevent infections in the digestive tract and control immune response (inflammation). These functional foods are being studied for benefits in colon cancer, skin infections, and irritable bowel syndrome (IBS). They produce lactic acid which lowers the intestine pH and inhibits bacterial pathogens such as *Clostridium, Salmonella, Shigella, E. coli,* etc. This helps in the production of a wide range of antimicrobial substances -acidophilin and bacteriocin etc. that help to control pathogenic bacteria, produce vitamins (especially Vitamin B and vitamin K) and act as barriers to prevent harmful bacteria from colonizing the intestine. Certain probiotics (*Lactobacillus bulcaricus)* may help prevent colon cancer by preventing the breakdown of enzymes (β- glucuronidase**)** that contribute to the growth of cancer causing agents. Probiotics are used to treat depression. Scientific studies have shown decline in nervousness and stress level from probiotic supplements, with a drop in inflammatory cytokines as a probable mechanism. Hence, probiotics are a promising

treatment for depression and other mental disorders, especially when combined with other gut-healing therapies [27-32].

NANOTECHNOLOGY CONCEPT IN FOOD INDUSTRY

Potential nano-carriers provide new chances for the food industry, based on definition of their substantial properties such as size, arrangement, morphology, surface area and its charge, to create nanoliposomes, nanoemulsions, nanoparticles, and nanofibers [33]. It is the immense assortment of structural arrays that make the nanosystems adaptable. The food grade nano particles (FGNP) fall into three capital categories: inorganic, surface functionalized materials and organic engineered nanomaterials. Worth mentioning, "top-down," "bottom up," biomimetic, and efficient congregations have been used in the dispensation of the nanomedicine. In the course of creation of the viral additive nanomaterials, alterable disassembly and reassembly in end result to ionic strength, temperature, and pH may occur. On confiscation, the nanomaterial produced from viruses goes through genomic RNA deletion, and then the viral capsid, acting as the core of the vaccine or treatment, may be consumed to encapsulate potential functional material. In the development of nanomedicine, these physical properties are exploited to play a fundamental role in cellular uptake, intracellular distribution, and possible accumulation within an organism's system, recently it has been also studied that immobilization of antibiotics on multiwall carbon nano-tubes increase the antimicrobial activity [34, 35]. Astonishingly, the world consists of nano-materials that previously occured in nature. Natural world has created nanotubes and nanoparticles, which exhibit them in a variety of configurations, such as sea spray, smoke, or volcanic ash. Nanotechnology has been advantageous in the global evolution of therapeutic science and has the capability to provide imminent treatments, and broadening currently existing therapies. Encapsulated drugs do not show evidence of the conventional pharmacokinetic outlines established in liberated drugs. In the formulation of FGNP requires a strategy, because the nanocarriers dictate the drugs overall distribution and efficacy, it has the luxury of directly interacting with the cell membrane and intracellular structures at ease.

NANOTECH ENHANCED SYNBIOTICS

There is research that has shown the benefits of combining the technology and current practices to promote a healthier colon. With having regular bowel movements, it reduces the effects of exotoxins released in the gut, which in turn will reduce the incidences of precancerous polyps and colon carcinoma with idiopathic

etiology. Nanotechnology has the competence for delivering the catalyst to it; premeditated situation, broadening time, and acknowledging the prebiotic to facilitate feed and supporter in a flourishing gut flora. This promising expertise turns out to be a immense advantage to persistent digestive disorders, and inflammatory bowel disease. To add on to the point, let us remember the recent investigation of gut and microbiome health and its relation to neuroscience and physical health. Evidence has shown increased level of stress hormones from the response of anxiety, depression, and gastrointestinal symptoms were associated with autism and had correlations between changes observed in the colon's micro flora, of those who did not suffer from neurological ailments [36]. A probable association amid ASD and gastroenterology, those with autism have revealed dysbiosis; a disturbance in the balance of the microbiota population organization and aberrations in the gut, with increased gastrointestinal permeability and dysmotility. A representation of MIA offspring illustrated the relation of augmented danger of ASD and amplified inflammatory factors found in the maternal blood, amniotic fluid, and placenta. When given the probiotic B. fragilis, it was found to correct the intestinal permeability in the MIA offspring [37]. The novel trend is to design healthy food with the use of nano-science and its desired characteristics and properties to create a food grade particle unique to the nano-scale that becomes an advantage for the whole health of its host.

One of the recent methodologies for FGNP that has been functional in the entrapment and deliverance of the heat-sensitive probiotics is PET. PET being a colloidal release system has the concept of encapsulating a bacterium in a gel-like suspension, then packing the matter into a miniature-sized finished product that has the enhanced power of functionality and the ability to control the release of the core, increasing the stability of the pharmaceutical grade nutrient [38-39]. It makes available the entrance to the probiotic to avoid the inappropriate environment such as the acid and bile-rich stomach. A study formed a goal to improve oral bioavailability and improve the efficacy of chemo-preventive compound DBM, through nano-emulsion. The nano-formation was from water, oil, and emulsifier under high speed and high-pressure homogenization [40-41], this compound is known to have anticancer effects, and getting through the harsh environment of the gastrointestinal tract was of extreme importance. Advanced studies described the use of microencapsulation of calcium alginate-starch and the assimilation of Hi-Maize improved its survival of the probiotic and were additionally enhancing the initiation

of the cryoprotectant glycerol; protecting it in temperatures of 20 degrees Celsius and slowing the effects of acid production and traveling through the stomach without any degradation [42]. With the market demand increasing for better-stabilized methods of deliveries and specific request towards lactose intolerant and vegetarian-friendly products, it called for an increase to cereal based probiotics. Bioavailability of a probiotic has benefited from nanoscience, being possible to design fermented beverages with synbiotic properties [43-44]. Reviews have put forward the surroundings of the gastrointestinal tract, has an augmented connection to the prevalence of polyps and colon cancer. Requiring for a plan to formulate tools and methods to elude the predicament is crucial. One study reported in rats that the stimulation growth of bifidobacteria leads to the inhibition colon cancer formation, attributed to lowering pH, and antitumor properties from the bacterium [45]. Such properties inhibited the growth of E.coli, and Clostridia in turn producing modulations to precarcinogens of the bacterium. Coupling nanotech with an effective therapy may help overcome the challenges encountered in colon related antineoplastic drug development and the prevention of tumor resistance from chemotherapy [46].

DISCUSSION AND CONCLUSION

The various studies in clinical nutrition conducted over the past 20 years have established the indirect role of prebiotic ingredients in promoting healthy and balanced intestinal microbiota. In addition, the administration of prebiotics reduces blood lipids and blood pressure, increases the synthesis and absorption of nutrients and has anti-carcinogenic action. Prebiotics also show interesting properties that have implications for the food processing industry and the content of its end-products. Administration of synbiotics as a food supplement is safe, simple, and convenient. Therefore, characterizing a new and novel synbiotic combination would find multifaceted use in disease prophylaxis and management for human use.

Nanotech enhanced synbiotics method is still an emerging field, with obstacles seen in the current market due to current mindset of consumers because of a market innovated with misleading labels of used and unused species. The commercialization of prebiotics and probiotics has seen minuscule movement in the field of food-nanotechnology regardless of research supporting the health claims has been a long and tedious process from lab to consumer. The advancements seen from nanotechnology within the last 20 years, has leaped the human body and the world forward

by creating a limitless environment of improvement and innovation. It has become an area of benefit in the gastrointestinal tract's health; from an infant in helping with colic to adults with the various digestive maladies. With drug delivery having the ability to be combined with nanotechnology, synbiotics as a concomitant with cytotoxic and anti-vascular chemotherapies makes this assembly an attractive approach for the treatment of gastrointestinal ailments. With statistics and research supporting the benefit of a happy gut in the prevention of carcinomas, the possible balance between the gut bacteria-brain links; such as depression, autism, and anxiety, nanotechnology can dramatically change the course of food technology, propel forward. The application of nanotechnology has, therefore, an immense potential in overcoming or circumventing the extra- and intracellular mechanisms associated with drug resistance. With nanotechnology partaking in the advancement of the field of gastroenterology, the "Golden Standard" has evolved from solely the use of imaging and colonoscopy, to find a formidable partnership in nanotechnology.

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