**MICROBIOME AND PERSONAL PROBIOTICS**

.Mankind has long wanted to live in space, which inspired the creation of space stations for extended manned space missions. A life support system must be developed. To maintain the fundamental conditions for human living in space, such as a constant body temperature, even pressure inside the body, and efficient waste evacuation. The three essential human needs of air, water, and food have received the majority of attention in this field thus far. Additionally, a life support system provides for an astronaut’s medical needs.

Longer space missions and improved health and immunity for the astronauts might also result from compensating for these changes. The significance of gut flora for both health and illness has long been recognised. Alterations in the balance of gut flora have been linked to a number of disorders, according to research [3]. The collection of flora genes found in the human genome was referred to as the “human metagenome” when the Human Genome Project was finished. Highlighting the microbiota’s critical function in maintaining health [4]. The importance of the microbiome on astronauts’ health and/or illness states is highlighted from this point of view. The development of probiotics for every type of astronaut would be advantageous given their unique dietary and health requirements. The intestinal Microbiome might then be replenished by consuming these healthy bacteria throughout lengthy trips.

**The microbiome of the human gut**

The phrase “gut health” is now often used in medical literature to refer to a healthy immune system, a normal intestinal flora, efficient digestion, and absorption [5]. But from a scientific perspective, it is still incredibly difficult to describe and/or measure gut health. The interactions between the microbiota and the gastrointestinal barrier seem to be an important factor in maintaining gut health. The digestive system helps in digestion and nutritional, mineral, and fluid absorption. The host, endocrine and osmoregulation, metabolism, systemic and mucosal tolerance, and osmoregulation Immunosuppression, The immune system’s activities include defence against potential diseases and toxins, peripheral to cerebral communication, and detoxification of harmful substances originating from the host or environment [6]. Astronauts’ health may benefit from an understanding of the importance of gut health and microbiome. Over the enormous expanse of the digestive system, beneficial and dangerous bacteria compete for supremacy. With such a wide exposure area, the immune system finds it difficult to stop germs from entering the blood and lymph.

A mix of potentially harmful and beneficial bacteria is thought to be normal, and it is necessary for a human gut to function dynamically and healthily. One way to maintain this balance is by ingesting probiotics or helpful microbes. Since Nobel Laureate Metchnikoff made the initial hypothesis regarding the health benefits of probiotics in the early 20th century, several bacterial strains have been rigorously investigated as prospective probiotics [7]. Probiotics are thought to improve health by lowering gut microbial illnesses [8–10]. The human gut’s surface size, apparent microbial balance, and influence on health serve as a reminder that this complex organ must not be overlooked as a contributing element to long-duration spaceflight health.

**Microgravity stress alters bacterial Virulence**

Studies have shown that certain bacteria have changed antibiotic sensitivities, altered growth regulation, and enhanced pathogenicity. Both in space and in real-world microgravity [15–19]. It has been challenging to carry out comprehensive genotypic and phenotypic analyses of bacterial responses to actual space settings due to significant logistical and technical difficulties. Wilson et al. Cultured Salmonella enterica Typhimurium using the same cultures on space shuttle flight STS-115. As ground-based controllers [15]. 73 conserved proteins and 167 transcripts with variable expression were discovered using global microarray and proteomic investigations. Non-binding protein Hfq was suggested as a potential A worldwide regulator is taking part in the reaction to spaceflight.. Similar results were obtained using a microgravity culture model that was mounted on the ground. In addition, S. Enterica Typhimurium grown in space exhibited enhanced virulence in animal models and an extracellular matrix buildup that was conducive to a biofilm [15].Growing S. Typhimurium in a similar space environment improved macrophage survival, increased virulence, increased resistance to environmental stresses (acid, osmotic, and thermal stress), and broad gene expression changes [20-22]. In low-shear simulated microgravity, the Caco-2 cell line, which resembles the gastrointestinal epithelium of mammals, increased its adhesion to adherent-invasive Escherichia coli [23]

The generation of the heat-labile enterotoxin from enterotoxigenic E. Coli was significantly boosted under simulated microgravity settings [18]. Candida albicans showed enhanced filamentation, biofilm community formation, phenotypic switching, and higher resistance to the antifungal drug amphotericin B after a 12-day stint in low-shear simulations of microgravity [24]. One virulence gene was among 163 differentially expressed genes in S. Typhimurium cultured in artificial microgravity The majority of virulence genes, including those involved in lipopolysaccharide production, were also expressed at low levels [22].

The possibility of the sigma factor, a transcription factor linked to a general stress response, was also ruled out since it had lowered gene expression in a microgravity simulation [25]. Full virulence in S. Typhimurium requires the Hfq pathway, but enhanced virulence in S. Typhimurium grown in real spaceflight and rotating wall vessel culture conditions is not brought on by increased expression of conventional genes that govern this bacterium’s virulence in normal gravity [26].

Many chronic, difficult-to-treat diseases, including as endocarditis, cystitis, and bacterial otitis media, have been related to biofilms, which are typically formed by most bacteria as a normal part of their life cycle [27]. Bacterial biofilm results in greater resistance to oxidative, osmolality, pH, and antibiotic stresses [28]. The development of bacterial biofilms, which increase bacterial survival by giving resistance to the immune system and antimicrobial treatments, may theoretically increase the chance and/or severity of infection on long-term space missions. It has been shown that Pseudomonas aeruginosa and E. Coli both benefit from reduced gravity in the growth of bacterial biofilms [29]. Rotating Wall vessel technology was used in a study by Crabbe et al. In 2008 to explore Microgravity’s impact on growth behaviours relating to P. Aeruginosa PAO1. A self-aggregating phenotype brought about by rotating wall vessel cultivation resulted in the development of biofilms. The same Researchers conducted a follow-up work in 2010 using microarrays to examine P. Aeruginosa PAO1’s reaction to low-shear modelled microgravity in rotating wall vessels and random position machines. In mimicked microgravity, P. Aeruginosa showed enhanced alginate synthesis and upregulation of AlgU-controlled Transcripts, including those encoding for stress-related proteins.

The study’s findings also suggested that Hfq was involved in P. Aeruginosa’s reaction to simulated microgravity. Hfq’s involvement in P. Aeruginosa’s response to real spaceflight was later validated in a different investigation [30].Additionally, there is worry that short-term spaceflight causes a rise in antibiotic resistance. When compared to E. Coli cultivated on the ground, the MIC for both colistin and kanamycin dramatically increased in the flying module. Staphylococcus aureus was shown to have a comparable rise in the MIC for oxacillin, thromycin, and chloramphenicol. This has given rise to worries that antibiotic effectiveness may be compromised during even brief orbital missions [3]. There has been speculation that a decrease in the Natural, There may be a rise in the prevalence of drug-resistant bacteria due to the increased variety of the gastrointestinal bacterial fauna in spaceflight. Additionally, it has been suggested that giving antibiotics either before or during the flight may encourage the formation of such resistant clones. Bacterial mutation, which happens more frequently in long-duration spaceflights, is another factor that promotes the emergence of medication resistance [9]. Overall, there is a chance that drug-resistant germs might infest the whole crew during a mission, creating a medical issue that is challenging to handle.

**Future perspective: considering probiotics as a countermeasure**

On Earth, probiotics have been shown to improve innate and adaptive immune responses. Oral bacteriotherapy employing probiotic bacterial strains is believed to enhance the intestine’s immunologic barrier by reducing inflammatory responses and intestinal IgA responses. A balance between proinflammatory and antiinflammatory cytokines seems to have a stabilising impact on the stomach. It has been proven that Lactobacillus rhamnosus GG may inhibit TNF-a-induced IL-8 synthesis in human colon adenocarcinoma (HT29) cells as well as reduce elevated faecal concentrations of TNF-a in people with atopic dermatitis and cow milk allergies. On the other hand, consumption of lactobacilli as live, attenuated bacteria or in fermented milk products increased the production of IFN-g by peripheral blood mononuclear cells [6]. The systemic and mucosal IgA response was boosted by oral lactobacilli treatment. In mice, oral administration of Bifidobacterium bifidum and Bifidobacterium breve boosted the IgA response to cholera toxin and improved the antibody response to ovalbumin [8].

The humoral immune response, including a rise in the IgA class of cells that release antibodies specific to the rotavirus, was increased in both children [60] and persons who took L. Rhamnosus GG [90]. Isolauri et al. Found that infants who got a reassortant live oral rotavirus vaccine together with L. Rhamnosus GG had a higher frequency of rotavirus-specific IgM class antibody-secreting cells. Additionally, there was a greater rate of rotavirus-specific IgA antibody class sero conversion in comparison to placebo patients. After 7 days of Lactobacillus casei treatment, the number of IgA+ cells and IL-6-producing cells rose.

Another study found that the injection of lactic acid bacteria induced the production of inflammatory cytokines including TNF-a, IFN-g, and IL-12 as well as regulatory cytokines like IL-4 and IL-10 from the gut immune cells in a dose- and strain-dependent way. It has been demonstrated that a number of lactobacilli strains enhance the ability of macrophages and other innate immune system cells to behave as immunopotentiators. Probiotics that can modify the gut immune system are many and have received thorough evaluation. According to Buckley et al., lactic acid bacteria-containing soy-based fermented food can help astronauts avoid health issues related to prolonged space travel. Given the importance of the human gut in proper digestion, nutrient absorption, and exposure to pathogens throughout its enormous surface area, a healthy digestive system is essential for a healthy individual. In space, an astronaut’s gut microbiota may alter as a result of things including food, way of life, use of antibiotics, various stressful conditions, and more. In light of potential immune system changes caused by changes in gut microflora, use of antibiotics in space, and changes in enhanced virulence and antibiotic resistance of bacteria, doctors who treat astronauts must keep in mind the importance of the intestinal microbiome to their health condition. This means that an astronaut’s health as well as the mission may be put at risk if their digestive system is affected.

**Microbiota in health and diseases**

Our knowledge of the human microbiota, or the microbial Community that resides inside the human body, has significantly increased as a result of the Human Microbiome Project (HMP) [11]. The knowledge that there are more microbial cells than human cells In order to analyse the microbiota in the GI tract, skin, oral cavity, nares, and vagina (in females) by a factor of 10 in the human body, the National Institutes of Health (NIH) developed HMP in 2007 [12–14]. Thanks to improvements in computational techniques and genetic technology, it is now feasible to do a full investigation of microbial compositions, even those that cannot be cultivated on microbiological media [15-18]. Numerous Findings from this five-year investigation were released after the HMP’s conclusion in 2012 [14].

Regardless of the place studied, there is a wide range of microbial diversity, and each system has dominating groups of species that represent its unique niche [13]. Variations in the microbiota occur throughout the course of a person’s lifetime and are influenced by both internal (host health) and external (environmental) variables [19]. In general, intrapersonal microbial community differences are less than interpersonal microbial community differences between persons [16,20].Understanding the function of the microbiota in the host’s health condition is unquestionably one of the top priorities of the HMP [12,14,15,21]. In the past, microbial illnesses tended to concentrate on specific pathogens; more recently, the approach has mainly assessed microbial populations and their interactions with the host to better understand a person’s health. A number of studies Have revealed that dysbiosis, a disturbance in the microbial Ecosystem, is responsible for various diseases and disorders.

According to reports, the HMP area that has gotten the most scientific focus is the GI system. According to metagenomics investigations of the gut microbiome, irritable bowel syndrome, Crohn’s disease, obesity, and other illnesses have all been connected to population changes [4, 11, 22–25]. Other disorders include irritable bowel syndrome, acute, traveler’s, and antibiotic-associated diarrhoea, as well as other forms of diarrhoea. On the other hand, new study findings have indicated that the microbiota of healthy individuals may assist avoid obesity and contribute to severe nutritional conditions [26,27].

**The skin microbiome**

The biggest organ in the human body is the skin. Its main purpose is to serve as a physical barrier that shields our bodies from outside damage. It also regulates body temperature, controls evaporation, senses touch, and stores lipids and water [20,28]. The skin constantly comes into touch with various substances because it serves as a barrier between internal organs and the outer world. Skin is frequently colonised by microscopic creatures including viruses, fungus, and bacteria that are present everywhere. Generally, they may be divided into three groups:

1. Transient microbes present intermittently,
2. Temporary Organisms that persist over a short period of time, and
3. Permanent inhabitants of the skin [9, 29]. Additionally, skin constantly goes through a process of self-renewal in which indigenous microbial cells are eliminated. In fact, some of the microbes found on the skin are thought to be mutualistic organisms and provide health benefits to the skin by secreting antibacterial substances, preventing pathogen colonisation, and influencing host immune responses [30]. The majority of the microbes found on the skin are commensal organisms and harmless to healthy people. On the other hand, if the physical barrier has been damaged by trauma or injury, commensal bacteria can still spread illnesses and infections [15,20]. Some pathogens are referred to be opportunistic pathogens that develop into infectious agents after the host’s immune system has been weakened by procedures, medical treatments, or other confounding events.

Based on historical culture techniques [9], it was believed that the types of bacteria that colonised the skin were restricted. These included species of Corynebacterium and Propionibacterium as well as Staphylococcus epidermidis and other coagulase negative staphylococci. The capacity to identify the microbial composition of the skin, even those that cannot be grown on microbiological medium, has subsequently been revolutionised by the introduction of molecular methods like metagenomics analysis [15,16,19].

Numerous variables, which may be broadly divided into host and environmental factors [28], influence the skin’s microbial ecology. The microenvironment of the sampling location, which is a reflection of skin physiology, has a significant impact on the skin microbiota [16,28]. The lowest diversity can be seen in sebaceous areas like the forehead, where Propionibacterium Species predominate. Contrarily, wet areas (such as the armpits, navel, and groyne) have a greater variety of microorganisms, with Staphylococcus and Corynebacterium species predominating [16,28]. Furthermore, skin regions with higher bacterial diversity, such as the forearm, hand, and buttock, may have diversity on par with or even larger than the gut microbiome.

Pathogens are discouraged from entering and colonising the skin because of the acidic environment created by sebum breakdown [28]. Another environmental component that directly affects the skin’s microbial flora is personal cleanliness. Skin conditions are altered by soaps, cosmetics, and skincare products (such moisturisers), which may then have an impact on the sorts of microorganisms that live on the skin. The section on probiotics and skin health has further information on this subject. Age, sex, and anatomical locations are some of the host-related characteristics. Skin microbiota vary with age, with the youngest and oldest groups having considerably different bacterial populations [19]. Soon after birth, a newborn obtains resident bacteria on the skin, and this affects the makeup of those bacteria. By birthing procedures [20, 30]. Changes in hormones during puberty stimulate the growth of lipophilic (or lipid-loving) Bacteria due to sebum production [19]. Physiological alterations Additionally, microbial community variation across genders is also influenced by anatomical variations [16].Skin illnesses can be brought on by altered lipid content and organisation when commensal bacteria turn into infectious agents. Acne, an inflammatory condition that affects 80% of teenage Americans, is one such example [3]. Puberty causes the lipid content to shift, which promotes the growth of lipophilic organisms such Propionibacterium acnes [25]. These bacteria use the metabolization of fatty acids to provide energy. Many different enzymes that harm the tissue lining of sebaceous glands are released in the sebum.

This causes the skin disorder known as acne vulgaris in association with activated immune responses [28]. The researchers also observed that Staphylococcus (S.) aureus was more prevalent in younger children, but that it was eventually replaced by lipophilic and other bacteria. This discovery might have significant effects on skin conditions like atopic dermatitis (or eczema), which are more common in youngsters but frequently go away by adolescence and adulthood [34]. Furthermore, impaired barrier function frequently contributes to skin disorders [20]. Impetigo furuncles, subcutaneous abscesses, ulcers, and other more serious systemic infections (such as toxic shock syndrome) are only a few of the cutaneous disorders that S. Aureus can cause [20,31,33]. S. Aureus is one of the most often reported skin pathogens. Patients with burns who have lost their epidermis (and maybe their dermis) are vulnerable to numerous assaults. Gram-positive bacteria like S. Aureus thrive in the first 48 hours. Aureus are the main colonisers. Gram negative opportunistic microbes, some of which have aggressive features and can cause infections that are lethal, take control as a result of this alteration [35].

 Additionally, skin microbiota has been linked to dermatological problems [15,25,28,34]. Atopic dermatitis (AD) is a chronic, severely inflamed skin condition that has increased more than twofold in developed nations over the past three decades [28]. S. Aureus is the main colonising species in many cutaneous infections in AD patients. A study that looked at the microbiomes of three distinct populations found a strong link between the variety of bacteria and the severity of illness [34]. In general, the sickness was worse when there was a lack oflow; however, when microbiota levels rose following therapy, they began to resemble those found in healthy skin. A thorough evaluation is crucial in treating AD patients because the change in the composition of the microbial community was a complicated process [25].

For psoriasis, another dermatological condition, the skin microbiome was determined. A chronic inflammatory skin disorder that affects 2% of the global population, the reason is mostly unclear. Different colonisation patterns between psoriasis lesions and unaffected skin locations were noted using molecular methods [30]. The three main skin microflora’s distributions varied greatly in their representations, indicating that a considerable ecological disturbance of the microbial community may have contributed to the patients’ psoriasis condition.

**Conclusion**

Applications and market share for probiotics are constantly growing, and this exponential expansion is not expected to stop. The lack of clinical research and scientific data for specific health applications is the major drawback to using probiotics. Because they were based on preliminary analyses and anecdotal evidence, many probiotic claims for foods have lost credibility. The same patterns and fallacies apply to personal care products as well. Additionally, it appears that the positive effects promoted by industry and others who make similar claims depend on the strain. Unfortunately, without sufficient data, the favourable results have been generalised and communicated to consumers (and even to health professionals). The fact that many commercially available products contain many microbes further complicates the situation, making it difficult to interpret the data and determine how each strain functions. Additionally, there is a paucity of information about safety, especially the long-term effects of probiotic organisms on current microbiomes and general health.

This presents a worry for young children and people who may be at danger of suffering catastrophic and unexpected consequences due to underlying health issues.Marketing personal care products that contain probiotics has additional challenges due to regulatory regulations. As was already mentioned, these products might fall under one of the numerous product categories (cosmetics, drugs, medical devices, and dietary supplements) that are subject to various rules under The FD&C Act, or they might be governed by rules that are specific to other subcategories of consumer goods. For instance, drug goods often need either adherence to a “monograph” for a certain medicine category as specified by the FDA’s Over-the-Counter (OTC) Drug Review or premarket FDA clearance through the New medicine Application (NDA) procedure. Contrarily, cosmetic items are often exclusively under post-market inspection.

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