

# MICROBIOME AND PERSONAL PROBIOTICS

Mankind has always yearned to live in space, which has inspired the creation of space stations for extended manned space missions. A life support system must be designed. To maintain the bare necessities for human existence in space, such as a constant body temperature, a constant pressure on the body, and proper waste disposal. The majority of study to far in this field has been devoted to basic human needs including air, water, and food. A life support system also handles the medical needs of astronauts.

In addition to improving the astronauts' health and immunity, compensating for these changes may also increase the length of their space missions. Mankind has long been aware of the significance of gut flora in both health and sickness. Changes in the balance of the gut flora and a number of illnesses have been linked by researchers [3]. The collection of flora genes found in the human genome was given the label "human metagenome" after the conclusion of the Human Genome Project. Highlighting the microbiome's critical function in maintaining health [4]. This viewpoint emphasises how important the microbiome is to astronauts' health and/or illness state. It would be helpful to develop probiotics for every crew member given the unique health and dietary requirements of astronauts while in space. 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 good immunological function, effective digestion and absorption, the absence of gastrointestinal lesions, and the existence of normal intestinal microflora [5]. However, it is still incredibly unclear from a scientific perspective what gut health is or how it can be described and/or evaluated. An crucial factor that aids in maintaining gut health appears to be the interactions between the gastrointestinal barrier and the microbiota. The gastrointestinal system helps in digestion and nutritional, mineral, and fluid absorption. The host, endocrine regulation, and osmoregulation metabolism, systemic tolerance, and mucosal tolerance Immunosuppression, protection against possible infections and poisons, communication from the periphery to the brain, and detoxification of poisonous chemicals coming from the host or environment [6] are all functions of the immune system. Understanding the significance of gut health and microbiota can be beneficial for astronauts' health. Bacteria that are healthy and those that are harmful fight it out for dominance over the vast surface of the digestive system. The immune system struggles to prevent pathogens from entering the blood and lymph with such a large exposure area.

A dynamic and healthy human gut depends on a balance of both potentially dangerous and helpful bacteria, which is regarded to be typical. Adding beneficial microorganisms or probiotics is one method of keeping this homeostasis. Numerous bacterial strains have been scientifically examined as potential probiotics since Nobel Laureate Metchnikoff made the first suggestion about the health advantages of probiotics in the early 20<sup>th</sup> century [7]. By reducing intestinal microbial infections, probiotics are believed to promote health [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**

Certain bacteria have been demonstrated in studies to exhibit increased pathogenicity, altered growth regulation, and altered responses to antibiotics. Both in real-world microgravity and in space [15–19]. Significant logistical and technical challenges have made it difficult to conduct in-depth genotypic and phenotypic investigations of bacterial responses to real-world space environments. On space shuttle flight STS-115, Wilson et al. Cultured *Salmonella enterica* Typhimurium using the same cultures. As controls on the ground [15]. Using global microarray and proteomic studies, 73 conserved proteins and 167 transcripts with differential expression were found. Hfq, a non-binding protein, was proposed as a possible Participating in the reaction to spaceflight is a

global regulator. 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]

In simulated microgravity conditions, the production of the heat-labile enterotoxin from enterotoxigenic *E. Coli* was dramatically increased [18]. After a 12-day exposure to low-shear simulated microgravity, *Candida albicans* displayed improved filamentation, biofilm community growth, phenotypic switching, and increased resistance to the antifungal medication amphotericin B [24]. 163 differentially expressed genes in *S. Typhimurium* grown in simulated microgravity were found to include one virulence gene. The majority of virulence genes, including those involved in lipopolysaccharide production, were also expressed at low levels [22].

Because it had decreased gene expression in a microgravity simulation, sigma factor, a transcription factor implicated in a general stress response, was also discarded as a potential explanation [25]. The Hfq pathway is required for full virulence in *S. Typhimurium*, but enhanced virulence of *S. Typhimurium* grown in actual spaceflight and rotating wall vessel culture conditions is not caused by increased expression of traditional genes that control this bacterium's virulence under normal gravity conditions [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**

Probiotics have been demonstrated to enhance both innate and adaptive immune responses on Earth. Through intestinal IgA responses and the reduction of inflammatory responses, oral bacteriotherapy using probiotic bacterial strains is thought to strengthen the intestine's immunologic barrier. It appears that a balance between proinflammatory and antiinflammatory cytokines causes a gut-stabilizing effect. It has been demonstrated that

Lactobacillus rhamnosus GG may lower increased faecal concentrations of TNF- $\alpha$  in individuals with atopic dermatitis and cow milk allergy and can block TNF- $\alpha$ -induced IL-8 production of human colon adenocarcinoma (HT29) cells. On the other hand, consumption of lactobacilli as live, attenuated bacteria or in fermented milk products increased the production of IFN- $\gamma$  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].

Children [60] and people who received L. Rhamnosus GG [90] both showed an increase in the humoral immune response, including an increase in the IgA class of cells that secrete antibodies specific to the rotavirus. Infants who received a reassortant live oral rotavirus vaccination together with L. Rhamnosus GG were shown to have a greater frequency of rotavirus-specific IgM class antibody-secreting cells, according to Isolauri et al. Additionally, compared to placebo participants, there was a higher rate of rotavirus-specific IgA antibody class sero conversion. IgA<sup>+</sup> cells and IL-6-producing cells increased in number after 7 days of Lactobacillus casei administration.

Another study found that the injection of lactic acid bacteria induced the production of inflammatory cytokines including TNF- $\alpha$ , IFN- $\gamma$ , 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. A healthy digestive system is crucial to a healthy person, given the significance of the human gut in good digestion, nutritional absorption, and exposure to pathogens over its considerable surface area. An astronaut's gut microbiota can change in space depending on factors including diet, lifestyle, antibiotic therapy, various stressful situations, and more. Doctors who care for astronauts must keep in mind the significance of the intestinal microbiome to their health condition in light of potential immune system changes caused by changes in gut microflora, antibiotic usage in space, and changes in enhanced virulence and antibiotic resistance of bacteria. This suggests that a compromised digestive system might be hazardous to both the astronaut's health and the mission.

### **Microbiota in health and diseases**

The Human Microbiome Project (HMP) has greatly improved our understanding of the human microbiota, or the microbial Community that lives inside the human body [11]. Realising that there are more microbial cells than human cells The National Institutes of Health (NIH) launched HMP in 2007 to evaluate the microbiota in the GI tract, skin, oral cavity, nares, and vagina (in females) by a factor of 10 in human body [12–14]. A thorough analysis of microbial compositions, even those that cannot be cultured on microbiological media, is now possible because to advancements in computational methods and genomic technology [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.

The GI system is perhaps the best studied site in the HMP and Yielded valuable scientific insights. Metagenomics analyses Of gut microbiome demonstrated many incidences that link The shift of populations with illnesses and disorders; these Include different types of diarrhea (e.g., acute, traveller's, and Antibiotic-associated), irritable

bowel syndrome, Crohn's Disease, obesity, and other conditions [4,11,22-25]. On the Other hand, microbiota from healthy individuals has been Attributed to potentially fighting against obesity and playing A role in severe malnutrition conditions, as shown by recent Research findings [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]. One of the most often mentioned skin pathogens, *S. Aureus* causes a number of cutaneous illnesses, including impetigo, furuncles, subcutaneous abscesses, ulcers, and other more serious systemic infections when penetrating into the blood stream (e.g., toxic shock syndrome) [20,31,33]. Burn victims whose epidermis (and at times dermis as well) have been destroyed are exposed to various assaults. Gramme positive bacteria, such as *S. Aureus*, are the primary colonisers during the first 48 hours. Then there is a change, and Gramme negative opportunistic organisms take over, some of which have aggressive traits and can result in infections that are fatal [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 of flow; 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 previously indicated, these items might come under one of the several product categories (cosmetics, medicines, medical devices, and dietary supplements) that are subject to distinct regulations under The FD&C Act, or they could be subject to regulations that are specific to other categories of consumer products. For instance, while cosmetic products are only subject to post-market surveillance, drug products must typically either receive premarket approval from the FDA through the New Drug Application (NDA) process or adhere to a "monograph" for a specific drug category as established by the FDA's Over-the-Counter (OTC) Drug Review.

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