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A Review: The Effect of Microgravity on Gut Beneficial Bacteria

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ABSTRACT

After decades of relatively quiet periods since the Apollo missions, human space travel has once again come to the forefront with many private and few government agencies vying for space tourism and space travel. India and China are planning long duration human space missions. America is planning a manned lunar mission followed by a Mars mission. Billionaires like Sir Richard Branson and Jeff Bezos have already flown to space and experienced microgravity while Elon Musk has gone public with his Mars plans. We are also searching for another earth like planet for our second home. Interplanetary missions and space tourism are likely to become common in the coming few decades. This will raise the important question of maintaining the health of space travelers while in the hazardous environment of space namely radiation, microgravity, the confined environment inside spacecraft, isolation, etc. Studying the health of the several hundreds of those, who traveled to the international space station and stayed there, has revealed numerous health risks for both short-term and long term space travel. Some of the health hazards include bone loss, muscle atrophy, decreased immunity, change in gut microflora, psychological disturbances, etc. A better understanding of the effects of microgravity on human health is essential for safe space travel and return to Earth. This review aims to discuss the effects of microgravity on the gut beneficial bacteria.

Keywords: Microgravity; Bacteria; Planet; Environment; Earth

INTRODUCTION

Microgravity arises in space as the orbiting body has an acceleration that is equal and opposite to acceleration due to the gravity of the orbiting body. For example, humans and objects onboard the international space station experience weightlessness, and hence float, as the earth's gravity is counteracted by the equal and opposite acceleration of the space station [1].

Microgravity is sometimes referred to as "zero gravity". However, both the terms are misleading. Gravity is neither micro nor zero but merely counteracted by the opposite acceleration of the orbiting object.

As of March 14, 2023, a total of 631 people from 41 countries have gone into space according to the Federation Aeronautique Internationale (FAI) criterion. Of those 631, three people only reached a sub-orbital flight, 597 people reached earth orbit, 24 travelled beyond low earth orbit and 12 walked on the moon.

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Space travellers have spent over 29,000 person-days (or a cumulative total of over 77 years) in space including over 100 person-days of spacewalks.

Analysis of the health of these astronauts has revealed information regarding health issues in space [2]. Prolonged exposure to microgravity and spacecraft environment consisting of excess carbon dioxide, lack of ultraviolet light, and radiation among other things can lead to profound health hazards. Some effects are very mild like facial oedema or an increase in height up to one inch [3]. Other effects are severe, and may not be reversible. An example of such a change is the loss of bone mineral density at an average rate of 1% per month with the corresponding recovery on Earth being very slow. Many other changes occur in the human body under microgravity like muscle atrophy and cardiovascular changes in short-term space missions. Other significant effects are orthostatic intolerance, ataxia, poor coordination, cardiac dysrhythmias, etc.

LITERATURE REVIEW

The Bioastronautics Roadmap

The health risk associated with space exploration is identified in the bioastronautics roadmap generated by NASA [4-8]. This is a framework for identifying, assessing, and reducing the risks of crew members in the hazardous environment of space. The roadmap identifies the risks and categorizes them into 5 main areas:

- Human health and countermeasures.
- Autonomous medical care.
- Behavioural health and performance.
- Radiation health.
- Advanced human support technologies.

Microgravity Simulation on Earth

Adequate research on microgravity is indispensable to understanding the impact of gravity on biological processes and organisms [9].

Since the numbers of people going into space are very few *in situ* studies are very constrained. This makes ground based simulated studies a very critical part of understanding the effects of microgravity on both short term and long term space stays. Further, these studies can be done in a cost-effective manner and with less associated risks to subjects. Standalone studies are also possible [10].

The ground simulators from microgravity can be modelled to simulate one physical aspect of microgravity. The most commonly used ground based facilities are based on following physical concepts.

- 2-D clinostat-one or two axes running fast and constantly in one direction.
- Random Positioning Machine (RPM)-two axes running with different speeds and directions.
- Rotating Wall Vessel (RWV) or rotating bioreactors for cell cultures and aquatic organisms.
- Diamagnetic levitation.

The most commonly used small-scale method for simulating microgravity on earth is the Rotating Wall Vessel (RWV) bioreactor that facilitates cellular models under simulated microgravity conditions [11].

RWV bioreactor is NASA designed tissue culture vessel that can be used to simulate microgravity while reducing the sheer turbulence associated with impeller-driven and stirred bio-reactors [12]. It is based on 2 important design principles (**Figure 1**).

- Solid-body rotation on the horizontal axis.
- Active or passive diffusion of oxygen through a silicone rubber membrane.

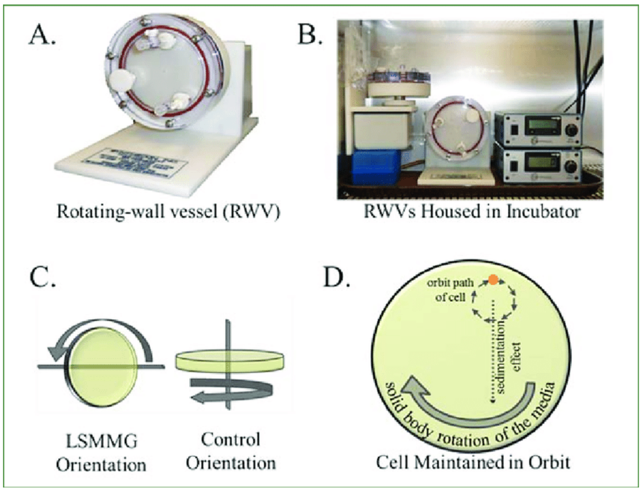

Figure 1: The rotating wall vessel bioreactor (Synthecon, Houston, Texas). A) Image of the NASA-designed RWV apparatus; B) RWV culture system in the incubator with their respective base units and power supply systems; C) The altered positioning of the RWV results in the two culture orientations, depicting the axis of rotation. The LSMMG (Low Sheer Model Microgravity) environment is achieved by rotation of the RWV on an axis parallel to the ground, whereas the axis of rotation in the control orientation is perpendicular to the ground; D) Depiction of the orbital path of a cell when cultured in the LSMMG orientation. The combination of the sedimentation effect, whereby gravity and lack of motility cause a cell to settle to the bottom of the vessel, and the clockwise solid body rotation of the media results in the continuous suspension of the cell in an orbit.

Effect of Microgravity on Various Human Body Systems

Till today, the majority of the research has been focused on the systematic effects of microgravity on human physiology, such as the neurological system, cardiovascular system, musculoskeletal system, gastrointestinal system, immune system, stem cells, blood cells, etc. (**Figure 2**).

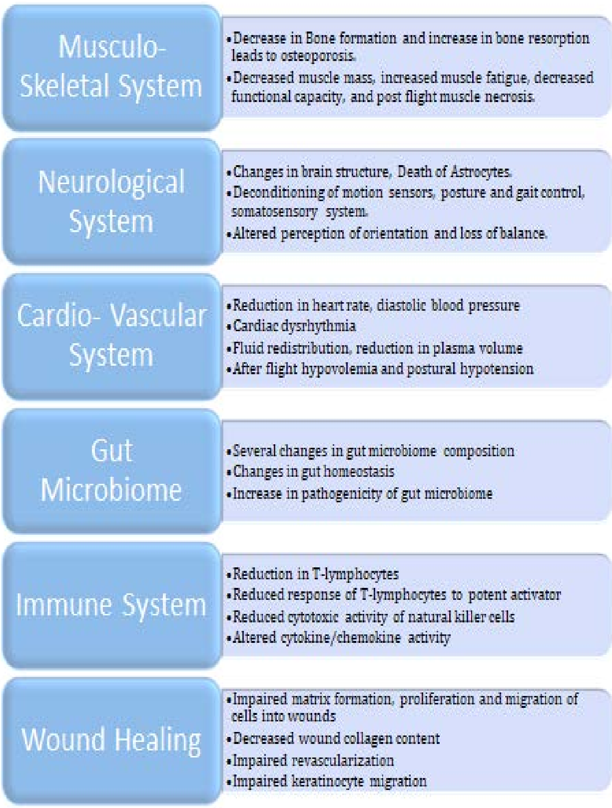

Figure 2: Effect of microgravity on various human physiological systems.

Gut Microbiome

The gut microbiome has a pivotal role in the regulation of the health and behaviour of the host. It affects digestion, metabolism, and immunity, and has been linked to changes in bones, muscles, and the brain [13-18]. Gut bacteria may exert their effects by the synthesis of molecules, their absorption, and through physiological effects on the host. Research has revealed that the microbiota protects against neurodevelopment disorders like Autism Spectrum Disorders (ASD) and schizophrenia. Few researchers have reported the beneficial properties of the gut microbiome against cancer [19].

The National Aeronautics and Space Administration (NASA) compared the gut microbiome of an astronaut and his twin who remained on Earth. Modifications were found in the gut microbiome of the astronaut during the one-year mission on board the International Space Station (ISS) while changes were not seen in his twin brother on Earth during the same period. A study, done using faecal samples of mice on board the ISS along with three control groups on earth, revealed modifications in the gut microbiome due to spaceflight. These changes were connected to an altered transcriptome in the liver of the same animals. Another study suggested that the overall number of microbes increased while their diversity went down under microgravity. Apart from this, the microbial count of *Serratia marcescens* and *Staphylococcus aureus* (pathogenic bacteria) was highly increased after space travel. Also, *S. aureus* was transmitted among the astronauts who indicates that pathogens can be transferred from person to person in a spaceship environment.

All these studies show that exposure to space can strongly influence the gut microbiota of space travellers, with the potential impairment of the homeostatic relationship with the host. The intestinal microbes play an important role in maintaining metabolic, immunological, and neurological health. Preserving eu-biotic microbiota during long-term space missions may help in reducing the unwanted effects on the human body and thus contribute to the success of the mission [20].

This could be achieved by optimizing diets to ensure adequate energy and fibre supply for SCFA (Short-Chain Fatty Acid) production while avoiding nutritional imbalances, as well as by integrating them with prebiotics, bioactive compounds, and probiotics for potentially synergistic effects. Probiotics are safe and along with prebiotics and bioactive compounds, they may be used both in traditional and latest forms can be used as a non-invasive alternative to protect space travellers against altered metabolism, satiety impairment, immune dysregulation, circadian rhythm changes, bone and muscle loss, as well as neurobehavioral disorders.

The human gut microbiome plays a crucial role in maintaining overall health and immunity, and disruptions to the microbiome can lead to health issues. Long term space travel can have significant effects on the gut microbiome, including changes in diversity, composition, and function. These changes may increase the risk of infectious diseases, metabolic disorders, and other health issues in space travellers. Strategies to maintain gut health in space include the use of probiotics, prebiotics, and symbiotic, as well as dietary interventions and lifestyle modifications. Probiotic and prebiotic supplementation has been shown to improve gut health and reduce the risk of infectious diseases in space like conditions. Dietary interventions, such as the inclusion of resistant starch and dietary fibre, can also promote the growth of beneficial gut bacteria and improve gut health. Lifestyle modifications, such as regular exercise and stress management, may also have positive effects on the gut microbiome in space travellers.

DISCUSSION

The authors of investigated the effects of simulated microgravity on the growth rate, acid tolerance, bile tolerance, and adhesion ability of *Lactobacillus acidophilus*. They found that simulated microgravity harmed the growth rate of *Lactobacillus acidophilus*, as well as its acid tolerance, bile tolerance, and adhesion ability. They suggest that the reduced growth rate and physiological changes seen in *Lactobacillus acidophilus* in simulated microgravity may have implications for the health of astronauts, as probiotics are often used to promote gastrointestinal health and prevent infections in space.

Probiotics have been proposed as a potential strategy to mitigate the negative effects of long duration space travel on human health, including changes in the gut microbiota and immune function. Studies done by Patricia Fajardo-Cavazos and Wayne L. Nicholson investigated the shelf life and survival of selected commercial probiotics (*Bifidobacterium* longum strain BB536, *Lactobacillus acidophilus* strain DDS-1, and spores of *Bacillus subtilis* strain HU58) during a simulated round-trip journey to Mars, including exposure to simulated space conditions and the simulated gastrointestinal tract. The study found that only spores of *Bacillus subtilis* were able to survive exposure to simulated space conditions and the simulated gastrointestinal tract, suggesting that they may be viable candidates for use during space travel.

Researchers propose a "designer diet" for astronauts that takes into account the impact of diet on the gut microbiome and overall human health during space travel. The proposed diet includes a variety of nutrient-rich foods, such as fruits, vegetables, whole grains, and lean protein sources, as well as prebiotics and probiotics to support the growth of beneficial gut bacteria. The article suggests that the designer diet could help mitigate the negative effects of space travel on human health, including changes in the gut microbiome, immune function, and bone health.

Several studies have shown that spaceflight can have significant effects on the composition of the gut microbiome of astronauts. The gut microbiome is essential in maintaining the physiological conditions of the host by regulating its immunity. The gut microbiome consists of an estimated 100 trillion microorganisms, including bacteria, protozoa, fungi, and viruses, and encodes more than 3 million genes that can produce thousands of metabolites, with various functions that impact the overall health of the host. Dysbiosis in the gut may result in the development of diseases and affect the immune system, while the microbiome may deliver protection against various disorders such as metabolic, inflammatory bowel, and allergic diseases. The two major bacterial species in the gut, Firmicutes and Bacteroidetes, need to have a balanced ratio for the maintenance of homeostasis in the host, with Firmicutes being involved in the metabolism and nutrition of the host and regulation of hunger and satiety through short-chain fatty acid synthesis and Bacteroidetes being associated with immunomodulation. Furthermore, the gut bacteria and their metabolites may influence the function of the tissues and organs that control circulatory system homeostasis, such as the blood vessel wall, blood cells, and the heart.

The microgravity environment has an effect on both the vascular physiology and gut microbiome composition, particularly through extended spaceflight travel, as shown by "the astronaut microbiome project," which studies the microbiome of astronauts with the aim of determining microbiome changes during space travel. For example, prolonged exposure to radiation can alter gut microbiome composition and disrupt gut homeostasis. Moreover, Analog mission projects such as the "MARS500 study" have supplemented the evidence of the significant role of the gut microbiome, where six astronauts were confined within an analogue mars-surface habitat over 520 days and examined for gut microbiota changes. Preliminary data have shown that astronaut microbiome composition becomes less diverse during spaceflight. The MARS500 study has shown that *F. prausnitzii*, the butyrate-producing members of the gut microbiota, were observed to alter in all subjects of the study, implicating the significance of short-chain fatty acid production, with possible inferences for the maintenance of the microbiome in the subjects. Recent studies using improved bioinformatics technology have identified several exact sequence variants that were significantly and differentially abundant over time. Overall, the impact of space travel on gut microbiome composition and astronaut health is an ongoing area of research.

CONCLUSION

Microgravity has a significant impact on human health and poses a challenge for long term space missions. Ground based simulators such as the RWV bioreactor have been used to simulate microgravity and study its effects on various human body systems. The gut microbiome, in particular, is significantly affected by spaceflight. Preserving eubiotic microbiota during long term space missions may help in reducing unwanted effects on the human body and contribute to the success of the mission. The research done to date in this field looks insufficient mainly because of the lack of a large number of subjects and the difficulties involved in simulating the space environment on the ground. Further research is necessary to understand the mechanisms underlying these changes and develop effective countermeasures to mitigate their impact on human health in space and interplanetary missions.

AUTHOR CONTRIBUTIONS

The idea of the article was given by Maulesh Gadani. The literature survey was done by Maulesh Gadani and Kedar Ahire. The article was written, and data analysis was done by Maulesh Gadani. The article was revised by all the authors.

CODE AVAILABILITY

Not applicable.

CONFLICT OF INTEREST

Maulesh Gadani declares that he has no conflict of interest. Kedar Ahire declares that he has no conflict of interest. Viral Shukla declares she has no conflict of interest.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

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