



## Space nutrition and the biochemical changes caused in Astronauts Health due to space flight: A review

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### ABSTRACT

Astronauts required food that is healthy, nutritious, and tasted good, while also meeting their dietary needs. To ensure the astronauts' nutritional needs are met, a Nutritional Status Assessment Supplemental Medical Objective (Nutrition SMO) is conducted. This involves collecting blood and urine samples from the astronauts, which are then tested and analysed. The assessment looks for indications of bone health, muscle loss, hormonal imbalances, gastrointestinal functions, cardiovascular health, iron metabolism, ophthalmic changes, and immune changes that occur during space flight under conditions of microgravity or weightlessness. It was discovered that iron levels in astronauts tend to increase due to the decrease in body volume during space flight. It requires skilful optimization considering nutrient delivery, shelf life, and packaging of space food, while minimizing resource usage and ensuring reliability, safety, and addressing the physiological and psychological effects on the crew members.

### 1. History

The history of space food dates back to the early days of human space exploration. When astronauts started on their first missions in the 1960s, scientists and engineers faced the challenge of providing them with suitable food for consumption in the harsh environment of space (Oluwafemi et al., 2018). Initially, space food was in the form of bite-sized cubes, freeze-dried powders, and semi-liquids. These early space meals were primarily developed to be lightweight, compact, and easy to store, as well as resistant to spoilage and contamination. They were also designed to require minimal preparation and to be consumed without creating crumbs or crumbs that could float around the spacecraft and potentially damage equipment (Oluwafemi et al., 2018; Gary et al., 1996). The Mercury and Gemini missions of the 1960s relied on food such as beef and vegetables in pureed form, which were packed into aluminum tubes. The food tubes were equipped with a nozzle that allowed astronauts to squeeze out the food and consume it directly from the tube. With the initiation of the Apollo program and the goal of

sending astronauts to the Moon, NASA sought to improve the quality and variety of space food. The Apollo missions introduced hot water for rehydrating freeze-dried food, enabling astronauts to enjoy meals that resembled more traditional dishes. These meals included shrimp cocktail, chicken and vegetables, and even ice cream (Oluwafemi et al., 2018; Gary et al., 1996).

The Skylab program in the 1970s marked another milestone in space food. Skylab astronauts had access to a refrigerator and a hot water dispenser, allowing them to enjoy a wider range of food, including fresh fruits and sandwiches. They also had the opportunity to grow and consume vegetables like lettuce and radishes in space, utilizing an on-board plant growth system (Gary et al., 1996). In more recent years, the International Space Station (ISS) has provided astronauts with improved culinary options. The ISS is equipped with a galley where astronauts can prepare meals using a variety of ingredients sent from Earth. These meals can be rehydrated, heated, or consumed as is. Additionally, astronauts have the opportunity to enjoy fresh produce grown on the ISS, such as lettuce, zinnias, and even red romaine lettuce (Gary et al., 1996;

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Douglas et al., 2020). Efforts have also been made to improve the taste and overall dining experience of space food. Astronauts now have access to a wider selection of condiments and seasonings to enhance the flavour of their meals. Special packaging and utensils have been designed to ensure that food is easy to handle and consume in a microgravity environment (Gary et al., 1996; Douglas et al., 2020).

## 2. Introduction

Space food refers to the specially designed meals and snacks that astronauts eat during their missions in space. When humans first started exploring space in the 1960s, scientists had to come up with ways to provide astronauts with food that would meet their nutritional needs while being suitable for consumption in a weightless environment. In August 1961, German Titov, a Soviet cosmonaut, became the first person to eat in space (Bourland, 1993). This marked the beginning of a journey of continuous development and improvement in space food. In August 1962, during the third manned Mercury flight, John Glenn, an American astronaut, became the first American to consume food in space. His meal consisted of applesauce and xylose sugar tablets. Since then, space food has undergone significant changes and advancements (Bourland, 1993).

It has evolved to meet the needs of astronauts and to ensure their sustenance during space missions. Space food is quite different from the food we eat on Earth. It needs to be lightweight, compact, and easy to store. It must also be able to withstand the extreme temperatures and lack of gravity in space. Scientists have developed various techniques to preserve and package space food, such as freeze-drying, dehydration, and irradiation, to make it safe and long-lasting. In the early days of space exploration, astronauts mostly ate foods in the form of cubes, powders, and purees. These foods were packed in tubes or pouches, allowing astronauts to squeeze them directly into their mouths. Over time, space food has evolved, and astronauts now have a wider range of options. They can rehydrate freeze-dried meals with water, warm up pre-packaged dishes, and even enjoy fresh produce grown onboard the International Space Station (Bourland, 1993).

## 3. Importance of proper nutrition in Astronauts voyage

Astronaut nutrition refers to the specific dietary needs and considerations for astronauts during space missions. It focuses on providing astronauts with adequate and balanced nutrition to support their health, well-being, and performance in the challenging environment of space (Obrist et al., 1993). A well-balanced diet ensures that astronauts receive the necessary nutrients to support their bodily functions, including muscle and bone health, cardiovascular health, immune function, and hormonal balance. Adequate water intake is vital for astronauts during spaceflights to prevent dehydration, support blood circulation, regulate body temperature, aid in nutrient absorption, maintain muscle function, promote bone health, cardiovascular health, immune function, and hormonal balance (Lane et al., 1994).

Adequate nutrition also helps prevent deficiencies and related health issues. Space travel exposes astronauts to a unique set of challenges, including changes in bone density, muscle loss, altered metabolism, and weakened immune function. Proper nutrition can help counteract these effects by providing the necessary nutrients to maintain bone and muscle mass, support metabolic processes, and boost the immune system (Obrist et al., 1993; Oluwafemi et al., 2021). Enjoyable and familiar food can have a positive impact on mood and morale, helping astronauts cope with the isolation and stress of space travel. As space agencies plan for longer-duration missions, such as missions to Mars, ensuring proper nutrition becomes even more critical (Obrist et al., 1993; Oluwafemi et al., 2021).

## 3.1. Nutritional composition of space food

Astronauts require a balanced intake of macronutrients, including carbohydrates, proteins, and fats. Carbohydrates provide energy, proteins support muscle maintenance and repair, and fats serve as a concentrated energy source. The specific proportions of macronutrients may vary depending on the mission duration and individual needs. Adequate intake of vitamins, minerals, and trace elements is essential for overall health and proper functioning of the body (Oluwafemi et al., 2021). Astronauts' diets are carefully formulated to ensure they receive sufficient amounts of these micronutrients. Special attention is given to calcium and vitamin D to support bone health, as well as iron to counteract potential iron overload in space. Maintaining proper hydration is crucial for astronauts in space. Adequate fluid intake helps prevent dehydration, supports physiological functions, and assists in waste removal (Oluwafemi et al., 2021; Taylor et al., 2020). Special water and fluid management systems are employed on spacecraft to ensure astronauts have access to clean drinking water and maintain proper hydration levels. Astronauts require a specific number of calories to meet their energy needs in space. The energy expenditure of astronauts can vary depending on their activities, and their diets are tailored to provide sufficient calories to sustain their daily activities and metabolic processes (Taylor et al., 2020; Kerwin & Seddon, 2002). Consideration is also given to the taste, variety, and palatability of space food to ensure that astronauts find their meals enjoyable. Providing familiar flavors and textures can help boost morale and maintain psychological well-being during space missions. Additionally, astronauts may have individualized nutrition plans based on their specific dietary needs, preferences, and any pre-existing medical conditions (Taylor et al., 2020; Kerwin & Seddon, 2002).

## 4. Comparison of the status of space food in historical and present times

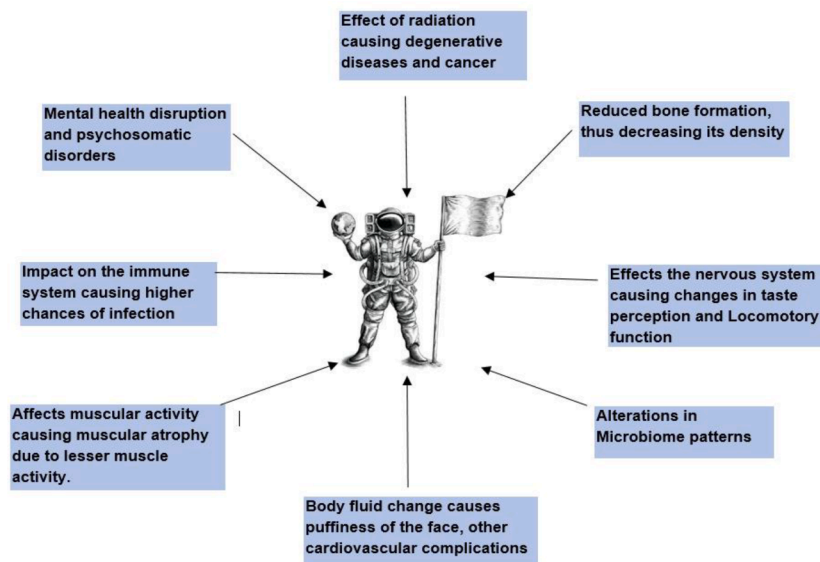
Historical view	Present scenario
In the early days of space exploration, space food was limited in variety, taste, and nutritional quality.	In the present era, space food has come a long way and has undergone significant improvements.
The primary focus was on providing astronauts with enough calories to sustain their energy levels. Food was often freeze-dried or thermally stabilized to extend its shelf life and reduce weight.	Space agencies and food scientists have made substantial efforts to enhance the quality, variety, taste, and nutritional value of space food.
Some early space food options included pureed meals, bite-sized cubes, and squeezed tubes of food. The selection was limited, and astronauts had to rehydrate their meals with water before consumption.	The focus has shifted towards providing balanced nutrition, improving flavor, and offering a wider range of meal options. Astronauts now have access to a more diverse menu that includes a variety of main courses, fruits, vegetables, snacks, desserts, and beverages.
The taste and texture of space food were often compromised, and astronauts reported difficulties in adapting to the eating experience in such gravitational alteration (Perchonok & Charles, 2002).	Food is prepared using advanced technology, such as freeze-drying and thermostabilization, to retain flavor, texture, and nutritional content. (Aleksey et al., 2021).

## 5. Challenges and future expectations

The field of space food still faces several challenges and holds future expectations as space exploration progresses. As space agencies plan for longer-duration missions, such as missions to Mars, sustaining astronauts' nutrition becomes a critical challenge. Developing food systems that can provide adequate nutrition for extended periods while maintaining freshness, taste, and nutritional value is a major focus. Scientists

continue to refine the nutrient composition of space food to optimize health, performance, and well-being. Research aims to identify specific nutritional requirements, such as personalized diets, tailored to individual astronauts' needs based on factors like genetics and physiological responses to microgravity. Minimizing resources, including water, energy, and packaging, is essential for long-duration missions where resupply is limited. Developing efficient food production and waste management systems is crucial to maximize resource utilization and minimize waste generation. Promoting psychological well-being through food is crucial for astronauts' mental health during long-duration missions. Enhancing the variety, taste, and comfort aspects of space food can contribute to astronauts' overall happiness, morale, and sense of connection to Earth (Douglas et al., 2021).

Innovations in food processing, flavor encapsulation, and texturization techniques are being explored to improve the sensory experience of eating in a microgravity environment. Personalized diets based on individual astronaut profiles, including dietary preferences, allergies, and health conditions, may become more prevalent (Douglas et al., 2021; Junaid et al., 2023). Developing food systems that can accommodate these individual needs and preferences will be crucial for maintaining astronauts' health and satisfaction during space missions. Ensuring food safety in space is essential to prevent contamination and adverse health effects (Junaid et al., 2023).



## 6. Alteration in the gravity in space with comparison to that on earth

The gravitational force experienced on Earth and in space differs significantly due to the presence or absence of massive celestial bodies. On the surface of the Earth, the gravitational force is relatively constant and is approximately 9.8 m per second squared ( $9.8 \text{ m/s}^2$ ). This value is known as the acceleration due to gravity or standard gravity (Cazenave & Jianli 2010). It keeps objects and people grounded, creating a downward force (Cazenave & Jianli, 2010).

In space, particularly in low Earth orbit, such as on the International Space Station (ISS), the force of gravity is significantly reduced compared to Earth's surface. This creates a condition known as microgravity. Astronauts in orbit experience a state of continuous freefall around the Earth, giving them the sensation of weightlessness. When traveling to more distant destinations, such as the Moon or other planets, the gravitational force decreases even further (Cazenave & Jianli, 2010;

Emily, 2003). This effect of microgravity, or the condition of experiencing very weak gravitational forces, has several effects on astronauts' health due to the significant changes it introduces to the human body's adaptation processes (Cazenave & Jianli, 2010; Emily, 2003).

## 7. Biochemical changes caused due to microgravity

Microgravity influences biochemical changes in the body because it disrupts the normal physiological conditions that organisms have evolved under on Earth. The absence of gravity's mechanical stress, alterations in fluid distribution, disruption of cellular signaling, sensory changes, and environmental factors in microgravity all contribute to the biochemical changes observed in the body. The body's adaptation mechanisms to microgravity also trigger complex biochemical responses (Kassemi & David, 2016). Few biochemical changes include:

- Bone and Muscle Loss
- Change in the mineral composition of the body
- Hormonal imbalances
- Abnormal digestion and absorption
- Abnormal Iron metabolism
- Impacts of oxidative stress
- Ophthalmological issues
- Reduced immune response

Biochemical changes caused in the astronauts due to space flight (Tesei et al., 2022).

### 7.1. Influence of microgravity on bone density

Microgravity reduces bone density primarily due to the absence of mechanical stress on the bones. On Earth, the force of gravity constantly acts on the skeletal system, subjecting it to mechanical loading during weight-bearing activities like walking or running. This loading stimulates bone remodeling, a process where old bone tissue is broken down by cells called osteoclasts, and new bone tissue is formed by cells called osteoblasts. In microgravity, the absence of constant mechanical stress significantly reduces the forces acting on the bones (Grimm et al., 2016). As a result, the normal bone remodeling process becomes imbalanced. Osteoclasts continue to break down old bone tissue, but the reduced osteoblast activity limits the formation of new bone tissue. This

imbalance leads to a net loss of bone mass and density over time. The reduction in bone density in microgravity is most pronounced in weight-bearing bones like the femur (thigh bone) and the spine. These areas experience the greatest decrease in mechanical loading due to the lack of gravity-induced compression and impact forces. The bone loss can result in osteoporosis, a condition characterized by weakened and porous bones, making astronauts more susceptible to fractures and injuries (Grimm et al., 2016; Man et al., 2022).

On Earth, gravity exerts a constant force on our bodies, and weight-bearing activities subject our bones to mechanical stress. This stress stimulates bone remodeling, where old bone tissue is broken down and replaced with new bone tissue. In microgravity, the absence of mechanical loading removes this stimulus, leading to a decrease in bone formation. In microgravity, bone breakdown by cells called osteoclasts continues as usual. However, the formation of new bone tissue by osteoblasts is reduced (Grimm et al., 2016; Man et al., 2022). The rate of bone resorption (breakdown) exceeds the rate of bone formation, resulting in a net loss of bone mass over time. This imbalance is a key factor in the reduction of bone density. Microgravity can disrupt the hormonal balance that regulates bone metabolism. One hormone affected is parathyroid hormone (PTH), which plays a role in maintaining calcium levels in the body. In microgravity, PTH levels may increase, leading to increased bone resorption as calcium is released from the bones. This further contributes to bone density loss (Man et al., 2022).

Calcium is essential for maintaining bone density, and its absorption in the intestines is influenced by factors like vitamin D and gravity. In microgravity, calcium absorption may be reduced, resulting in decreased availability of calcium for bone mineralization and maintenance. Weight-bearing activities, such as walking and running, help stimulate bone formation. The lack of mechanical stress on the bones further contributes to the decrease in bone density (Man et al., 2022; Nagaraja & Diana, 2013). Osteocytes are specialized bone cells involved in sensing mechanical stress and communicating with osteoblasts and osteoclasts to regulate bone remodeling. In microgravity, the altered mechanical environment affects the function of osteocytes, disrupting their ability to sense and respond to mechanical cues, which further impairs bone formation (Man et al., 2022; Nagaraja & Diana, 2013).

#### 7.1.1. Change in the mineral composition of the body

Microgravity influences the mineral composition of the body by disrupting the normal processes of absorption, distribution, and excretion of minerals. The reduced mechanical loading on the bones in microgravity leads to decreased calcium absorption and increased calcium excretion, contributing to bone loss. Other minerals like phosphorus, magnesium, iron, zinc, and electrolytes may also be affected due to changes in metabolism, fluid shifts, and altered distribution (Nagaraja & Diana, 2013). In microgravity, the reduced mechanical loading on the bones leads to decreased calcium absorption and increased calcium excretion.

The altered calcium metabolism can contribute to the loss of bone mineral density and increase the risk of osteoporosis (Nagaraja & Diana, 2013; West, 2000). During microgravity, the imbalance in bone remodeling affects phosphorus metabolism. The reduced osteoblast activity and increased bone resorption lead to the release of phosphorus from the bones, potentially resulting in altered phosphorus levels in the body (West, 2000). Magnesium plays a crucial role in enzyme function, muscle contraction, and bone health. Microgravity can impact magnesium homeostasis by altering its absorption and excretion. The changes in fluid distribution and electrolyte balance in microgravity may affect magnesium levels in the body (West, 2000; Fitts et al., 2001). Increased iron absorption and changes in iron distribution have been observed, potentially leading to higher iron levels in the body. These alterations may have implications for iron storage and utilization (West, 2000; Fitts et al., 2001). Microgravity can affect zinc metabolism, leading to altered zinc levels in the body. Changes in zinc absorption,

excretion, and distribution may impact its availability for cellular functions (Fitts et al., 2001; Iwase et al., 2020).

#### 7.1.2. Influence on the muscle activity

Changes in mineral composition due to microgravity can influence muscle activity through various mechanisms such as Calcium plays a crucial role in muscle contraction. In microgravity, altered calcium regulation can occur due to changes in mineral composition. Calcium ions are released from storage sites in muscle cells during muscle contraction. Disruptions in calcium metabolism can lead to impaired muscle contraction and reduced force generation. Magnesium is another essential mineral involved in muscle function. It acts as a cofactor in numerous biochemical reactions, including muscle relaxation. Changes in magnesium levels or its interaction with other minerals in microgravity can affect muscle relaxation, leading to muscle stiffness or spasms. Potassium is necessary for maintaining proper muscle cell excitability (Iwase et al., 2020; Schneider et al., 2015). In microgravity, alterations in potassium levels can impact the excitability of muscle cells. This can affect the ability of muscles to respond to nerve signals and result in reduced muscle performance or coordination.

Sodium is critical for muscle cell function, including maintaining the proper balance of fluids and transmitting nerve signals for muscle contraction (Schneider et al., 2015). Changes in sodium levels due to altered mineral composition in microgravity can disrupt muscle cell function and impair muscle performance. Phosphorus is an essential component of adenosine triphosphate (ATP), the primary energy source for muscle contractions. Changes in phosphorus levels or its availability in microgravity can affect ATP synthesis and energy metabolism in muscle cells, leading to decreased muscle endurance and performance (Schneider et al., 2015; Aubert et al., 2005).

#### 7.1.3. Effect of altered mineral composition on the muscle proteins

Changes in mineral composition due to microgravity can induce various alterations in muscle proteins, which can impact muscle structure and function. Collagen is a protein that forms the structural framework of muscles and connective tissues. In microgravity, changes in mineral composition can disrupt collagen synthesis, organization, and cross-linking. This can lead to a decrease in the integrity and strength of muscle fibers and connective tissues, potentially resulting in muscle atrophy and increased susceptibility to injuries (Schneider et al., 2015; Aubert et al., 2005).

Actin and myosin are the primary contractile proteins in muscle fibers whose interactions enable muscle contraction. Changes in mineral composition can affect the binding and sliding movements of actin and myosin filaments, altering the contractile properties of muscle fibers resulting in reduced muscle force generation and impaired muscle function. Disruptions in mineral composition, particularly calcium levels, can influence the binding affinity between troponin and calcium, affecting the regulation of muscle contraction.

Titin is the largest known protein and contributes to muscle elasticity and passive tension. Changes in mineral composition can affect the structure and properties of titin, leading to alterations in muscle elasticity and stiffness (Schneider et al., 2015; Aubert et al., 2005). This can impact muscle function, especially during stretching or lengthening movements. Proteolytic enzymes are responsible for the breakdown of muscle proteins during muscle protein turnover. Changes in mineral composition, particularly calcium and magnesium levels, can influence the activity of proteolytic enzymes. Altered enzyme activity can affect the balance between muscle protein synthesis and degradation, leading to changes in muscle mass and strength (Aubert et al., 2005).

#### 7.2. Hormonal imbalances

Microgravity can cause hormonal imbalances in astronauts due to the unique physiological changes they experience in space. Microgravity disrupts the normal processes of calcium metabolism in the body,

leading to imbalances in hormones involved in calcium regulation, such as parathyroid hormone (PTH) and calcitonin. The altered calcium levels can affect bone health and lead to bone density loss. Vitamin D, which is crucial for calcium absorption and bone health, may become insufficient in astronauts due to reduced sun exposure. This deficiency can further impact calcium regulation and bone metabolism. Microgravity even reduces the secretion of growth hormone, which plays a vital role in maintaining muscle mass and regulating protein metabolism (Aubert et al., 2005; Ronca et al., 2014). The decline in growth hormone levels may contribute to muscle loss and decreased protein synthesis in astronauts.

Insulin-like Growth Factor 1 (IGF-1, regulated by growth hormone, is involved in muscle growth and repair. In microgravity, decreased growth hormone levels can lead to lower IGF-1 levels, affecting muscle health and regeneration. The stress response in microgravity can result in altered cortisol levels. Elevated cortisol levels due to stress can have various effects on metabolism, immune function, and bone health. Microgravity-induced stress can also impact the levels of adrenaline and noradrenaline, hormones involved in the “fight-or-flight” response. Changes in these hormones can affect cardiovascular function and overall stress response (Ronca et al., 2014).

#### 7.2.1. Hormonal imbalances caused in male and female astronauts due to microgravity ((Ronca et al., 2014; Felice, 2021)

Changes in Female Astronauts	Changes in Male Astronauts
Alterations in Estrogen hormone secretion	Alterations in Testosterone hormone secretion.
Hormone fluctuations due to altered menstrual cycle, disturbed circadian rhythm and changes in the body composition	Mechanism behind testosterone alteration is unknown, but it causes stress, disrupted sleep pattern, altered physical activity and change in circadian rhythm in the male astronauts.
Altered Estrogen even has an impact on the bone density of female astronauts.	Altered testosterone levels even have an impact on the secretion of the Growth hormone in the male astronauts.
Irregular menstrual cycle is even associated with disruptions in hypothalamic-pituitary-ovarian axis, which in turn elevates stress and alters the energy balance.	Reduced mechanical loading and even altered muscle stimulation can affect the bone density.

#### 7.3. Abnormal digestion and absorption

Digestion and absorption are disturbed due to microgravity primarily because the absence of gravity alters the normal functioning of the gastrointestinal system. In microgravity, the absence of gravitational forces significantly impacts the motility of the gastrointestinal tract. Peristaltic movements, which help propel food through the digestive system, are diminished or altered. This can result in slower transit times and inefficient movement of food through the digestive tract, leading to digestive disturbances (Yang et al., 2020).

In microgravity, fluids in the body shift towards the upper body, causing fluid volume changes and redistribution. This can result in a decrease in blood volume and an increase in fluid accumulation in the head, leading to a condition known as “puffy face syndrome.” The altered fluid dynamics can affect the function of the digestive system. Microgravity can disrupt the normal functioning of the stomach, leading to gastrointestinal discomfort and gastric upset.

The gut microbiome, the community of microorganisms in the gastrointestinal tract, plays a crucial role in digestion and nutrient absorption. Microgravity can lead to changes in the composition and diversity of the gut microbiome, which can impact the breakdown and absorption of nutrients. These alterations may also contribute to gastrointestinal issues and nutrient deficiencies. Due to the effects of microgravity on digestion and absorption, astronauts may have altered nutritional requirements. Nutritional supplements and meal plans are

designed to meet the unique needs of astronauts during space missions (Yang et al., 2020; Amidon et al., 1991).

#### 7.3.1. Deficiencies caused

Microgravity can affect the digestion and absorption of macronutrients such as carbohydrates, proteins, and fats. Insufficient intake or inadequate absorption of these macronutrients can lead to deficiencies. Reduced absorption of micronutrients like vitamin D, calcium, and iron can lead to deficiencies (Amidon et al., 1991; Heer et al., 1999). Vitamin D and calcium are important for bone health, and their deficiency can increase the risk of bone loss and osteoporosis. Iron deficiency can lead to anemia and impaired oxygen transport in the body. Vitamin B12 absorption can be affected by microgravity-related changes in the gastrointestinal tract that can result in anemia, neurological problems, and fatigue.

Microgravity-induced alterations in calcium metabolism and reduced calcium absorption can contribute to bone demineralization and increased risk of bone fractures. Changes in fluid distribution and altered kidney function in microgravity can disrupt electrolyte balance and can lead to muscle cramps, weakness, and other physiological disturbances. Microgravity can affect the availability and absorption of vitamin C, which is crucial for immune function, collagen synthesis, and antioxidant defense (Heer et al., 1999).

#### 7.4. Abnormal iron metabolism

Microgravity can lead to fluid redistribution in the body, causing changes in blood volume and fluid accumulation in the upper body. This redistribution can affect iron distribution in the body, leading to altered iron metabolism. Iron may accumulate in certain areas or organs, such as the head, due to the fluid shifts, while other regions may experience decreased iron levels. Microgravity conditions can result in higher iron levels in the body. The contraction of body volume in microgravity can lead to an excess of iron, as the same amount of iron becomes concentrated in a smaller overall volume. This excess iron can have implications for iron metabolism and homeostasis (Chen et al., 2019). While iron levels may be higher in microgravity, the mass of hemoglobin (the molecule that carries oxygen in red blood cells) and the mass of red blood cells may experience a slight or negligible decrease. This suggests that the production or maintenance of hemoglobin and red blood cells may be affected by microgravity conditions (Chen et al., 2019; Nay et al., 2020).

Additionally, in microgravity, the body experiences a contraction of volume due to the absence of gravity’s compressive forces. This contraction leads to an increased concentration of substances, including iron, within the reduced volume. As a result, the same amount of iron becomes concentrated in a smaller overall volume, leading to higher iron levels (Nay et al., 2020).

Iron plays a role in determining the shape and characteristics of the oxygen dissociation curve, which represents the relationship between oxygen saturation and partial pressure of oxygen in the blood. Any alterations in iron metabolism can modify the shape of the curve, affecting the ability of hemoglobin to release oxygen to tissues. This can result in impaired gas exchange and reduced oxygen availability. Improper iron metabolism can affect the efficiency of oxygen uptake by red blood cells in microgravity. This can hinder the ability of the body to extract oxygen from the lungs and transport it to the tissues. Consequently, astronauts may even experience difficulties in meeting their oxygen demands, leading to physiological challenges and decreased exercise capacity (Horeau et al., 2022; Smith, 2002).

Improper iron metabolism in microgravity conditions can contribute to anemic conditions in astronauts because there is a redistribution of bodily fluids, including blood. This fluid shift can lead to a decrease in total blood volume and alterations in blood flow dynamics. As a result, iron, which is essential for the production of red blood cells and hemoglobin, may not be efficiently transported or utilized, leading to

anemia. Microgravity conditions can also increase iron loss from the body (Horeau et al., 2022; Smith, 2002). In microgravity, the altered bone metabolism and reduced physical stress on the skeletal system can affect bone marrow function and red blood cell production. This impairment can result in a decrease in red blood cell count, leading to anemia (Smith, 2002; Milojevic & Weckwerth, 2020).

### 7.5. Impacts of oxidative stress

Microgravity can cause oxidative stress in astronauts by several mechanisms such as microgravity disrupts the normal gravity-dependent cellular processes and alters the cellular environment. This disruption can lead to an imbalance between the production of reactive oxygen species (ROS) and the body's antioxidant defense systems. ROS are highly reactive molecules that can damage cells and biomolecules, leading to oxidative stress. It can trigger an immune response and chronic low-grade inflammation in the body. Inflammatory processes involve the release of ROS as a defense mechanism (Nguyen et al., 2021).

However, in the microgravity environment, this inflammatory response can become dysregulated, resulting in excessive ROS production and subsequent oxidative stress. Mitochondria, the energy-producing organelles in cells, are particularly susceptible to oxidative damage. Microgravity can impair mitochondrial function and disrupt the electron transport chain, which is involved in energy production. This disruption can lead to an accumulation of ROS within the mitochondria, causing oxidative stress. Microgravity even induces changes in fluid distribution within the body, leading to fluid shifts from the lower body to the upper body. This altered fluid distribution affects blood flow, oxygen delivery, and waste removal (Nguyen et al., 2021; Tian et al., 2017). Reduced blood flow and oxygen delivery can compromise tissue function and increase the production of ROS, contributing to oxidative stress. Astronauts in space are exposed to higher levels of radiation compared to Earth due to the absence of the protective shield provided by Earth's atmosphere. Radiation exposure directly generates ROS and can cause oxidative stress. The combination of microgravity-induced oxidative stress and radiation-induced oxidative stress can have a synergistic effect on astronauts' health (Tian et al., 2017).

Galactic cosmic rays (GCR) originating outside the solar system and solar particles emitted by the sun during solar flares (solar particle events) are the most common source of ionizing radiations that the astronauts are exposed to. Such environment can easily generate the ROS radicals through the interaction with water molecules in their bodies. This oxidative stress thus causes cellular dysfunction, DNA mutations, potential long term risks such as increased risk of cancer and other degenerative diseases (Kennedy, Guan, & Ware, 2007).

#### 7.5.1. Effect of antioxidants against oxidative stress

Antioxidants act as scavengers, donating electrons to stabilize these free radicals and prevent them from causing further harm. By doing so, antioxidants help maintain the balance between oxidative stress and antioxidant defense systems in the body. They protect cells from oxidative damage, support proper cellular function, and reduce the risk of chronic diseases associated with oxidative stress. Including antioxidant-rich foods in the diet and supplementing with antioxidants can provide an additional defense against oxidative stress and promote overall health and well-being (Tian et al., 2017; Zheng et al., 2015). Antioxidants can play a crucial role in mitigating the impact of oxidative stress caused by microgravity in astronauts. Antioxidants counteract the harmful effects of ROS by donating electrons to stabilize them.

Additionally, antioxidants can prevent oxidative damage to DNA, reducing the risk of genetic mutations (Zheng et al., 2015). Some antioxidants have the ability to regenerate endogenous antioxidants within the body, such as glutathione and vitamins C and E. These endogenous antioxidants are critical for maintaining the antioxidant defense system. By replenishing and recycling these antioxidants, the overall capacity to

combat oxidative stress is enhanced. Antioxidants can help regulate the inflammatory response, which is often heightened in conditions of oxidative stress. By suppressing excessive inflammation, antioxidants can indirectly reduce the generation of ROS and minimize the overall oxidative burden on cells and tissues. Antioxidants can even support cellular repair mechanisms and facilitate tissue recovery from oxidative damage. They can promote the activation of repair enzymes and aid in the removal of damaged molecules. This can contribute to the restoration of normal cellular function and reduce the long-term impact of oxidative stress (Mao et al., 2016).

Astronauts definitely need antioxidants in space to counteract the harmful effects of increased radiation exposure and oxidative stress encountered during extended space missions. In the microgravity environment of space, astronauts are exposed to higher levels of cosmic radiation, which can generate free radicals in their bodies. These free radicals can damage cells and DNA, potentially leading to various health issues. Antioxidants, such as vitamins C and E, help neutralize these free radicals by donating electrons, reducing their potential harm (Mao et al., 2016).

### 7.6. Reduced immune response

#### 7.6.1. General immune response of the human body on earth

On Earth, the immune response consists of two primary components: the antibody-mediated immune response (also known as humoral immunity) and the cell-mediated immune response. The antibody-mediated immune response involves the production and action of antibodies, which are proteins produced by B cells (a type of lymphocyte). This response is particularly effective against extracellular pathogens, such as bacteria and viruses in the bloodstream or other body fluids (Green et al., 2021). This includes the following response sequence. B cells have receptors on their surface that can recognize specific antigens (proteins or other molecules on the surface of pathogens). When a B cell encounters its specific antigen, it becomes activated and undergoes differentiation. This process leads to the production of plasma cells, which are specialized B cells that secrete large quantities of antibodies. Antibodies produced by plasma cells bind to the antigens on the surface of pathogens, neutralizing them and marking them for destruction. The antibodies can activate other components of the immune system, such as complement proteins or phagocytes, to eliminate the pathogens (Green et al., 2021).

The cell-mediated immune response involves the action of T cells, another type of lymphocyte. This response is crucial for combating intracellular pathogens, such as viruses that infect host cells or cancer cells. The key steps in the cell-mediated immune response are a sequence. Antigen-presenting cells (APCs), such as macrophages, engulf pathogens and present pieces of the pathogens (antigens) on their surface. T cells have receptors that can recognize specific antigens presented by APCs. When a T cell encounters its specific antigen, it becomes activated. Activated T cells differentiate into various effector T cell types, such as cytotoxic T cells or helper T cells, depending on the type of antigen encountered. Cytotoxic T cells directly kill infected or abnormal cells by releasing toxic substances, while helper T cells assist other immune cells in coordinating the immune response (Zayzafoon et al., 2005).

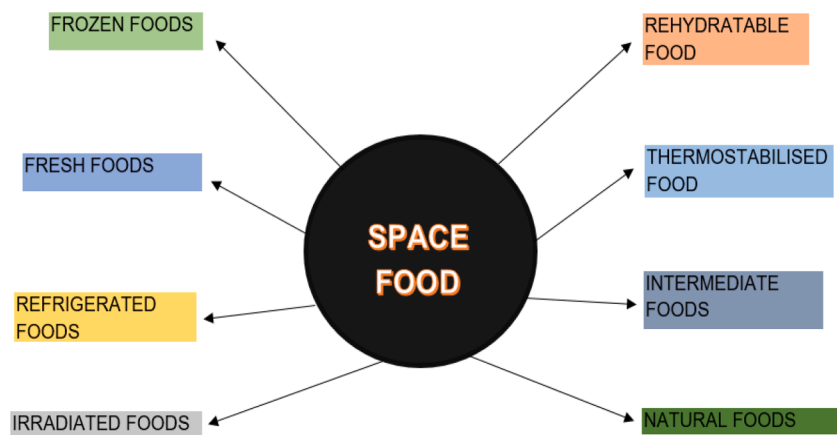
#### 7.6.2. Immune response of astronauts in space

The immune response that occurs in astronauts' bodies in space can be influenced by the unique conditions of the space environment, including microgravity, radiation exposure, and confinement. Microgravity can disrupt the signaling pathways that regulate immune cell activation and communication. This can lead to changes in immune cell function, such as impaired immune cell activation and reduced immune cell-to-cell interactions. Microgravity has been associated with decreased activity of immune cells, such as decreased production of certain cytokines (signaling molecules) and impaired phagocytosis (the ability of immune cells to engulf and destroy pathogens) (Zayzafoon

et al., 2005; Cogoli, 1993). Microgravity can even cause changes in the expression of genes related to immune function. This can affect the production of immune factors and the overall immune response. Since, astronauts are exposed to higher levels of radiation in space, which can have detrimental effects on the immune system. Radiation can directly damage immune cells and suppress immune function. This can lead to a weakened immune response, making astronauts more susceptible to infections and diseases. The confined environment of a spacecraft can also impact the immune response in astronauts. The reduced exposure to diverse microorganisms in space can affect the development and regulation of the immune system. This may result in alterations in immune cell populations and their functionality (Cogoli, 1993).

### 7.6.3. Ophthalmological issues

The fluid shift that occurs in microgravity leads to increased fluid pressure in the head, affecting the optic nerve and potentially causing vision disturbances. Additionally, the increased intracranial pressure experienced in microgravity can impact visual function. Astronauts may develop a condition called Visual Impairment and Intracranial Pressure Syndrome (VIIP), which involves changes in visual acuity, optic disc swelling, and other eye abnormalities. Microgravity can also induce corneal and refractive changes, leading to alterations in visual acuity (Mader et al., 2011). The exact mechanisms underlying this increase are



not yet fully understood but may involve alterations in cerebrospinal fluid dynamics (Mader et al., 2011; Aleci, 2020). VIIP is characterized by changes in visual acuity, flattening of the back of the eyeball (posterior globe flattening), optic disc swelling, and other ophthalmic abnormalities. VIIP is believed to be linked to fluid shifts, altered blood flow regulation, and changes in cerebrospinal fluid dynamics associated with microgravity (Aleci, 2020).

## 8. Types of space foods in the earlier decades

In the early days of space exploration, the historical space foods had several unique characteristics and challenges. The variety of space foods was relatively limited compared to the wide array of options available today (Douglas, et al., 2020; Kumar & Gaikwad, 2023). Mercury-Atlas Program (1961–1963): Mercury astronauts ate bite-sized cubes of food compressed into aluminum tubes. These tubes contained items like pureed beef, vegetables, and fruit. Applesauce was also provided in a squeezable tube for easy consumption in microgravity (Kumar & Gaikwad, 2023). Gemini Program (1965–1966): Gemini astronauts had a wider variety of bite-sized cubes, including beef, vegetables, and fruit. They had access to a range of beverages like coffee, tea, and fruit juices (Kumar & Gaikwad, 2023). Apollo Program (1968–1972): Apollo astronauts could rehydrate their food by adding water. Meals included

shrimp cocktail, chicken and vegetables, and beef and gravy. They had bite-sized snacks like dried fruits, nuts, and candy-coated chocolates. (Kumar & Gaikwad, 2023). Skylab Program (1973–1974): Skylab astronauts had better packaging that allowed for easier rehydration and improved food quality. They had access to a wider range of meals, including bacon squares, scrambled eggs, chicken and rice, steak, and even special meals for holidays (Kumar & Gaikwad, 2023).

## 9. Recent developments in the space foods

Space missions can have a significant impact on astronauts' health, including changes in bone density, muscle loss, hormonal imbalances, and immune system functioning. Developing advanced space food ensures that astronauts receive adequate nutrition to support their physical health and well-being during space travel. Proper nutrition is essential for optimal cognitive function, concentration, and performance. Space missions can be mentally and emotionally demanding (Grover et al., 2022). Advances in space food can provide options for individuals with specific dietary needs, such as vegetarian, vegan, or gluten-free diets. Ensuring the safety and longevity of space food is crucial for successful missions. Advanced packaging and preservation techniques can extend the shelf life of food, maintain its nutritional integrity, and minimize the risk of contamination or spoilage (Grover et al., 2022).

Types of Space food for the Astronauts (Akbar, 2019).

## 10. Space food is divided into eight categories (Gustafson et al., 2013)

### 10.1. Rehydratable food

Rehydratable space food refers to food products that are specifically designed to be rehydrated with water before consumption. Rehydratable space food typically comes in the form of dehydrated or freeze-dried meals (Jiang et al., 2020). These meals undergo a process where the water content is removed, leaving behind lightweight and compact food items. To prepare the food for consumption, astronauts add a specific amount of water to the meal, allowing it to rehydrate and regain its original texture and flavor (Jiang et al., 2020; Cooper & Douglas, 2011). The water used for rehydration is carefully controlled and provided in limited quantities to prevent excessive waste or excessive moisture accumulation in the spacecraft environment. Rehydratable food reduces the weight and volume of food during transportation, making it more efficient in terms of resource utilization and storage. Additionally, rehydration helps to restore the original texture and taste of the food, enhancing its palatability and providing a more satisfying eating experience for astronauts (Cooper & Douglas, 2011).

### 10.2. Thermo-stabilized food

Thermo-stabilized space food refers to a type of packaged food that is heat-treated and sterilized to ensure its safety, extend its shelf life, and withstand the challenging environmental conditions of space travel. Unlike rehydratable space food, thermo-stabilized meals are ready to eat without the need for additional preparation or rehydration. Thermo-stabilized space food goes through a rigorous thermal processing method such as retort sterilization or high-temperature short-time (HTST) processing (Varghese et al., 2014). It allows for long shelf life, reducing the need for frequent resupply missions. The food can withstand temperature fluctuations, extreme conditions, and the absence of gravity during space travel. It also eliminates the need for refrigeration or special storage requirements, simplifying logistics and resource management (Varghese et al., 2014; Hollender et al., 1970). Examples of thermo-stabilized space food include ready-to-eat meals like sandwiches, fruits, vegetables, meat, and dessert items. These meals are carefully formulated to provide balanced nutrition, meet dietary requirements, and ensure the astronauts receive the necessary sustenance for their space missions (Varghese et al., 2014; Hollender et al., 1970).

### 10.3. Intermediate moisture food

Intermediate moisture space food, also known as semi-moist space food, refers to a type of space food that has a moisture content between that of dry food and wet food. It falls in the middle of the spectrum in terms of water activity, which is the measure of water availability for microbial growth. Intermediate moisture space food is designed to have a longer shelf life compared to wet or perishable food, while still maintaining a soft and palatable texture (Voorhies et al., 2019).

The moisture content of intermediate moisture space food typically ranges from 15% to 45%, which provides a favorable environment for microbial control and inhibits the growth of bacteria, yeast, and mold. This is achieved through various preservation methods such as sugar or salt addition, pH adjustment, and packaging techniques that maintain a controlled atmosphere. The advantages of intermediate moisture space food include its extended shelf life, reduced weight and volume compared to wet food, and the ability to retain a desirable texture and flavor. It offers astronauts a wider variety of food options, including snacks, confectioneries, and other semi-moist food items that provide sensory satisfaction and contribute to their overall well-being during space missions (Cao, 2022).

### 10.4. Natural food

Natural form space food refers to food that is minimally processed and retains its original form, texture, and nutritional composition. It is designed to provide astronauts with a more natural and fresh food experience during space missions, resembling the food they would consume on Earth. Natural form space food focuses on preserving the inherent qualities of fresh food while ensuring its safety, stability, and suitability for consumption in a microgravity environment. This type of space food undergoes minimal processing steps to maintain its nutritional value and sensory attributes (Tang et al., 2021).

These foods are typically washed, sanitized, and packaged to maintain their freshness and prevent spoilage. Special packaging techniques, such as modified atmosphere packaging, are often used to extend the shelf life and preserve the quality of the food. Examples of natural form space food include fresh fruits, vegetables, nuts, and seeds that are carefully chosen for their nutritional content and suitability for space travel (Tang et al., 2021). These foods are rich in vitamins, minerals, fiber, and antioxidants, providing astronauts with a variety of essential nutrients necessary for their health and well-being (Tang et al., 2021).

### 10.5. Irradiated food

Irradiated space food refers to food that has undergone a process called food irradiation which involves exposing food to ionizing radiation, such as gamma rays, X-rays, or electron beams, to help control or eliminate harmful microorganisms, pests, and parasites that may be present in the food (Krzysztof & Aleksandra, 2022). Irradiated space food offers several advantages for space missions. It helps ensure the safety and quality of the food by reducing the risk of foodborne pathogens, spoilage microorganisms, and pests that could cause illness or spoilage during extended periods of storage. It also helps to extend the shelf life of the food, reducing the need for frequent resupply missions and enhancing the efficiency of space missions (Krzysztof & Aleksandra, 2022; Kim & Rhee, 2020).

### 10.6. Frozen food

Frozen space food are the meals and food items that are prepared and stored at extremely low temperatures to keep them frozen during space missions. In the context of space travel, frozen space food offers several advantages. First, freezing helps to inhibit the growth of microorganisms, including bacteria and molds, which can cause food spoilage and foodborne illnesses. By keeping the food frozen, the growth and activity of these microorganisms are significantly slowed down or halted (Watkins et al., 2022).

Second, freezing helps to preserve the taste, texture, and nutritional content of the food. It helps to retain the flavors and aromas of the ingredients, as well as the natural texture and appearance. Freezing also helps to retain the essential nutrients present in the food, ensuring that astronauts receive adequate nutrition during their missions (Watkins et al., 2022). When it is time for astronauts to consume the frozen space food, they follow specific instructions to rehydrate or reheat the meals using specialized equipment available on the spacecraft. This allows them to enjoy a variety of dishes, including entrees, desserts, and side dishes, while in the microgravity environment of space (Watkins et al., 2022).

### 10.7. Fresh food

Fresh space food refers to meals and food items that are consumed by astronauts during space missions and are prepared using fresh ingredients. Unlike other types of space food that undergo preservation methods like freezing or dehydration, fresh space food aims to provide astronauts with a more natural and enjoyable dining experience in space (Rahul, 2023). To ensure the freshness and quality of the ingredients, special packaging and storage methods are employed. For example, fresh produce may be packaged in sealed containers with controlled atmospheres to maintain their freshness and prevent spoilage. Astronauts utilize advanced technologies and systems, such as hydroponics or aeroponics, to grow plants and provide the necessary conditions for their cultivation. Fresh space food offers several benefits to astronauts (Rahul, 2023; Häuplik-Meusburger, 2014).

### 10.8. Refrigerated food

Unlike frozen space food, which is kept at much colder temperatures, refrigeration allows for a slightly higher temperature range that keeps the food chilled but not frozen. Refrigerated space food offers several advantages for astronauts (Charles, 1998). It helps to preserve the quality, taste, and nutritional value of the food while providing a wider variety of meal options compared to shelf-stable or rehydratable alternatives. Refrigeration helps to slow down the growth of microorganisms, such as bacteria and molds, that can cause food spoilage and pose health risks (Charles, 1998). These systems are designed to maintain a stable temperature range, typically between 2 °C and 4 °C (36 °F and 39 °F), to keep the food at a chilled state. The packaging of refrigerated space food



is designed to be lightweight, compact, and easy to handle in the microgravity environment of space (Charles, 1998).

### 11. Additional aspects and factors of consideration

Foods that are stored and eaten in the microgravity environment of space are specially designed to address the challenges posed by weightlessness. Various important factors are taken into consideration, such as the packaging, delivery of vitamins, concentration of nutrients, and ensuring a long shelf life for the food. These aspects are crucial to ensure that the food remains safe, nutritious, and enjoyable for astronauts during their space missions (Nishanth, 2023). The main goal is to provide astronauts with the necessary 2500 calories per day while maximizing the energy from fats. By increasing the caloric density of the foods and reducing the moisture content to 10%, it is possible to achieve a mass savings of approximately 22% (Nishanth, 2023; Paola & Martina, 2022). The shelf life of space food is of utmost importance during its production and storage. Research on shelf life has shown that canned thermo-stabilized food can last for up to three years. These foods were stored under different conditions: 50 percent relative humidity at 4.4 °C (control), 22 °C (storage temperature of actual flight food), and 35 °C (accelerated temperature) (Paola & Martina, 2022).

Among the food items, meat products were found to maintain their quality for the longest period, up to three years, even without refrigeration. Starches and vegetable side dishes, on the other hand, can maintain their quality for 1 to 4 years if not refrigerated (Paola & Martina, 2022). To ensure optimal performance of astronauts during space missions, it is crucial to provide them with the right amount and quality of nutrition. In space missions, fat-soluble vitamins are particularly important compared to water-soluble vitamins (Paola & Martina, 2022; Raut, et al., 2021). Among the vitamins, riboflavin, vitamin A, and vitamin C were found to degrade the most. To address this issue, encapsulated vitamin fortification or innovative methods of vitamin stabilization may be necessary (Raut et al., 2021). The packaging of space food, along with several other crucial factors, plays a vital role in the transportation and storage of food for long-duration space missions. The goal is to ensure that the quality of the food is maintained and that there is minimal degradation of vitamins and nutrients (Raut et al., 2021; Chaloulakou et al., 2022).

### 12. Opportunities in space food

Space food research presents an opportunity to develop highly nutritious meals that meet the specific dietary requirements of astronauts. This can lead to advancements in nutritional science and contribute to better health outcomes for space travelers. Creating space food involves unique culinary challenges. There is an opportunity to explore new cooking techniques, flavors, and food presentations, pushing the boundaries of culinary arts and expanding the gastronomic experience for astronauts (Enfield et al., 2022).

Developing sustainable food production systems for space missions can have broader implications for food production on Earth. Research in space food can help in optimizing resource usage, reducing waste, and developing efficient cultivation methods, which are crucial for sustainable agriculture. Space food research can contribute to food security efforts by developing techniques for growing food in extreme environments, such as arid regions or regions affected by climate change. (Enfield et al., 2022; Shukla, 2020).

### 13. Conclusion

Space food plays a crucial role in the success of space missions by providing astronauts with the necessary nutrition to support their health, well-being, and performance in the challenging conditions of space. One important aspect to consider is the biochemical changes that occur in the human body during space missions. Microgravity and other

factors in the space environment can lead to alterations in bone density, muscle activity, hormonal balance, digestion and absorption, iron metabolism, ophthalmological issues, immune response, and oxidative stress. Space food must be designed to counteract these effects and provide the necessary nutrients to support the astronauts' physiological functions. Different types of space foods have been developed to meet the specific needs of astronauts. These include rehydratable, thermo-stabilized, intermediate moisture, natural form, irradiated, frozen, fresh, and refrigerated options. The continuous improvement and innovation in space food technology are essential to address the challenges faced in providing nutritionally balanced meals in the unique environment of space.

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### Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

### Data availability

No data was used for the research described in the article.

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### References

- Akbar, H. (2019). Possible Malaysian contribution to future space food during long-duration space mission. *ASM Science*, 12, 162–171. [https://www.researchgate.net/publication/335060457\\_Possible\\_Malaysian\\_Contribution\\_to\\_Future\\_Space\\_Food\\_during\\_Long-duration\\_Space\\_Mission](https://www.researchgate.net/publication/335060457_Possible_Malaysian_Contribution_to_Future_Space_Food_during_Long-duration_Space_Mission).
- Aleci, C. (2020). From international ophthalmology to space ophthalmology: The threats to vision on the way to Moon and Mars colonization. *International Ophthalmology*, 40, 775–786. <https://doi.org/10.1007/s10792-019-01212-7>
- Aleksey, B., Elena, S. B., Ekaterina, P., & Polina, R. (2021). The current state and future trends of space nutrition from a perspective of astronauts' physiology. *International Journal of Gastronomy and Food Science*, 24, Article 100324. <https://doi.org/10.1016/j.ijgfs.2021.100324>
- Amidon, G. L., Gary, A., & DeBrincat, N. N. (1991). Effects of gravity on gastric emptying, intestinal transit, and drug absorption. *Journal of Clinical Pharmacology*, 31, 968–973.
- Aubert, A. E., Frank, B., & Bart, V. (2005). Cardiovascular function and basics of physiology in microgravity. *Acta Cardiologica*, 6, 129–151. <https://doi.org/10.2143/AC.60.2.2005024>
- Bourland, C. T. (1993). The development of food systems for space. *Trends in Food Science and Technology*, 4, 271–276. [https://doi.org/10.1016/0924-2244\(93\)90069-M](https://doi.org/10.1016/0924-2244(93)90069-M)
- Cao, X. (2022). Research progress on the effects of microgravity and space radiation on astronauts' health and nursing measures. *Open Astronomy*, 31, 300–309. <https://doi.org/10.1515/astro-2022-0038>
- Cazenave, A., & Jianli, C. (2010). Time-variable gravity from space and present-day mass redistribution in the Earth system. *Earth and Planetary Science Letters*, 298, 263–274. <https://doi.org/10.1016/j.epsl.2010.07.035>
- Chaloulakou, S., Kalliopi, A. P., & Dimitrios, K. (2022). Physiological alterations in relation to space flight: The role of nutrition. *Nutrients*, 14, 4896. <https://doi.org/10.3390/nu14224896>
- Charles, T. (1998). Advances in food systems for space flight. *Life Support & Biosphere Science*, 5, 71–77. <https://pubmed.ncbi.nlm.nih.gov/11540467/>.
- Chen, X., et al. (2019). Iron overload as a high risk factor for microgravity-induced bone loss. *Acta Astronautica*, 164, 407–414. <https://doi.org/10.1016/j.actastro.2019.07.034>
- Cogoli, A. (1993). Space flight and the immune system. *Vaccine*, 11, 496–503. [https://doi.org/10.1016/0264-410X\(93\)90217-L](https://doi.org/10.1016/0264-410X(93)90217-L)
- Cooper, M., & Douglas, P. M. (2011). Developing the NASA food system for long-duration missions. *Journal of Food Science*, 76:R40–R48. doi: 10.1111/j.1750-3841.2010.01982.x.

- Douglas, G. L., Wheeler, R. M., & Fritsche, R. F. (2021). Sustaining astronauts: Resource limitations, technology needs, and parallels between spaceflight food systems and those on Earth. *Sustainability Science*, 13, 9424. <https://doi.org/10.3390/su13169424>
- Douglas, G. L., Zwart, S. R., & Smith, S. M. (2020). Space food for thought: Challenges and considerations for food and nutrition on exploration missions. *Journal of Nutrition*, 150(9), 2242–2244. <https://doi.org/10.1093/jn/nxaa188>
- Emily, M. H. (2003). *The impact of gravity on life. Evolution on planet Earth* (pp. 143–159). Academic Press. DOI:10.1016/B978-012598655-7/50036-7.
- Enfield, R., et al. (2022). The future of 3D food printing: Opportunities for space applications. *Critical Reviews in Food Science and Nutrition*, 4, 1–14. <https://doi.org/10.1080/10408398.2022.2077299>
- Felice, J. V. (2021). Aging-like metabolic and adrenal changes in microgravity: State of the art in preparation for Mars. *Neuroscience and Biobehavioral Reviews*, 126, 236–242. <https://doi.org/10.1016/j.neubiorev.2021.01.028>
- Fitts, R. H., Danny, R., & Riley, J. JW. (2001). Functional and structural adaptations of skeletal muscle to microgravity. *Journal of Experimental Biology*, 204, 3201–3208. <https://doi.org/10.1242/jeb.204.18.3201>
- Gary, A. P., Robert, D. H., & Bruce, A. M. (1996). Time, space, and life history: Influences on food webs. *Food Webs: Integration of Patterns & Dynamics*, 435–460. [https://doi.org/10.1007/978-1-4615-7007-3\\_38](https://doi.org/10.1007/978-1-4615-7007-3_38)
- Green, M. J., et al. (2021). Immunity in space: Prokaryote adaptations and immune response in microgravity. *Life*, 11, 112. <https://doi.org/10.3390/life11020112>
- Grimm, D., et al. (2016). The impact of microgravity on bone in humans. *Bone*, 87:44–56. <https://doi.org/10.1016/j.bone.2015.12.057>
- Grover, Y., et al. (2022). Developments and scope of space food. *Current Nutrition & Food Science*, 8, 248–258. <https://doi.org/10.2174/1573401317666210809113956>
- Gustafson, A., Christian, J. W., Lewis, S., Moore, K., & Jilcott, S. (2013). Food venue choice, consumer food environment, but not food venue availability within daily travel patterns are associated with dietary intake among adults, Lexington Kentucky 2011. *Nutrition Journal*, 12, 17. <https://doi.org/10.1186/1475-2891-12-17>
- Häuplik-Meusburger, S. (2014). Astronauts orbiting on their stomachs: The needs to design for the consumption and production of food in space. *Architectural Design*, 84: 114–117. <https://doi.org/10.1002/ad.1841>
- Heer, M., et al. (1999). Calcium metabolism in microgravity. *European Journal of Medical Research*, 4, 357–360. <https://doi.org/10.3390/nu4122047>
- Hollender, H. A., Klicka, M. V., & Smith, M. C. (1970). Food technology problems related to space feeding. *Life Sciences and Space Research*, 8, 265–279. <https://pubmed.ncbi.nlm.nih.gov/11826888/>
- Horeau, M., et al. (2022). Iron metabolism regulation in females and males exposed to simulated microgravity: Results from the randomized trial Artificial Gravity Bed Rest—European Space Agency (AGBRESA). *The American Journal of Clinical Nutrition*, 116, 1430–1440. <https://doi.org/10.1093/ajcn/nqac205>
- Jiang, J., et al. (2020). Current processing and packing technology for space foods: A review. *Critical Reviews in Food Science and Nutrition*, 60, 3573–3588. <https://doi.org/10.1080/10408398.2019.1700348>
- Junaid, A. P., Somya, N., Saghir, A., & Rayees, A. S. (2023). Recent developments in space food for exploration missions: A review. *Life Sciences and Space Research*, 36, 123–124. <https://doi.org/10.1016/j.lssr.2022.09.007>
- Kassemi, M., & David, T. (2016). Prediction of renal crystalline size distributions in space using a PBE analytic model. 1. Effect of microgravity-induced biochemical alterations. *American Journal of Physiology-Renal Physiology*, 311, F520–F530. <https://doi.org/10.1152/ajprenal.00401.2015>
- Kennedy, A. R., Guan, J., & Ware, J. H. (2007). Countermeasures against space radiation induced oxidative stress in mice. *Radiation and Environmental Biophysics*, 46, 201–203.
- Kerwin, J., & Seddon, R. (2002). Eating in space—from an astronaut's perspective. *Nutrition*, 18, 921–925. [https://doi.org/10.1016/s0899-9007\(02\)00935-8](https://doi.org/10.1016/s0899-9007(02)00935-8)
- Kim, H. W., & Rhee, M. S. (2020). Space food and bacterial infections: Realities of the risk and role of science. *Trends in Food Science and Technology*, 106, 275–287. <https://doi.org/10.1016/j.tifs.2020.10.023>
- Krzysztof, L., & Aleksandra, S. (2022). What food will we be eating on our journey to Mars? *Biotechnology and Biotechnological Equipment*, 36, 165–175. <https://doi.org/10.1080/13102818.2022.2060135>
- Kumar, L., & Gaikwad, K. K. (2023). Advanced food packaging systems for space exploration missions. *Life Science Space Research (Amsterdam)*, 37, 7–14. <https://doi.org/10.1016/j.lssr.2023.01.005>
- Lane, H. W., Smith, S. M., Rice, B. L., & Bourland, C. T. (1994). Nutrition in space: Lessons from the past applied to the future. *American Journal of Clinical Nutrition*, 60 (5), 801S–805S. <https://doi.org/10.1093/ajcn/60.5.801S>
- Mader, T. H., et al. (2011). Optic disc edema, globe flattening, choroidal folds, and hyperopic shifts observed in astronauts after long-duration space flight. *Journal of Ophthalmology*, 118, 2058–2069. <https://doi.org/10.1016/j.optha.2011.06.021>
- Man, J., et al. (2022). The effects of microgravity on bone structure and function. *NPJ Microgravity*, 8:9. <https://doi.org/10.1038/s41526-022-00194-8>
- Mao, X. W., et al. (2016). Simulated microgravity and low-dose/low-dose-rate radiation induces oxidative damage in the mouse brain. *Radiation Research*, 185:647–657. <https://doi.org/10.1667/RR14267.1>
- Milojevic, T., & Weckwerth, W. (2020). Molecular mechanisms of microbial survivability in outer space: A systems biology approach. *Frontiers in Microbiology*, 15, 923. <https://doi.org/10.3389/fmicb.2020.00923>
- Nagaraja, M. P., & Diana, R. (2013). The current state of bone loss research: Data from spaceflight and microgravity simulators. *Journal of Cellular Biochemistry*, 114, 1001–1008. <https://doi.org/10.1002/jcb.24454>
- Nay, K., et al. (2020). Simulated microgravity disturbs iron metabolism and distribution in humans: Lessons from dry immersion, an innovative ground-based human model. *FASEB Journal*, 34, 14920–14929. <https://doi.org/10.1096/fj.202001199RR>
- Nguyen, H. P., et al. (2021). The effects of real and simulated microgravity on cellular mitochondrial function. *npj Microgravity*, 7, 44. <https://doi.org/10.1038/s41526-021-00171-7>
- Nishanth, M. (2023). Space food technology: Historical background, present prospective and future aspects. <https://www.thepharmajournal.com/archives/?year=2023&vol=12&issue=5&ArticleId=20336>
- Obirst, M., et al. (1993). Space food experiences: Designing passenger's eating experiences for future space travel scenarios. *Frontiers of Computer Science*, 1, 3. <https://doi.org/10.3389/fcomp.2019.00003>
- Oluwafemi, F. A., et al. (2018). Space food and nutrition in a long term manned mission. *Advances in Astronautics Science and Technology*, 1, 1–21. <https://doi.org/10.1007/s42423-018-0016-2>
- Oluwafemi, F. A., et al. (2021). A review of astronaut mental health in manned missions: Potential interventions for cognitive and mental health challenges. *Life Sciences in Space Research (Amsterdam)*, 8, 26–31. <https://doi.org/10.1016/j.lssr.2020.12.002>
- Paola, P., & Martina, H. (2022). Space food for the future: Nutritional challenges and technological strategies for healthy and high-quality products. *In-Space Manufacturing and Resources: Earth and Planetary Exploration Applications*, 34, 251–268. <https://doi.org/10.1002/9783527830909.ch13>
- Perchonok, M., & Charles, B. (2002). NASA food systems: past, present, and future. *Nutrition*, 18, 913–920. [https://doi.org/10.1016/s0899-9007\(02\)00910-3](https://doi.org/10.1016/s0899-9007(02)00910-3)
- Rahul, W. (2023). Evolution of space food, category, challenges and packaging. *Journal of Pharmaceutical Innovation*, 12:1233-1244. <https://www.thepharmajournal.com/archives/2023/vol12issue6/PartO/12-5-284-846.pdf>
- Ronca, A. E., Baker, E. S., Bavendam, T. G., Beck, K. D., Miller, V. M., Tash, J. S., et al. (2014). Effects of sex and gender on adaptations to space: Reproductive health. *Journal of Women's Health*, 23, 967–974. <https://doi.org/10.1089/jwh.2014.4915>
- Satoshi, I., Naoki, N., Kunihiko, T., & Tadaaki, M. (2019). Effects of microgravity on human physiology. Beyond LEO- human health issues for deep space exploration. *IntechOpen*. DOI: 10.5772/intechopen.90700.
- Schneider, S., et al. (2015). Feasibility of monitoring muscle health in microgravity environments using Myoton technology. *Medical & Biological Engineering & Computing*, 53, 57–66. <https://doi.org/10.1007/s11517-014-1211-5>
- Shukla, A. D. (2020). Space foods: The food for zero gravity. *Agri Mirror: Future India*, 1: 70-79. <https://aiasa.org.in/wp-content/uploads/2020/09/15.pdf>
- Smith, S. M. (2002). Red blood cell and iron metabolism during space flight. *Nutrition*, 18, 864–866. [https://doi.org/10.1016/s0899-9007\(02\)00912-7](https://doi.org/10.1016/s0899-9007(02)00912-7)
- Tang, H., et al. (2021). Long-term space nutrition: A scoping review. *Nutrients*, 14, 194. <https://doi.org/10.3390/nu14010194>
- Taylor, A. J., et al. (2020). Factors affecting flavor perception in space: Does the spacecraft environment influence food intake by astronauts? *Comprehensive Reviews in Food Science and Food Safety*, 19, 3439–3475. <https://doi.org/10.1111/1541-4337.12633>
- Tesei, D., Jewczynko, A., Lynch, A. M., & Urbaniak, C. (2022). Understanding the complexities and changes of the astronaut microbiome for successful long-duration space missions. *Life*, 12(4), 495. <https://doi.org/10.3390/life12040495>
- Tian, Y., et al. (2017). The impact of oxidative stress on the bone system in response to the space special environment. *International Journal of Molecular Sciences*, 18, 2132. <https://doi.org/10.3390/ijms18102132>
- Varghese, K. S., et al. (2014). Technology, applications and modelling of ohmic heating: A review. *Journal of Food Science & Technology*, 51:2304-2317. <https://doi.org/10.1007/s13197-012-0710-3>
- Voorhies, A. A., Mark, O., Mehta, S., et al. (2019). Study of the impact of long-duration space missions at the International Space Station on the astronaut microbiome. *Scientific Reports*, 9, 9911. <https://doi.org/10.1038/s41598-019-46303-8>
- Watkins, P., et al. (2022). Long term food stability for extended space missions: A review. *Life Sciences and Space Research*, 32, 79–95. <https://doi.org/10.1016/j.lssr.2021.12.003>
- West, J. B. (2000). Historical perspectives: Physiology in microgravity. *Journal of Applied Physiology*, 89, 379–384. <https://doi.org/10.1152/jappp.2000.89.1.379>
- Yang, J.-Q., et al. (2020). The effects of microgravity on the digestive system and the new insights it brings to the life sciences. *Life Sciences and Space Research*, 27, 74–82. <https://doi.org/10.1016/j.lssr.2020.07.009>
- Zayzafoom, M., Valerie, E. M., & Jay, M. (2005). Microgravity: The immune response and bone. *Immunological Reviews*, 208, 267–280. <https://doi.org/10.1111/j.0105-2896.2005.00330.x>
- Zheng, H., Qiong, F. H., & Le, J. (2015). Higher plants in space: Microgravity perception, response, and adaptation. *Microgravity Science and Technology*, 27, 377–386. <https://doi.org/10.1007/s12217-015-9428-y>