World Journal of Biology Pharmacy and Health Sciences
eISSN: 2582-5542
Cross Ref DOI: 10.30574/wjbphs
Journal homepage: https://wjbphs.com/

(Review Article)

Microgravity-Induced Alterations in Drug Pharmacokinetics: Implications for Space Medicine

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World Journal of Biology Pharmacy and Health Sciences, , 2026, 27(01), 127–130

Publication history: Received on 13 June 2026; revised on 18 July 2026; accepted on 21 July 2026

Article DOI: https://doi.org/10.30574/wjbphs.2026.27.1.0397

Abstract

Space flight poses distinct challenges for human physiology and environment that might result in significant changes in pharmacokinetics (PK) of drugs that could affect safety and efficacy of pharmacotherapy in space. Microgravity causes alteration in body fluid shifts, cardiovascular system, gastroenterology, liver, kidney and body composition function thus affecting processes of drug absorption, distribution, metabolism and elimination (ADME). Moreover, space radiation and drug storage can impair the stability of the drugs thus affecting performance of the medications. The purpose of the current review is to explore the influence of microgravity on the pharmacokinetics of drugs and to evaluate the implications of this effect for pharmacotherapy during human space flight based on space flight, analogs, and recent research findings. Existing research indicates that space flight-related adaptation may result in clinically meaningful changes in the PK of the drugs; however, the magnitude of this impact is unknown because of limited data from human space flight as well as methodological variability in the available studies.

Keywords: Microgravity; Pharmacokinetics; Space flight; Absorption; Distribution; Metabolism; Elimination

1. Introduction

As the progress in human exploration of space increases, including plans for long-term missions on the Moon and Mars, there is a growing need for the development of efficient healthcare measures ensuring astronauts health and mission success. The use of medications in order to prevent and treat not only common but also specific space related conditions is very important; yet, the unique conditions of space can affect their effectiveness. One of the challenges associated with the use of medications in space and which can influence their efficiency is related to microgravity, which affects human physiology in many ways. The exposure to microgravity leads to many changes in physiology in such systems as cardiovascular system, gastrointestinal system, liver, kidneys, musculoskeletal system, and immune system, resulting in alterations in body fluids distribution, organ perfusion, and metabolism. These physiological changes may influence pharmacokinetics (PK) of medications, including their absorption, distribution, metabolism, and elimination (ADME). Also, the long-term storage under conditions of spaceflight and exposure to ionizing radiation can lead to loss of drug stability, and, therefore, it is important to learn about the behavior of medications in the space environment.

Even with increased attention towards the discipline of space pharmacology, information on how microgravity affects drug pharmacokinetics is scanty because of the few studies done during flights and the use of ground analogs and animal models. Research shows that the physiological adjustments associated with microgravity may affect the pharmacokinetics of various drugs; however, their extent and clinical significance are still unclear. It is imperative to understand these drug changes to ensure development of evidence-based dose adjustment regimens, guarantee medication stability, reduce adverse drug effects, and promote individualized medicine in astronauts on long space

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missions. The purpose of this narrative review paper is to evaluate the available evidence on the effect of microgravity on drug pharmacokinetics and assess its clinical implications to astronaut medication during flights.

2. Literature search strategy

The search for scientific literature was carried out using PubMed as a source of scientific articles concerning the influence of microgravity on pharmacokinetics of drugs used in manned space flights. The period of searching the literature was from January 2015 to June 2025, and the literature search was limited to English articles. For the search in PubMed the Medical Subject Headings (MeSH) terms and key words such as microgravity, spaceflight, human spaceflight, pharmacokinetics, drug absorption, drug distribution, drug metabolism, drug excretion, ADME, drug stability, astronauts, and space medicine were used. The articles selected were screened using their titles and abstracts and then read in their full texts. The scientific literature included all original research articles, clinical trials, observational studies, reviews, guidelines, and experts' opinions about the effect of microgravity on the pharmacokinetics of drugs in human space flight. Animal experiments, in vitro studies, conference papers without full texts, duplicate articles, articles in other languages, and unrelated to the issue of pharmacokinetics in space articles were not used.

3. Effect of Microgravity on Drug Pharmacokinetics and Its Implications for Space Medicine

3.1. Overview

Microgravity can be considered one of the main features of the space environment and affects human physiology in a way that can considerably influence drug pharmacokinetics (PK). Spaceflights lead to fluid shifts toward the head, decreased plasma volume, cardiovascular deconditioning, modification of the function of the gastrointestinal tract, modification of the physiological processes of the liver and kidneys, musculoskeletal atrophy, and the immune system. They affect the processes of drug absorption, distribution, metabolism, and excretion (ADME), thus affecting the drug exposure, effectiveness, and safety. With regard to planning prolonged flights to the Moon and Mars by space agencies, pharmacokinetic changes have to be understood in order to provide appropriate pharmacotherapy in the conditions of space medicine, when medication is limited and cannot be resupplied quickly.

3.1.1. Effect of Microgravity on Drug Absorption

Drug absorption is the first step in the pharmacokinetics which can be affected by microgravity. The absorption of drugs through the oral route requires the normal functioning of the processes of gastric emptying, intestinal motility, and splanchnic circulation along with the appropriate gastric pH. Changes in the physiology of the gastrointestinal system, including gastric emptying delay, decreased intestinal transit and changes in the splanchnic circulation caused by space flight conditions can affect the speed and the degree of drug absorption. In this case, the drugs can demonstrate their delayed effect, low bioavailability or increased variation between individuals in particular when using these drugs in the conditions of acute medical emergency situations, for example antiemetics, analgesics and antibiotics.

3.1.2. Effect of Microgravity on Drug Distribution

Physiological effects caused by microgravity play a major role in drug distribution. First, the cephalad shift of body fluids and a decrease in blood volume will affect the fluid compartments in the body as well as tissue perfusion, which could impact the volume of distribution of both hydrophilic and lipophilic drugs. Second, exposure to microgravity leads to muscle atrophy, loss of bone mass, and changes in body composition that may affect the distribution of drugs in the tissues and their protein binding in plasma.

3.1.3. Effect of Microgravity on Drug Metabolism

Drug metabolism might change while traveling through space due to alterations in the blood flow of the liver, oxidative stress, disruption in circadian rhythm, and regulation of hepatic drug-metabolizing enzymes. Despite the fact that there is not much scientific data about changes in CYP450 activity, the above-mentioned factors might affect metabolism and generation of either active or non-active metabolites of drugs. This might result in a reduction in drug efficiency and inter-individual differences, which calls for more research in this sphere.

3.1.4. Effect of Microgravity on Drug Excretion

Drugs' elimination is still one more pharmacokinetic process that is influenced by microgravity. Space travel affects the renal blood flow, body fluid volume, GFR, renal tubular functions, and electrolyte balance. Cephalad fluid shift at the initial stage results in enhanced diuresis and fluid reduction of plasma volume. However, on the contrary, prolonged spaceflights contribute to renal adaptation, which may influence the excretion of renally eliminated drugs. Thus, changes in renal clearance of drugs will result in drug accumulation or reduced concentrations of drugs, particularly renally eliminated drugs.

3.1.5. Pharmaceutical Stability in the Space Environment

Apart from changes in physiology that impact pharmacokinetics, there are unique problems associated with drugs in outer space. Ionizing radiation, microgravity, vibrations during takeoff, variations in temperature, and extended storage periods can lead to instability of medications and their loss of effectiveness and even degradation. As astronauts depend on limited reserves of medicines available on board, having few opportunities for resupply during long missions, the preservation of drug quality is an essential consideration for any space mission plan.

3.1.6. Clinical Implications for Space Medicine

Although the field of space pharmacology is gaining more attention, there still exist several knowledge gaps related to the impact of microgravity on pharmacokinetics of medications. Most information is gained from analogs on Earth, experiments with animals, or studies conducted with a small number of astronauts, making it not applicable for long-term space flights. For future research, there is a need to conduct in-flight pharmacokinetic studies, develop standard experiments, and research the effect of microgravity in combination with other factors such as space radiation, disrupted circadian rhythm, and genotypic differences on drug disposition. Innovations such as pharmacogenomics, AI-assisted dose calculation, therapeutic drug monitoring in real-time, PBPK modeling, and specialized space medication formulas will definitely be used in the future to implement personalized medicine and ensure safe pharmacotherapy.

3.1.7. Future Perspectives and Research Needs

While there is much more attention paid to space pharmacology nowadays, still much is unknown about the influence of microgravity on the pharmacokinetics of drugs. Some of the recent works have studied the area of depharmacogenomics, artificial intelligence-assisted dose optimization, real-time therapeutic drug monitoring, physiologically-based pharmacokinetics (PBPK), and even space-specific pharmaceutical formulations—all of which will be crucial for the further development of personalized medicine and drug administration under microgravity. Some of the new approaches, such as pharmacogenomics, artificial intelligence-assisted dose optimization, real-time therapeutic drug monitoring, physiologically-based pharmacokinetics (PBPK), and space-specific pharmaceutical formulations, will be crucial for the further development of personalized medicine and drug administration under microgravity.

4. Discussion

The results of the reviewed literature suggest that microgravity causes many physiological changes that can affect every aspect of pharmacokinetics of a drug, such as its absorption, distribution, metabolism, and elimination (ADME). Changes in the functioning of the gastrointestinal tract, headward movement of body fluids, decreased plasma volume, altered function of the liver and kidneys, and musculoskeletal changes may all play a role in causing variability in drug pharmacokinetics in microgravity. Moreover, the special nature of space flight environment, the ionizing radiation present in space, and long-term storage conditions can affect the stability and efficiency of the drug, thus creating an additional challenge for pharmacological treatment in space. However, the extent of these pharmacokinetic changes is unknown due to lack of human studies conducted during flights.

The above-mentioned changes in the drug pharmacokinetics have significant clinical importance for the astronauts, especially when it comes to prolonged missions in which medical supplies are scarce and any resupply or emergency evacuation is impossible. The change in the pharmacodynamics of drugs can cause delays in therapy onset, decreased efficiency of treatment, and increase in adverse effects, especially concerning medications prescribed for treating various infections, cardiovascular disorders, pain, motion sickness, and other emergencies. Thus, the impact of microgravity on the drug pharmacokinetics should be considered when choosing appropriate medication, dose adjustment, and storing medicines in space.

Even though there is significant progress in space pharmacology, many gaps still exist in the field of the influence of microgravity on drug pharmacokinetics in humans. The following research should aim at performing pharmacokinetic studies under microgravity conditions using a wider astronaut sample and various medicines. Moreover, studying the impact of all the above-mentioned factors on the behavior of drugs in space will give a better insight into this issue. This will help develop evidence-based guidelines for space medication, space-friendly forms of drugs, and personalized pharmacotherapy, which will promote the well-being of astronauts and success of future space flights to the Moon, Mars, and other planets.

5. Conclusion

However, microgravity leads to different physiological changes that have the potential of influencing pharmacokinetic changes through the ADME process, whereas the unique characteristics of the space environment may lead to changes in the stability and effectiveness of the drugs. Nevertheless, considering the existing evidence, it is evident that the present knowledge on the influence of the above-mentioned changes on the use of drugs in human spaceflight is limited due to the few human studies conducted in-flight and due to the differences in methodology used by the previous researchers. In view of the future plans to carry out spaceflights to other planets such as the Moon and Mars, pharmacotherapy will be instrumental in ensuring the well-being of astronauts during missions. This narrative review is meant to demonstrate the importance of studying the effects of microgravity on pharmacokinetics in order to ensure proper drug selection, dosing schedules, and development of new drugs that can be taken in space. The main areas of future study include conducting pharmacokinetic tests in-flight, assessing the stability of the drugs in the space environment, and integrating the concepts of pharmacogenomics and therapeutic drug monitoring and drug delivery systems.

Compliance with ethical standards

Disclosure of Conflict of Interest

No conflict of interest to be disclosed.

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