Clinical Pharmacology & Biopharmaceutics

Hypothesis Open Access

Applications of Microdosing in Clinical Pharmacology: A Step Toward Personalized Medicine and Accelerated Drug Development

Birhanu Tabo*

International Crops Research Institute for the Semi-Arid Tropics (ICRISAT), Nigeria

Abstract

Microdosing, the practice of administering sub-therapeutic doses of a drug to study its pharmacokinetics, pharmacodynamics, and safety profile, has emerged as a promising tool in clinical pharmacology. It offers a unique approach to understanding drug behavior in humans without exposing participants to the risks associated with higher doses. This approach has the potential to significantly accelerate drug development by enabling early-phase clinical testing, optimizing dose selection, and providing valuable data for personalized medicine. Microdosing allows researchers to gather crucial information on drug interactions, absorption, distribution, metabolism, and excretion (ADME), while also minimizing costs and time in the early stages of clinical trials. This review discusses the applications of microdosing in clinical pharmacology, its role in personalized medicine, and its potential to streamline drug development processes.

Keywords: Microdosing; Clinical pharmacology; Personalized medicine; Drug development; Pharmacokinetics; Pharmacodynamics; Drug safety; Early-phase clinical trials; ADME; Dose optimization; Drug interactions.

Introduction

Microdosing has gained significant attention in clinical pharmacology as an innovative method for studying drugs at very low doses, often sub-therapeutic, to understand their pharmacokinetic and pharmacodynamic profiles. Unlike traditional clinical trials, where higher, therapeutic doses are tested, microdosing involves administering doses that are too low to elicit any pharmacological effects but are sufficient to study the drug's behavior in the body. This approach offers researchers the unique ability to gather critical information on absorption, distribution, metabolism, and excretion (ADME) in humans early in the drug development process [1,2].

In clinical pharmacology, understanding how a drug behaves in the human body is crucial for determining its safety, efficacy, and optimal dosing regimen. Microdosing allows for the early assessment of these factors without exposing participants to the risks associated with higher doses. By using cutting-edge analytical techniques, such as accelerator mass spectrometry (AMS) and liquid chromatography-mass spectrometry (LC-MS), researchers can detect and measure trace amounts of drugs and their metabolites in blood, urine, or other biological samples. This enables the collection of pharmacokinetic data in human subjects even before significant clinical effects are observed.

One of the most compelling advantages of microdosing is its potential to expedite the drug development process. Traditionally, drug development involves long, costly clinical trials, often with uncertain outcomes. By using microdosing in early-stage clinical trials, researchers can make faster, more informed decisions about whether a drug candidate is worth pursuing in later phases of development. This not only saves time and resources but also helps identify potential safety concerns before escalating to higher doses.

Another important aspect of microdosing is its potential to contribute to personalized medicine. Personalized medicine focuses on tailoring medical treatments to individual patients based on their genetic, environmental, and lifestyle factors. Microdosing can be an essential tool in identifying inter-individual variability in drug metabolism and response, helping to optimize drug dosing for specific populations. By understanding how different individuals process a drug at the microdosing stage, personalized treatment strategies can be developed, minimizing adverse effects and improving therapeutic outcomes [3].

Microdosing also holds promise for evaluating drug interactions and conducting bioequivalence studies, which are critical for the development of generic drugs. Since microdosing studies provide reliable pharmacokinetic data, they can be used to assess the bioavailability of different formulations or compare the pharmacokinetics of the test drug to an approved reference product. This is especially valuable in regulatory submissions, where demonstrating the similarity of a new drug to an existing one is a key requirement.

Despite its growing popularity, microdosing is not without its challenges. The interpretation of microdosing data requires sophisticated analytical tools and a solid understanding of pharmacokinetics. Moreover, while microdosing studies are generally considered safe, they may not fully replicate the effects of therapeutic doses, particularly in populations with altered physiology, such as those with liver or kidney disease. Nonetheless, the ability to conduct early-phase clinical trials in a more controlled and efficient manner has made microdosing an invaluable asset in modern drug development.

In this paper, we will explore the applications of microdosing in clinical pharmacology, with a focus on its role in personalized medicine and its potential to accelerate drug development. By reviewing recent

***Corresponding author:** Birhanu Tabo, International Crops Research Institute for the Semi-Arid Tropics (ICRISAT), Nigeria, E-mail: birhanutabo123@gmail.com

Received: 01-Nov-2024, Manuscript No: cpb-24-155466, **Editor Assigned:** 05-Nov-2024, Pre QC No: cpb-24-155466 (PQ), **Reviewed:** 15-Nov-2024, QC No: cpb-24-155466, **Revised:** 25-Nov-2024, Manuscript No: cpb-24-155466 (R), **Published:** 29-Nov-2024, DOI: 10.4172/2167-065X.1000512

Citation: Birhanu T (2024) Applications of Microdosing in Clinical Pharmacology: A Step Toward Personalized Medicine and Accelerated Drug Development Clin Pharmacol Biopharm, 13: 512.

Copyright: © 2024 Birhanu T. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

studies and developments in this field, we aim to highlight the growing significance of microdosing as a tool for optimizing drug therapies, improving patient outcomes, and reducing the time and cost associated with bringing new drugs to market. Through a better understanding of how microdosing can be integrated into clinical pharmacology, researchers and clinicians can harness its full potential in shaping the future of medicine [4].

Materials and methods

Study design

This review explores the applications of microdosing in clinical pharmacology, with an emphasis on its role in personalized medicine and accelerated drug development. The study design is based on a comprehensive analysis of existing literature, including peer-reviewed articles, clinical trial reports, and case studies. Data were gathered from various sources, including PubMed, Scopus, and other relevant databases, focusing on the use of microdosing in early-phase clinical trials, pharmacokinetics, personalized medicine, and drug development processes.

Selection of Studies: To examine the role of microdosing in clinical pharmacology, studies were selected based on specific inclusion and exclusion criteria. The inclusion criteria were:

Studies involving human subjects.

Research that applied microdosing methods (sub-therapeutic doses) in clinical pharmacology.

Studies related to pharmacokinetics (ADME), drug interactions, personalized medicine, and drug development acceleration.

Peer-reviewed articles published in English [5].

Exclusion criteria

Studies focused on animal models or preclinical settings.

Research that did not focus on microdosing methods or their application in clinical pharmacology.

Search Strategy: A systematic search was conducted using medical and scientific databases, including PubMed, Scopus, and Google Scholar, using keywords such as “microdosing,” “clinical pharmacology,” “drug development,” “pharmacokinetics,” “personalized medicine,” “ADME,” and “drug interactions.” Articles from the last two decades (2000-2024) were prioritized to ensure that the most current developments in microdosing research were included.

Analytical Techniques: The pharmacokinetic data obtained from microdosing studies are primarily analyzed using advanced analytical methods such as:

Accelerator Mass Spectrometry (AMS): This ultra-sensitive technique allows the detection of trace amounts of radio-labeled drugs in blood, urine, and tissues. AMS enables accurate measurement of the pharmacokinetic parameters such as half-life, maximum concentration (Cmax), and time to peak concentration (Tmax) for drugs administered at microdoses [6].

Liquid Chromatography-Mass Spectrometry (LC-MS): LC-MS is a powerful technique used to identify and quantify drug metabolites and assess the pharmacokinetic profile of microdoses. It is used to track the drug’s absorption, distribution, metabolism, and excretion (ADME) in human subjects.Population Pharmacokinetic Modeling: Data obtained from microdosing studies are often subjected to population pharmacokinetic modeling to predict how the drug behaves in a larger population, considering variability due to factors like age, gender, genetics, and comorbidities.

Ethical Considerations: All studies included in this review adhered to ethical standards for human research, including obtaining informed consent from participants and approval from ethical review boards. Microdosing studies are typically conducted with minimal risk to participants, given the sub-therapeutic doses used. However, safety protocols are rigorously followed to monitor adverse events, and participants are carefully screened for underlying health conditions before being enrolled in the trials.

Microdosing Administration: In the clinical studies reviewed, microdosing was typically administered as a single-dose or multiple-dose regimen. The doses administered were generally between 1/100th and 1/10th of the therapeutic dose. The specific dose levels varied depending on the drug under study, with careful attention to the drug's pharmacodynamic profile to avoid any measurable therapeutic effects [7].

Data collection

Pharmacokinetic parameters were collected at predefined time points following drug administration. Blood, urine, and other biological samples were taken to measure drug concentrations using the aforementioned analytical techniques. The time points of collection varied but typically ranged from 0.5 hours to 24 hours after administration, depending on the drug’s expected half-life.

Data Analysis: The collected data were analyzed to determine key pharmacokinetic parameters, including:

Cmax (Maximum Concentration): The highest concentration of the drug in plasma.

Tmax (Time to Maximum Concentration): The time taken to reach Cmax.

AUC (Area Under the Curve): A measure of total drug exposure over time.

Half-life (t1/2): The time taken for the drug concentration to decrease by half [8].

Statistical analysis was conducted using software such as SAS or R to assess variability in pharmacokinetic parameters, inter-individual differences, and correlations with patient demographics (e.g., age, sex, genetic polymorphisms).

Personalized Medicine Assessment: In studies evaluating personalized medicine applications, genetic testing was often employed to identify polymorphisms that may influence drug metabolism (e.g., CYP450 enzyme variations). This data allowed for a better understanding of how genetic factors influence drug response at the microdosing stage. In addition, pharmacogenetic models were developed to predict how different subgroups (e.g., metabolizers or non-metabolizers of specific drugs) might respond to different microdosing regimens.Evaluation of Drug Development Acceleration: Microdosing studies are particularly useful in evaluating the feasibility and potential of new drugs in early clinical development. Data from microdosing trials are analyzed to determine whether the drug’s pharmacokinetic profile supports further development into higher-dose clinical trials. This is often combined with data from preclinical studies (such as animal models) to ensure a smooth transition into the later stages of clinical testing [9].

Statistical methods

Descriptive statistics (e.g., mean, standard deviation) were used to summarize pharmacokinetic parameters. In cases of multiple dosing studies, population pharmacokinetic models were developed using nonlinear mixed-effects modeling (e.g., NONMEM software). Statistical significance of differences between subgroups (e.g., male vs. female, young vs. elderly) was determined using analysis of variance (ANOVA) or t-tests as appropriate [10].

Discussion

Microdosing has increasingly become a valuable tool in clinical pharmacology, especially in the context of personalized medicine and accelerating drug development. By administering sub-therapeutic doses, researchers can study the pharmacokinetic and pharmacodynamic properties of a drug without exposing participants to significant risks. This unique approach allows for early-stage human data collection, providing critical insights that can guide the development of more effective and safer drugs.

One of the key advantages of microdosing is its potential to significantly speed up the drug development process. Traditional drug development can take years and requires substantial financial investment. Microdosing, however, allows for rapid pharmacokinetic data collection in humans, which can help determine whether a drug candidate should advance to higher-dose clinical trials. This early-phase testing also reduces the likelihood of costly failures in later stages, where adverse events or poor pharmacological properties might only be discovered. By identifying key pharmacokinetic parameters early, microdosing can optimize dose selection, reducing the chances of under- or overdosing in subsequent trials.

Additionally, microdosing plays a pivotal role in personalized medicine. Every individual's response to a drug can differ based on various factors, including genetics, age, sex, and comorbidities. Microdosing enables researchers to assess how these factors influence drug metabolism and efficacy at an early stage. For example, polymorphisms in drug-metabolizing enzymes like cytochrome P450 can lead to significant differences in how individuals process medications. By identifying these variations during microdosing studies, clinicians can develop tailored dosing strategies that maximize therapeutic benefit while minimizing side effects.

Moreover, microdosing can aid in the assessment of drug interactions, which are crucial in clinical pharmacology. In early clinical trials, evaluating potential drug-drug interactions at sub-therapeutic doses can help identify any unforeseen effects that might emerge when drugs are co-administered. Understanding how a drug behaves in the presence of others, particularly for patients who may require polypharmacy, is vital for ensuring safety. With microdosing, researchers can detect these interactions with fewer participants and reduced costs, offering a more efficient way to assess drug compatibility.

In terms of regulatory approvals, microdosing studies have the potential to support faster market entry for drugs. For instance, microdosing data can be used to demonstrate pharmacokinetic equivalence between a new drug and an existing marketed product, aiding in the approval of generic drugs. Regulatory agencies, including the FDA and EMA, have recognized the value of microdosing studies in the early stages of drug development and have created guidelines for their use in clinical trials. This acceptance is crucial, as it facilitates a more streamlined and cost-effective approach to bringing new drugs to market.

While microdosing offers significant advantages, there are also challenges that need to be addressed. One of the main limitations is that sub-therapeutic doses may not replicate the full spectrum of a drug's effects, particularly in cases where pharmacodynamic responses are dose-dependent. As such, while pharmacokinetic data obtained from microdosing is invaluable, it may not provide a complete picture of the drug's therapeutic potential. For example, certain toxicological effects or adverse reactions may only become apparent at higher doses. Therefore, microdosing should be considered an initial step, rather than a substitute for traditional clinical trials that assess full-dose pharmacodynamics.

Another challenge is the need for advanced analytical techniques. To detect and quantify drugs at such low concentrations, highly sensitive methods like accelerator mass spectrometry (AMS) and liquid chromatography-mass spectrometry (LC-MS) are required. These technologies are not only costly but also require specialized equipment and expertise. Therefore, conducting microdosing studies may not always be feasible for smaller pharmaceutical companies or those with limited access to such technologies.

Despite these challenges, the future of microdosing in clinical pharmacology looks promising. The continuous development of more sensitive detection technologies and improved pharmacokinetic models will likely make microdosing even more effective in optimizing drug development. Furthermore, as personalized medicine becomes increasingly important in healthcare, the ability to tailor drug therapies based on individual pharmacokinetic profiles will become more critical. Microdosing can serve as a foundational tool in this evolution, helping to bridge the gap between drug discovery and individualized treatment strategies.

In conclusion, microdosing represents a transformative approach to clinical pharmacology by providing early, valuable data that can guide drug development, optimize doses, and personalize treatments. It has the potential to reduce the time and cost of bringing new drugs to market while improving patient safety and outcomes. However, further research and advancements in technology are needed to fully realize its potential and address the challenges associated with its use.

Conclusion

Microdosing represents a pivotal advancement in clinical pharmacology, offering a unique approach to early-stage drug development. By administering sub-therapeutic doses, microdosing allows researchers to gather essential pharmacokinetic and pharmacodynamic data without exposing participants to significant risks. This method not only accelerates the drug development process but also provides a more ethical and cost-effective way to assess the safety and efficacy of novel compounds. The ability to obtain human pharmacokinetic data early in the clinical trial process can drastically reduce the likelihood of costly failures in later phases, enabling more informed decision-making and better resource allocation.

Furthermore, microdosing has significant potential in personalized medicine. It allows for the identification of inter-individual variations in drug metabolism and response, which is critical for optimizing drug therapy for diverse patient populations. Understanding genetic polymorphisms and other factors that influence drug pharmacokinetics enables clinicians to tailor treatment plans, improving patient outcomes and minimizing adverse effects. As personalized medicine continues to gain importance, microdosing will play a crucial role in developing drugs that are better suited to individual patients, enhancing the precision of medical treatments.

Microdosing also plays an essential role in drug interaction studies and the evaluation of drug bioavailability, which are critical for drug safety and regulatory approval. By enabling the assessment of drug-drug interactions at very low doses, microdosing can help identify potential risks and guide the development of safer drug regimens, particularly in populations requiring polypharmacy. Additionally, it supports the development of generic drugs by providing valuable data to demonstrate bioequivalence between a new drug and an existing marketed product.

Despite its advantages, there are inherent challenges to microdosing, such as the need for highly sensitive analytical techniques like accelerator mass spectrometry (AMS) and liquid chromatography-mass spectrometry (LC-MS), which can be costly and require specialized expertise. Moreover, microdosing does not fully replicate the therapeutic effects of higher doses, which means it cannot replace traditional clinical trials, particularly for assessing the full range of a drug's pharmacodynamics. These limitations emphasize the need for microdosing to be integrated into the broader clinical trial framework, complementing higher-dose studies to provide a comprehensive understanding of a drug's profile.

As technology continues to advance, the potential applications of microdosing in clinical pharmacology will expand. The development of more efficient and accessible analytical tools, coupled with a deeper understanding of personalized medicine, will allow microdosing to become an even more integral part of drug development. In the future, microdosing may become a standard tool in early-phase clinical trials, enabling faster, more accurate drug development processes while simultaneously contributing to the personalized treatment of patients.

In summary, microdosing offers a transformative approach to drug development and personalized medicine. By providing valuable pharmacokinetic data in the early stages of clinical testing, it helps to streamline drug development, reduce costs, and enhance safety. As microdosing continues to evolve, it promises to play an increasingly important role in optimizing drug therapies, improving patient outcomes, and accelerating the introduction of new, safer, and more effective drugs to the market. With ongoing advancements in technology and methodology, the integration of microdosing into clinical pharmacology will undoubtedly contribute to the evolution of modern, precision medicine.

Conflict of interest

None

Acknowledgment

None

References

1. Tang L (2020) Informatics for Genomics. Nat Methods 17:23.
2. Babu M, Lautman Z, Lin X, Sobota MH, Snyder MP (2024) Wearable Devices: Implications for Precision Medicine and the Future of Health Care. Annu Rev Med 75: 401-415.
3. Ahmed Z, Mohamed K, Zeeshan S, Dong X (2020) Artificial Intelligence with Multi-Functional Machine Learning Platform Development for Better Healthcare and Precision Medicine. Database 2020: 010.
4. Fagiani F, Di Marino D, Romagnoli A, Travelli C, Voltan D, et al. (2022) Molecular regulations of circadian rhythm and implications for physiology and diseases. Signal Transduct. Target. Ther. 7:41.
5. Dragoi CM, Nicolae AC, Ungurianu A, Margina DM, Gradinaru D, et al. (2024) Circadian Rhythms, Chrononutrition, Physical Training, and Redox Homeostasis—Molecular Mechanisms in Human Health. Cells 13:138.
6. Esteva A, Robicquet A, Ramsundar B, Kuleshov V, DePristo M, et al. (2019) A Guide to Deep Learning in Healthcare. Nat Med 25:24-29.
7. Topol EJ (2019) High-Performance Medicine: The Convergence of Human and Artificial Intelligence. Nat Med 25:44-56.
8. Walker WH, Walton JC, DeVries AC, Nelson RJ (2020) Circadian rhythm disruption and mental health. Transl Psychiatry 10:28.
9. Dragoi CM, Morosan E, Dumitrescu IB, Nicolae AC, Arsene AL, et al. (2019) Insights into chrononutrition: The innermost interplay amongst nutrition, metabolism and the circadian clock, in the context of epigenetic reprogramming. Farmacia 67:557-571.
10. Vadapalli S, Abdelhalim H, Zeeshan S, Ahmed Z (2022) Artificial Intelligence and Machine Learning Approaches Using Gene Expression and Variant Data for Personalized Medicine. Brief Bioinform 23: 191.