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The Effects of Physical Activity on Drug Pharmacokinetics and Efficacy and Their Relevance in Sports Doping

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Abstract

Background: Physical exercise brings about physiological adaptations that may influence drug absorption, distribution, metabolism and excretion (ADME) and thus therapeutic efficacy and interpretation of anti-doping testing. Interest in exercise-drug interactions is expanding, but the research base is still piecemeal and mostly limited to specific classes of drugs and anti-doping situations.

Objective: This narrative review aimed to summarize the existing evidence of the effects of physical activity on drug pharmacokinetics and therapeutic efficacy and implications for sports doping.

Methods: Using PubMed database, a narrative review was performed to identify original studies published in the English language in the last 10 years. We included human studies investigating the influence of exercise on medication pharmacokinetics, therapeutic effect or anti-doping significance. Ten articles published between 2022 and 2025 were included in the narrative synthesis after title, abstract and full-text screening against pre-defined eligibility criteria.

Results: The reviewed studies showed consistent evidence that physical activity alters the pharmacokinetic processes by changing physiological factors such as blood flow, hydration status, renal function and metabolic activity, leading to interindividual differences in drug disposition and therapeutic response. These effects were more pronounced for inhaled β 2 -agonists and non-steroidal anti-inflammatory medications and could affect the assessment of urine drug concentrations in the context of anti-doping tests. Metabolite profiling and enantioselective analysis are examples of new pharmacometric approaches that have improved the differentiation between therapeutic use of drugs and prohibited administration.

Conclusion: Physical activity is an important determinant of pharmacokinetic variability with major implications for therapeutic efficacy and anti-doping interpretation. The combination of exercise physiology and pharmacokinetic evidence may lead to a more customized medication and to more accurate and equitable decision making in doping control.

Keywords: physical activity, pharmacokinetics, drug efficacy, doping in sport, health.

INTRODUCTION

Regular physical activity is widely recognized as one of the most effective non-pharmacological strategies for preventing chronic diseases and improving overall health. In addition to its established role in enhancing cardiovascular, metabolic, musculoskeletal, and mental health, exercise has increasingly been incorporated into the management of various chronic conditions alongside pharmacological therapy to optimize clinical outcomes and functional capacity (Izquierdo et al., 2025). Consequently, a growing proportion of physically active individuals, including recreational exercisers and competitive athletes, routinely use medications for the treatment of acute and chronic medical conditions. Among athletes, analgesics, non-steroidal anti-inflammatory drugs (NSAIDs), and anti-asthmatic medications are among the most frequently used therapeutic agents (Gjelstad et al., 2023). The increasing coexistence of exercise and pharmacological treatment highlights the importance of understanding how physical activity may influence drug behavior and therapeutic outcomes.

Physical activity induces a wide range of physiological adaptations that extend beyond improvements in physical performance. Acute and chronic exercise increases cardiac output, redistributes blood flow toward active skeletal muscles, enhances endothelial function, and promotes skeletal muscle angiogenesis and metabolic remodeling (Ross et al., 2023; Sun et al., 2024). Exercise also alters renal and hepatic perfusion, modifies hydration status, and influences metabolic activity, all of which are essential for meeting the increased physiological demands associated with exercise (Wang et al., 2026). These adaptations not only support exercise performance but also influence the physiological processes governing drug disposition, suggesting that exercise may contribute to pharmacokinetic variability among physically active individuals.

Drug pharmacokinetics describes the processes of absorption, distribution, metabolism, and excretion (ADME), which collectively determine systemic drug exposure, tissue concentrations, therapeutic efficacy, and the occurrence of adverse effects (Mahalakshmi et al., 2024). Because these processes are highly dependent on physiological conditions, alterations in organ perfusion, membrane transport, metabolic activity, and renal function induced by physical activity may substantially modify drug disposition. Consequently, exercise-induced physiological adaptations have the potential to influence medication effectiveness, safety, and individualized dosing strategies.

Growing evidence indicates that the influence of physical activity on pharmacokinetics is not merely theoretical but has been demonstrated across several therapeutic agents. Exercise-related changes in gastrointestinal perfusion may influence drug absorption, whereas alterations in tissue blood flow, hepatic metabolism, renal clearance, and hydration status may affect drug distribution, metabolism, and excretion, thereby modifying systemic drug exposure and therapeutic response (Chung et al., 2024; Izquierdo et al., 2025). The magnitude of these changes depends on multiple factors, including exercise intensity, duration, hydration status, environmental conditions, and individual physiological characteristics. Collectively, these findings suggest that physical activity represents an important source of pharmacokinetic variability that should be considered in both clinical pharmacology and sports medicine.

Recent pharmacokinetic studies have provided increasing evidence that exercise may influence the disposition of medications commonly used by athletes and physically active individuals. Model-based analyses of inhaled salbutamol have demonstrated substantial interindividual variability in plasma and urinary drug concentrations, potentially affecting the interpretation of anti-doping testing (Courlet et al., 2022). Similarly, therapeutic and supratherapeutic administration of vilanterol has been

shown to produce distinct urinary pharmacokinetic profiles following exercise, leading to the proposal of evidence-based urinary decision limits to improve anti-doping interpretation (Østergaard et al., 2023). Exercise-related physiological changes have also been suggested to influence the pharmacokinetics and therapeutic responses of other medications, including NSAIDs commonly prescribed for sports-related musculoskeletal injuries (Selig et al., 2022). Together, these findings indicate that exercise-induced pharmacokinetic variability may have clinically relevant implications for medication use in physically active populations.

Understanding these exercise-induced pharmacokinetic alterations is particularly important in sports medicine because many therapeutic agents are regulated under the World Anti-Doping Agency (WADA) Prohibited List. Several medications remain permitted for therapeutic use within specific dosage limits; however, physiological changes associated with exercise may influence drug absorption, metabolism, and elimination, thereby affecting urinary drug concentrations used during doping control (Bizjak et al., 2023). This issue is especially relevant for inhaled β_2-agonists, which are permitted within defined therapeutic limits but remain closely monitored because excessive systemic exposure may enhance athletic performance (Courlet et al., 2022; Østergaard et al., 2023). Therefore, accurate interpretation of anti-doping findings requires a comprehensive understanding of both pharmacokinetic variability and exercise-induced physiological adaptations.

Despite increasing research interest, current evidence remains fragmented. Most published studies have focused on individual drug classes, particularly inhaled β_2-agonists, specific pharmacokinetic parameters, or anti-doping regulations, whereas relatively few have integrated the broader relationships among physical activity, drug pharmacokinetics, therapeutic efficacy, and sports doping within a single

conceptual framework (Damjanovic et al., 2025). Likewise, existing reviews have generally discussed medication use in athletes or anti-doping issues separately rather than examining how exercise-induced physiological adaptations collectively influence drug disposition and therapeutic outcomes across different pharmacological agents (Alorfi, 2026). Consequently, clinicians, sports physicians, and anti-doping authorities still lack an integrated evidence base to support the interpretation of exercise-related pharmacokinetic variability in clinical and sporting settings.

Therefore, this narrative review aims to synthesize current evidence regarding the effects of physical activity on drug pharmacokinetics and therapeutic efficacy and to discuss their implications for sports doping. By integrating findings from exercise physiology, clinical pharmacology, and anti-doping research, this review seeks to provide a comprehensive framework for understanding exercise–drug interactions and their relevance to individualized pharmacotherapy and evidence-based anti-doping decision-making.

METHODS

Design Study

This study employed a narrative review design to synthesize current evidence regarding the effects of physical activity on drug pharmacokinetics, therapeutic efficacy, and their implications for sports doping. A narrative review was considered appropriate because the available literature comprises heterogeneous study designs, pharmacological agents, exercise protocols, and outcome measures, making quantitative synthesis inappropriate. This approach enabled a comprehensive interpretation of existing evidence while identifying emerging themes, knowledge gaps, and future research directions.

The review was guided by the following research questions: (1) How does physical activity influence drug pharmacokinetics? (2) How do exercise-induced pharmacokinetic changes affect therapeutic efficacy? and (3) What are the implications of these findings for sports doping?

Eligibility Criteria

Eligible studies included original research articles and review articles published in peer-reviewed journals that: (1) involved human participants or addressed clinically relevant pharmacokinetic and anti-doping evidence; (2) investigated the effects of physical activity or exercise on drug pharmacokinetics, therapeutic efficacy, or their relevance to sports doping; (3) were published in English within the last 10 years; and (4) were directly relevant to the objectives of this review.

Studies were excluded if they were conference abstracts, editorials, commentaries, letters to the editor, case reports, animal studies, in vitro studies, or publications that did not address the relationship between physical activity, pharmacokinetics, therapeutic efficacy, or sports doping.

Search Strategy

A literature search was conducted in the PubMed and Scopus databases. PubMed and Scopus were selected because it provides comprehensive coverage of peer-reviewed biomedical, pharmacological, and sports medicine literature relevant to the objectives of this review. The search strategy combined keywords related to physical activity, exercise, pharmacokinetics, drug efficacy, athletes, and sports doping using Boolean operators (AND and OR). The following search strategy was applied *("physical activity" OR exercise) AND ("drug efficacy" OR pharmacokinetics) AND (athlete OR doping)*. The search was limited to English-language publications published within the previous ten years. Initially, 45 records were identified across the two databases. After duplicate removal and application of the predefined eligibility criteria, records proceeded to title and abstract screening, followed by full-text assessment. Ultimately, ten

studies met the inclusion criteria and were included in the narrative synthesis.

Study Selection

The retrieved records were screened in several stages according to the predefined eligibility criteria. First, titles and abstracts were independently assessed by two reviewers to determine their relevance to the objectives of the review. Potentially eligible articles subsequently underwent full-text assessment to confirm their eligibility. Any disagreements regarding study selection were resolved through discussion until consensus was achieved. Ultimately, ten studies met the eligibility criteria and were included in the narrative synthesis. The study selection process is illustrated in the study flow diagram.

Data Extraction

A standardized data extraction form was developed to ensure consistent collection of relevant information from each included study. The extracted data included the first author, publication year, country, study design, participant characteristics, investigated drug(s), type of physical activity or exercise, pharmacokinetic outcomes, therapeutic efficacy outcomes, anti-doping relevance, and the principal findings. Data extraction was independently performed by two reviewers, and any discrepancies were resolved through discussion until consensus was reached.

Data Synthesis

A narrative synthesis approach was employed because of the methodological heterogeneity among the included studies. The findings were organized into three predefined themes: (1) the effects of physical activity on drug pharmacokinetics, (2) the influence of physical activity on therapeutic efficacy, and (3) the implications of exercise-induced pharmacokinetic variability for sports doping.

Similarities, differences, and emerging trends across the included studies were critically compared to identify common mechanisms, clinical implications, and current knowledge gaps. Meta-analysis was not performed because substantial heterogeneity existed in study designs, exercise interventions, pharmacological agents, and reported outcome measures.

RESULTS

Characteristics of Included Studies

A total of ten studies met the eligibility criteria and were included in this narrative review. The studies were published between 2022 and 2025 and comprised experimental studies, prospective pharmacokinetic studies, model-based analyses, pharmacometric studies, and review articles. The majority of the included studies investigated inhaled β_2-adrenergic agonists, including salbutamol, vilanterol, fenoterol, and salmeterol, whereas additional studies evaluated non-steroidal anti-inflammatory drugs (NSAIDs), oral anticoagulants, and selective androgen receptor modulators (SARMs). Overall, the evidence was synthesized into three major themes: (1) the effects of physical activity on drug pharmacokinetics, (2) the influence of physical activity on therapeutic efficacy, and (3) the implications of exercise-induced pharmacokinetic variability for sports doping. The characteristics of the included studies are summarized in Table 1.

Table 1. Characteristics of the Included Studies

No.	Author (Year)	Study Design	Population	Drug(s) Investigated	Physical Activity	Main Outcome	Primary Theme
1	Courlet et al. (2022)	Model-based meta-analysis	Data from 13 pharmacokinetic studies	Salbutamol	Exercise-related therapeutic use	Evaluated plasma and urinary pharmacokinetics and assessed WADA urinary threshold for differentiating therapeutic and prohibited use	Pharmacokinetics; Anti-doping
2	Østergaard et al. (2023)	Prospective pharmacokinetic study	25 trained men and women	Vilanterol	One hour of exercise after inhalation	Determined urinary concentrations following therapeutic and supratherapeutic inhalation and proposed a urinary decision limit	Pharmacokinetics; Anti-doping
3	Hostrup et al. (2025)	Experimental study	12 healthy young men	Salbutamol	Skeletal muscle assessment after oral administration	Investigated enantioselective distribution of salbutamol in skeletal muscle and plasma	Pharmacokinetics; Drug efficacy
4	Cheibub et al. (2023)	Experimental study	Five elite female judo athletes	Fenoterol	Rapid weight loss and rehydration protocol	Demonstrated altered urinary drug excretion during dehydration and recovery	Pharmacokinetics; Anti-doping
5	Mashal et al. (2025)	Analytical and pharmacokinetic study	Mountain ultra-trail runners	Ibuprofen and other NSAIDs	Endurance running	Evaluated NSAID detection and pharmacokinetic changes associated with prolonged exercise	Pharmacokinetics
6	Minardi et al. (2024)	Narrative review	Athletes with atrial fibrillation	Oral anticoagulants	Competitive and recreational sports	Discussed anticoagulant management and therapeutic considerations for physically active individuals	Drug efficacy

No.	Author (Year)	Study Design	Population	Drug(s) Investigated	Physical Activity	Main Outcome	Primary Theme
7	Slíž & Mikuš (2025)	Review article	Anti-doping studies	SARMs	Sports performance	Summarized advances in analytical methods for SARM detection and biomarker identification	Anti-doping
8	Cricco et al. (2025)	Narrative review	Athletes using inhaled medications	β_2-agonists and inhaled corticosteroids	Competitive sports	Reviewed pharmacological effects, therapeutic use, and potential performance enhancement	Drug efficacy; Anti-doping
9	Jacobson & Hostrup, (2022)	Original research	Athletes	Salmeterol	Exercise-related use	Evaluated urinary threshold for distinguishing therapeutic administration from potential misuse	Pharmacokinetics; Anti-doping
10	Thoueille et al., (2026)	Pharmacometric study	Pharmacokinetic datasets	Salmeterol	Therapeutic inhalation	Developed pharmacometric approaches to improve interpretation of salmeterol concentrations in doping control	Pharmacokinetics; Anti-doping

Effects of Physical Activity on Drug Pharmacokinetics

The included studies consistently demonstrated that physical activity influences drug pharmacokinetics by modifying physiological processes involved in drug absorption, distribution, metabolism, and excretion (ADME). Exercise-induced alterations in blood flow, hydration status, renal function, and metabolic activity were repeatedly identified as the principal mechanisms contributing to pharmacokinetic variability. Although the magnitude of these effects differed among drug classes and exercise conditions, the overall evidence indicates that physical activity represents an important source of interindividual variability in drug disposition.

Among the included studies, inhaled β_2-adrenergic agonists were the most extensively investigated. A model-based meta-analysis demonstrated substantial variability in plasma and urinary salbutamol concentrations following therapeutic inhalation, indicating that urinary concentrations near the World Anti-Doping Agency (WADA) decision threshold may overlap between therapeutic and prohibited use (Courlet et al., 2022). Similarly, a prospective pharmacokinetic study evaluating vilanterol reported dose-dependent increases in urinary parent drug concentrations following therapeutic and supratherapeutic inhalation combined with exercise. Based on these findings, evidence-based urinary decision limits were proposed to improve the interpretation of anti-doping testing (Østergaard et al., 2023).

Exercise-induced dehydration also affected drug elimination. An experimental study involving elite female judo athletes demonstrated that rapid weight loss followed by rehydration produced a transient increase in urinary fenoterol excretion during the recovery period, suggesting temporary drug retention during dehydration and subsequent release after rehydration (Cheibub et al., 2023). Similar observations were reported for NSAIDs, where prolonged endurance exercise was associated

with altered ibuprofen pharmacokinetics, particularly drug clearance, potentially influencing detection windows during anti-doping analysis (Mashal et al., 2025).

Collectively, these findings demonstrate that exercise-induced physiological adaptations substantially contribute to pharmacokinetic variability. The magnitude and direction of these changes appear to depend on drug characteristics, exercise intensity, hydration status, and individual physiological responses, emphasizing the importance of considering physical activity when interpreting pharmacokinetic outcomes.

Physical Activity and Drug Efficacy

Beyond altering pharmacokinetic profiles, the included studies suggest that physical activity may also influence therapeutic efficacy and drug responses. Exercise-related physiological adaptations can modify systemic drug exposure, tissue distribution, and target-organ responses, potentially affecting both clinical effectiveness and safety.

Evidence regarding inhaled β_2-adrenergic agonists demonstrated that these medications remain essential for the management of asthma and exercise-induced bronchoconstriction in athletes. However, supratherapeutic exposure may produce systemic effects extending beyond bronchodilation, including skeletal muscle hypertrophy, enhanced sprint performance, and cardiovascular stimulation, thereby increasing concerns regarding their potential ergogenic effects (Cricco et al., 2025). In addition, experimental evidence showed that orally administered salbutamol exhibited enantioselective distribution within skeletal muscle despite similar systemic administration, suggesting that tissue-specific drug disposition may contribute to variability in pharmacological responses among athletes (Hostrup et al., 2025)

Therapeutic considerations were also reported for oral anticoagulants. Evidence indicates that anticoagulant therapy remains

necessary for athletes with atrial fibrillation to reduce thromboembolic risk, although participation in competitive sports requires individualized treatment strategies because exercise may increase trauma-related bleeding risk. Direct oral anticoagulants were identified as promising alternatives because of their relatively predictable pharmacokinetic profiles compared with vitamin K antagonists (Minardi et al., 2024).

Overall, the available evidence suggests that physical activity influences therapeutic outcomes not only through alterations in drug pharmacokinetics but also through changes in tissue distribution and physiological responsiveness. These findings highlight the importance of considering exercise-related factors when optimizing pharmacotherapy in physically active individuals.

Implications for Sports Doping

The reviewed studies consistently identified exercise-induced pharmacokinetic variability as a major challenge in anti-doping science. Physiological factors associated with exercise, including hydration status, exercise intensity, renal function, and metabolic activity, substantially influence urinary drug concentrations and may complicate the differentiation between legitimate therapeutic use and prohibited drug administration.

Several studies demonstrated that pharmacokinetic modelling provides valuable support for interpreting urinary drug concentrations beyond the use of fixed concentration thresholds. Model-based analyses of salbutamol improved the interpretation of urinary concentrations commonly encountered during doping control (Courlet et al., 2022), whereas pharmacokinetic evaluation of vilanterol supported the establishment of evidence-based urinary decision limits capable of distinguishing therapeutic from supratherapeutic administration (Østergaard et al., 2023).

Additional evidence suggests that exercise-related physiological responses should also be considered during interpretation of anti-doping findings. Enantioselective analysis of salbutamol demonstrated differential distribution between skeletal muscle and plasma, indicating that tissue-specific pharmacokinetics may provide additional discriminatory information during anti-doping investigations (Hostrup et al., 2025). Likewise, dehydration and rehydration protocols frequently used in weight-category sports substantially altered urinary fenoterol excretion profiles, emphasizing the importance of physiological status during sample interpretation (Cheibub et al., 2023). Furthermore, recent advances in anti-doping analysis, including metabolite profiling, biomarker identification, and high-resolution mass spectrometry, have expanded opportunities to improve analytical specificity and extend detection windows for prohibited substances such as SARMs (Slíž & Mikuš, 2025).

Overall, the reviewed evidence demonstrates a progressive shift from concentration-based anti-doping interpretation toward mechanism-based approaches that integrate pharmacokinetic modelling, advanced analytical techniques, and exercise-induced physiological variability. These developments may improve the accuracy and fairness of anti-doping decision-making while reducing the risk of misclassification among athletes receiving legitimate therapeutic treatment.

DISCUSSION

Physical Activity as a Determinant of Drug Pharmacokinetics

The present review demonstrates that physical activity is an important determinant of drug pharmacokinetic variability. Rather than acting as an external factor accompanying drug administration, exercise induces coordinated physiological adaptations that influence drug absorption, distribution, metabolism, and excretion (ADME). Consequently, pharmacokinetic parameters obtained under resting

conditions may not accurately represent drug disposition in physically active individuals, particularly athletes exposed to varying exercise intensities and environmental conditions.

The included studies consistently identified exercise-induced alterations in cardiovascular and metabolic function as the primary mechanisms underlying pharmacokinetic variability. Redistribution of blood flow from the splanchnic circulation toward active skeletal muscles may modify gastrointestinal drug absorption, tissue distribution, and hepatic drug metabolism. Simultaneously, dehydration associated with prolonged or high-intensity exercise reduces plasma volume and may temporarily alter renal perfusion, whereas subsequent rehydration accelerates urinary drug elimination. These physiological responses provide a plausible explanation for the variability in urinary drug concentrations reported for inhaled β_2-adrenergic agonists and other renally excreted medications included in this review (Courlet et al., 2022; Østergaard et al., 2023; Cheibub et al., 2023).

Importantly, the reviewed evidence indicates that the magnitude of exercise-induced pharmacokinetic alterations is not uniform across individuals or therapeutic agents. Variability appears to be influenced by multiple interacting factors, including exercise intensity, duration, hydration status, environmental conditions, drug characteristics, and individual physiological responses. These observations suggest that physical activity should be recognized as a clinically relevant source of pharmacokinetic variability rather than merely a potential confounding factor. Future pharmacokinetic studies should therefore incorporate standardized exercise protocols and physiological monitoring to improve the applicability of pharmacokinetic data to physically active populations.

Clinical Implications for Medication Use in Physically Active Individuals

The interaction between exercise and pharmacokinetics has important implications for clinical practice because alterations in systemic

drug exposure may influence therapeutic efficacy, safety, and individualized treatment strategies. Although exercise is generally considered beneficial for health, the accompanying physiological adaptations may modify medication responses, emphasizing the need to interpret pharmacological outcomes within the context of physical activity.

This review identified inhaled β_2-adrenergic agonists as the therapeutic class most frequently investigated. These medications remain essential for managing asthma and exercise-induced bronchoconstriction among athletes; however, excessive systemic exposure has been associated with physiological effects extending beyond bronchodilation, including skeletal muscle hypertrophy, enhanced exercise performance, and cardiovascular stimulation (Cricco et al., 2025). Furthermore, the demonstration of enantioselective salbutamol distribution within skeletal muscle suggests that tissue-specific pharmacokinetics may contribute to interindividual variability in therapeutic responses despite similar systemic exposure (Hostrup et al., 2025).

Evidence from anticoagulant therapy further illustrates the complexity of medication management in physically active populations. Although direct oral anticoagulants provide relatively predictable pharmacokinetic profiles compared with vitamin K antagonists, participation in competitive or contact sports may increase trauma-related bleeding risk, requiring individualized therapeutic decision-making (Minardi et al., 2024). Collectively, these findings indicate that optimizing pharmacotherapy in physically active individuals requires consideration of both pharmacokinetic variability and the physiological demands associated with different exercise modalities.

Implications for Anti-Doping Science

One of the principal findings of this review is that exercise-induced pharmacokinetic variability has important implications for anti-doping

science. Current anti-doping regulations primarily rely on urinary drug concentrations to distinguish therapeutic medication use from prohibited administration. However, the reviewed evidence demonstrates that urinary drug concentrations are influenced not only by the administered dose but also by exercise-induced physiological changes, including alterations in hydration status, renal clearance, metabolic activity, and tissue distribution.

This challenge is particularly evident for inhaled β_2-adrenergic agonists, where individuals receiving identical therapeutic doses may exhibit markedly different urinary drug concentrations because of normal physiological variability associated with exercise (Courlet et al., 2022; Østergaard et al., 2023). Similarly, rapid dehydration and subsequent rehydration, which are common practices in weight-category sports, have been shown to substantially modify urinary drug excretion patterns (Cheibub et al., 2023). These findings indicate that interpretation based solely on fixed urinary concentration thresholds may not adequately reflect actual drug administration.

Recent advances in pharmacometric modelling, metabolite profiling, enantioselective analysis, and high-resolution mass spectrometry represent promising approaches for improving anti-doping interpretation. Rather than relying exclusively on concentration-based thresholds, these techniques incorporate pharmacokinetic behaviour and physiological variability to better differentiate legitimate therapeutic use from prohibited drug administration (Slíž & Mikuš, 2025). Such developments support a gradual transition toward more individualized and evidence-based anti-doping strategies while maintaining fairness in competitive sports.

Research Gaps and Future Perspectives

Despite increasing interest in exercise-related pharmacokinetic variability, several important knowledge gaps remain. First, the current

evidence is heavily dominated by studies investigating inhaled β_2-adrenergic agonists, whereas considerably fewer studies have evaluated other therapeutic drug classes commonly used by physically active individuals, including antibiotics, antihypertensive agents, antidiabetic medications, and biological therapies. Consequently, the available evidence cannot yet be generalized across all pharmacological agents.

Second, most included studies involved relatively small cohorts of healthy athletes or trained individuals under controlled experimental conditions. Although these designs provide valuable mechanistic insights, their findings may not be directly applicable to broader populations such as recreational exercisers, older adults, women, or individuals with chronic diseases. Future prospective studies involving larger and more diverse populations are therefore required to improve the external validity of current evidence.

Finally, advances in precision medicine offer promising opportunities for future research in exercise pharmacology. The integration of pharmacokinetic modelling, wearable physiological monitoring, biomarker analysis, and artificial intelligence may facilitate individualized medication dosing while simultaneously improving anti-doping interpretation. Such multidisciplinary approaches have the potential to support safer pharmacotherapy, more accurate anti-doping decision-making, and better health outcomes for physically active individuals.

CONCLUSION

This narrative review highlights that physical activity is an important determinant of drug pharmacokinetics, influencing drug absorption, distribution, metabolism, and excretion through exercise-induced physiological adaptations. These alterations contribute to interindividual variability in drug disposition and may subsequently affect therapeutic efficacy as well as the interpretation of urinary drug concentrations used

in anti-doping testing. The reviewed evidence emphasizes that exercise-related physiological factors, including hydration status, exercise intensity, metabolic activity, and renal function, should be considered when evaluating pharmacokinetic outcomes in physically active individuals.

The findings further suggest that integrating exercise physiology with pharmacokinetic evidence may support more individualized pharmacotherapy while improving the accuracy and fairness of anti-doping decision-making. However, the current evidence remains concentrated on a limited number of therapeutic agents, particularly inhaled β_2-adrenergic agonists. Therefore, future research should investigate a broader range of drug classes using larger and more diverse populations, while incorporating advanced pharmacometric approaches to strengthen the evidence base for exercise-informed clinical practice and anti-doping policies.

AUTHOR'S CONTRIBUTION

Kayla Bachmid contributed to conceptualization, literature searching, data curation, formal analysis, and preparation of the original manuscript. Vania Malva Syakira contributed to literature searching, data curation, and manuscript revision. Vika Auralya Zalvany Harrisma Putri contributed to conceptualization, methodology, supervision, validation, and critical review of the manuscript. All authors read and approved the final version of the manuscript.

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