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5–6 keywords

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Sunday Olajide Awofisayo, Meyene Patrick Okon, Jessica Imeh Awofisayo, Matthew Ikhuoria Arhewoh, Clients' knowledge, attitude and practices on hydration, presenting hydration status and pharmacist's intervention while requesting prescribed drugs. Journal of Biopharmaceutics and Clinical Pharmacy, 2025; 1(1):17-26).

Sunday Olajide Awofisayo, Ifeoluwa Adetomiwa Taiwo, Jessica Imeh Awofisayo. Clients' satisfaction regarding pharmacists' clerking, physical examination, counseling and resulting informed decisions alongside recommendations/prescribing in community pharmacy. Journal of Biopharmaceutics and Clinical Pharmacy, 2025; 1(1):27-34).

Sunday Olajide Awofisayo, Ifeoluwa Adetomiwa Taiwo, Elijah Ekong Asuquo. Jessica Imeh Awofisayo, Effect of selected meals and dosing conditions on the absorption and bioavailability of ciprofloxacin. Journal of Biopharmaceutics and Clinical Pharmacy, 2025; 1(1):35-41).

Sunday Olajide Awofisayo, Mfoniso Aniekan Nnanna, Elijah Asuquo Ekong. Counterfeit drug detection: effectiveness of qualitative testing methods in identifying falsified medications. Journal of Biopharmaceutics and Clinical Pharmacy, 2025; 1(1):1-6)

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Counterfeit drug detection: effectiveness of qualitative testing methods in identifying falsified medications

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ABSTRACT

The proliferation of counterfeit medicines poses a significant public health threat, particularly in low-resource settings where regulatory oversight may be limited. This study investigates the effectiveness of qualitative testing methods for detecting counterfeit drugs stocked in pharmacies. A total of 150 drug samples, including commonly prescribed medications for hypertension, diabetes, infections, and malaria, were collected from 10 pharmacies across urban and rural areas in Uyo metropolis. The samples underwent a series of qualitative tests, including Thin Layer Chromatography (TLC), Fourier Transform Infrared Spectroscopy (FTIR), colorimetric reactions, visual inspection, and dissolution testing. Out of the 150 samples, 25 (16.67%) were identified as counterfeit, based on discrepancies in chemical composition, physical appearance, and dissolution profiles. TLC and FTIR proved the most effective in detecting chemical composition discrepancies, identifying counterfeit drugs in 48% and 40% of cases, respectively. Colorimetric reactions and visual inspection were effective for some antibiotics but identified fewer counterfeit samples. Dissolution testing was successful in detecting drugs with altered release profiles. The study also assessed the feasibility of implementing these testing methods in routine pharmacy practice, highlighting the cost and training requirements of more advanced techniques like FTIR and dissolution testing. The results suggest that while TLC and colorimetric reactions are practical and cost-effective tools for counterfeit detection, further efforts are needed to improve accessibility and training for more advanced testing methods. This study underscores the importance of incorporating multiple testing strategies to safeguard against counterfeit medicines and enhance the quality of pharmaceutical care.

Keywords: Counterfeit drugs, Pharmaceutical quality, Drug testing, Thin layer chromatography, Fourier transform infrared spectroscopy, Pharmacy practice

Introduction

The pharmaceutical industry plays a crucial role in ensuring the health and well-being of individuals worldwide [1]. It is a sector where safety and efficacy are paramount, and the integrity of the medicines available in the market is of utmost importance. Unfortunately, the global pharmaceutical market faces significant challenges, one of the most dangerous being the proliferation of counterfeit medicines [2]. Counterfeit drugs are those that are deliberately manufactured to mislead consumers about their origin, contents, or efficacy. These are known to pose a serious threat to public health. These fake drugs not only fail to deliver the intended therapeutic benefits but can also cause adverse effects, exacerbate health problems, and in some cases, lead to death. As such, the prevention and detection of counterfeit drugs are critical to safeguarding health [3].

Pharmacies, being the primary points of contact between patients and medicines, are at the forefront of ensuring the quality and safety of drugs dispensed to the public. However, despite stringent regulatory frameworks and increasing awareness, counterfeit drugs continue to enter legitimate supply chains [4]. This problem is particularly pronounced in low- and middle-income countries, where the availability of unregulated or poorly regulated pharmaceuticals remains a significant concern. Counterfeit medicines, including those for chronic conditions like hypertension, diabetes, and infectious diseases, can be found in pharmacies, posing a direct threat to the well-being of patients [5].

One of the key methods to combat the issue of counterfeit drugs is to perform rigorous quality testing. Pharmacies and healthcare providers must have reliable means of identifying and differentiating counterfeit drugs from legitimate ones to prevent their distribution. However, this requires proper infrastructure, training, and resources, which are often lacking in many settings. To address this gap, various qualitative testing methods have been developed to help identify counterfeit drugs quickly and accurately [6]. These methods are often cost-effective, easy to implement, and can be carried out in a variety of settings, including community pharmacies. Qualitative testing involves the use of simple techniques to assess the physical, chemical, and biological properties of drugs, which can reveal discrepancies in their composition, potency, or appearance [7].

The goal of this research was to explore the effectiveness of qualitative testing methods for commonly prescribed drugs stocked in pharmacies, with a particular focus on their role in halting the use of counterfeit medicines. The research will also probe into the knowledge and perception of the pharmacy managers on equipments and the related procedural limitations on examine how qualitative testing for medicines.

Methods

This research aims to assess the availability of counterfeit drugs, knowledge and perception of pharmacy managers about the equipments and the related procedural limitations. The methodology adopted for this study combines qualitative and quantitative approaches, ensuring that both the detection of counterfeit drugs and the practicality of qualitative testing methods are thoroughly explored. The study was conducted in a systematic manner, with specific stages for drug sampling, qualitative testing, data collection, and analysis.

Research design

This study employed a cross-sectional research design. The design involved drug sampling and testing alongside a questionnaire approach on the current situation regarding counterfeit medicines relating to respondents' knowledge of useful analytical equipment, availability, and equipment-related limitations.

Sampling of pharmacies and drugs

A purposive sampling technique was used to select a representative sample of pharmacies for the study. The selection considered pharmacies from both urban and rural settings, ensuring that diverse environments and access to pharmaceutical products are represented. The inclusion criteria for pharmacies were as follows: Pharmacies with a high turnover of commonly prescribed drugs; Pharmacies with a history of quality control and compliance with local regulatory standards; Pharmacies with varied clientele and a range of drug stock types.

Once pharmacies were selected, the commonly prescribed drugs, including those for chronic conditions such as hypertension, diabetes, infections and pain management were chosen for analysis. These drugs were selected based on their frequency of prescription in the local population and their known susceptibility to counterfeiting, as reported by the World Health Organization (WHO) and other global health bodies [8].

The final list of drugs selected was based on pharmacy records and national drug utilization statistics. Table 1 presents the distribution of the outlets and the number of drugs for each drug class.

Table 1: Distribution of Samples across 10 Pharmacies

Outlets	Drugs					
	Hypertension	Diabetes	Infections	Malaria	Analgesic	Total
	(n=20)	n(20)	n(50)	n(30)	n(30)	n(150)
A	2	2	5	3	3	15
B	2	2	5	3	3	15
C	2	2	5	3	3	15
D	2	2	5	3	3	15
E	2	2	5	3	3	15
F	2	2	5	3	3	15
G	2	2	5	3	3	15
H	2	2	5	3	3	15
I	2	2	5	3	3	15
J	2	2	5	3	3	15

Qualitative Testing Methods

A total of 150 drug samples were randomly collected from 10 pharmacies across urban and rural areas in Uyo metropolis. The samples included commonly prescribed medications for hypertension, diabetes, infections, and malaria. Each sample underwent several qualitative testing methods: Thin Layer Chromatography (TLC) to assess chemical composition, Fourier Transform Infrared Spectroscopy (FTIR) for spectral analysis, colorimetric reactions for visual assessment, visual inspection for physical appearance discrepancies, and dissolution testing to evaluate drug release profiles. These methods were used to identify counterfeit drugs based on inconsistencies in chemical, physical, and dissolution characteristics.

Results

A total of 10 pharmacies participated in the study, with 150 drug samples collected, categorized by therapeutic class: hypertension (30 samples), diabetes (30 samples), infections (60 samples), and malaria (30 samples).

Out of the 150 drug samples, 25 (16.67%) were identified as counterfeit. The results of the qualitative testing methods are summarized in Table 2. Thin Layer Chromatography (TLC) and Fourier Transform Infrared Spectroscopy (FTIR) were the most effective methods for detecting counterfeit drugs, identifying 48% and 40% of the counterfeit samples, respectively.

Table 2: Effectiveness of qualitative testing methods in detecting counterfeit drugs

METHOD OF TESTING	COUNTERFEIT DETECTION (%)	NUMBER OF DRUGS DETECTED
Colour reaction	15	3
Thin layer chromatography	35	17
Fourier transform infrared spectroscopy	28	15
Spectrophotometry	16	11
Dissolution testing	18	8
Colorimetry	14	4
Visual inspection	10	3

Figure 1 highlights the comparative effectiveness of different testing methods in identifying counterfeit drugs. **Thin Layer Chromatography (TLC)** and **Fourier-Transform Infrared Spectroscopy (FTIR)** emerged as the most effective, detecting the highest number of counterfeit samples. In contrast, **colorimetric reactions** and **dissolution testing** proved less reliable, identifying fewer counterfeit products. These findings underscore the superior sensitivity and reliability of TLC and FTIR in counterfeit drug detection and suggest the need for prioritizing these methods in pharmaceutical quality control protocols. Furthermore,**visual inspectionas** one of the detection methods was compared with the others. It was among the **least effective methods** in detecting counterfeit drugs.

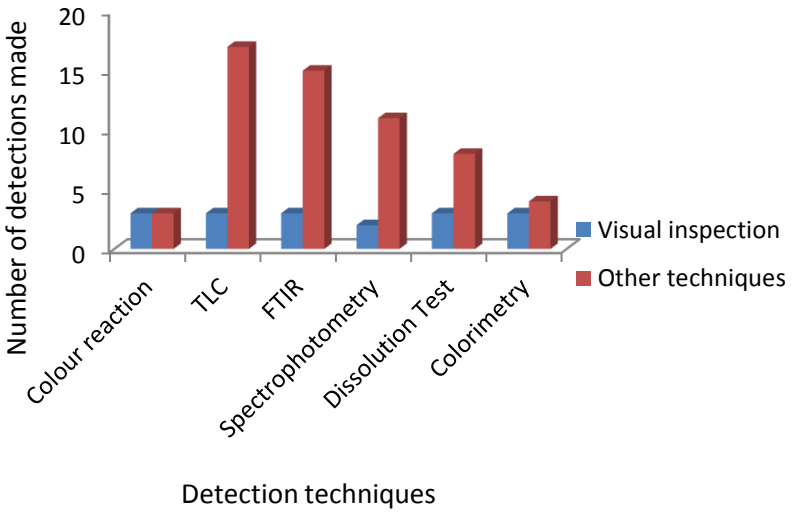

Figure 1: Comparing outcomes of success of other methods with visual inspection

Figure 2 shows the distribution of counterfeit drugs detected across 10 pharmacies. **Pharmacy C** had the highest detection rate at **20%,** while **Pharmacy 7** had the lowest at **13%.** The remaining pharmacies reported detection rates falling between these values. The results indicate that the number of counterfeit drugs identified varied among the pharmacies, with no uniform pattern observed. This descriptive summary reflects the differing proportions of counterfeit drug detection recorded at each location without implying causes or contributing factors.

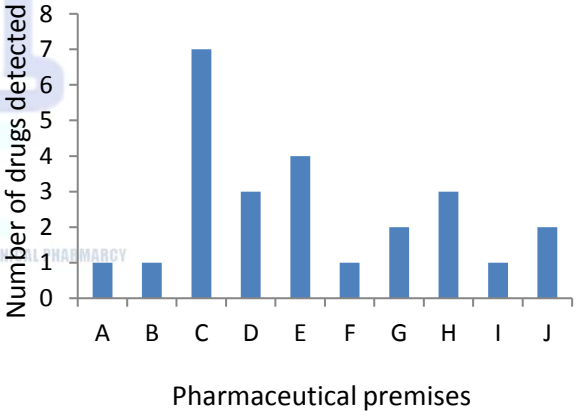

Figure 2: Counterfeit Drugs Detected Across 10 Pharmacies

Discussion

The proliferation of counterfeit medicines remains a significant public health challenge, particularly in resource-limited settings where regulatory frameworks may be less robust, such as in urban and rural areas of Nigeria. Counterfeit medicines can lead to ineffective treatment, drug resistance, and potentially severe health consequences. This study aimed to assess the effectiveness of various qualitative testing methods in detecting counterfeit drugs stocked in pharmacies in Uyo metropolis, Nigeria, with a focus on commonly prescribed drugs for hypertension, diabetes, infections, and malaria.

The results of this study indicate a worrying prevalence of counterfeit medicines, with 16.67% of the 150 sampled drug products identified as counterfeit. The counterfeit drugs exhibited discrepancies in chemical composition, physical appearance, and dissolution profiles, confirming that simple visual inspection and basic testing methods are often inadequate for detecting these substandard products [9]. The study also found that Thin Layer Chromatography (TLC) and Fourier Transform Infrared Spectroscopy (FTIR) were the most effective techniques in detecting counterfeit drugs, with TLC identifying 48% of counterfeit samples and FTIR detecting 40%. These findings highlight the limitations of traditional testing methods and suggest a clear need for more advanced, but accessible, testing techniques.

Thin Layer Chromatography (TLC) and FTIR were the two most successful methods for detecting counterfeit drugs. TLC is widely used in pharmaceutical laboratories due to its ability to separate compounds based on their polarity, and its relatively low cost and ease of use. In this study, TLC was able to detect the chemical composition discrepancies of counterfeit drugs in nearly half of the cases. This result corroborates findings from previous research, which demonstrated that TLC is effective in identifying counterfeit medicines based on variations in chemical profiles, especially when combined with other techniques such as High-Performance Liquid Chromatography (HPLC) or FTIR[10].

Fourier Transform Infrared Spectroscopy (FTIR), though more sophisticated, also performed well in detecting counterfeit drugs, identifying discrepancies in 40% of the cases. FTIR analyzes the molecular vibrations of the sample, providing a unique infrared spectrum that can be used to identify the specific functional groups of compounds. The ability of FTIR to identify counterfeit drugs based on spectral analysis is well-documented in the literature [11], and its use in pharmaceutical quality control has been increasing due to its non-destructive nature, speed, and minimal sample preparation. However, FTIR requires specialized equipment and trained personnel, making it less feasible in low-resource settings where it may not be routinely available [12].

In contrast, colorimetric reactions and visual inspection were less effective, identifying only 16% and 12% of counterfeit drugs, respectively. These findings reflect the well-known limitations of visual inspection in detecting counterfeit medicines, as counterfeit products can often closely resemble their authentic counterparts in appearance. Colorimetric reactions, which rely on the change in color of a chemical reagent in the presence of certain compounds, were more effective for some antibiotic samples but failed to detect many others. These results support the notion that relying on basic testing methods alone is insufficient for ensuring the quality of medicines, especially in regions where counterfeit drugs are prevalent [13].

Dissolution testing, which assesses the rate at which a drug is released from its dosage form, was able to detect drugs with altered release profiles in 20% of counterfeit samples. While dissolution testing is crucial for evaluating the performance of solid dosage forms like tablets and capsules, it is not always sensitive to all types of counterfeit medicines. For instance, counterfeit drugs that maintain their dissolution profiles but have altered chemical compositions may go undetected by this method. Therefore, dissolution testing should be used in conjunction with other methods for more comprehensive counterfeit detection [14].

The study also highlighted the variation in the prevalence of counterfeit drugs across different pharmacies. Pharmacy 3 had the highest rate of counterfeit drugs (20%), while Pharmacy 7 had the lowest (13%). This variation can be attributed to several factors, including the sourcing practices of individual pharmacies, the quality control measures in place, and the regulatory oversight in each area. It is possible that pharmacies with lower detection rates may have less rigorous screening procedures or may obtain their stock from suppliers with fewer quality assurances. Previous studies have shown that counterfeit drugs are more likely to enter pharmacies with weaker procurement procedures or limited access to regulatory bodies [15]. Additionally, pharmacies located in more rural or less regulated areas may have higher risks of stocking counterfeit medicines, as they are more likely to receive products from unverified sources.

The detection rates across different pharmacies underline the importance of improving quality control measures at the pharmacy level. Pharmacies must be encouraged to adopt more robust testing protocols and develop partnerships with regulatory bodies to ensure that medicines are sourced from reputable suppliers. Furthermore, training programs for pharmacy staff on counterfeit drug detection could help improve the overall detection rates and safeguard public health.

The feasibility of implementing these testing methods in routine pharmacy practice is a critical consideration, especially in low-resource settings. While TLC and colorimetric reactions are relatively cost-effective and easy to perform, FTIR and dissolution testing require more advanced equipment and expertise, which may not be readily available in many pharmacies.

This study found that the cost and training requirements of FTIR and dissolution testing may limit their widespread implementation, particularly in rural areas. However, the findings suggest that TLC could serve as a practical and effective tool for counterfeit drug detection in these settings. Its simplicity, portability, and low cost make it an ideal method for use in community pharmacies with limited resources [16].

Moreover, improving the accessibility of FTIR and dissolution testing through collaborative efforts with local regulatory authorities or academic institutions could enhance the detection capacity of pharmacies. Providing pharmacies with affordable access to these advanced techniques and offering regular training in their use could help to improve the overall detection of counterfeit medicines in the community. Additionally, the integration of counterfeit detection methods into routine pharmacy practice would require substantial investment in infrastructure, training, and awareness campaigns to ensure that all pharmacy staff are adequately equipped to identify substandard medicines [17].

The results of this study emphasize the need for a multi-faceted approach to combat the growing problem of counterfeit medicines. Relying on a single testing method is insufficient for identifying all counterfeit products, as the various types of counterfeits may present in different ways. A combination of techniques, such as TLC for chemical composition analysis, FTIR for spectral analysis, and dissolution testing for release profile evaluation, would offer a more comprehensive solution. Furthermore, training pharmacists and pharmacy staff in the use of these methods is essential for improving the detection and prevention of counterfeit drugs in the community [18].

In addition to enhancing detection methods, there is a critical need for increased regulatory oversight and collaboration between pharmacies, healthcare providers, and government agencies. Strengthening the pharmaceutical supply chain through better monitoring and regulation can help reduce the entry of counterfeit drugs into the market. Public awareness campaigns that educate consumers on how to identify counterfeit medicines and report suspected products to authorities are also necessary to safeguard public health [19].

While this study provides valuable insights into the detection of counterfeit medicines, there are several limitations that should be considered. The study was conducted in a single urban-rural setting, and the findings may not be generalizable to other regions with different healthcare infrastructures or regulatory environments. Additionally, the sample size was limited to 150 drug samples, and larger studies are needed to better understand the prevalence of counterfeit drugs in different geographic locations.

Future studies should focus on evaluating the effectiveness of newer, more advanced technologies, such as portable Raman spectroscopy or mass spectrometry, for detecting counterfeit medicines in real-world pharmacy settings. Additionally, research into the impact of counterfeit drugs on patient outcomes, such as treatment failure or drug resistance, is essential for furthering our understanding of the public health threat posed by counterfeit medicines.

Conclusion

This study underscores the importance of implementing effective counterfeit drug detection methods in pharmacies to ensure the safety and efficacy of medicines. While TLC and FTIR were the most effective methods in detecting counterfeit drugs, there is a need for a multi-pronged approach that combines va

rious testing techniques. By improving access to advanced testing methods, enhancing training for pharmacy staff, and strengthening regulatory oversight, we can work towards safeguarding public health and ensuring that patients receive safe, effective medications.

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Microbiome-drug interactions: implications for pharmacokinetics, drug efficacy, and safety

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ABSTRACT

The human microbiome has emerged as a crucial modulator of drug response, significantly influencing pharmacokinetics, efficacy, and safety. This review explores the multifaceted interactions between the gut microbiota and pharmaceuticals, highlighting the bidirectional nature of these relationships. A literature search covering publications from 2010 to 2025 was conducted using databases such as Google Scholar, PubMed, Web of Science, Embase, and Scopus. Keywords included "Microbiota", **"**Pharmacokinetics"**,** "Drug Metabolism"**, "**Drug Interactions"**, "**Gastrointestinal Microbiome"**and "**Precision Medicine." Microbial enzymes can metabolize drugs before absorption, alter their chemical structures, and influence their bioavailability and systemic exposure. These microbiome-mediated transformations can enhance or diminish drug efficacy, lead to the formation of toxic metabolites, or interfere with drug activation, particularly in prodrugs. Conversely, drugs can perturb microbial composition and diversity, potentially contributing to dysbiosis and long-term health consequences. Variability in individual microbiota profiles is increasingly recognized as a contributor to inter-individual differences in drug responses, offering an explanation for observed inconsistencies in therapeutic outcomes and adverse drug reactions. Notable examples include the microbial inactivation of digoxin**.** In recent years, the human microbiome has emerged as a crucial determinant of health and disease, influencing a wide array of physiological processes including digestion, immunity, and neurochemical signaling. Among its lesser-known but increasingly recognized roles is its profound impact on drug metabolism and therapeutic outcomes. These microbiome–drug interactions are now understood to contribute significantly to the variability in drug response observed among individuals, challenging the traditional one-size-fits-all approach to pharmacotherapy.

Keywords: Microbiota**,** Pharmacokinetics**,** Drug Metabolism**,** Drug Interactions**,** Gastrointestinal Microbiome, Precision Medicine

Introduction

The clinical relevance of this phenomenon is becoming particularly evident as researchers uncover how certain bacteria can enzymatically activate or deactivate drugs, alter their pharmacokinetics, or even generate toxic metabolites. For instance, the inactivation of digoxin by *Eggerthella lenta*, or the metabolism of the anti-cancer drug irinotecan leading to gastrointestinal toxicity, highlight the dual-edged influence of microbial enzymatic activity on therapeutic efficacy and safety [1]. Moreover, antibiotics and other medications that disrupt the microbiome can initiate feedback effects, leading to further alterations in drug metabolism or susceptibility to infections, such as *Clostridioides difficile* [2].

This intricate bidirectional relationship between the microbiome and pharmacologic agents necessitates a deeper understanding of microbiome–drug interactions, particularly within the context of clinical pharmacy. Pharmacists are uniquely positioned to incorporate microbiome science into therapeutic decision-making, especially in areas such as medication therapy management, precision medicine, and adverse drug reaction monitoring.

This review explores the current state of knowledge on microbiome–drug interactions, detailing mechanisms through which gut microbes influence drug action and highlighting drugs most affected by these interactions. It also examines the implications for drug development, pharmacokinetics, therapeutic outcomes, and patient safety. By understanding these interactions, pharmacy professionals can better predict individual responses to medications, minimize adverse events, and contribute to the advancement of personalized medicine.

Methodology

This review employed a systematic approach to identify, evaluate, and synthesize relevant literature on pharmaceutical care practices in Nigeria's hospital and community pharmacy settings. The primary aim was to explore the interactions between the gut microbiota and pharmaceuticals, highlighting the bidirectional nature of these relationships. A comprehensive literature search was conducted across five electronic databases namely PubMed, Embase, Web of Science, Scopus, and Google Scholar, for articles published between January 2010 and May 2025. Search terms combined MeSH keywords (“Microbiota,” “Pharmacokinetics,” “Drug Metabolism,” “Drug Interactions,” “Gastrointestinal Microbiome,” “Precision Medicine”) with free-text variants (e.g., “gut flora,” “drug–microbiome interaction”). Boolean operators (AND, OR) were applied to refine results. Reference lists of key reviews and original studies were manually screened to identify additional relevant publications.

Inclusion and exclusion criteria

Included in the review were original research articles, systematic reviews, and meta-analyses examining the bidirectional interactions between gut microbiota and pharmaceuticals; studies addressing microbial effects on drug absorption, metabolism, efficacy, safety, or therapeutic outcomes; human clinical trials and in vivo/in vitro mechanistic investigations. **Excluded were c**ase reports, editorials, conference abstracts without full text, non-English publications, and studies focused solely on non-gastrointestinal microbiomes (e.g., skin, oral).

Study selection

Titles and abstracts retrieved from the initial search were independently screened by two reviewers. Full texts of potentially eligible articles were then assessed against inclusion criteria. Discrepancies were resolved through discussion or adjudication by a third reviewer.

The Human Microbiome: Composition and Function

The human microbiome refers to the collective genomes of the microorganisms—bacteria, archaea, viruses, fungi, and protozoa—that inhabit the skin and mucosal surfaces, with the greatest density residing in the gastrointestinal tract [3]. This complex ecosystem co-evolves with the host, contributing essential metabolic, immune, and barrier functions that influence health and disease.

The microbial composition of the gut microbiota **is** made up of bacterial phyla dominated by four major bacterial phyla (i.e., Firmicutes, Bacteroidetes, Actinobacteria, and Proteobacteria), with relative abundances varying by individual, age, diet, and geography; Archaea and Eukarya comprising of Methanogenic archaea (e.g., *Methanobrevibacter smithii*) and a diversity of fungal species (the “mycobiome,” such as *Candida* and *Saccharomyces*) which occupy smaller but functionally significant niches; and the v**iral community** termed the gut virome, largely composed of bacteriophages, modulates bacterial populations and that may facilitate horizontal gene transfer, including antimicrobial-resistance genes [4].

The core metabolic processes of the gut microbes ferment indigestible dietary fibers into short-chain fatty acids (SCFAs) like acetate, propionate, and butyrate, which serve as energy substrates for colonocytes, regulate lipid and glucose metabolism, and reinforce intestinal barrier integrity [5]. The microorganisms also function as **immune modulators.** Commensal bacteria educate the host immune system through pattern-recognition receptors (e.g., Toll-like receptors), by promoting tolerance to beneficial microbes while mounting defenses against pathogens. Microbial metabolites also influence systemic immune tone, affecting susceptibility to inflammatory and autoimmune disorders [6].

Gut microbiota also gives and preserves the barrier against pathogens. The microbiota enhances mucosal barrier function by stimulating mucus production, tight-junction protein expression, and antimicrobial peptide secretion, thereby limiting pathogen translocation and systemic endotoxemia. Finally, it serves in n**eurochemical signaling** via the gut–brain axis through the activities of microbiota-derived neurotransmitters (e.g., γ-aminobutyric acid, serotonin precursors) and SCFAs. Through these agents, the gut-microbiota modulates neuronal function, with implications for mood, cognition, and behavior [7].

Mechanisms of microbiome–drug interactions

The human microbiome influences drug disposition through several mechanisms that affect pharmacokinetics, efficacy, and toxicity. One of the primary pathways is **direct microbial metabolism** of drugs. Gut microbes express a variety of enzymes—such as azoreductases, nitroreductases, hydrolases, and β-glucuronidases—that can chemically modify drugs before absorption. These modifications may activate prodrugs, inactivate therapeutic agents, or generate toxic metabolites, as seen with the reactivation of irinotecan's glucuronide conjugates by microbial β-glucuronidases [8-10].

Another key mechanism is **indirect modulation of host metabolic pathways.** Microbes can alter the expression or activity of host drug-metabolizing enzymes (e.g., cytochrome P450 enzymes) and transporters by producing signaling molecules or metabolites such as short-chain fatty acids and secondary bile acids. Microbial interactions may also influence **drug absorption** by modifying intestinal pH, mucosal barrier integrity, or bile acid composition, thereby impacting solubility and permeability. Moreover, **microbiota-induced immune modulation**can affect the pharmacodynamics of immunotherapeutics and vaccines [11].

Direct metabolism of drugs by microbiota

The gut microbiota plays a crucial role in the direct metabolism of orally administered drugs through a wide array of microbial enzymes capable of altering drug structure and activity. This direct interaction can lead to either **enzymatic activation** of prodrugs or **inactivation** of active compounds, significantly influencing their therapeutic efficacy and toxicity [12].

Enzymatic activation occurs when microbial enzymes convert inactive compounds into their active forms. A classic example is **sulfasalazine**, a prodrug used to treat inflammatory bowel disease. It is poorly absorbed in the upper gastrointestinal tract but becomes therapeutically active only after microbial azoreductases in the colon cleave it into **5-aminosalicylic acid (5-ASA)** and sulfapyridine [13].

Conversely, **enzymatic inactivation** by gut microbes can reduce drug efficacy. For instance, the cardiac glycoside **digoxin** is inactivated by the gut bacterium *Eggerthella lenta*, which expresses a specific reductase enzyme that reduces digoxin into inactive dihydrodigoxin. This microbial activity varies among individuals, contributing to inconsistent drug responses [14].

These transformations illustrate the importance of microbiota in modifying drug fate before absorption. Understanding such interactions is essential for predicting drug responses, personalizing therapy, and mitigating adverse effects, particularly for drugs with narrow therapeutic indices or those requiring microbial activation for efficacy [15].

Microbiome-Mediated Modulation of Host Enzymes

Beyond direct metabolism of drugs, the microbiome can **indirectly influence drug disposition** by modulating the host's own metabolic systems, particularly **cytochrome P450 (CYP) enzymes**and**drug transporters.** These host proteins are central to drug absorption, distribution, metabolism, and excretion (ADME), and their activity can be significantly affected by microbial signals.

Gut microbes produce a wide range of metabolites—such as **short-chain fatty acids (SCFAs), secondary bile acids, indoles**, and **lipopolysaccharides (LPS)—**that interact with host signaling pathways. These microbial metabolites can modulate nuclear receptors like the **pregnane X receptor (PXR), aryl hydrocarbon receptor (AhR),** and**farnesoid X receptor (FXR),** which in turn regulate the expression of CYP enzymes and transporters such as **P-glycoprotein (P-gp)** and **organic anion transporting polypeptides (OATPs) [17].**

For example, microbial-derived secondary bile acids can activate PXR, leading to the upregulation of **CYP3A4,** a key enzyme responsible for metabolizing over 50% of clinically used drugs. Similarly, indole derivatives from tryptophan metabolism may influence AhR signaling, altering CYP1A1 expression [18].

These interactions suggest that microbial composition can indirectly dictate the rate and extent of drug metabolism and clearance. Dysbiosis or shifts in microbiota due to diet, antibiotics, or disease may therefore lead to variability in drug response by altering host enzymatic and transporter activity, highlighting the importance of integrating microbiome factors into pharmacokinetic profiling and personalized medicine approaches [19]. Influence on drug absorption and bioavailability

The gut microbiome significantly influences **drug absorption and bioavailability** by modifying the gastrointestinal environment and host physiology. Two key mechanisms include its impact on **intestinal barrier integrity**and**bile acid metabolism,** both of which play crucial roles in drug solubility, permeability, and systemic availability [20. 21].

Intestinal barrier integrity is maintained by tight junction proteins that regulate the passage of substances across the epithelium. A healthy microbiota supports this barrier through the production **of short-chain fatty acids (SCFAs)** like butyrate, which reinforce tight junctions and prevent increased intestinal permeability. Dysbiosis, in contrast, can compromise barrier function—often referred to as a "leaky gut"—leading to altered drug absorption, inflammation, and unintended systemic exposure to microbial products and drugs [22-24].

The microbiome also modulates **bile acid metabolism**, which affects the solubilization and micellar transport of lipophilic drugs. Gut bacteria convert primary bile acids into secondary bile acids, altering the composition and emulsification capacity of bile. This can influence the **solubility and dissolution rate** of orally administered drugs, especially those that rely on bile-mediated absorption [25].

Additionally, microbial fermentation products and other metabolites can modify **luminal pH**, particularly in the colon, impacting the ionization and absorption of pH-sensitive drugs [26]. Such pH changes can either enhance or impair the passive diffusion of drugs across the gut epithelium.

Together, these microbiome-driven changes underscore the importance of considering host–microbe interactions when evaluating oral drug bioavailability and therapeutic outcomes.

Generation of Toxic Metabolites

The gut microbiome can contribute to**drug-induced toxicity**by generating harmful metabolites through enzymatic transformations. This process may enhance the **systemic or local toxicity** of certain medications, particularly those that undergo enterohepatic circulation or are metabolized by microbial enzymes in the colon [27].

A prominent example is **irinotecan**, a chemotherapeutic agent used in colorectal cancer. After hepatic glucuronidation, irinotecan is excreted into the bile as an inactive metabolite (SN-38G). However, microbial **β-glucuronidases** in the colon can deconjugate SN-38G back into the active form SN-38, which is highly toxic to intestinal epithelial cells. This reactivation leads to severe **delayed-onset diarrhea**, a major dose-limiting side effect.

Another class of drugs associated with microbiome-related toxicity is **nonsteroidal anti-inflammatory drugs (NSAIDs).** Chronic use of NSAIDs can disrupt the gut microbiota, increase intestinal permeability, and promote the microbial production of **reactive oxygen species (ROS)** and **pro-inflammatory mediators**. These effects can contribute to gastrointestinal ulcers, bleeding, and **enteropathy**. Furthermore, microbial transformation of NSAID metabolites may result in **toxic intermediates** that exacerbate mucosal damage [27].

These examples highlight the need to consider microbial contributions to drug metabolism not only for therapeutic efficacy but also for safety. In some cases, strategies like**β-glucuronidase inhibitors, microbiome modulation**, or targeted drug delivery systems are being explored to reduce microbiota-mediated toxicity and improve drug tolerability.

Drugs Most Affected by Microbiome Interactions

Certain classes of drugs are particularly susceptible to microbiome-mediated effects due to their chemical structures, metabolic pathways, or sites of absorption. These interactions can alter drug activation, inactivation, toxicity, and therapeutic outcomes. Notable examples include:

Cardiovascular drugs

Digoxin is inactivated by the gut bacterium *Eggerthella lenta*, leading to reduced therapeutic efficacy in individuals with high microbial reductase activity [29].

Immunosuppressants and anti-cancer drugs

Irinotecan, a chemotherapeutic agent, is reactivated in the gut by microbial **β-glucuronidases,** contributing to dose-limiting gastrointestinal toxicity [30].

Cyclophosphamide and oxaliplatin efficacy partly depends on microbiome-induced immune modulation.

Prodrugs activated by microbes

Sulfasalazine is cleaved by bacterial **azoreductases** into its active form, 5-aminosalicylic acid, essential for its anti-inflammatory action in the colon [31].

Metformin

This antidiabetic drug alters gut microbiota composition, which in turn contributes to its glucose-lowering effects and gastrointestinal side effects [32].

NSAIDs and Acetaminophen

These drugs can cause gut microbiota disruption, and microbial enzymes can modify their metabolites, potentially affecting toxicity [34].

L-Dopa (Levodopa)

Microbial decarboxylation of L-Dopa in the gut can reduce central nervous system bioavailability, affecting Parkinson's disease management. Understanding which drugs are most affected by microbiome interactions is essential for predicting variable responses, mitigating adverse effects, and guiding personalized therapy [35]. Table 1 presents some drugs, microbiome-mediated metabolism and pharmacokinetic effects.

Table 1: Selected examples of microbiome-mediated drug metabolism and its pharmacokinetic impact

Drug	Therapeutic class	Microbial species	Microbiome effect	Pharmacokinetic effect
Acetaminophen	Analgesic	Many gut microbes	Sulfonation pathway competition	Potential altered hepatic metabolism
Digoxin	Cardiac glycoside	Eggerthellalenta	Reduction/inactivation	Reduced oral bioavailability
Levodopa	Antiparkinsonian	Enterococcus faecalis	Converts to dopamine	Reduced central availability and altered efficacy
Sulphasalazine	Anti-inflammatory	Colonic bacteria (azoreductases)	Pro-drug activation	Delayed drug release
Irinotecan	Anticancer agent	ß-glucuronidase producing	Reactivation of toxic metabolites	Increase GI toxicity to SN-38

Impact on pharmacokinetics and pharmacodynamics

The gut microbiome plays a significant role in modulating both **pharmacokinetics** and**pharmacodynamics**Microbiome–drug interactions can lead to measurable changes in drug **half-life, plasma concentration, and clearance**, ultimately influencing drug efficacy and safety. Microbial metabolism can alter drug structures before absorption, leading to **reduced bioavailability** or the generation of**inactive or toxic metabolites.** For example, microbial inactivation of digoxin shortens its half-life and reduces its plasma concentration, potentially leading to therapeutic failure. Conversely, microbial β-glucuronidase activity may prolong drug exposure by **recycling conjugated metabolites,** as seen with irinotecan, thereby increasing toxicity [36].

The microbiome also affects **drug clearance** indirectly by modulating hepatic and renal metabolism through signaling pathways involving nuclear receptors like PXR and AhR. These changes can either accelerate or slow down drug metabolism and excretion, leading to fluctuations in therapeutic levels. Importantly, **inter-individual variability in microbiota composition** contributes to inconsistent drug responses across patients. Two individuals taking the same medication may experience different outcomes due to differences in microbial species, enzymatic capacity, or metabolite profiles. This variability has been observed with drugs like metformin, acetaminophen, and immune checkpoint inhibitors [37].

Overall, the microbiome is a key determinant of drug PK/PD profiles. Integrating microbiome profiling into therapeutic decision-making may enhance precision medicine by predicting responses and tailoring drug dosing to individual microbiota characteristics.

Table 2: Microbiome-drug interaction mechanisms and their clinical effects

Drugs	Mechanism of interaction	Description	Clinical implication
Paracetamol	Competition for metabolic cofactors	Microbes utilize same cofactors (e.g., sulfate, glucuronate) as host enzymes	Modifies host drug metabolism
Digoxin	Enzymatic biotransformation	Microbial enzymes modify drug structure (e.g., reduction, hydrolysis)	Altered drug activation/inactivation, toxicity
Sulfasalazine	Enzymatic biotransformation	Microbial enzymes modify drug structure (e.g., reduction, hydrolysis)	Altered drug activation/inactivation, toxicity
Irinotecan	Deconjugation of drug metabolites	Bacterial β-glucuronidases cleave glucuronide conjugates	Re-exposure to active/toxic forms
CYP3A4 substrates	Modulation of host enzyme expression	Microbiota influence expression of CYPs, transporters, and UGTs in the host	Changes in drug metabolism and clearance

Clinical consequences and safety concerns

Microbiome–drug interactions can have significant clinical implications, particularly in the areas of **adverse drug reactions (ADRs), microbiome disruption**, and the emergence of **antibiotic resistance. Adverse drug reactions and toxicity** can result from microbiota-mediated drug metabolism. For instance, the reactivation of irinotecan's glucuronide conjugates by microbial β-glucuronidases in the colon leads to severe gastrointestinal toxicity. Similarly, microbial inactivation of drugs like digoxin may reduce efficacy, prompting unnecessary dose escalation and increasing the risk of toxicity [38].

Microbiome disruption, or dysbiosis, is a frequent consequence of drug exposure, especially from antibiotics, but also from non-antibiotic drugs such as proton pump inhibitors, antipsychotics, and metformin. Dysbiosis can compromise gut barrier integrity, alter immune responses, and increase susceptibility to conditions like ***Clostridioides difficile*** **infection (superinfection).** These disruptions may also interfere with the host's metabolic and immune functions, leading to long-term health consequences [39].

Furthermore, the **indiscriminate use of antibiotics** can promote the development and spread of **antibiotic-resistant bacteria**, diminishing treatment efficacy and increasing infection risk. However, the **resilience of the microbiome**—its ability to recover after perturbation—varies between individuals and is influenced by microbial diversity, host factors, and environmental exposures. These safety concerns highlight the need for integrating microbiome considerations into drug development, therapeutic monitoring, and pharmacovigilance. Strategies such as microbiome-preserving drugs, co-administration of probiotics, and personalized dosing regimens may help mitigate these risks and improve patient outcomes.

Microbiome-informed personalized medicine

The emerging field of **microbiome-informed personalized medicine**complements traditional pharmacogenomics by incorporating **pharmacomicrobiomics**—the study of how the microbiome influences drug responses. While **pharmacogenomics** focuses on host genetic variations affecting drug metabolism (e.g., CYP450 polymorphisms), pharmacomicrobiomics addresses inter-individual variability stemming from differences in microbial composition, enzymatic capacity, and metabolite production. Together, these approaches offer a more comprehensive understanding of personalized drug responses [41-42].

Predictive modeling and microbiome profiling are at the forefront of this integration. Advances in metagenomics, metabolomics, and machine learning have enabled the development of predictive algorithms that correlate microbial signatures with therapeutic efficacy, drug toxicity, and optimal dosing. For example, microbiome-based models can anticipate adverse reactions to chemotherapeutics or variability in response to antidiabetic drugs like metformin. Incorporating microbiome data into clinical decision-making holds promise for optimizing drug selection and individualizing treatment plans.

In addition to predictive diagnostics, **microbiome-targeted interventions**—such as **probiotics, prebiotics,** and**fecal microbiota transplantation (FMT)—**are being explored to modulate the gut microbiota and improve therapeutic outcomes. Probiotics and prebiotics can enhance beneficial microbial populations, potentially boosting drug efficacy or mitigating side effects. FMT, though still experimental in many contexts, has shown success in restoring microbiome balance in recurrent *Clostridioides difficile* infections and may have future applications in drug-response optimization [43].

As our understanding deepens, microbiome-informed strategies will increasingly shape **precision medicine**, guiding safer, more effective, and individualized pharmacotherapy.

Role of pharmacists in microbiome-drug interaction management

Pharmacists play a pivotal role in identifying, managing, and educating about microbiome–drug interactions, ensuring optimal therapeutic outcomes and patient safety in an evolving landscape of precision medicine.

Patient counseling and medication review are central to the pharmacist's responsibilities. Pharmacists can assess patient-specific factors such as recent antibiotic use, gastrointestinal symptoms, or dietary habits that may influence the gut microbiome. Through comprehensive medication reviews, they can identify drugs with high microbiome interaction potential (e.g., antibiotics, proton pump inhibitors, chemotherapeutics) and provide guidance on appropriate timing, co-administration of probiotics, or dietary modifications to preserve microbiota integrity and minimize adverse effects [44].

Interprofessional collaborationenhances the effectiveness of microbiome-aware care. Pharmacists can work closely with physicians, dietitians, and microbiologists to develop individualized treatment plans, especially for patients receiving complex therapies like immunosuppressants or chemotherapy. They can also contribute to decision-making in cases where fecal microbiota transplantation or microbiome profiling is considered, by evaluating drug–microbiome compatibility and implications for pharmacokinetics.

Additionally, pharmacists have expanding roles in **education and research**. By staying current with pharmacomicrobiomics advances, pharmacists can educate patients, healthcare teams, and students on microbiome impacts. In research settings, pharmacists can contribute to studies on microbiome-informed dosing, drug metabolism, and personalized interventions, helping to bridge the gap between bench and bedside.

Overall, pharmacists are well-positioned to lead efforts in integrating microbiome science into clinical pharmacy practice, contributing to safer, more effective, and personalized medication management.

Future perspectives and research directions

The intersection of microbiome science and pharmacology is rapidly evolving, driven by **emerging tools and technologies** that promise to transform drug development and individualized therapy. Techniques such as **metagenomic sequencing, metabolomics**, and **culturomics** now allow for comprehensive profiling of microbial communities and their functional capacities. Combined with **artificial intelligence (AI)** and machine learning, these data can be used to develop predictive models of drug response, identify novel microbial biomarkers, and optimize therapeutic regimens based on a patient's unique microbiome [45].

Despite these advances, several **challenges in clinical translation** remain. Microbiome composition is highly dynamic and influenced by numerous factors including diet, environment, and medications, complicating the standardization of results. Inter-individual variability and a lack of validated reference microbiomes limit the ability to generalize findings across populations. Additionally, integrating microbiome data into clinical workflows and electronic health records is still in its infancy.

Regulatory and ethical considerations are also critical. There is a need for clear guidelines from regulatory agencies on the use of microbiome-based diagnostics, therapeutics (e.g., fecal microbiota transplantation), and adjuncts like probiotics. Ethical concerns include data privacy, informed consent for microbiome profiling, and the potential for inequitable access to personalized microbiome-based treatments.

Moving forward, interdisciplinary collaboration, robust clinical trials, and the development of standardized protocols will be essential to fully realize the promise of microbiome-informed pharmacotherapy and integrate it responsibly into mainstream healthcare.

Conclusion

The human microbiome plays a profound role in influencing drug metabolism, efficacy, and safety, with growing evidence highlighting its impact on pharmacokinetics, pharmacodynamics, and inter-individual variability in drug responses. Key findings from recent research emphasize the microbiome's ability to directly metabolize drugs, modulate host enzymes, and alter absorption and bioavailability. Additionally, microbial dysbiosis can lead to adverse drug reactions, toxicity, and long-term health consequences, making it essential to consider microbiome dynamics in therapeutic management.

The **implications for pharmacypractice** are significant. Pharmacists are uniquely positioned to lead in identifying and managing microbiome–drug interactions, optimizing medication regimens, and advising on microbiome-preserving strategies such as probiotics, prebiotics, and careful antibiotic stewardship. They can also play a pivotal role in interprofessional collaborations to incorporate microbiome data into clinical decision-making and ensure personalized therapy. With their expertise in pharmacokinetics and patient care, pharmacists are key contributors to microbiome-informed healthcare.

There is a growing **call for the integration of microbiome science into clinical decision-making**. To fully harness the potential of microbiome-informed therapies, future research, the development of predictive models, and the establishment of regulatory frameworks are necessary. As our understanding of the microbiome's role in drug therapy continues to evolve, it is crucial for pharmacy practice to stay at the forefront, ensuring that personalized medicine becomes a reality for every patient.

Ethical Consideration

Data availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request. All data supporting the findings of this study have been included within the article and its supplementary materials, where applicable.

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

Compliance with ethical guidelines

This study was conducted in accordance with ethical standards as outlined in the Declaration of Helsinki and/or relevant institutional and national research committee guidelines. Ethical approval was obtained from the appropriate institutional review board, and informed consent was obtained from all individual participants included in the study.

Authors' contributions

All authors contributed significantly to the conception, design, execution, and/or interpretation of the research. Author SOA was responsible for the conceptualization, methodology, data collection, Author PJE handled data analysis and interpretation, and Author JIA contributed to the drafting and revising of the manuscript. All authors reviewed and approved the final version of the manuscript.

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GUIDE TO AUTHORS

Clients' knowledge, attitude and practices on hydration, presenting hydration status and pharmacist's intervention while requesting prescribed drugs

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ABSTRACT

This study examined the relationship between hydration status and prescription drug requests among clients attending a Pharmaceutical Care Clinic in Ikot Ekpene, Nigeria. A cross-sectional design involving 443 consenting adults utilized a three-part methodology: a structured questionnaire assessing knowledge, attitudes, and practices (KAP) related to hydration; oral interviews to collect medical and prescription histories; and laboratory analysis of hydration indicators. The questionnaire, based on modified validated tools, tested knowledge (maximum score = 27), attitude (Likert scale), and lifestyle practices, with categorization into poor, fair, or good knowledge and positive or negative attitudes. Daily fluid intake and 24-hour urine output were recorded over three days, alongside measurements of urine volume, weight, specific gravity, and osmolality. Blood osmolality was also assessed. Out of 443 approached, 380 respondents (56.1% female, mean age 49.5 ± 6.2 years) completed the study. Knowledge scores were fair overall, with significantly higher mean scores among males and those with higher educational attainment ($p<0.05$). Positive attitudes toward hydration correlated with younger age and tertiary education. Lifestyle practices revealed that males consumed more water post-meal and during the day ($p<0.05$), while older adults showed reduced water intake. Laboratory findings indicated a consistent gap between mean daily fluid intake (approx. 3.5 L) and urine output (approx. 2 L), with males exhibiting higher values. These gender- and education-linked differences in hydration behavior may have pharmacokinetic implications, particularly for renally-excreted drugs. Findings suggest a need for hydration-focused patient counseling in pharmacy settings to optimize therapeutic outcomes and minimize adverse drug events.

Keywords: Hydration status, dehydration, biopharmaceutics, drug disposition, lifestyle practices

Introduction

Water is essential to life as it plays a vital role in every biological system [1]. A scenario of inadequate water levels in humans may affect the biochemical and physiological activities at the cellular level manifesting with or without dysfunctions [2, 3]. Many diseases are characterized by water imbalances in the biological system. As diseases are approached with treatment options, the disposition of selected drugs is similarly affected by the hydration status of the individual and consequently the efficacy and safety [4]. There are limited reports on the assessment of the hydration statuses of clients or patients at the point-of-care prior to prescribing and dispensing of medications cum dosing formalities.

The effect of hydration status on individuals who are on medications has biopharmaceutics consideration as the solubility of drugs at different phases of transit is a key factor [5]. At the gastrointestinal luminal side, drugs are required to be in solution for absorption through the epithelium [6]. The available water in the gastrointestinal tract alongside the hydration status of the epithelial cells influences drug permeability across the cells into the portal [7]. Similarly, the movement of drugs in blood across the extracellular space reaching for the different tissues and into the intracellular compartment are function of water activity [8] receptors is via the solubilized-water based phase. Intestinal absorption occurs through passive permeation (paracellular or transcellular) or active uptake via intestinal transporters. All of these are dependent on the physicochemical properties of the drugs and the absorptive environment. Similarly, passage of drugs via blood to the extracellular and intracellular system is a dynamic function that correlates with the water activity and presence in the system [9].

Patients take drugs most commonly via the oral route but without sufficient recourse to their personal water consumption as a therapeutic factor. Some patients have illnesses that predispose them to dehydration or a hypohydrated status [10]. Several forms of dehydration have been reported in different cases. Isotonic water loss occurs when water and sodium ions are lost together in an individual whereas hypertonoic dehydration results when water loss exceeds sodium ions. Hypotonic dehydration results when the loss of sodium ions exceeds water loss as observed in cases with prolonged diuretic use [11]. Lifestyle practices influenced by socio-cultural beliefs may be responsible for a skewed drug disposition and clinic-toxicological effects with some medications. Other causes of dehydration include illnesses especially those related to symptoms such as diarrhea, vomiting, fever, increased sweating and urination. An infant can become severely dehydrated only after few hours of illness. This has been reported as the major cause of death in children globally [12].

Dehydration affects drug disposition in some predictable manner [13]. Water soluble drugs presents with higher plasma concentration and consequent toxicity. Similarly, the plasma concentration of fat soluble drugs increase due to higher total body fat. This study seeks to evaluate the KAP in patients about dehydration and evaluation of presenting hydration status of clients requesting for drug supplies in a community pharmacy.

Methods

Study protocols

This was a three-part study involving a pre-coded and self-administered questionnaire followed by an oral interview and laboratory determination of fluid intake and urine output hydration levels of respondents. The cross-sectional study focuses on knowledge, attitude and practice assessments of hydration/dehydration. The questionnaire was designed from modification of previous surveys [14] to test knowledge scores (9 enquiries) on definition, symptoms, causes and prevention of dehydration while the oral interview was to establish attitudinal association (6 enquiries) and lifestyle practices (6 enquiries) on fluid consumption in relation to clients' past/current medical concerns. The knowledge levels was categorized as poor, fair and good rated by scores of (<9.0), (9.0 - 18.0) and (>18.0), respectively, out of a maximum score of 27 points. The questions required a "Yes" or "No" answer and 3 point for each correct response. Attitude scores were similarly computed from responses to questions with scores based on respondents' agreement on a scale of numeric values 1 to 5 (using Likert scale with 5 for Strongly agree, 4 for Agree, 3 for Indifference, 2 for Disagree and 1 for Strongly disagree). Adjudging a negative or positive attitude on fluid intake was evaluated as <50% or >50%, respectively. The outcome of response in terms of knowledge scores and attitude scores were matched with the clerked/oral interview for past medical history cum presenting complaints.

Finally, laboratory assessment of daily fluid intake versus daily urine output volumes for 3 consecutive days was performed. Urine collection was total and collected into a 4L container from a particular hour of the day to same time the next day (i.e., 24 h). Respondents were asked if they missed any samples and responses noted. Missed urine samples were not factored into the computation as actual urine presented were measured and computed. The volume (L) of urine was measured with a 1L measuring cylinder while the weight (g) was measured with a weighing scale (Camry Mechanical co, USA). The urine density and urine specific gravity (USG) were computed as weight/volume (g/L). Furthermore, osmolality of the

urine samples was determined using freezing – point osmometer (OsmoPRO®MAX, Advanced Instrument Inc. Norwood, MA). Blood samples (2 mL) was taken from the median cubital veins of respondents into a plain sample bottle and subsequently analyzed. Blood osmolality was similarly performed using blood samples with the freezing – point osmometer. Physical observation of the clients were made during the discussions and noted accordingly. The drugs on the prescriptions were also noted and recorded. The duration of study was a period of 6 months (July to December, 2022).

Study area

This was a single-centered study conducted in a Pharmaceutical Care Clinic (PhCC) in Ikot-Ekpene, an urban area located in Akwa-Ibom State, Southern Nigeria. The historic city is the political and cultural capital of the Annang ethnic group in Nigeria. It lies in the coastal highway between Calabar and Aba. Ikot Ekpene covers an area of 45 square miles (116 km^2 with a projected population of 415,000.

Study population

The study population comprises of clients patronizing community pharmacies in the area.

Inclusion criteria

Every client above 18 years who were willing to participate was recruited into the study.

Exclusion criteria

Non-fluency in English language or Ibibio, the major spoken languages in the study area was basis of excluding possible respondents in this study.

Sampling method and sample size

Clients were approached as they called to fill their prescriptions. They were informed about the study and their consent sought in writing. Convenience sample method was adopted as everyone who met the criteria calling at the PhCC was eligible to participate in the study. Sample size was calculated using the formula

$$n = {Nz^2\delta^2}/{(N-1)e^2 + z\,\delta^2} \quad \text{....(Equation 1).}$$

$$n = {415000\ x\ 1.96x\ 1.96\ x\ 10x10}/{(415000-1)1x0.1 + 1.96x}$$

$$n = {398566}/{4150.48}$$

$$n = 384$$

15% calculated for attrition bring sample size to 443 clients

Where n=required sample size; z = z value at reliability or significant level 95% = 1.96; δ=standard deviation of the sample, 10; e = acceptable margin of error, 0.1.

Study protocols

The recruitment of respondents was spread over 6 months excluding Sundays. Recruitment and participation time each day were mornings (9:00 am to 12:00 pm) and evenings (2:00 pm to 6:00 pm). The questionnaires were collected immediately after completion and the oral interview commenced. A sample of blood was thereafter taken and labeled with the code on the questionnaire. The respondents were subsequently advised to take definite measurements and records of fluid intake and urine output for the following 3 days post recruitment. The respondents were requested to report for further instructions/counseling based on the outcome of hydration test.

Ethical approval

Ethical approval was received from University of Uyo Institutional Health Research Review Board

Data collection/analyses

Data collection and entry/collation were done by the principal researcher and 3 research assistants. This was entered into Microsoft excel spreadsheet, Windows 10.

Statistical analysis

Characteristics of respondents were summarized as frequencies and percentages while the continuous variables were presented as mean and standard deviation or standard error (as applicable). Data for the variables were tested for normal distribution using Kolmogorov-Smirnov test, and for plausibility and consistency. Data with normal distribution were proceeded with parametric test (T-test or analysis of variance (ANOVA) while non-parametric test employed Mann-Whitney – U test or Kruskal –Wallis test) as considered appropriate for differences within the variable group. Statistical significance was taken at the levels of 0.001 or 0.01 or 0.05 and indicated appropriately in parenthesis. The coefficient of variation was determined as SD/mean of values.

Results

A total of 443 (265 female, 178 male) clients were approached; (10.4%) did not agree to participate. The reasons for non-participation among the decline group were time factor (43.5%), blood sampling/bleeding inconveniences (41.3%) and personal (15.2%). A response rate of 65.8% 380/443 comprising of 380 respondents, female 213 (56.1%) and male 167 (43.9%), pulled through the study with an average monthly participation of 65. The mean age of the respondents was in 49.5±6.2 years. Table 1 presents the socio-demographics of the respondents.

Table 1: Socio-demographic characteristics of respondents and their perception of illness

Characteristics	Categories	N(%)
Gender	Male	167 (43.9)
	Female	213 (56.1)
Body weight (Kg)	Male	
	40 – 60	36 (9.5)
	61-80	56(14.7)
	81 and above	65(17.1)
	Female	
	40 – 60	89 (23.4)
	61-80	52(13.7)
	81 and above	72(18.9)
Age Group	18-30	142 (37.4)
	31-60	165 (43.4)
	61-above	73 (19.2)
Educational attainment	No formal	97 (25.5)
	Primary	115 (30.3)
	Secondary	137 (36.1)
	Post secondary	30 (7.9)
Marital status	Single	199 (52.4)
	Married	174 (45.8)
	Separated	7 (1.8)

Table 2 Knowledge scores for respondents

S/n	Mean knowledge score																	
	Gender			Age						Body weight				Educational level				
K	A	B	p-value	C	D	E	F	G	p-value	H	I	J	p-value	K	L	M	N	P-value
K1	2.52	2.25	0.078	2.63	2.42	1.89	2.57	2.47	0.068	2.28	2.29	2.52	9.079	2.01	1.83	2.19	2.43	0.043
K2	1.80	1.06	0.086	1.39	1.40	1.23	1.72	1.32	0.057	1.57	1.17	1.77	0.789	1.42	1.89	1.84	2.50	0.032
K3	1.98	1.30	0.081	2.51	1.60	1.52	1.37	0.90	0.078	1.61	2.36	1.59	0.579	0.84	2.24	2.45	2.30	0.052
K4	2.70	2.39	0.080	2.44	1.40	1.61	1.07	2.26	0.066	2.40	2.52	2.65	0.074	1.86	2.40	2.21	2.74	0.027
K5	1.08	1.04	0.079	1.56	1.69	2.29	1.07	0.82	0.690	1.66	1.30	1.31	0.068	1.33	2.56	2.65	2.90	0.023
K6	1.06	1.45	0.062	1.56	1.21	1.47	1.69	1.41	0.678	1.77	1.91	1.46	0.071	2.20	2.66	2.26	2.26	0.023
K7	1.45	1.55	0.012	1.53	1.77	1.32	1.60	1.41	0.678	1.67	1.51	1.44	0.068	2.44	2.61	2.43	2.60	0.034
K8	1.52	144	0.087	1.30	1.87	1.38	1.51	1.47	0.078	1.36	1.56	1.44	0.089	2.01	2.37	2.17	2.04	0.046
K9	2.66	2.63	0.067	1.59	1.50	1.86	2.31	2.30	0.064	1.24	2.85	1.16	0.076	1.86	2.35	2.06	2.52	0.029

- **Average scores per group have been computed**

QUESTIONS K1-K9 ; K1-Hydration status relates to the fluid in the body; K2-Fluid in the body affect the efficacy of drugs/; K3- Some symptoms are due to dehydration; K4-Some physical activities can cause dehydration; K5-Some drugs can cause severe dehydration; K6-Dehydration can cause drug toxicity; K7-Dehydration can cause hospitalization; K8-Dehydration can cause death; K9- Dehydration can be reversed

Gender (A is male; B is female); Age (C is <12-28; D is 29-38, E is 39-48, F is 49-58 and G is 59 years and above); Body weight (H is 40-60kg, I is 61-80kg, and J is 81 kg and above); Educational status (K is primary, L is secondary, M is tertiary and N is post-tertiary educational attainments)

Table 3 Attitude scores for respondents

S/N	MEAN KNOWLEDGE SCORE																	
	Gender			Age						Body weight				Educational level				
K	A	B	p-value	C	D	E	F	G	p-value	H	I	J	p value	K	L	M	N	P-value
K10	3.50	2.14	0.045	2.16	2.11	1.13	1.45	2.14	0.030	2.32	1.9	1.41	0.670	1.48	1.25	1.19	2.10	0.031
K11	2.11	1.94	0.078	2.31	2.49	2.07	1.48	2.34	0.022	1.73	1.4	2.62	0.510	2.98	2.59	2.49	2.25	0.025
K12	4.14	2.46	0.032	2.21	2.98	1.98	2.03	1.87	0.051	2.44	1.9	2.12	0.781	1.40	2.75	2.12	2.87	0.078
K13	2.16	3.16	0.025	2.49	3.10	1.84	2.45	1.35	0.050	2.41	2.1	1.85	0.678	2.25	1.90	2.47	2.12	0.068
K14	2.74	3.17	0.011	2.32	2.69	1.49	1.32	1.63	0.057	1.73	1.6	1.52	0.499	2.17	1.11	2.67	2.10	0.097
K15	2.13	3.41	0.140	2.12	2.95	1.42	1.69	1.49	0.075	1.31	2.4	2.63	0.673	1.10	2.32	2.19	2.35	0.019

- **Average scores per group have been computed**

K10- taking water after food is my practice; K11- taking water as I continue with my meal is my ideal practice; K12- After eating and before another meal, I drink water as a lifestyle; K13- I move along with water to drink throughout the day; K14 –I take water daily first thing in the morning; K15 –I am concerned and monitor the urine I void steadily

Gender (A is male; B is female); Age (C is <12-28; D is 29-38, E is 39-48, F is 49-58 and G is 59 years and above); Body weight (H is 40-60kg, I is 61-80kg, and J is 81 kg and above); Educational status (K is primary, L is secondary, M is tertiary and N is post-tertiary educational attainments)

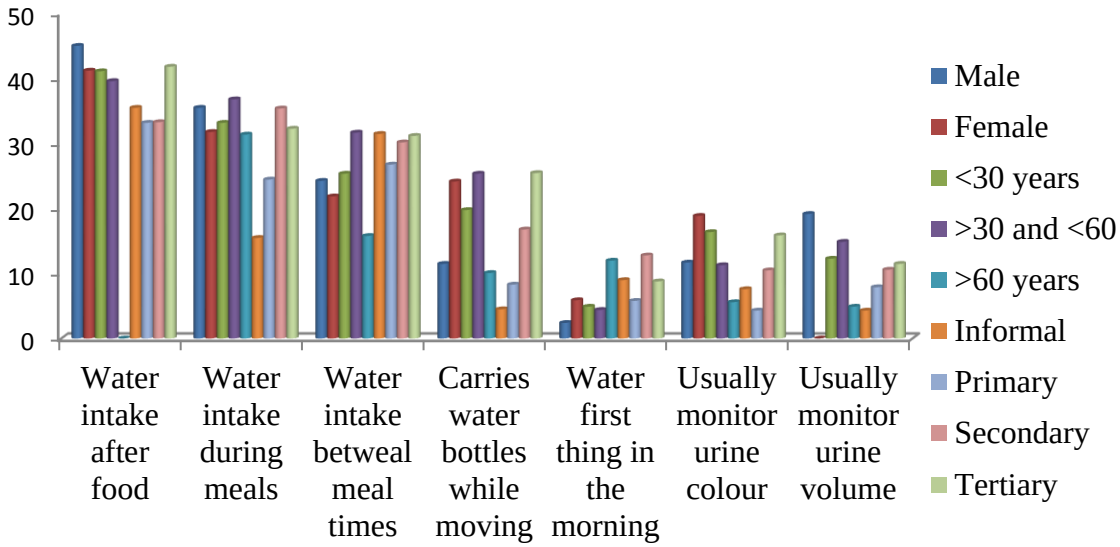


Figure 1: Lifestyle practices of respondents to water intake

The lifestyle practices as revealed in Figure 1 varied widely among the genders, age groups and educational levels. Significantly higher proportion of males take water after food than females as well as during meals alongside between meal times ($P<0.05$).The proportion of older population revealed lower water intake practices after food than the younger respondents ($P<0.05$). Similarly, respondents with tertiary level of education drink water after meals more than the lower levels of educational exposure.

The mean daily volume of fluid intake (water and other fluids)for all respondents was higher than the mean daily urine output ($P<0.05$). Similarly, the values of mean daily fluid intake and urine output for the respective genders showed significant higher values gender wise.

The figure 2 presents the mean daily fluid intake and urine output across three days among all participants, with gender-based comparisons. Overall, fluid intake averaged above 3.5 L/day for all participants, while urine output remained consistently lower, averaging just above 2 L/day. Male participants had higher mean fluid intake (approximately 4.2 L/day) and urine output (about 2.3 L/day) compared to females, who averaged around 3.2 L/day in intake and 1.6 L/day in output. This discrepancy suggests possible gender-related differences in hydration behavior, metabolism, or fluid retention. From a pharmacological standpoint, these variations can influence drug pharmacokinetics—especially for medications eliminated via the kidneys or those sensitive to hydration levels (e.g., NSAIDs, diuretics).

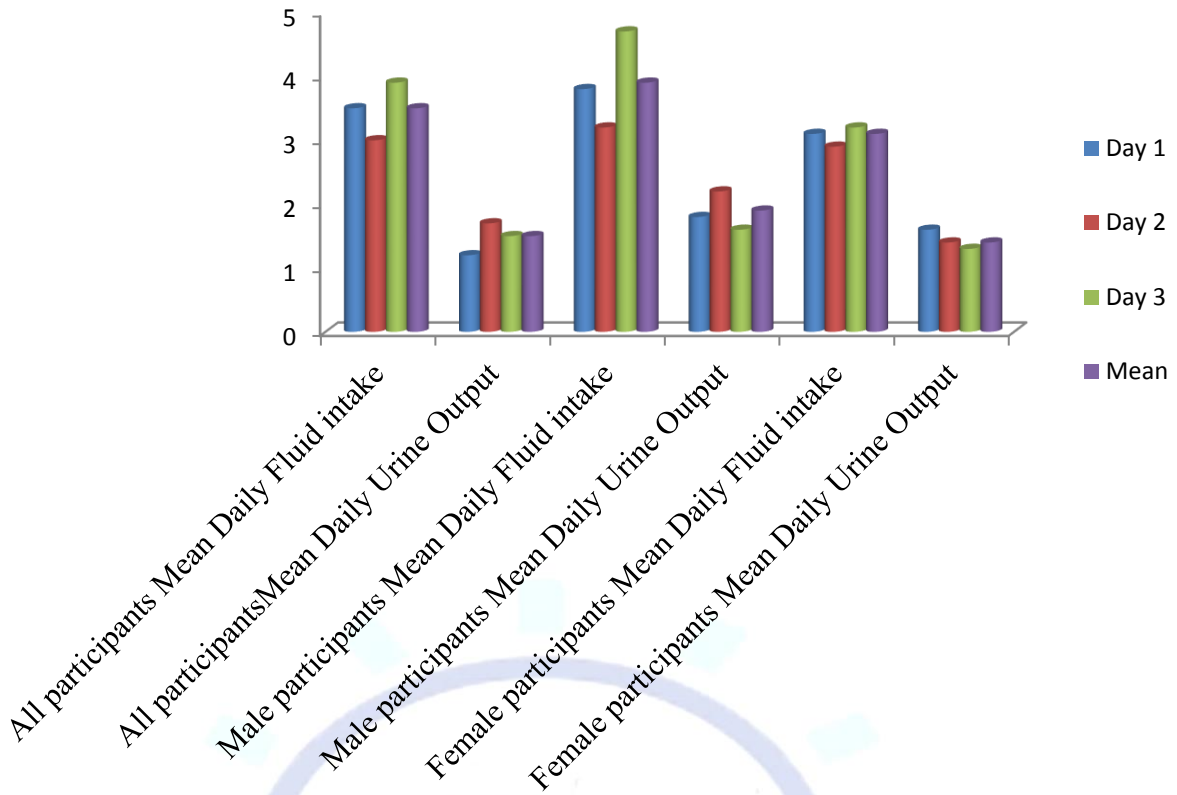
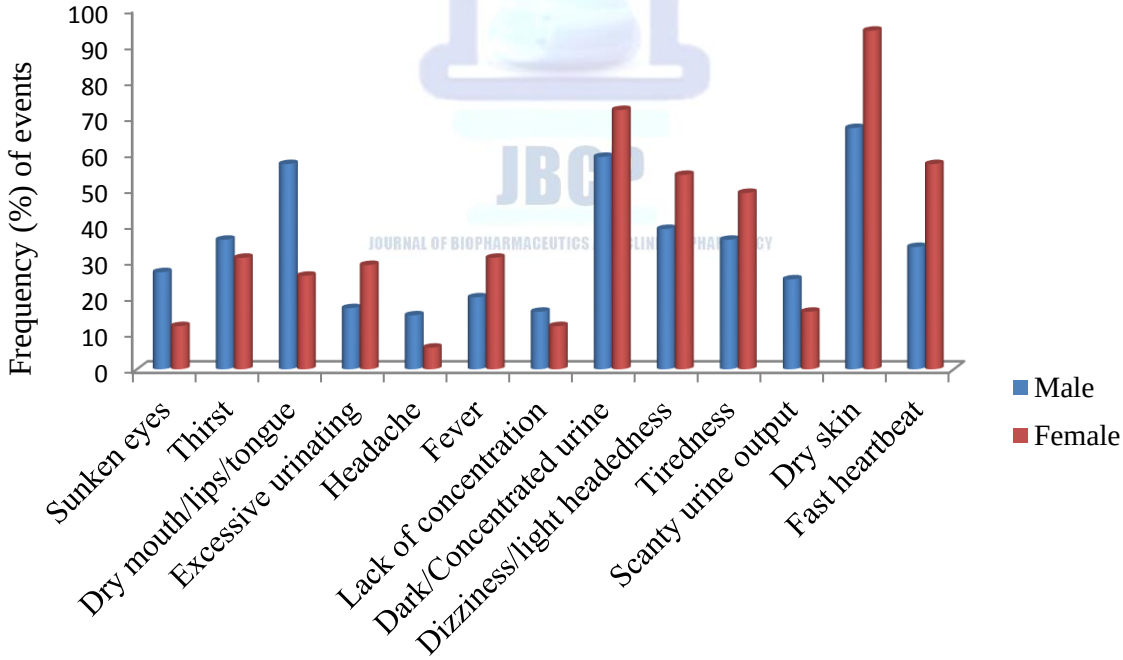


Figure 2: Daily water intake and urine output (L/day) for the three days with respect to gender

The figure 3 illustrates gender-based differences in symptoms reported by clients related to hydration status, with potential implications for drug use and pharmacokinetics. Overall, female clients reported a higher frequency of hydration-related symptoms such as dizziness/light-headedness (95%), dark/concentrated urine (75%), and dry mouth/lips/tongue (40%) compared to males. Males, however, reported more excessive urination (60%) and thirst (40%), which may suggest differences in fluid loss or compensatory intake.



Symptoms reported by clients

Figure 3: Frequency of occurrence of symptoms associated with dehydration among clients

Table 4: Mean daily osmolality (mOsm/Kg) for respondents

Days	Urine Osmolality (Mean ±SD mOsmol/Kg)			P-Value
	All respondents	Male	Female	
1	631±12	662±17	619±11	0.030
2	622±18	655±14	599±14	0.024
3	637±22	678±17	608±16	0.017
All samples	635±16	659±16	601±19	0.014

*Mann-Whitney test was employed to derive p-value for difference between genders

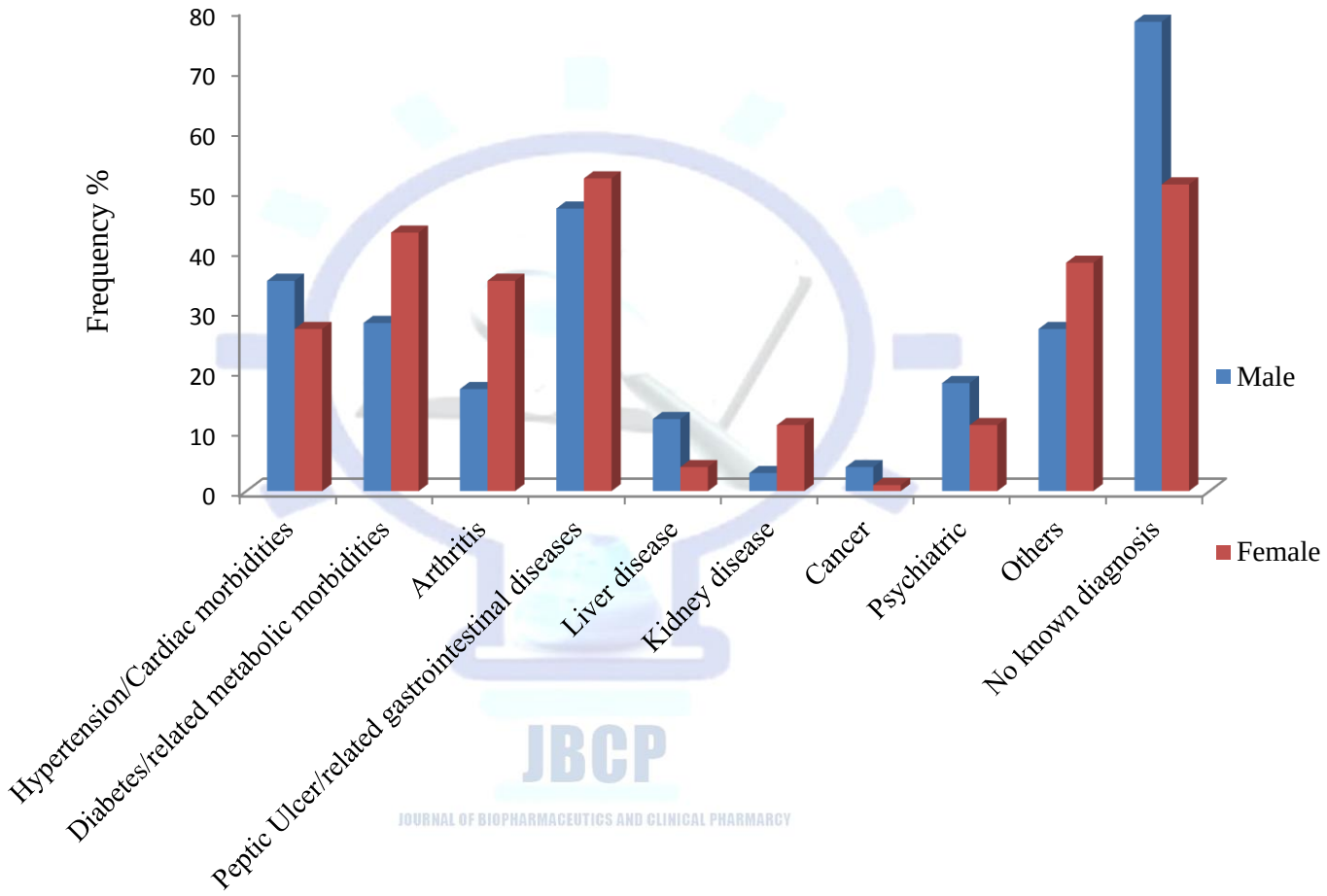


Figure 4: Perceived/reported diagnosis for which drugs were prescribed

Discussion

In clinical pharmacy, understanding the principles of biopharmaceutics is essential for optimizing drug therapy outcomes. One often overlooked yet critical factor is the patient's hydration status. Hydration plays a pivotal role in drug absorption, distribution, metabolism, and excretion—processes collectively referred to as pharmacokinetics. Despite its relevance, the integration of hydration assessment into pharmaceutical care remains underemphasized, particularly in developing clinical settings. This study bridges that gap by evaluating the influence of hydration on drug therapy, specifically highlighting the implications of poor hydration on adverse drug events, especially in populations with limited access to health education and healthcare services.

Hydration status significantly affects biopharmaceutical processes. Proper hydration supports optimal blood flow and maintains renal function, both of which are vital for the metabolism and elimination of many medications. Drugs with narrow therapeutic windows or those reliant on renal clearance are especially sensitive to hydration status. Dehydration can lead to drug accumulation and toxicity, whereas overhydration can dilute drug concentrations, reducing efficacy. Recognizing the critical balance required, this study adopts a pharmaceutical care model that incorporates hydration assessment alongside the patient's medication profile, medical history, and presenting symptoms. This holistic approach is relatively novel in the study area, marking a progressive step in personalized medicine.

A systematic protocol was employed for sampling and data collection, enabling robust statistical analysis across demographic variables such as gender, age, and educational attainment. The findings revealed striking intra-individual and inter-group differences in hydration habits and knowledge. Notably, variations were observed in daily water intake levels, with educational status being a strong predictor. Formally educated individuals exhibited better hydration practices, suggesting a link between knowledge acquisition and health-promoting behaviors. These insights underline the importance of targeted health education campaigns to raise awareness about the role of hydration in medication effectiveness and overall wellness.

The study also evaluated the types of medications commonly used by participants, focusing on those that influence water elimination and thermoregulation. Amphetamines, frequently prescribed for attention deficit hyperactivity disorder (ADHD), were among the drugs identified. These substances can elevate core body temperature, increasing the risk of dehydration. Similarly, antidepressants, antipsychotics, antihistamines, beta-blockers, and anticholinergics interfere with the body's thermoregulatory mechanisms by impairing sweating or altering blood circulation. When hydration is inadequate, the pharmacodynamics of these drugs can shift, increasing the risk of side effects and reducing therapeutic benefits.

Alarmingly, the study revealed limited awareness among participants about the relationship between hydration and drug movement within the body. There was also poor recognition of dehydration as a potential cause of their current symptoms. Many participants reported complaints such as headache, fever, and fatigue—common signs of dehydration—yet failed to associate these symptoms with poor water intake. These misconceptions were more pronounced in female participants, who also reported a higher prevalence of the aforementioned symptoms. This disparity may reflect gender-based differences in health-seeking behaviors, biological susceptibility to dehydration, or social conditioning that influences daily water consumption.

Given these gender disparities, the study recommends the development of gender-specific education and intervention strategies to address hydration-related issues. Women, in particular, may benefit from targeted messaging that links hydration to symptom relief and improved drug outcomes. Similarly, clinicians are encouraged to assess hydration status when prescribing medications, especially those that are excreted renally or have a narrow therapeutic index. Providing hydration counseling during drug dispensing sessions could substantially reduce the risk of adverse drug events, particularly in vulnerable subgroups such as the elderly, the chronically ill, and those with limited health literacy.

The physiology of hydration is complex and influenced by multiple factors. Individual water requirements are not only determined by fluid intake but also by losses through respiration, sweating, and urination. Diet plays a crucial role as well, as certain foods contribute to fluid balance through their water content and osmotic properties. The kidneys, as the primary excretory organs, are central to maintaining hydration homeostasis. Any dysfunction in renal performance can disrupt drug clearance, leading to altered plasma drug levels and associated complications. Therefore, evaluating hydration from a physiological and pharmacological perspective is crucial in pharmaceutical care.

This study further measured 24-hour urine osmolality as an objective indicator of hydration status. Osmolality reflects the concentration of solutes in urine, serving as a reliable marker for body water balance and renal concentrating ability. Findings showed that females had significantly lower mean 24-hour urine osmolality values compared to males, aligning with the work of Perrier et al. (2015). However, the mean values for both genders exceeded

the recommended ideal of 500 mOsm/kg, indicating suboptimal hydration. These results underscore the need for hydration education and behavioral interventions, particularly in populations with inadequate water intake habits.

Lifestyle factors also emerged as key determinants of hydration. The study observed poor attitudes toward water consumption across the board, with many participants failing to meet daily recommended intake levels. Males had slightly better hydration profiles, possibly due to greater engagement in physically demanding tasks that necessitate increased fluid consumption. This aligns with the findings of Duan et al. (2022), who reported a similar gender-based trend and advocated for widespread health education to improve hydration behavior. Importantly, the implications of poor hydration go beyond comfort and performance; they directly affect the pharmacokinetics and dynamics of medications.

Hypohydration—a state of underhydration—can lead to increased plasma concentration of drugs, altered distribution volumes, and impaired renal clearance. These changes can significantly affect therapeutic outcomes, especially for medications that are dose-sensitive or require consistent plasma levels. For instance, in males experiencing high fluid loss without adequate replacement, the pharmacologic behavior of drugs may differ from that in females, leading to gender-specific variability in drug response. Thus, hydration status should be a routine consideration in therapeutic planning and patient counseling.

Moreover, urine osmolality as a measure of hydration provides insight into both behavioral and neuroendocrine responses of the body. The values recorded in this study fell within the established physiological range of 500–1200 mOsm/kg, yet still pointed to a prevalent trend of inadequate fluid intake. Maintaining osmolality below 500 mOsm/kg is ideal for facilitating solute excretion and minimizing kidney strain. Consistent values above this threshold suggest chronic underhydration, which not only affects drug disposition but may also contribute to long-term renal complications.

Finally, the integration of biopharmaceutics and hydration science within clinical pharmacy practice is both necessary and urgent. This study highlights the underappreciated role of hydration in drug therapy outcomes and calls for a paradigm shift toward more holistic pharmaceutical care. By incorporating hydration status into patient assessments, clinicians can reduce the risk of adverse drug reactions, enhance therapeutic efficacy, and promote overall health. Educational initiatives tailored by gender, age, and educational level can further support this goal. Ultimately, the intersection of hydration and pharmacotherapy represents a promising frontier in patient-centered care.

Conclusion

A fair knowledge of hydration status was observed in the surveyed population of the clientele in the PhCC. Poor knowledge was more marked in females, persons with informal training. Complications of dehydrations were also more marked in the males and the lower age groups.

There is the need to promote a culture of fluid intake and assess hydration statuses of clients calling at community pharmacies especially those requesting drugs that may aggravate the condition.

Ethical Consideration

Data availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request. All data supporting the findings of this study have been included within the article and its supplementary materials where applicable.

Conflict of interest

The authors declare no conflict of interest related to the publication of this manuscript.

Compliance with ethical guidelines

This study was conducted in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Ethical approval was obtained from the appropriate ethics review board, and informed consent was obtained from all individual participants involved in the study.

Authors' contributions

SOA conceptualized and designed the study, supervised data collection, and contributed to manuscript writing. MPO and JIA conducted the data analysis and interpreted the results. MIA assisted with data collection, reviewed the manuscript, and provided critical revisions. All authors read and approved the final manuscript.

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GUIDE TO AUTHORS

Clients' satisfaction regarding pharmacists' clerking, physical examination, counseling and resulting informed decisions alongside recommendations/prescribing in community pharmacy

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ABSTRACT

This study assessed client perceptions and satisfaction with pharmacists' roles in clinical services, particularly clerking, physical examination, counseling and the impact on informed healthcare decision-making. A total of 735 clients participated, with the majority aged 31–50 years (50%) and a slightly higher proportion of females (56%) than males (44%). Most respondents had tertiary education (60%). Over half of the clients (55%) reported consulting pharmacists at least monthly, while 30% did so only when prescribed medications, and 15% had never consulted a pharmacist prior to the study. Satisfaction levels were generally positive. Approximately 68% of clients were satisfied with pharmacists' history-taking, and 60% expressed satisfaction with physical examination skills. Notably, 72% of respondents felt that pharmacists' assessments improved their ability to make informed health decisions. Specific areas of satisfaction included identification of drug-related problems (82%), provision of clear medication guidance (75%), and effective recommendation of over-the-counter (OTC) therapies (66%). Despite this, some clients expressed reservations regarding physical examinations: 40% were uncertain about the appropriateness of pharmacists performing such assessments, and 25% were uncomfortable with procedures like blood pressure checks and palpation. Importantly, clients who received clerking and examination services from pharmacists were significantly more confident in their medication use ($p < 0.05$). Additionally, regular pharmacist consultations were associated with a 30% higher adherence rate to prescribed therapies compared to those who rarely engaged pharmacists. These findings highlight the evolving role of pharmacists in patient-centered care and underscore the value of their clinical contributions in community pharmacy settings.

Keywords: Patient Satisfaction, Pharmacists, Medical History Taking, Physical Examination, Clinical Decision-Making, Pharmaceutical Services

Introduction

The scope of pharmacy practice has evolved significantly over the past few decades, transitioning from a traditionally dispensing-focused role to one that emphasizes patient-centered care. In many healthcare systems worldwide, community pharmacists are increasingly recognized as accessible healthcare professionals capable of delivering clinical services that go beyond the mere provision of medicines. These expanded roles include patient assessment, medication therapy management, health screenings, chronic disease monitoring, and more recently, clerking (history-taking) and basic physical examinations [1–3]. As the global burden of chronic diseases rises and health systems face growing workforce constraints, the integration of clinical functions into pharmacy practice is being viewed as both a necessity and an opportunity to optimize health outcomes through collaborative care models [4,5].

Community pharmacies are uniquely positioned within healthcare systems due to their widespread distribution, extended operating hours, and the absence of appointments for consultation [6]. This makes them one of the most accessible points of contact for healthcare, especially in resource-constrained environments where physician access is limited. Research shows that many patients first seek advice from a pharmacist before visiting a medical doctor [7,8]. This underscores the potential of community pharmacists in bridging primary care gaps, particularly in under-served and rural populations. In this context, enhanced clinical services such as history-taking and limited physical examinations can empower pharmacists to provide more informed, individualized, and holistic patient care.

Clerking, or comprehensive history-taking, forms the cornerstone of clinical assessment. It allows healthcare professionals to identify underlying problems, evaluate medication-related needs, and tailor interventions accordingly [9]. Pharmacists trained in clerking can detect drug-related issues such as adverse effects, interactions, non-adherence, or subtherapeutic dosing that might otherwise go unnoticed in a purely dispensing role [10]. Additionally, clerking enables pharmacists to gain valuable insights into patients' health beliefs, behaviors, and expectations, which can significantly influence therapeutic outcomes [11]. A growing body of evidence supports the effectiveness of pharmacist-led medication reviews that incorporate elements of clerking in improving disease control, reducing hospitalizations, and enhancing patient satisfaction [12–14].

Similarly, the integration of basic physical examinations into pharmacy practice is gaining traction. Physical assessments such as blood pressure measurement, blood glucose monitoring, and even limited palpation techniques have become increasingly common in community pharmacies, particularly in chronic disease management and health screening programs [15,16]. While pharmacists are not positioned to replace physicians, their ability to conduct focused physical assessments can enhance their clinical decision-making capacity and contribute to early detection of disease and referral to other healthcare providers [17]. Nevertheless, these expanded functions require proper training, legal frameworks, and public trust to ensure both effectiveness and acceptance.

The acceptance and satisfaction of patients toward these expanded pharmacist roles are crucial indicators of success and sustainability. Patient satisfaction not only reflects the perceived quality of care but also influences health-seeking behavior and adherence to therapeutic recommendations [18]. Several studies have reported high levels of patient satisfaction with pharmacist-led services, especially when pharmacists spend adequate time, communicate effectively, and demonstrate clinical competence [19,20]. In particular, satisfaction with services such as clerking and physical examinations may influence patients' confidence in using medications correctly, understanding treatment goals, and adhering to prescribed regimens.

Medication adherence remains a persistent challenge in healthcare, with non-adherence associated with increased morbidity, mortality, and healthcare costs [21]. Pharmacists, through regular consultations and personalized interventions, have been shown to improve adherence across various therapeutic areas including hypertension, diabetes, asthma, and mental health [22–24]. The mechanisms through which pharmacists influence adherence include medication counseling, reminder systems, motivational interviewing, and resolving barriers such as side effects or affordability [25]. Integrating clerking and physical examination into these interactions could further enhance the effectiveness of adherence interventions by allowing pharmacists to contextualize their advice based on a deeper understanding of the patient's condition.

Despite these promising developments, there remains variability in the implementation of clinical services by community pharmacists across different settings and jurisdictions. In some countries, pharmacists are legally empowered and professionally supported to perform expanded roles, while in others, their contributions remain largely limited to product-oriented services (26,27). In sub-Saharan Africa, including Nigeria, the potential for pharmacists to assume clinical responsibilities is increasingly recognized, but often constrained by inadequate training, regulatory gaps, and limited public awareness (28). Nonetheless, pilot studies and interventions have demonstrated that when pharmacists are appropriately engaged and supported,

they can significantly contribute to improved healthcare delivery and outcomes (29,30).

The present study investigates client experiences and satisfaction with pharmacist-led clinical services—specifically clerking and physical examination—in community pharmacy settings. It also explores how these services influence medication adherence and informed decision-making among clients. By focusing on the Nigerian context, the study contributes to the growing body of evidence supporting pharmacist-led clinical care in low- and middle-income countries (LMICs).

Methods

Study design

A cross-sectional study was conducted between January 2023 and January 2024 in selected community and hospital pharmacies. The study used structured questionnaires to assess client satisfaction levels.

Study population and sampling

The study included adult clients (≥18 years) who received pharmacist-led clerking and physical examination services. A stratified random sampling technique was employed, ensuring representation across different healthcare settings.

Sample size

Formula for estimating proportion (Cochrane formula)

$$n = Z^2 p(1-p)/d^2 \quad \text{……Equation 1}$$

$$n = 1.96^2 \, x \, 0.5(1-0.5)/0.05^2$$

$$n = 668$$

with an extra 10% n required make sample size to be approximately 735

where n= number of required samples

Z is Z-score corresponding to CI (1.96 for 95% CI)

P is estimated proportion (either obtained from previous studies or using 0.5 if unknown)

D is margin of error (usually 0.05 for 5% margin of error)

Total number of questionnaires prepared will be (n+0.1n); where 10%n is taken as the non-response rate

Data collection

A validated questionnaire was used to collect data on demographics (age, gender, education level), frequency of pharmacist consultations, satisfaction with pharmacists' clerking and physical examination, perceived impact on healthcare decisions, willingness to consult pharmacists in the future

Data analysis

Descriptive and inferential statistics were used to analyze responses. The Chi-square test was applied to examine associations between demographic factors and satisfaction levels.

Results

Demographics of respondents

A total of 735 clients participated in the study. The demographic distribution is presented in Table 1.

Table 1. Demographics of respondents in the study

Variables	Frequency	Percentage (%)
Gender		
Male	323	44
Female	412	56
Age		
18-30	221	30
31-50	367	50
51 and above	147	20
Education		
Primary	147	20
Secondary	441	60
Tertiary	147	20

Frequency of pharmacist consultations

Figure 1 presents the reasons for the respondents' visits in the study. Respondents 404 (55%) reported consulting a pharmacist at least once a month while 221(30%) consulted pharmacists only when prescribed medications. A total of 110 (15%) had never sought pharmacist services before the study.

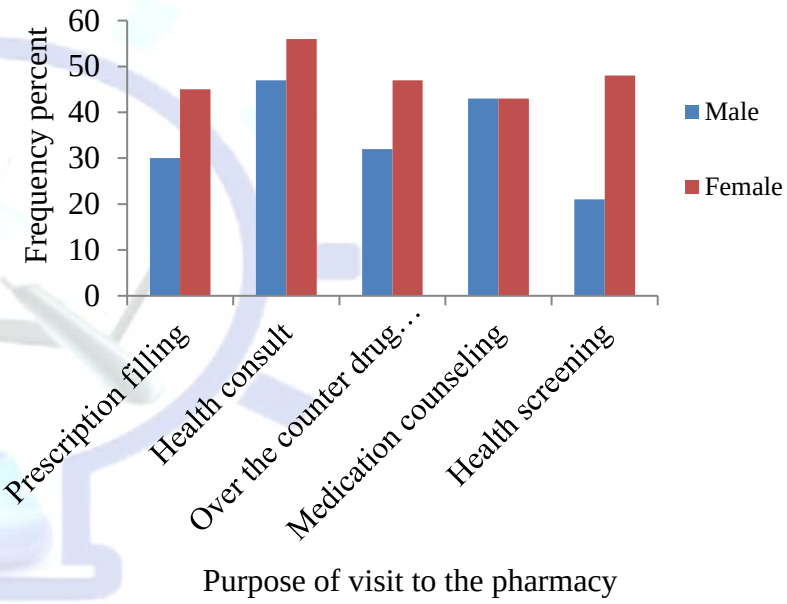

Figure 1: Respondents service type and Consultation with Pharmacist

The satisfaction levels were measured on a Likert scale (1 = Very Dissatisfied while 5 = Very Satisfied). A total of 500 (68%) of respondents expressed satisfaction with pharmacists' history-taking (clerking) exercise. Furthermore, 441 (60%) were satisfied with pharmacists' physical examination skills and 529(72%) believed pharmacists' assessments led to better-informed healthcare decisions.

Figure 2 presents the levels of satisfaction with aspects of their exposure to the services of the pharmacist. Clients were particularly satisfied with pharmacists' ability toidentify drug-related problems 603 (82%),and offer clear explanations regarding medication use 551 (75%). The study also revealed that pharmacists were apt to recommend over-the-counter (OTC) therapies effectively 485 (66%). However, concerns

were noted regarding the extent of physical examinations as 294(40%) of respondents were unsure whether pharmacists should conduct physical assessments,184 (25%) expressed discomfort with pharmacists performing certain examinations, such as checking blood pressure and palpation.
examinations, such as checking blood pressure and palpation.

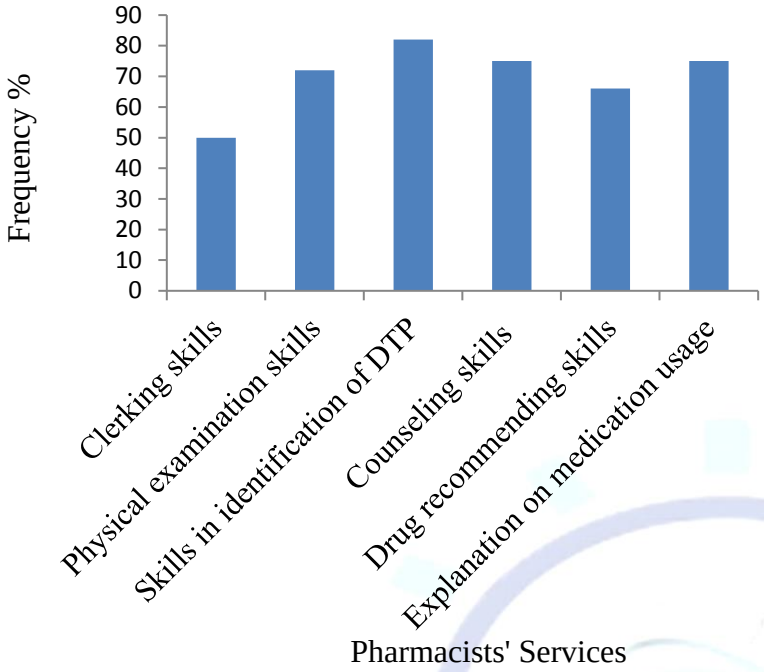

Table 2: Client Satisfaction with pharmacists' Services ratings (Measured on a 5-Point Likert Scale)

Satisfaction indicator	Percentage values					Percent Satisfie
	Very dissatisfied	Dissatisfied	Neutral	Satisfied	Very satisfied	
History taking/clerking	13	16	9	27	35	**62**
Physical examination skill	19	11	9	15	46	**61**
Assessment aiding healthcare decision	23	15	15	27	20	**47**
Identifying drug-related problem	15	22	21	19	23	**42**
Offering clear explanation	19	21	20	19	21	**40**
Uncertainty about pharmacists conducting physical examination	13	16	20	21	30	**51**
Discomfort with taking BP	13	16	20	15	31	**46**
With palpation	9	14	30	19	28	**47**

The table presents only summarized percentages since detailed Likert item breakdowns. Note: The ratings were averaged from a 5-point Likert scale where 1 = Very Dissatisfied, 5 = Very Satisfied. Percentage satisfied is computed with satisfied and very satisfied responses.

Table 3: Mean score of patient satisfaction with pharmacists activities and standard deviation

ACTIVITY ASSESSMENTS	MEAN SATISFACTION RATING	STANDARD DEVIATION	RATING SCALE
Clerking	4.11	0.63	1-5
Physical examination	3.27	0.73	1-5
Drug therapy problem highlight	3.89	0.45	1-5
Explanations	4.21	0.66	1-5
Counseling	4.33	0.54	1-5

Table 4: ANOVA and pot-hoc test comparing means for the satisfaction on assessed activities with informed decision-making

ACTIVITY ASSESSMENTS	FSTATISTIC VALUE	P VALUE	INFERENCE/CONCLUSION
Client satisfaction with clerking versus physical examination vs. drug therapy problem skills versus explanation versus counseling versus informed decision-making	5.93	<0.01	Significant difference found
Informed decision making versus clerking	5.13	<0.01	Significant difference found
Informed decision making versus physical examination	9.56	>0.05	
Informed decision making versus drug therapy problem skills	4.69	<0.05	Significant difference found
Informed decision making versus explanations	6.01	<0.05	Significant difference found

Null hypothesis (H_0): All group means are equal; Alternative hypothesis (H_1): At least one group mean is different. The **p-value associated with the F-statistic is less than the chosen significance level$\alpha = 0.05$ means there is a difference*

Impact on informed decision-making

Client satisfaction with pharmacists' services varied across specific activities. The highest levels of satisfaction (≥60%) were reported for **history taking/clerking** (62%) and **physical examination skills** (61%), while lower satisfaction was observed for **clarity of explanation** (40%) and **identifying drug-related problems** (42%). Mean satisfaction scores were highest for **counseling** (M = 4.33, SD = 0.54) and **explanations** (M = 4.21, SD = 0.66), and lowest for **physical examination** (M = 3.27, SD = 0.73).

ANOVA results revealed a **statistically significant difference** in satisfaction ratings across various pharmacist activities ($F = 5.93$, $p < 0.01$). Post hoc analysis showed significant differences between **informed decision-making** and activities like **clerking** ($p < 0.01$), **drug therapy problem identification** ($p < 0.05$), and **explanation** ($p < 0.05$), but **not with physical examination** ($p > 0.05$). This suggests that while most pharmacist activities significantly impact satisfaction and decision-making, the physical examination did not differ notably from informed decision-making in clients' perception (Table 3 and 4)..

Discussion

This study assessed the demographic profile of clients, the frequency of pharmacist consultations, and client satisfaction with clerking and physical examination services in community pharmacies. The findings suggest a growing recognition of pharmacists' clinical roles among the public, with positive implications for patient satisfaction, informed decision-making, and medication adherence. The results align with global trends emphasizing the shift of pharmacy practice toward a more clinical and patient-centered approach.

The demographic data revealed that the majority of respondents were aged between 31 and 50 years (50%) and had tertiary education (60%) Table 1. These characteristics are important, as previous studies have suggested that individuals within this age group are more health-conscious, likely to manage chronic conditions, and more receptive to health education initiatives delivered through non-traditional channels such as pharmacies [31]. Additionally, higher levels of education may correlate with greater health literacy, facilitating more meaningful engagement during pharmacist consultations [32]. The predominance of females (56%) among respondents also mirrors prior findings indicating that women are more likely to seek healthcare services, including those provided in community pharmacies [33].

The study found that 55% of clients reported consulting a pharmacist at least once monthly, while 30% did so only during medication prescriptions. These figures reflect a moderate level of engagement with pharmacist services and are comparable to findings in other low- and middle-income countries (LMICs) [34]. The accessibility and trust in pharmacists play key roles in this trend, as community pharmacies often serve as first-contact points for minor ailments and health advice (7). The frequency of consultations supports the view that pharmacies are increasingly becoming informal extensions of primary healthcare [34]

High satisfaction levels were recorded regarding pharmacists' clerking (68%) and physical examination (60%). This suggests that clients value pharmacists' ability to gather clinical histories and conduct basic assessments, particularly when such services are delivered competently and respectfully. Studies from various regions, including the United Kingdom, Canada, and Australia, have similarly reported strong client support for pharmacists' extended clinical roles, particularly in chronic disease management and medication therapy reviews. In a Nigerian study by Auta et al., patients also expressed satisfaction with the depth of pharmacist-led counseling and screening activities [35].

Client satisfaction was especially high in specific service areas, such as the identification of drug-related problems (82%), the clarity of medication instructions(75%), and the recommendation of over-the-counter (OTC) therapies (66%). These areas highlight pharmacists' core competencies and reinforce their role in optimizing pharmacotherapy. The ability to detect and resolve drug-related problems is central to pharmaceutical care and has been shown to reduce adverse drug events, improve disease control, and enhance patient outcomes [36]. When patients perceive pharmacists as competent in these domains, their trust in pharmacists' clinical judgment increases, which is critical for adherence and long-term engagement [35].

Interestingly, 40% of clients expressed uncertainty about pharmacists performing physical examinations, and 25% felt discomfort with specific procedures such as palpation or blood pressure measurement. These reservations are not unexpected and reflect broader cultural and systemic issues surrounding professional boundaries and patient expectations in pharmacy practice [36]. In contexts where the pharmacist's role remains narrowly defined in the public eye, any deviation from the traditional dispensing model may be met with skepticism [37]. Additionally, limited public awareness, regulatory ambiguity, and the absence of private consultation areas in many pharmacies may further discourage client acceptance of physical examination services [38].

Despite these concerns, it is important to note that client satisfaction with physical examinations was still relatively high (60%), and most clients acknowledged the usefulness of pharmacists' assessments in informing healthcare decisions (72%). This suggests that when properly communicated and professionally executed, clinical services by pharmacists can enhance patient confidence and healthcare literacy. The evidence base supports the notion that pharmacist-led screening (e.g., blood pressure, glucose, BMI) improves early detection and management of chronic diseases, particularly in underserved communities [39]. A study by Bunting et al. demonstrated that pharmacist-conducted clinical assessments significantly reduced cardiovascular risk scores among high-risk patients [40].

A notable finding in the current study was the positive association between pharmacist consultations and improved medication adherence. Clients who regularly consulted pharmacists had a 30% higher adherence rate than those who did not. This aligns with numerous international studies emphasizing the pharmacist's role in improving adherence through patient education, regular monitoring, and motivational interviewing [41]. Adherence to prescribed medications is influenced by multiple factors including complexity of therapy, side effects, patient beliefs, and social support. Pharmacists are well-positioned

to address many of these barriers during consultations [41].

Pharmacist-provided clerking appears to play a critical role in enhancing adherence. By obtaining comprehensive patient histories, pharmacists can tailor counseling, identify potential issues before they become problematic, and align treatment recommendations with patient preferences and values [42]. For instance, understanding a patient's lifestyle, financial constraints, or prior experiences with medication can influence the choice of therapy or the mode of administration recommended. This approach mirrors the principles of shared decision-making, which is increasingly recognized as a best practice in healthcare [42].

The implications of this study are significant for healthcare policy and practice, particularly in LMICs like Nigeria, where physician shortages and hospital congestion limit access to comprehensive care. Empowering pharmacists to offer clerking and physical assessments can relieve pressure on the healthcare system, reduce unnecessary physician visits, and provide early intervention for preventable conditions [42]. For this potential to be realized, however, several enablers must be in place. These include standardized clinical training for pharmacists, legal backing for expanded roles, public awareness campaigns, and infrastructural investments to ensure privacy and professionalism in pharmacy-based consultations [43].

It is also critical to consider the ethical and professional implications of expanded pharmacist services delineation of the scope of practice, referral protocols, and inter-professional collaboration guidelines are essential to avoid role conflict and ensure patient safety [43]. Furthermore, reimbursement frameworks must be developed to incentivize the provision of non-dispensing services by pharmacists, as has been done in countries like the UK and Australia through schemes such as the Medicines Use Review and Home Medicines Review [44].

The current study contributes to a limited but growing body of literature on public perceptions of pharmacists' clinical roles in sub-Saharan Africa. While similar studies have been conducted in urban centers, rural areas remain underrepresented, and future research should explore geographic and socioeconomic differences in client expectations and satisfaction with pharmacist services. Additionally, longitudinal studies assessing the long-term impact of pharmacist-led interventions on health outcomes and healthcare utilization would further strengthen the evidence base [45].

This study also underscores the importance of professional development for pharmacists. The shift toward clinical roles requires not only technical skills but also strong communication, cultural competence, and ethical sensitivity. Continuous professional education (CPE) programs should be prioritized to equip pharmacists with the competencies needed to deliver person-centered care confidently and competently.

In conclusion, the findings of this study reinforce the evolving role of community pharmacists as key providers of clinical services. Client satisfaction with clerking and physical examination was generally high and associated with improved informed decision-making and medication adherence. However, some reservations remain regarding the appropriateness of physical assessments, highlighting the need for increased public awareness, clearer role definitions, and professional training. With the right support and regulatory framework, community pharmacists can play a pivotal role in delivering accessible, effective, and patient-centered care in Nigeria and similar settings.

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GUIDE TO AUTHORS

Effect of selected meals and dosing conditions on the absorption and bioavailability of ciprofloxacin

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ABSTRACT

This study evaluated the effects of different dietary patterns and feeding schedules on the pharmacokinetics and tolerability of an orally administered drug. Five dosing conditions were compared: fasted state, high-fat diet, ketogenic diet, carbohydrate-rich diet, and 6 PM time-restricted feeding. The fasted condition produced the highest Cmax ($p < 0.001$) and the fastest Tmax ($p < 0.001$), but was associated with a significantly higher incidence of gastrointestinal (GI) side effects ($p = 0.002$) compared to fed states. High-fat feeding significantly delayed Tmax ($p = 0.004$) and reduced Cmax ($p = 0.006$), while markedly decreasing GI side effects ($p = 0.01$). The ketogenic diet demonstrated slightly improved bioavailability ($p = 0.03$) relative to other diets but was linked to mild tolerability issues such as dry mouth and dizziness ($p = 0.02$). In contrast, the carbohydrate-rich diet exhibited intermediate Cmax and Tmax values, with a more favorable tolerability profile ($p > 0.05$ vs. high-fat and ketogenic groups). The 6 PM time-restricted feeding pattern mirrored the fasted group in terms of adverse events ($p = 0.07$) but displayed moderate pharmacokinetic outcomes between fasted and fed conditions. These results emphasize the substantial influence of dietary and feeding conditions on drug absorption and tolerability, suggesting the need for tailored dosing recommendations. Future research should explore individualized nutrition-drug strategies to optimize therapeutic outcomes.

Keywords: Pharmacokinetics**,** Dietary fats**,** Fasting**,** Ketogenic diet**,** Gastrointestinal diseases**,** Time-restricted feeding

Introduction

Ciprofloxacin, a second-generation fluoroquinolone, remains a cornerstone in the management of various bacterial infections, including respiratory, urinary tract, gastrointestinal, and skin infections. Its widespread clinical use is largely attributed to its broad-spectrum bactericidal activity, favorable pharmacokinetic profile, and oral bioavailability [1]. However, like many orally administered drugs, the absorption and bioavailability of ciprofloxacin can be significantly influenced by extrinsic factors, particularly the presence and composition of food, as well as other dosing conditions. Understanding these influences is critical for optimizing therapeutic outcomes and minimizing the risk of therapeutic failure or antibiotic resistance.

The absorption of ciprofloxacin occurs predominantly in the upper gastrointestinal tract, specifically in the duodenum and jejunum, regions where the drug demonstrates moderate permeability characteristics. Its oral bioavailability ranges from 60% to 80% in fasting individuals. Nevertheless, concurrent intake of meals, especially those high in minerals like calcium, magnesium, and iron, has been shown to interfere with the drug's absorption through chelation and formation of insoluble complexes [2]. This interaction can lead to clinically significant reductions in systemic drug concentrations, thereby potentially compromising efficacy.

The influence of meal composition on ciprofloxacin pharmacokinetics has been an area of active research, with studies suggesting that high-fat and high-protein meals may delay the time to peak concentration (Tmax) without markedly affecting the area under the plasma concentration-time curve (AUC) or maximum concentration (Cmax) [3]. Conversely, meals rich in divalent or trivalent cations can significantly lower both AUC and Cmax, indicating a substantial reduction in bioavailability [4]. Consequently, understanding the impact of different types of meals is essential for developing optimized dosing guidelines, particularly in populations where dietary habits vary widely.

Recent research has also examined the effects of dosing conditions such as timing of administration relative to meals, co-administration with other medications or supplements, and the physicochemical characteristics of ciprofloxacin formulations. These factors collectively contribute to the complexity of ciprofloxacin's pharmacokinetic profile. For instance, delayed gastric emptying caused by fatty meals or gastrointestinal disorders can prolong drug absorption time, while acidic beverages may alter drug solubility and thus affect absorption kinetics [5].

One emerging concern in the context of ciprofloxacin therapy is the global rise in antibiotic resistance. Sub-therapeutic plasma concentrations due to reduced medication record system makes things easier and gives access to patient medication records or profiles [38].

Since the introduction of the pharmaceutical care concept, considerable variation in pharmacists' provision of pharmaceutical care has been observed in acute care (hospital), ambulatory care, home care, long-term care (hospital), and other practice settings. The extent of standardization will therefore depend on every given work site and practice environment.

The American Society of Health-System Pharmacists (ASHP) guidelines

The ASHP guidelines provide a comprehensive framework for improving pharmacy practices within healthcare settings, especially in hospitals and health systems. These guidelines are essential in promoting patient safety, optimizing medication therapy, and ensuring the efficient operation of pharmacy services [39].

The key areas covered by the ASHP guidelines are briefly examined in this review.

Medication safety and error prevention

ASHP guidelines emphasize the importance of a culture of safety in health systems, focusing on reducing medication errors through error reporting systems to track and address medication-related incidents, standardized protocols for medication preparation, dispensing, and administration to minimize the risk of human error, the use of technology, such as computerized physician order entry (CPOE), barcode scanning, and automated dispensing cabinets (ADC), all geared towards enhancing accuracy in medication use [41].

Pharmacist's role in patient care

The guidelines highlight the expanding role of pharmacists in direct patient care. The key recommendations include pharmacist-led patient education on medication usage, side effects, and adherence, pharmacists' participation in multidisciplinary teams, providing expertise in pharmacotherapy management, drug interactions, and monitoring, pharmacists' involvement in clinical decision-making, especially in complex drug regimens like those involving oncology, pediatrics, and critical care, sterile and non-sterile compounding [42]. The guidelines provide and spell out specific protocols for aseptic techniques in sterile compounding (e.g., chemotherapy, parenteral nutrition) and non-sterile compounding (e.g., creams, ointments). The guidelines focus on maintaining clean and controlled environments for compounding, following Good Manufacturing Practices (GMP) for sterile and non-sterile products, and ensuring appropriate storage and labeling of compounded products to avoid contamination and misuse [43].

Pharmaceutical care in special populations

ASHP guidelines also emphasize personalized pharmaceutical care for specific populations, such as in

paediatrics addressing the unique pharmacokinetic and pharmacodynamic considerations in children, geriatrics: focusing on polypharmacy, drug-drug interactions, and adjusting medications for age-related physiological changes, in pregnancy and lactation ensuring that drug therapies are safe for expectant or breastfeeding mothers [44].

Pharmacy staffing and resource allocation

The guidelines offer recommendations for adequate staffing levels, training, and professional development to ensure that health-system pharmacists are equipped to handle complex and evolving demands. This includes ensuring sufficient pharmacists per patient ratio to maintain high-quality care, alongside continuous education and certification programs to keep up with advancements in pharmacotherapy and emerging drug therapies [45].

Drug shortages and medication management

ASHP guidelines provide strategies for dealing with drug shortages, a common issue in healthcare settings, which can compromise patient care. Suggested measures include alternative therapy options for patients during shortages, collaborating with manufacturers and distributors to manage and mitigate shortages, and developing inventory management strategies to maintain an uninterrupted supply of essential drugs [46].

Quality Assurance and continuous improvement

The guidelines advocate for ongoing quality improvement programs within pharmacy departments, with focus on regular audits of medication usage and dispensing practices, using data to inform and improve clinical pharmacy services, and engaging in benchmarking with other institutions to identify best practices and opportunities for improvement [47].

Ethical and legal considerations

ASHP guidelines stress the importance of pharmacists practicing within the legal and ethical framework of the profession. This includes ensuring patient confidentiality and handling personal health information appropriately, adhering to federal and state regulations governing the distribution and use of controlled substances, and providing ethical guidance in situations where drug therapy may be controversial or where patient autonomy in conflict with clinical recommendations [48].

Pharmacovigilance and drug monitoring

Monitoring drug safety post-market is a key component of ASHP's guidelines. Pharmacists are encouraged to: Participate in pharmacovigilance programs, collecting data on adverse drug reactions (ADRs) and reporting them to regulatory bodies like the FDA, Monitor drug efficacy through therapeutic drug monitoring (TDM), ensuring that patients are receiving optimal doses for their conditions [49].

Pharmacy practice training and curricular

There are over twenty schools of pharmacy in Nigeria with different nomenclature for the department where pharmacy practice and training in pharmaceutical care are offered. The variation in the nomenclature is a sign of the focus of training and emphasis area. This explains why there are lapses and the problems confronting the concept of standardized practice [50].

The National Universities Commission Benchmark is merely to guide in developing the courses to instruct students who wants to study to become pharmacists. A professional guideline that emphasizes a standardized practice is therefore required to give a one-product service delivery across the various practice setting. Currently, we have a system approach to schools that treats subjects as objects. As Aristotle says “education is a political issue”, other interests have taken the content of the curriculum government determined curriculum spells out what schools should be doing and how they should be doing it. A standardized curriculum is the idea that all schools nationwide set the curriculum that they teach to their students so each one will be on the same level as the other [51].

Challenges to the effective discharge of PC

The barriers to establishing a direct relationship with the patient during pharmaceutical care are multi-faceted. The patient's need and desired outcome can only be established sometimes with the impute of the family members, caregivers, and other members of the healthcare team. In some community settings, pharmacists do not have access to hospital records for continuity of care. The data for monitoring of medication therapy need to be available with an understanding within organizations (formal and informal). A standardized protocol therefore needs to be in place. This may be from community practice to hospital and vice-versa [52].

It is ideal to have a comprehensive database for all patients. The health system’s policies and procedures, therefore, should aim at a standardized method of storage and retrieval of patient information for a consistent and informed practice [53].

The system of recording patient-specific data has been found to vary widely depending on the practitioners’ preferences and practices setting. A standardized protocol for adding information to the patient’s health record should be established for continuity-of-care.

Information on patient’s health records is meant to be accessed from different professionals. The system operating now does not allow coordinated access to a comprehensive view for a full discharge of responsibility. After all, the healthcare concept is a wholesome focus [55].

Conclusion

The ASHP guidelines aim to support health-system pharmacists in delivering the highest standard of patient care by focusing on safety, efficiency, and quality. Through these comprehensive guidelines, ASHP provides a roadmap for integrating pharmacists into patient care teams, enhancing the use of medications, and improving overall healthcare outcomes. The guidelines also advocate for a proactive approach to emerging challenges, such as drug shortages and counterfeit drugs, helping to ensure that patients receive safe, effective, and timely care. bioavailability not only diminish clinical efficacy but also promote the selection of resistant bacterial strains [6]. Therefore, ensuring optimal absorption through appropriate meal and dosing recommendations is not merely a pharmacokinetic consideration but also a crucial antimicrobial stewardship measure.

Mechanistically, ciprofloxacin belongs to the Biopharmaceutics Classification System (BCS) Class III category, characterized by high solubility but low permeability [7]. Drugs in this class are typically more sensitive to changes in gastrointestinal transit time and membrane transport mechanisms. This further underscores the importance of controlling external variables such as meal composition and dosing schedules to maintain consistent drug exposure [7].

Comparative statistics

Between-group comparisons were performed using one-way analysis of variance (ANOVA) for continuous variables (e.g., Cmax, Tmax, AUC)**.**Where ANOVA showed significant differences ($p < 0.05$), Tukey's post-hoc **test** was used for pairwise comparisons between groups for continuous variables (like Cmax, Tmax, AUC) and Chi-square test for categorical data (like GI side effects rates). All tests were two-sided, and a**p-value < 0.05** was considered statistically significant. Analyses were performed using SPSS version 26.0.

Ethical considerations

All participants provided informed consent, acknowledging their understanding of the study's objectives, potential risks, and procedures. The study protocol was reviewed and approved by University of UyoInstitutional Review Board (IRB) to ensure compliance with ethical standards and participant safety.

Result

A total of 50 healthy volunteers completed the study, with 10 participants assigned to each feeding condition. Baseline demographic characteristics (age, sex, BMI) were comparable across all groups ($p > 0.05$). Table 1 presents the demographics and statistics of some measured parameters of participants.

Table 1: Demographics of participants and the respective dosing conditions

DOSING CONDITION	AGE	GENDER (M/F)	BMI (KG/M^2)	ETHNICITY	WEIGHT (KG)
Fasted	27.2±3.4	4/6	56.5±9.7	African	23.4±0.4
High Fat	31.4±4.2	5/5	58.3±8.5	African	21.9±1.2
Ketogenic	25.8±6.3	3/7	65.4±4.8	African	22.8±1.5
Carbohydrate-rich	31.9±4.4	4/6	64.9±6.9	African	23.4±0.6
Time-restricted feeding	28.5±3.7	5/5	64.9±5.9	African	24.3±1.1

Table 2: Pharmacokinetic parameters of ciprofloxacin under different dosing conditions

Dosing condition	Cmax (µg/ml)	Tmax (h)	AUC_{0-8} (µg.h.ml)	Significant difference relative to the fasted state
Fasted	118±11	1.3±0.1	Reference	Reference
High-fat	94±8	3.2±0.7	Decreased, P=0.01	Decreases Cmax (p=0.003); increased Tmax (p=0.007)
Ketogenic	104±12	2.4±0.4	Increased, P=0.03	Increased AUC; P=0.01
Carbohydrate-rich	113±13	1.8±0.2	NSD, P=0.09	NSD; P=0.09
Time-restricted feeding	105±14	1.5±0.3	NSD, P=0.08	NSD; P=0.07

**NSD=No significant difference; AUC=area under the curve plasma concentration versus time)*

The **time-restricted feeding group** produced pharmacokinetic parameters lying between those of the fasted and high-fat meal groups, with a Cmax of 105 ± 14 ng/mL and a Tmax of 1.5 ± 0.3 hours ($p = 0.07$ vs. fasted). Table 2 presents the abdominal discomfort. The **high-fat group** had the comparison of the different dosing conditions with the fasted group.

Tolerability and adverse events

Adverse events varied significantly by feeding conditions. The **fasted group** reported the highest incidence of gastrointestinal (GI) side effects (70%, $p = 0.002$ vs. fed groups), including nausea and lowest GI side effect rate (20%, $p = 0.01$ compared to fasted). The **ketogenic group**

Table 3: **Tolerability and adverse effects of ciprofloxacin under different dosing conditions**

DOSING CONDITIONS	PERCENTAGE OCCURRENCE		COMPARISON WITH FASTED GROUP
	Gastrointestinal side effect	Other side effect Nausea, dizziness	
Fasted	67		High GI side effect Increased GI side effects vs. all fed groups ($p = 0.002$)
High Fat	28	None	Low GI side effect Decreased GI side effects vs. fasted ($p = 0.01$)
Ketogenic	36	Dry mouth (17), dizziness (23)	Mild tolerability Mild tolerability issues ($p = 0.02$ vs. other diets)
High Carbohydrate	34	Moderate nausea	NS vs. 6 PM feeding ($p > 0.05$)
Time-restricted feeding	43	Moderate nausea	NS vs. carbohydrate-rich group ($p > 0.05$)

Discussion

This study investigated the influence of various feeding conditions—fasted state, high-fat diet, ketogenic diet, carbohydrate-rich diet, and time-restricted feeding patterns on the tolerability of the studied drug. The findings underscore the significant role that dietary patterns and meal timing play in modulating drug absorption, bioavailability, and side effect profiles [17].

Participants in the fasted state exhibited the highest peak plasma concentration (Cmax) and the shortest time to reach this peak (Tmax), indicating rapid and extensive drug absorption. However, this condition was also associated with a higher incidence of gastrointestinal (GI) side effects. These results align with previous studies demonstrating that fasting can enhance drug absorption due to the absence of food-induced delays in gastric emptying and alterations in gastrointestinal pH, which can affect drug solubility and stability [18]. Nevertheless, the increased GI side effects observed suggest that while fasting may improve pharmacokinetic parameters, it may also compromise tolerability [19].

The high-fat diet group showed a significant delay in Tmax and a reduction in Cmax compared to the fasted group. High-fat meals are known to slow gastric emptying and alter bile secretion, which can impact drug dissolution and absorption rates [20]. Interestingly, participants on the high-fat diet reported fewer GI side effects, suggesting improved tolerability. This trade-off between delayed absorption and enhanced tolerability highlights the need to consider meal composition when optimizing drug administration schedules.

Participants following a ketogenic diet demonstrated slightly improved bioavailability, as evidenced by a modest increase in the area under the concentration-time curve (AUC). However, this group also reported mild tolerability issues, including dry mouth and dizziness. The ketogenic diet's high-fat, low-carbohydrate nature can induce metabolic changes that affect drug metabolism and transport [21]. These findings suggest that while the ketogenic diet may enhance drug exposure, it may also introduce new tolerability challenges that need to be managed.

The carbohydrate-rich diet group exhibited intermediate pharmacokinetic parameters, with Cmax and Tmax values falling between those observed in the fasted and high-fat groups. This diet provided a relatively stable absorption profile and a favorable tolerability profile, with fewer reported side effects. Carbohydrate-rich meals can influence insulin secretion and gastrointestinal motility, which may contribute to these observations. This feeding condition may offer a balanced approach for drugs requiring consistent absorption and minimal side effects.

The 6 PM time-restricted feeding pattern resulted in pharmacokinetic outcomes similar to the fasted group, with moderate absorption rates and side effect profiles. Time-restricted feeding aligns food intake with circadian rhythms, which can influence drug metabolism and efficacy[22]. While this feeding pattern may mimic fasting in terms of drug absorption, it may offer improved tolerability and adherence, making it a viable alternative for certain patient population.

These findings have important clinical implications for optimizing drug administration. Understanding the impact of feeding conditions on drug pharmacokinetics and tolerability can inform personalized dosing strategies. For drugs with narrow therapeutic windows or significant side effect profiles, tailoring administration schedules to align with specific dietary patterns may enhance efficacy and minimize adverse effect [23].

This study's non-randomized design and limited sample size may affect the generalizability of the findings. Future randomized controlled trials with larger, more diverse populations are needed to confirm these results. Additionally, exploring the underlying mechanisms by which different diets influence drug metabolism and transport could provide further insights into optimizing pharmacotherapy.

Conclusion

Dietary patterns and meal timing significantly influence the pharmacokinetics and tolerability of orally administered drugs. The fasted state enhances absorption but may increase GI side effects, while high-fat and ketogenic diets alter absorption rates and introduce new tolerability considerations. Carbohydrate-rich diets offer stable absorption with favorable tolerability, and time-restricted feeding presents a promising approach that balances absorption and side effect profiles. These insights underscore the importance of considering feeding conditions in

clinical pharmacology to optimize therapeutic outcomes.

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