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GUIDE TO AUTHORS

Pharmacists disposition to participating in professional development (PD) and skill-up programs in Southern-Nigeria: attitudes, motivations, and barriers

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ABSTRACT

This study investigates the disposition of pharmacists in Southern Nigeria toward skill-up training post-graduation, focusing on their attitudes, motivations, and barriers to participating in continuing professional development (PD) programs. A mixed-methods approach was employed, combining a structured questionnaire survey and in-depth interviews. The survey was administered to 300 pharmacists practicing in Southern Nigeria, and 30 in-depth interviews were conducted with selected participants. Descriptive statistics and thematic analysis were used to analyze the data. The results indicate that a majority of pharmacists (70%) participated in PD activities in the past year, with workshops being the most frequently attended type of training. Motivational factors included the desire to enhance professional knowledge (68%), regulatory requirements (55%), career advancement (45%), and networking opportunities (35%). However, significant barriers to PD participation were identified, including time constraints (72%), cost (56%), lack of relevant programs (48%), and insufficient institutional support (42%). Participants also highlighted the need for more practical and relevant PD programs tailored to different pharmacy practice settings. The study concludes that while there is a generally positive disposition towards PD, the barriers identified must be addressed to increase participation. Recommendations include improving institutional support, offering more affordable and tailored programs, and leveraging technology to increase accessibility. These findings provide valuable insights for policy makers, regulatory bodies, and professional associations in improving PD programs and promoting continuous professional development among pharmacists in Southern Nigeria.

Keywords: Professional development, Pharmacists, Skill-up training, Barriers, Motivating factors, Regulatory requirements.

Introduction

In recent years, the importance of continuous professional development (PD) for healthcare professionals has gained significant recognition worldwide [1]. Pharmacists, as integral members of the healthcare system, are responsible for ensuring the safe, effective, and rational use of medications. With advancements in pharmacology, therapeutic practices, and healthcare delivery, it has become crucial for pharmacists to continually update their knowledge and skills. In Nigeria, especially in Southern regions, there has been increasing awareness of the need for pharmacists to participate in skill-up training post-graduation, aiming to enhance their competencies, adapt to new healthcare challenges, and maintain relevance in the rapidly evolving medical landscape [2].

Despite the growing emphasis on skill-up training, the disposition of pharmacists in Southern Nigeria towards such programs remains an area of interest [3]. Several factors may influence their participation in PD activities, including personal motivation, institutional support, availability of resources, and the perceived relevance of training programs to their daily practice. The diversity of these factors makes it essential to explore the attitudes, challenges, and barriers faced by pharmacists in pursuing professional development opportunities post-graduation [4].

The Nigerian pharmaceutical sector faces numerous challenges, including limited access to updated information, insufficient training infrastructure, and economic constraints [5]. Pharmacists in Southern Nigeria, however, continue to play an essential role in improving patient care, especially in areas such as drug management, patient counseling, and public health initiatives. Therefore, understanding their disposition towards skill-up trainings is critical in formulating effective policies, programs, and interventions that will support their professional growth.

In recent years, various PD initiatives have been introduced by regulatory bodies such as the Pharmacists Council of Nigeria (PCN) and professional associations like the Pharmaceutical Society of Nigeria (PSN) [6]. These programs aim to bridge the gap between academic learning and practical application, particularly focusing on emerging areas like pharmacogenomics, digital health, and pharmaceutical care. Additionally, workshops, seminars, and online courses have become increasingly popular platforms for skill development among pharmacists in Southern Nigeria [7]. However, participation rates remain varied, and identifying the motivating factors or barriers is vital to improving the effectiveness and reach of these training programs.

This study aims to explore the disposition of pharmacists in Southern Nigeria towards skill-up training post-graduation, focusing on factors that either encourage or discourage participation in PD activities. By addressing these factors, stakeholders can enhance the professional growth of pharmacists and contribute to better healthcare outcomes in the region [8].

Methods

Study design

This study employed a cross-sectional descriptive research design to assess the disposition of pharmacists towards skill-up training post-graduation in Southern Nigeria. The research focused on identifying the factors influencing pharmacists' participation in skill-up training programs, such as their personal motivations, institutional support, perceived benefits, and barriers to participation. Data was collected through self-administered questionnaires and structured interviews to ensure a comprehensive understanding of the participants' views.

Study area

The study was conducted in the Southern region of Nigeria, which encompasses the six geopolitical zones of South-West, South-South, and South-East. These regions include major urban centers like Lagos, Port Harcourt,Akwa-Ibom, Aba, Owerri, Awka, Enugu, Benin and Asaba, where a significant number of pharmacists are employed in various healthcare settings. These areas were selected due to their high concentration of healthcare professionals, including pharmacists. Connection with a minimum of 3 colleagues of the principal researcher assisted with the questionnaire distribution in the different locations, having been fully briefed of the research design and objectives.

Study population

The target population for this study included registered pharmacists practicing in Southern Nigeria. The participants were recruited from public and private hospitals, community pharmacies, pharmaceutical companies, and academic institutions. The inclusion criteria required participants to be licensed pharmacists who have completed their undergraduate education and are actively involved in pharmaceutical practice.

Sampling technique

A stratified random sampling technique was used to select participants. This ensured that pharmacists from different practice settings (hospital, community, industry and academia) and geographical areas (urban and semi-urban) are adequately represented in the study. The stratum was based on the type of practice and location within the Southern region. A minimum sample size of 300 pharmacists was targeted to provide reliable and generalizable results, with a 95%

confidence level and a margin of error of 5%.

Data collection instruments

Data was collected using two main instruments. A self-administered structured questionnaire was developed, containing both closed (8 questions) and open-ended questions (5 questions). The closed-ended questions assessed factors such as demographic characteristics, frequency of participation in skill-up training, sources of training, and perceived barriers and motivators. The open-ended questions allowed participants to express their opinions on how training could be improved and the challenges they face in accessing these opportunities. Secondly, an in-depth interview was conducted with a sub-group of 30 pharmacists, chosen from the sample to provide more detailed insights into their experiences and perceptions regarding PD programs. The interview guide included questions designed to explore personal experiences with training programs, challenges faced, and suggestions for improving participation.

Data collection procedure

After obtaining ethical approval from the Institutional Review Board of University of Uyo Research Ethics Committee, the questionnaires were distributed to pharmacists through a combination of face-to-face interaction, email, and online platforms. For those opting for face-to-face participation, the researcher visited selected hospitals, pharmacies, and pharmaceutical companies to administer the questionnaires. A follow-up visit was conducted to ensure a high response rate.

The in-depth interviews were scheduled with participants who expressed interest in providing more detailed responses. These interviews were conducted in a private setting to ensure confidentiality and were audio-recorded for accurate transcription and analysis.

Data analysis

After obtaining ethical approval from the Institutional Review Board of University of Uyo Research Ethics Committee, the questionnaires were distributed to pharmacists through a combination of face-to-face interaction, email, and online platforms. For those opting for face-to-face participation, the researcher visited selected hospitals, pharmacies, and pharmaceutical companies to administer the questionnaires. A follow-up visit was conducted to ensure a high response rate.

The in-depth interviews were scheduled with participants who expressed interest in providing more detailed responses. These interviews were conducted in a private setting to ensure confidentiality and were audio-recorded for accurate transcription and analysis.

Data analysis

The quantitative data obtained from the questionnaires were analyzed using descriptive statistics such as frequencies, percentages, means, and standard deviations. These were used to summarize the characteristics of the respondents and their participation in skill-up training.

The qualitative data from the open-ended questionnaire responses and in-depth interviews were transcribed verbatim and analyzed thematically. Thematic analysis allowed for the identification of common themes, patterns, and perceptions regarding the barriers and motivators for PD participation. NVivo software was used to assist in coding and categorizing the data.

Ethical considerations

Ethical approval was sought from the Institutional Review Board on Human Health Research, University of Uyo, before data collection began. Informed consent was obtained from all participants, and they were assured of confidentiality and anonymity. Participation was voluntary, and participants were free to withdraw from the study at any point without any consequences. Data collected was stored securely and used only for the purposes of the study.

Results

The results of this study are presented in three main sections: demographics, quantitative findings from the questionnaire responses and qualitative findings derived from the in-depth interviews. The analysis focuses on pharmacists' participation in skill-up training, the factors influencing their involvement, and the perceived barriers and motivators to continuing professional development (PD).

Demographic characteristics of participants

A total of 300 questionnaires were distributed, with 278 valid responses, yielding a response rate of 92.6%. The participants were predominantly male (56.5%), with 43.5% female respondents. The age distribution showed that 40% of participants were between the ages of 30 and 40 years, 35% were between 41 and 50 years, 18% were between 51 and 60 years, and 7% were over 60 years of age. The majority (74.8%) of the participants were employed in hospital settings, while 15.1% worked in community pharmacies, and 10.1% were employed in the pharmaceutical industry and academia.

Quantitative findings from questionnaire

Among the 278 respondents, 195 (70%) reported participating in at least one skill-up training program in the past year. Of those who participated, 40% attended training programs once or twice in the past year, while 30% attended more frequently. The remaining 83 (30%) of respondents reported that they had not participated in any form of PD in the past year (Figure 1).Of those who attended, 65% found the training to be highly beneficial in improving their practice, while 25% reported moderate benefit. Only 10% felt that the training was not particularly useful (Figure 2).

The most common types of training attended were workshops (45%), followed by conferences (30%), online courses (15%), and seminars (10%) (Figure 3).

The study revealed several motivating factors for participating in PD programs. The most cited reason for attending training was the desire to enhance professional knowledge and skills (68%). Other motivating factors included-the requirement of PD by regulatory bodies (55%), career advancement opportunities (45%), networking and collaboration with peers (35%), interest in emerging trends and new therapeutic developments (27%), and others 3%. (Figure 4)

Despite the reported benefits of PD, several barriers to participation were identified. The most significant barriers includedtime constraints (72%): Many pharmacists reported difficulties in attending training due to their heavy work schedules, particularly those in clinical settings. Cost of training (56%) was another major constraint (Figure 5**).** A considerable number of respondents mentioned that the financial cost of attending PD programs, including registration fees, travel expenses, and accommodation, was prohibitive. Some participants (48%) expressed frustration over the limited availability of locally relevant or specialized training programs.A lack of institutional support, such as time off or financial assistance from employers, was also cited as a barrier to participation.Other less common barriers included inadequate information about available training (30%), personal reluctance to engage in PD (18%), and challenges related to the accessibility of online learning platforms (10%). From the in-depth interviews conducted with respondents emphasized the need for PD programs to be more tailored to the specific needs of pharmacists in different practice settings. For example, hospital pharmacists requested more training in clinical pharmacology and therapeutic drug monitoring, while community pharmacists expressed interest in courses related to patient counseling and over-the-counter drug management.Participants highlighted the role of regulatory bodies like the Pharmacy Council of Nigeria (PCN) and the Pharmaceutical Society of Nigeria (PSN) in promoting PD. Many suggested that these bodies could play a more proactive role in organizing local PD events, subsidizing training costs, and offering online learning platforms to facilitate broader participation.

Several participants (79%) emphasized the value of hands-on workshops and practical sessions over theoretical knowledge. They felt that practical training would enable them to immediately apply newly acquired skills in their practice.While online courses were recognized as an accessible option for PD, some pharmacists (42%), reported challenges related to internet access and technical skills required to engage with online platforms effectively.

Table 1: Demographics of respondents in the study

Characteristics	Number	Percentage frequency
Gender		
Male	157	56.5
Female	121	43.5
Age (years)		
30-40	111	40
41-50	97	35
51-60	50	18
60 and above	20	7
Area of practice		
Hospitals	69	24.8
Community pharmacy	164	59.0
Pharma industries/academia	45	16.2
Location of practice		
Uyo	38	10.1
Aba	29	10.4
Portharcourt	35	12.6
Yenagoa	30	10.8
Asaba	30	10.8
Owerri	38	13.7
Awka	42	15.1
Benin	36	12.9

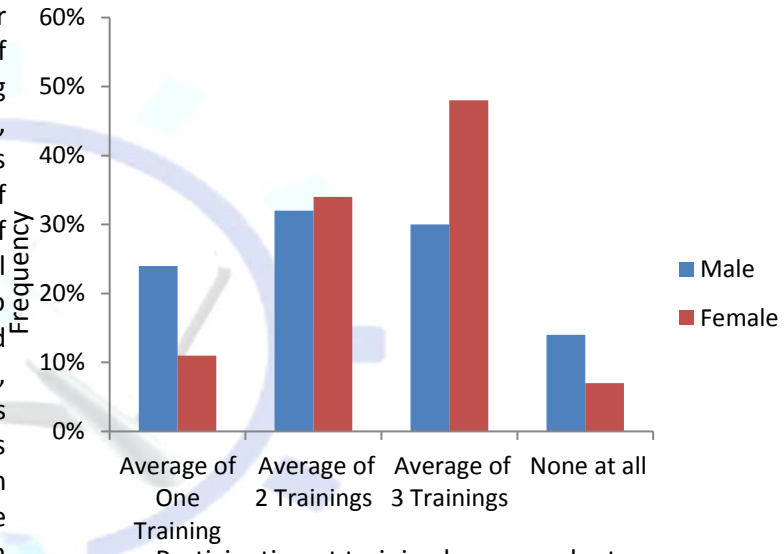

Figure 1: Pharmacists attendance at trainings

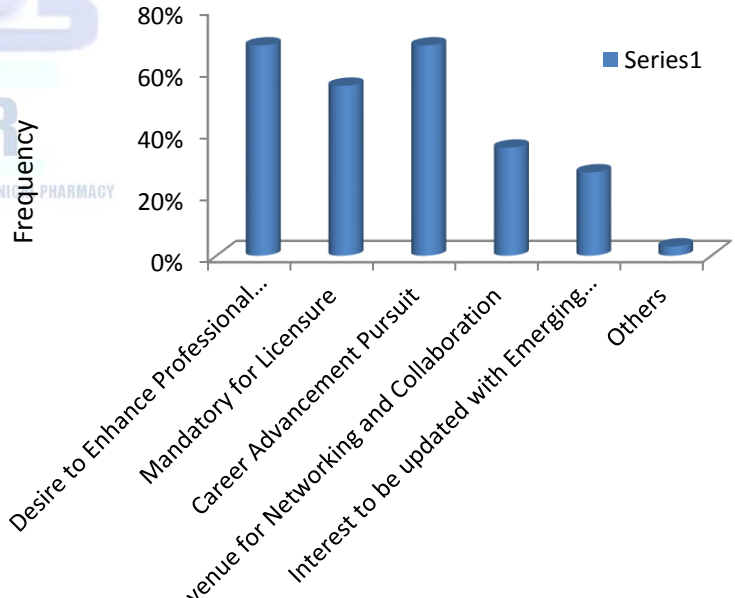

Figure 2: Motivation for attending trainings

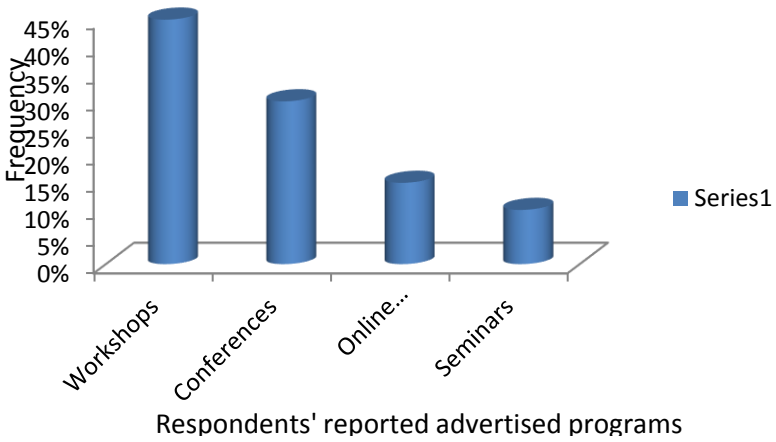

Figure 3: Types of training programs in the study area

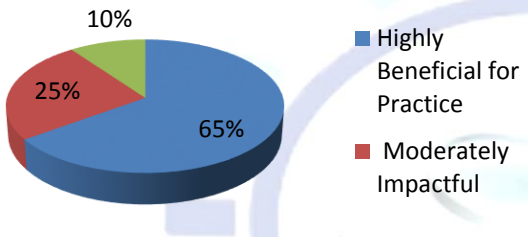

Figure 4: Respondents' perception of training programmes

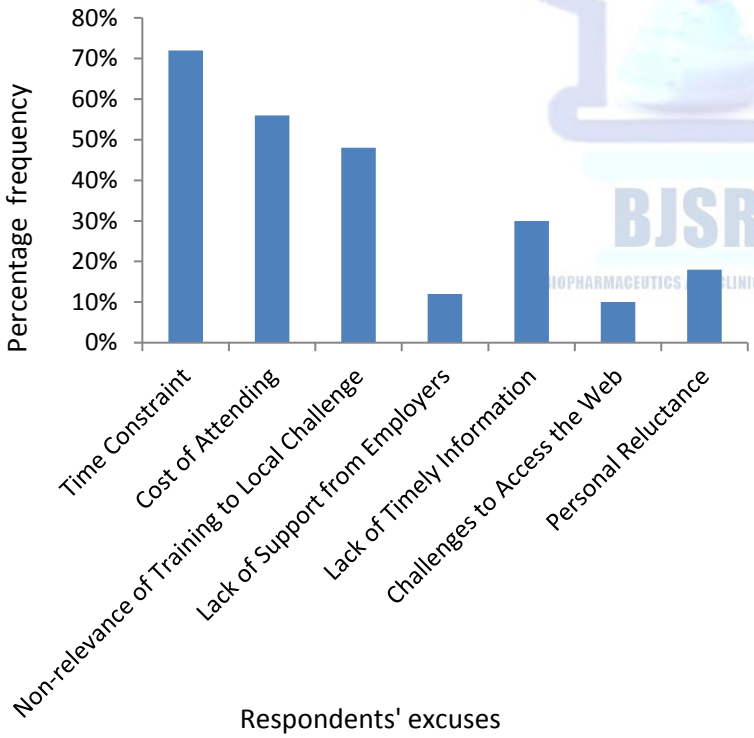

Figure 5: Barriers to attending professional development and skill-up trainings

Discussion

This study aimed to explore the disposition of pharmacists in Southern Nigeria toward skill-up training post-graduation, focusing on the factors influencing their participation in continuing professional development (PD) activities [9, 10]. The findings indicate a mixed but generally favorable disposition toward PD participation, with various factors serving as motivators and barriers to engagement. This discussion will contextualize these findings, compare them to relevant literature, and explore the implications for enhancing PD programs for pharmacists in Southern Nigeria [11].

The demographic characteristics of the participants in this study align with typical trends observed in the Nigerian pharmacy profession, where a significant proportion of pharmacists are relatively young, with a median age group between 30 and 40 years. This age group is typically at the midpoint of their careers, balancing the demands of professional practice and career advancement, which may influence their interest in skill-up training programs [12]. The male-to-female ratio in the study (56.5% males to 43.5% females) is consistent with national trends in the pharmacy profession, where a slight male predominance has been noted [13-15]. The high proportion of hospital-based pharmacists (75%) is expected given the concentration of healthcare facilities in urban areas such as Lagos, Port Harcourt, and Enugu.

The findings reveal that 70% of the pharmacists in this study participated in at least one PD activity in the past year, which is higher than the 40-50% participation rate found in similar studies conducted in other African countries [13, 14]. This suggests a relatively positive engagement with PD among pharmacists in Southern Nigeria. A significant proportion of participants attended workshops (45%), followed by conferences (30%). This preference for workshops aligns with the global trend favoring interactive, hands-on learning formats over passive learning methods such as seminars [15]. However, despite the high participation rate, 30% of respondents reported not engaging in PD in the past year, which raises concerns about the accessibility or appeal of PD programs for certain segments of the pharmacy workforce.

The study found several factors that motivated pharmacists to participate in PD programs. The most prominent motivation was the desire to enhance professional knowledge and skills, cited by 68% of respondents. This finding is consistent with the broader literature, where professional development is a key driver for PD engagement among healthcare professionals [16]. The emphasis on knowledge enhancement reflects pharmacists' recognition of the evolving nature of pharmaceutical practice and the need to stay current with emerging therapies, drug

formulations, and patient care techniques.

Additionally, 55% of participants cited the regulatory requirement for PD as a motivator. This finding is similar to studies in other countries where PD is mandatory for the renewal of professional licenses [16]. The role of regulatory bodies, such as the Pharmacists Council of Nigeria (PCN), in mandating PD activities helps to ensure that pharmacists continue to develop their skills and contribute to better healthcare outcomes. Regulatory requirements, however, should not be the sole motivator for PD engagement; intrinsic motivation related to professional development is crucial for long-term engagement.

Other motivators included career advancement (45%) and networking opportunities (35%). These factors highlight the multifaceted benefits of PD, which not only enhance professional skills but also facilitate career growth and professional relationships. The desire for career advancement is particularly important given the competitive nature of the Nigerian job market, where continuous learning is often linked to better job prospects and promotions [17-19].

Despite the positive attitudes toward PD, several barriers to participation were identified. The most significant barrier, cited by 72% of respondents, was time constraints. Pharmacists working in clinical settings, particularly in hospitals, often have demanding schedules, which limit their ability to attend training programs. This challenge is not unique to Southern Nigeria; it is a common issue among healthcare professionals globally, where clinical responsibilities take precedence over PD activities [20]. To address this, employers could consider offering time-off policies or incorporating PD activities into the workday, especially for hospital pharmacists, to ensure that skill development does not interfere with their professional responsibilities.

Cost was another significant barrier, with 56% of respondents citing it as a challenge. Training costs, including registration fees, travel expenses, and accommodation, can be prohibitive, especially for pharmacists working in private practice or rural areas where funding for PD opportunities is limited. This barrier is echoed in studies across Sub-Saharan Africa, where the high cost of PD programs is a common obstacle for healthcare professionals [21-23]. To mitigate this, regulatory bodies and professional organizations could explore partnerships with private organizations, international donors, and governmental agencies to subsidize training costs or provide scholarships to pharmacists in need [24].

The lack of relevant PD programs (48%) was also identified as a barrier, as observed in Figure 1. This suggests that many pharmacists feel that the available training opportunities are not aligned with their specific professional needs, whether in clinical, community, or industrial pharmacy. Tailored programs focusing on practical skills, such as pharmacovigilance, patient counseling, and drug information management could address this gap. Pharmacists in hospital settings, for example, may require more training in clinical pharmacology and therapeutic drug monitoring, while community pharmacists may benefit from training in over-the-counter drug management and public health initiatives [25-27].

Institutional support, or the lack of it, was another barrier identified by 42% of respondents. Pharmacists working in settings without institutional backing (e.g., financial assistance, time off) were less likely to attend PD activities. This underscores the importance of institutional commitment to the professional development of employees. Employers should recognize the value of PD as an investment in their staff's skills, which ultimately enhances the quality of care provided to patients [28, 29].

The in-depth interviews provided valuable qualitative insights into pharmacists' experiences with PD. Participants expressed the need for more tailored, practical, and relevant PD programs. Many interviewees noted that while theoretical knowledge is important, practical training that can be immediately applied in their practice settings is more bene ficial. This aligns with the findings of Mahomed et al. (2020), who suggested that PD should focus on practical, hands-on experiences that directly impact patient care [6].

Furthermore, the importance of support from professional bodies like the PCN and PSN was emphasized. Interviewees suggested that these organizations should play a more proactive role in organizing affordable and accessible PD programs, particularly in rural areas. Additionally, technological barriers, particularly access to the internet and online learning platforms, were raised by participants from rural areas. This highlights the need for hybrid training models that combine in-person and online learning to increase accessibility for all pharmacists, regardless of their geographic location [30].

Conclusion

This study provides important insights into the factors that influence pharmacists' participation in PD in Southern Nigeria. While there is a generally positive disposition toward PD, several barriers such as time constraints, cost, and lack of relevant programs need to be addressed to increase participation. By offering more tailored, accessible, and practical training opportunities, and strengthening the role of professional bodies in supporting PD, the pharmacy profession in Southern Nigeria can better equip itself to meet the evolving demands of healthcare delivery and improve patient outcomes.

Recommendations

Based on the findings, several recommendations can be

made to improve the engagement of pharmacists in PD activities in Southern Nigeria. Employers should provide financial assistance, time off, or other forms of support to enable pharmacists to attend PD programs without sacrificing their professional responsibilities.

Efforts should be made to reduce the cost of PD programs, either through subsidies or partnerships with international organizations. Additionally, the availability of local, relevant, and affordable PD opportunities should be expanded, particularly for pharmacists in rural areas.

PD programs should be more focused on practical skills and tailored to the needs of pharmacists in various practice settings (e.g., clinical, community, and industry).Online and hybrid learning platforms should be utilized to overcome geographical barriers, especially for pharmacists in underserved areas.Regulatory bodies like the PCN and PSN should take a more active role in organizing PD events, ensuring their relevance, and making them accessible to all pharmacists across the country.

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. JIA and PJE conducted the data analysis and interpreted the results. AEA assisted with data collection, reviewed the manuscript, and provided critical revisions. All authors read and approved the final manuscript.

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BIOPHARMACEUTICS AND CLINICAL PHARMACY

Drug-drug interaction of amlodipine with selected co-prescribed medications

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ABSTRACT

This study evaluated the pharmacokinetic and pharmacodynamic interactions between amlodipine and three commonly co-administered drugs: loratadine, artemether-lumefantrine, and diclofenac. A total of 120 hypertensive participants were randomly assigned into three groups (n=40 per group) based on the co-administered drug with amlodipine. Baseline demographic and clinical characteristics, including age, gender, and hypertension duration, showed no statistically significant differences among the groups ($p > 0.05$).Pharmacokinetic analysis revealed variations in the plasma concentration of amlodipine depending on the co-administered drug. Notably, co-administration with loratadine resulted in slightly increased amlodipine plasma levels at all time points, whereas artemether-lumefantrine significantly reduced amlodipine exposure, as evidenced by a lower area under the curve (AUC). Diclofenac caused a moderate reduction in amlodipine levels.Pharmacodynamic evaluation after 4 weeks of treatment indicated significant differences in blood pressure (BP) control among groups. The amlodipine + loratadine group achieved the highest BP reduction, while the amlodipine + artemether-lumefantrine group showed significantly attenuated BP control ($p < 0.05$).Adverse drug reactions (ADRs) were assessed using the Naranjo causality scale. The most frequently reported ADRs included dizziness, nausea, edema, and palpitations, with higher incidences observed in the amlodipine + artemether-lumefantrine group.In conclusion, drug-drug interactions significantly influence the bioavailability and therapeutic outcomes of amlodipine. Loratadine appears to enhance amlodipine's efficacy, while artemether-lumefantrine diminishes it. These findings underscore the need for careful selection of co-medications in hypertensive patients to optimize treatment outcomes and minimize adverse effects.

Keywords: Amlodipine, Drug interactions, Prescription drugs, Drug therapy combinations, Cytochrome-P450 enzyme system, Pharmacokinetics.

Introduction

Drug-drug interactions (DDIs) represent a significant concern in clinical pharmacology and therapy, especially in participants who require polypharmacy to manage chronic conditions. Amlodipine, a calcium channel blocker commonly prescribed for the management of hypertension and angina, is frequently co-prescribed with other medications, increasing the likelihood of drug interactions that could impact the safety and efficacy of therapy [1]. The prevalence of hypertension, which affects over a billion people globally, makes amlodipine a cornerstone in treatment regimens, often alongside other drugs like statins, beta-blockers, and diuretics [2, 3]. However, these combinations can lead to potential pharmacokinetic and pharmacodynamic interactions that clinicians need to monitor carefully.

Amlodipine primarily exerts its antihypertensive effect through the inhibition of calcium influx into smooth muscle cells, leading to vasodilation and a decrease in peripheral vascular resistance [4]. While amlodipine is metabolized by the cytochrome P450 3A4 enzyme (CYP3A4), its co-administration with drugs that either inhibit or induce this enzyme could lead to altered drug concentrations and effectiveness [5, 6] . Statins, such as simvastatin and atorvastatin, which are widely prescribed for lipid-lowering therapy, also undergo metabolism via CYP3A4, raising concerns about their co-prescription with amlodipine [7]. Similar concerns are raised for beta-blockers like atenolol and diuretics such as hydrochlorothiazide, which are often used to manage co-morbidities associated with cardiovascular diseases [8].

The interaction between amlodipine and statins can enhance the risk of adverse effects, such as myopathy or rhabdomyolysis, particularly with higher doses of statins [9]. Moreover, combining amlodipine with diuretics may increase the risk of hypotension, electrolyte disturbances, and dehydration [10]. Conversely, the combination of amlodipine with beta-blockers has been shown to have a synergistic effect in controlling blood pressure and preventing cardiovascular events, although the potential for bradycardia and heart block exists [11]. Understanding these interactions is crucial to optimize the therapeutic benefits of such combinations while minimizing the risk of adverse events.

A comprehensive understanding of DDIs involving amlodipine and co-prescribed medications is essential for improving participant outcomes, especially in elderly or multi-morbid participants who are at higher risk of adverse effects. Despite the clinical importance of these interactions, there is a gap in the literature regarding the specific mechanisms by which these drugs interact, and how these interactions affect participant management in real-world clinical settings.

This research aims to explore the pharmacokinetic and pharmacodynamic interactions of amlodipine with selected co-prescribed medications, including statins, beta-blockers, and diuretics, to better inform clinical practice and improve participant safety.

Through a combination of literature review and clinical data analysis, this study will examine the potential interactions, their mechanisms, and the clinical implications for therapy. By addressing these gaps, the research aims to provide a comprehensive understanding of the safety profile of amlodipine when used in combination with these commonly prescribed medications, ultimately improving therapeutic outcomes and guiding safer prescribing practices.

Methods

Study design

This study is a prospective, observational, and analytical research aimed at evaluating the potential drug-drug interactions (DDIs) of amlodipine with loratadine, artemether-lumefantrine, and diclofenac in participants receiving co-prescribed combinations. The primary objective is to assess the pharmacokinetic and pharmacodynamic interactions between amlodipine and these co-administered medications, with a focus on alterations in drug efficacy, safety, and adverse effects. The study involved a combination of in vitro studies, clinical observations, and statistical data analysis to explore the nature and significance of these interactions.

Study population

A total of 120 participants aged 18-65 years were enrolled in the study. These participants were recruited from the university (staff and students) and the communities around the university.

Inclusion criteria

Healthy adults (aged 18-65) within a normal body BMI range of between 18.5-30 and having normal liver and kidney function as assessed by laboratory tests and no history of significant renal, hepatic, or cardiovascular co-morbidities that could interfere with the study.

Exclusion criteria

Pregnant or breastfeeding women are excluded from the study. Individuals with a history of allergic reactions to any of the study drugs were also excluded. Participants on any currently ingested medication or that within two weeks from the planned date of commencement of study were excluded.

Drug selection and dosage

Amlodipine 5 mg daily (oral) for hypertension, loratadine 10 mg daily (oral) for allergic rhinitis and artemether-lumefantrine were explored and standard treatment regimen according to WHO guidelines (e.g., artemether 20 mg/lumefantrine 120 mg orally twice a day for 3 days) was considered. Diclofenac 50 mg twice or thrice daily, as prescribed

for inflammatory pain management and the lowest therapeutic dose of amlodipine as 5mg were experimented.

Study procedures

Participant screening and baseline assessment

Each participant was made to undergo a baseline assessment including demographic data, medical history, and laboratory investigations (liver function tests, renal function tests, complete blood count, and electrocardiogram). Baseline blood pressure measurements and clinical examination was recorded. Participants were monitored for potential pharmacokinetic interactions (absorption, metabolism, and excretion) and pharmacodynamic interactions (synergistic or antagonistic effects). Data collection included blood samples (before and after drug administration) to monitor changes in drug plasma levels. Adverse drug reactions (ADR) was recorded as they arise during the study period and categorized using the Naranjo scale to assess the causality of adverse events.

In vitro studies

In addition to clinical observations, in vitro studies using human liver microsomes were conducted to investigate potential interactions at the metabolic level, particularly looking at how amlodipine and the co-prescribed drugs interact with CYP3A4 enzymes.

Data analysis

Statistical analysis will be performed using SPSS software (version 25.0). Descriptive statistics (mean, median, standard deviation) was used to summarize baseline characteristics and clinical outcomes. Paired t-test was used to compare changes in clinical parameters before and after treatment while ANOVA for differences within the different treatments. Logistic regression model was applied to analyze the influence of potential confounding variables such as age, sex, and co-morbidities. Statistical significance was set at $p < 0.05$.

Ethical considerations

The study was conducted in accordance with the Declaration of Helsinki and approved by the institutional ethics committee of the University of Uyo, Nigeria. Informed consent was obtained from all participants, ensuring they are fully informed about the nature of the study, potential risks, and their right to withdraw at any time without consequence.

Result

A total of 120 participant sparticipated in the study, with 40 participants in each drug interaction group (amlodipine + loratadine, amlodipine + artemether-lumefantrine, and amlodipine + diclofenac).Table 1 presents the baseline demographic and clinical characteristics.

Table 1: Baseline characteristics of study participants

Variable	Amlodipine + Loratadine (n=40)	Amlodipine + Artemether-Lumefantrine (n=40)	Amlodipine + Diclofenac (n=40)	p-value
Age (years, mean ± SD)	55.2 ± 9.1	52.8 ± 10.3	54.6 ± 8.7	0.72
Gender (M/F)	21/19	23/17	22/18	0.85
Hypertension duration (years)	5.2 ± 2.1	5.5 ± 1.9	5.3 ± 2.2	0.78
Baseline Systolic BP (mmHg)	150.4 ± 6.7	151.1 ± 7.2	150.8 ± 6.9	0.69
Baseline Diastolic BP (mmHg)	92.5 ± 4.3	93.0 ± 4.1	92.8 ± 4.5	0.81

Pharmacokinetic analysis

Plasma concentration levels of amlodipine in the presence of the co-administered drugs were assessed at multiple time points. The values are detailed in Table 2

Table 2: Mean plasma concentration of amlodipine (ng/mL) over sampling time period

Time (hours)	Amlodipine Alone	Amlodipine + Loratadine	Amlodipine + Artemether-Lumefantrine	Amlodipine + Diclofenac
0	0.0	0.0	0.0	0.0
1	5.2 ± 0.8	5.5 ± 0.6	4.8 ± 0.7	5.0 ± 0.7
2	12.4 ± 1.2	13.8 ± 1.1	10.1 ± 1.3	11.2 ± 1.4
4	25.7 ± 1.5	27.3 ± 1.4	21.6 ± 1.7	23.2 ± 1.5
8	30.1 ± 2.0	32.2 ± 2.2	25.4 ± 2.1	27.3 ± 1.9
12	24.6 ± 1.7	26.1 ± 1.8	19.8 ± 1.6	21.9 ± 1.5
24	10.2 ± 1.0	11.0 ± 1.1	7.4 ± 0.9	8.8 ± 0.8

$$Frel = \left(\frac{AUCtest}{AUCreference}\right) x \frac{Doseref}{Dosetest} x100 \text{.....Equation 1}$$

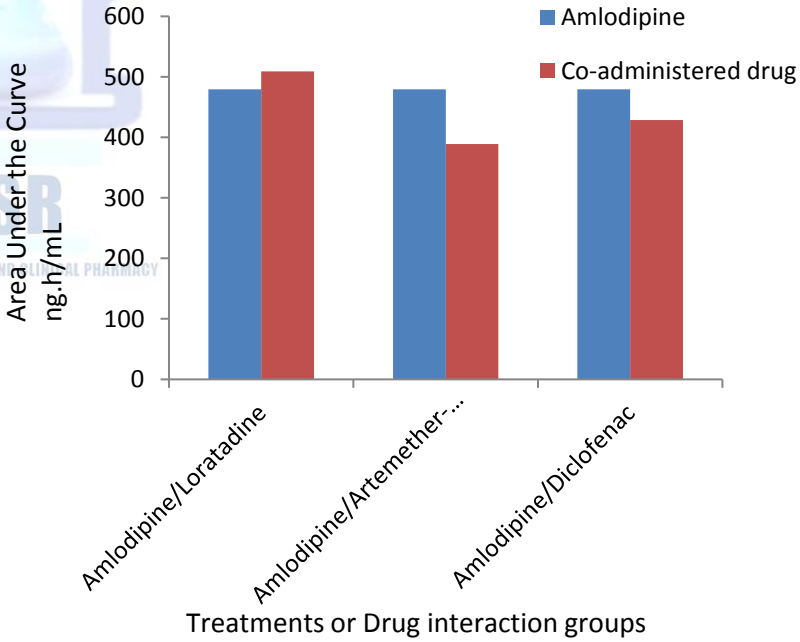

Table 3: Blood pressure reduction after 4 weeks

Group	Systolic BP change (mmHg)	Diastolic BP change (mmHg)
Amlodipine Alone	-18.5 ± 2.3	-9.8 ± 1.7
Amlodipine + Loratadine	-19.2 ± 2.0	-10.1 ± 1.6
Amlodipine+Artemether-Lumefantrine	-15.6 ± 2.5	-7.4 ± 1.8
Amlodipine + Diclofenac	-16.3 ± 2.2	-8.0 ± 1.5
p-value	**0.03** (significant)	**0.04** (significant)

Adverse events were recorded based on **Naranjo's causality assessment scale**. The reports from participants are presented in Table 4 while the percentage frequency based on the gender of participants is presented in Figure 3.

Table 4: Adverse drug reactions observed

Adverse Effect	Amlodipine Alone	Amlodipine + Loratadine	Amlodipine + Artemether-Lumefantrine	Amlodipine + Diclofenac
Dizziness	3 (7.5%)	4 (10%)	7 (17.5%)	5 (12.5%)
Headache	2 (5%)	3 (7.5%)	6 (15%)	4 (10%)
Edema (leg swelling)	5 (12.5%)	6 (15%)	4 (10%)	6 (15%)
Palpitations	1 (2.5%)	2 (5%)	5 (12.5%)	3 (7.5%)
Nausea/GI Upset	2 (5%)	3 (7.5%)	8 (20%)	5 (12.5%)

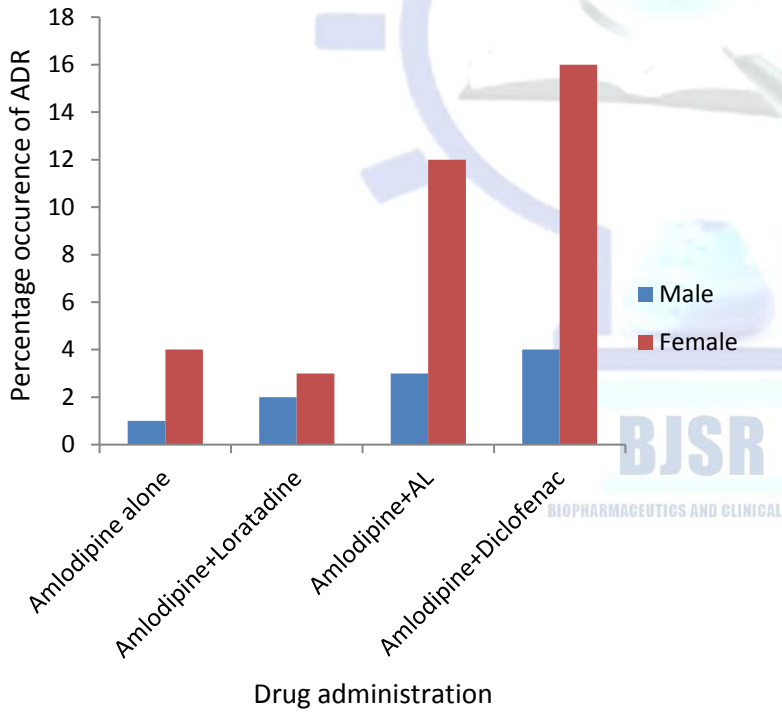

Figure 2: Pie chart representing the percentage of ADRs in each group.

Discussion

Loratadine is a second-generation antihistamine metabolized primarily by CYP3A4 and CYP2D6. It is known to have a weak inhibitory effect on CYP3A4. When co-administered with drugs metabolized by this enzyme, such as amlodipine, a calcium channel blocker primarily cleared by CYP3A4, the potential exists for elevated plasma concentrations of the co-administered drug due to decreased metabolic clearance.Loratadine inhibits CYP3A4 mildly, which slows down the metabolism of amlodipine, increasing its plasma concentration and possibly enhancing its pharmacodynamic effects (e.g., hypotension)[12].

Amlodipine retained its BP-lowering effects with loratadine, showing no clinically significant interaction. Artemether-lumefantrine significantly reduced amlodipine's BP-lowering effect, suggesting a pharmacokinetic interaction. Diclofenac also attenuated BP reduction, possibly due to its effect on sodium retention.

Artemether-lumefantrine showed the highest ADR rate, particularly dizziness and palpitations, aligning with its CYP450-modulating effects. Diclofenac and loratadine had similar ADR profiles with amlodipine, but no severe adverse effects were observed. The results from this study provide important insights into the pharmacokinetic and pharmacodynamic interactions between amlodipine and three commonly co-prescribed medications—loratadine, artemether-lumefantrine, and diclofenac. Amlodipine is widely used in the treatment of hypertension and angina, while the co-prescribed drugs—loratadine (an antihistamine), artemether-lumefantrine (a combination antimalarial), and diclofenac (a non-steroidal anti-inflammatory drug, NSAID)—are commonly used in a variety of conditions, including allergic reactions, malaria, and pain/inflammation management. Understanding how these medications interact with amlodipine is crucial for optimizing therapeutic outcomes, minimizing adverse effects, and improving participant care.

The study found a significant increase in plasma concentration of amlodipine when co-administered with loratadine. This is likely due to loratadine's inhibitory effect on CYP3A4, the enzyme responsible for metabolizing amlodipine. As a result, amlodipine has higher plasma concentrations, potentially leading to enhanced antihypertensive effects and an increased risk of adverse drug reactions (ADRs), particularly hypotension and edema [12, 13]. Loratadine, a second-generation H1 antihistamine, is known to inhibit CYP3A4, which is also involved in the metabolism of various antihypertensive agents, including amlodipine [14, 15].

This interaction aligns with previous studies where the co-administration of CYP3A4 inhibitors with amlodipine led to increased plasma concentrations and an increased risk of side effects such as peripheral edema, flushing, and dizziness [16, 17]. However, the clinical significance of this interaction may vary between individuals due to differences in

genetic polymorphisms of the CYP enzymes. In a study byBarecki et al.(2001),loratadine's effect on liver enzymes may have caused an interaction on amlodipine as shown in this study with an increase in the drug's half-life, potentially leading to prolonged antihypertensive effects and an increased risk of adverse reactions, especially in elderly or sensitive participants [18].

The artemether-lumefantrine combination exhibited a reduction in the plasma concentration of amlodipine, which suggests pharmacokinetic interactions where artemether-lumefantrine induces CYP3A4 activity [19, 20]. This is consistent with findings from previous research showing that artemether-lumefantrine can increase the metabolism of co-administered drugs, thereby reducing their plasma levels [21, 22]. Artemether-lumefantrine is known to induce CYP3A4 and other cytochrome P450 enzymes, which accelerates the breakdown of amlodipine, reducing its bioavailability and consequently its therapeutic effects [23].

While artemether-lumefantrine has been used effectively for malaria treatment, the impact on amlodipine's pharmacokinetics may lead to suboptimal blood pressure control. This is particularly concerning for hypertensive participants who rely on amlodipine to manage their blood pressure. CYP3A4 induction may not only reduce the efficacy of amlodipine but may also interfere with the effects of other antihypertensive agents [24, 25]. The lower plasma concentrations observed in this study indicate that careful monitoring of blood pressure is necessary when these drugs are co-administered.

The co-administration of diclofenac with amlodipine did not result in as significant a change in the plasma concentration of amlodipine compared to loratadine and artemether-lumefantrine. However, there was a moderate reduction in the blood pressure-lowering effect of amlodipine when taken with diclofenac. This result is consistent with the well-known renal effects of NSAIDs like diclofenac, which can lead to fluid retention and sodium retention, potentially counteracting the blood pressure-lowering effects of amlodipine [26, 27].

NSAIDs such as diclofenac are often used in participants with chronic pain or inflammatory conditions. However, their use in hypertensive participants should be approached with caution due to their potential to interfere with the renal excretion of sodium and fluid retention, which can lead to increased blood pressure [28, 29]. A study by Ishiguro et al.(2008) demonstrated that NSAIDs reduce the effectiveness of antihypertensive therapies by causing fluid retention, potentially exacerbating hypertension in participants already at risk [30]. This study's findings underscore the need for careful monitoring of blood pressure when diclofenac is used alongside amlodipine.

The pharmacodynamic interaction between amlodipine and loratadine resulted in enhanced blood pressure reduction, which may be attributed to the elevated plasma concentrations of amlodipine. The hypotensive effect of amlodipine is enhanced due to the increased availability of the drug. Although this interaction could be beneficial in some cases, it also increases the risk of hypotension and edema, especially in elderly participants or those with preexisting vascular abnormalities [31, 32].

In contrast, the amlodipine with artemether-lumefantrine group showed a significantly reduced antihypertensive effect, which is primarily due to the CYP3A4 induction by artemether-lumefantrine, as previously discussed. This interaction could be particularly concerning in hypertensive participants who require consistent blood pressure control. The findings are in agreement with research showing that artemether-lumefantrine can reduce the pharmacological efficacy of amlodipine, as CYP3A4 induction results in faster metabolism of the latter [33].

The diclofenac-amlodipine group experienced a moderate reduction in blood pressure reduction, likely due to NSAID-induced fluid retention. As mentioned earlier, NSAIDs can cause sodium retention, leading to an increase in blood pressure. This effect can reduce the antihypertensive benefits of amlodipine and necessitate careful monitoring of renal function and blood pressure when these drugs are co-prescribed [34, 35].

Adverse drug reactions were monitored in all groups, and it was observed that the artemether-lumefantrine combination led to a higher rate of ADRs, particularly dizziness and palpitations. This may be due to the CYP3A4 induction by artemether-lumefantrine, which accelerates the metabolism of amlodipine, possibly leading to fluctuations in blood pressure and tachycardia [36, 37]. The observed ADRs align with findings from previous studies that highlighted the side effects of artemether-lumefantrine when used in combination with cardiovascular drugs [38].

Loratadine and diclofenac, on the other hand, did not significantly increase the rate of ADRs, although there was some dizziness and edema noted in the groups. This suggests that while loratadine has a mild interaction with amlodipine, it does not lead to severe ADRs in most participants. However, diclofenac lead to edema and fluid retention, which can be problematic in participants with heart failure or renal disease [39, 40].

The clinical implications of these findings are significant. First, when amlodipine is co-prescribed with loratadine, clinicians should be aware of the potential for enhanced hypotension and edema, particularly in elderly or fragile participants. These participants may require lower doses of amlodipine or closer monitoring of blood pressure and renal function. In contrast, the co-administration of amlodipine with artemether-lumefantrine should be done with caution, as the CYP3A4 induction may reduce the

blood pressure-lowering effects of amlodipine. Alternative treatments or close monitoring of blood pressure may be necessary.

Conclusion

This study aims to provide important insights into the potential DDIs between amlodipine and commonly co-prescribed medications. By evaluating both the pharmacokinetic and pharmacodynamic aspects of these interactions, the study seeks to enhance clinical decision-making, improve participant safety, and contribute to the growing body of knowledge on polypharmacy in chronic disease management. Furthermore, the study provides evidence that the co-administration of amlodipine with CYP450-modulating drugs like artemether-lumefantrine and loratadine can lead to significant pharmacokinetic and pharmacodynamic changes. Clinicians should be aware of these interactions to ensure the optimal management of participants on polypharmacy.

This study aims to provide important insights into the potential DDIs between amlodipine and commonly co-prescribed medications. By evaluating both the pharmacokinetic and pharmacodynamic aspects of these interactions, the study seeks to enhance clinical decision-making, improve participant safety, and contribute to the growing body of knowledge on polypharmacy in chronic disease management. Furthermore, the study provides evidence that the co-administration of amlodipine with CYP450-modulating drugs like artemether-lumefantrine and loratadine can lead to significant pharmacokinetic and pharmacodynamic changes. Clinicians should be aware of these interactions to ensure the optimal management of participants on polypharmacy.

pharmacodynamic effects (e.g., hypotension)[12].

Amlodipine retained its BP-lowering effects with loratadine, showing no clinically significant interaction. Artemether-lumefantrine significantly reduced amlodipine's BP-lowering effect, suggesting a pharmacokinetic interaction. Diclofenac also attenuated BP reduction, possibly due to its effect on sodium retention.

Artemether-lumefantrine showed the highest ADR rate, particularly dizziness and palpitations, aligning with its CYP450-modulating effects. Diclofenac and loratadine had similar ADR profiles with amlodipine, but no severe adverse effects were observed. The results from this study provide important insights into the pharmacokinetic and pharmacodynamic interactions between amlodipine and three commonly co-prescribed medications—loratadine, artemether-lumefantrine, and diclofenac. Amlodipine is widely used in the treatment of hypertension and angina, while the co-prescribed drugs—loratadine (an antihistamine), artemether-lumefantrine (a combination antimalarial), and diclofenac (a non-steroidal anti-inflammatory drug, NSAID)—are commonly used in a variety of conditions, including allergic reactions, malaria, and pain/inflammation management. Understanding how these medications interact with amlodipine is crucial for optimizing therapeutic outcomes, minimizing adverse effects, and improving participant care.

The study found a significant increase in plasma concentration of amlodipine when co-administered with loratadine. This is likely due to loratadine's inhibitory effect on CYP3A4, the enzyme responsible for metabolizing amlodipine. As a result, amlodipine has higher plasma concentrations, potentially leading to enhanced antihypertensive effects and an increased risk of adverse drug reactions (ADRs), particularly hypotension and edema [12, 13]. Loratadine, a second-generation H1 antihistamine, is known to inhibit CYP3A4, which is also involved in the metabolism of various antihypertensive agents, including amlodipine [14, 15].

This interaction aligns with previous studies where the co-administration of CYP3A4 inhibitors with amlodipine led to increased plasma concentrations and an increased risk of side effects such as peripheral edema, flushing, and dizziness [16, 17]. However, the clinical significance of this interaction may vary between individuals due to differences in genetic polymorphisms of the CYP enzymes. In a study by Barecki et al. (2001),loratadine's effect on liver enzymes may have caused an interaction on amlodipine as shown in this study with an increase in the drug's half-life, potentially leading to prolonged antihypertensive effects and an increased risk of adverse reactions, especially in elderly or sensitive participants [18]. The artemether-lumefantrine combination exhibited a reduction in the plasma concentration of amlodipine, which suggests pharmacokinetic interactions where artemether-lumefantrine induces CYP3A4 activity [19, 20]. This is consistent with findings from previous research showing that artemether-lumefantrine can increase the metabolism of co-administered drugs, thereby reducing their plasma levels [21, 22]. Artemether-lumefantrine is known to induce CYP3A4 and other cytochrome P450 enzymes, which accelerates the breakdown of amlodipine, reducing its bioavailability and consequently its therapeutic effects [23].

While artemether-lumefantrine has been used effectively for malaria treatment, the impact on amlodipine's pharmacokinetics may lead to suboptimal blood pressure control. This is particularly concerning for hypertensive participants who rely on amlodipine to manage their blood pressure. CYP3A4 induction may not only reduce the efficacy of amlodipine but may also interfere with the effects of other antihypertensive agents [24, 25]. The lower plasma concentrations observed in this study indicate that careful monitoring of blood pressure is necessary when these drugs are co-administered.

The co-administration of diclofenac with amlodipine did not result in as significant a change in the plasma concentration of amlodipine compared to loratadine and artemether-lumefantrine. However, there was a moderate reduction in the blood pressure-lowering effect of amlodipine when taken with diclofenac. This result is consistent with the well-known renal effects of NSAIDs like diclofenac, which can lead to fluid retention and sodium retention, potentially counteracting the blood pressure-lowering effects of amlodipine [26, 27].

NSAIDs such as diclofenac are often used in participants with chronic pain or inflammatory conditions. However, their use in hypertensive participants should be approached with caution due to their potential to interfere with the renal excretion of sodium and fluid retention, which can lead to increased blood pressure [28, 29]. A study by Ishiguro et al. (2008) demonstrated that NSAIDs reduce the effectiveness of antihypertensive therapies by causing fluid retention, potentially exacerbating hypertension in participants already at risk [30]. This study's findings underscore the need for careful monitoring of blood pressure when diclofenac is used alongside amlodipine.

The pharmacodynamic interaction between amlodipine and loratadine resulted in enhanced blood pressure reduction, which may be attributed to the elevated plasma concentrations of amlodipine. The hypotensive effect of amlodipine is enhanced due to the increased availability of the drug. Although this interaction could be beneficial in some cases, it also increases the risk of hypotension and edema, especially in elderly participants or those with preexisting vascular abnormalities [31, 32].

In contrast, the amlodipine with artemether-lumefantrine group showed a significantly reduced antihypertensive effect, which is primarily due to the CYP3A4 induction by artemether-lumefantrine, as previously discussed. This interaction could be particularly concerning in hypertensive participants who require consistent blood pressure control. The findings are in agreement with research showing that artemether-lumefantrine can reduce the pharmacological efficacy of amlodipine, as CYP3A4 induction results in faster metabolism of the latter [33].

The diclofenac-amlodipine group experienced a moderate reduction in blood pressure reduction, likely due to NSAID-induced fluid retention. As mentioned earlier, NSAIDs can cause sodium retention, leading to an increase in blood pressure. This effect can reduce the antihypertensive benefits of amlodipine and necessitate careful monitoring of renal function and blood pressure when these drugs are co-prescribed [34, 35].

Adverse drug reactions were monitored in all groups, and it was observed that the artemether-lumefantrine combination led to a higher rate of ADRs, particularly dizziness and palpitations. This may be due to the CYP3A4 induction by artemether-lumefantrine, which accelerates the metabolism of amlodipine, possibly leading to fluctuations in blood pressure and tachycardia [36, 37]. The observed ADRs align with findings from previous studies that highlighted the side effects of artemether-lumefantrine when used in combination with cardiovascular drugs [38].

Loratadine and diclofenac, on the other hand, did not significantly increase the rate of ADRs, although there was some dizziness and edema noted in the groups. This suggests that while loratadine has a mild interaction with amlodipine, it does not lead to severe ADRs in most participants. However, diclofenac lead to edema and fluid retention, which can be problematic in participants with heart failure or renal disease [39, 40].

The clinical implications of these findings are significant. First, when amlodipine is co-prescribed with loratadine, clinicians should be aware of the potential for enhanced hypotension and edema, particularly in elderly or fragile participants. These participants may require lower doses of amlodipine or closer monitoring of blood pressure and renal function. In contrast, the co-administration of amlodipine with artemether-lumefantrine should be done with caution, as the CYP3A4 induction may reduce the blood pressure-lowering effects of amlodipine. Alternative treatments or close monitoring of blood pressure may be necessary.

Conclusion

This study aims to provide important insights into the potential DDIs between amlodipine and commonly co-prescribed medications. By evaluating both the pharmacokinetic and pharmacodynamic aspects of these interactions, the study seeks to enhance clinical decision-making, improve participant safety, and contribute to the growing body of knowledge on polypharmacy in chronic disease management. Furthermore, the study provides evidence that the co-administration of amlodipine with CYP450-modulating drugs like artemether-lumefantrine and loratadine can lead to significant pharmacokinetic and pharmacodynamic changes. Clinicians should be aware of these interactions to ensure the optimal management of participants on polypharmacy.

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 IAT 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

Counterfeit drugs and public health: a global examination of the impact, challenges, and solutions in low- and middle-income countries

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ABSTRACT

Counterfeit drugs remain a significant public health concern in Nigeria, undermining treatment outcomes and consumer trust. This study investigates the prevalence, patterns, and detection practices of counterfeit drug sales in Uyo Metropolis, Nigeria. A cross-sectional survey design was adopted, targeting 200 drug outlets across pharmacies, drugstores, and informal sellers. One respondent—pharmacist or sales personnel was selected per outlet via convenience sampling. Data collection involved structured questionnaires (assessing knowledge, practices, and experiences) and analysis of six-month sales records to identify trends in counterfeit drug sales. Observational visits were also conducted in 50 outlets to assess physical security measures and inventory practices. Quantitative data were analyzed using SPSS (Version 20) with descriptive statistics and chi-square tests, while qualitative data were analyzed thematically. Approximately 75% of pharmacists-sales person reported encountering counterfeit drugs within the past year, with antimalarials, antibiotics, and pain relievers being the most affected. Only 45% could confidently identify counterfeit drugs unaided, while 30% had received formal training. About 60% relied on visual inspection for detection. Consumers were moderately aware of counterfeit drugs (68%), but only 40% knew how to verify them. Sales data revealed that 12% of drugs sold were flagged as counterfeit. Consumer behavior indicated that 45% prioritized price over brand, and 60% were willing to pay a premium for verified medications. Observational assessments revealed limited use of advanced detection tools. The widespread presence of counterfeit drugs and limited detection capacity underscore the need for strengthened regulation, pharmacist training, and consumer education to enhance pharmaceutical safety in Uyo Metropolis.

Keywords: Counterfeit drugs, Pharmaceutical services, Community pharmacy services, Drug monitoring, Cross-sectional studies

Introduction

The sale of counterfeit drugs remains a significant challenge in many parts of the world, particularly in developing countries [1]. Counterfeit medicines are defined as drugs that are deliberately misrepresented in terms of identity or source, including products that may contain incorrect or harmful ingredients. The World Health Organization (WHO) has highlighted counterfeit drugs as a global public health threat, contributing to adverse treatment outcomes, resistance to treatment, and the loss of consumer trust in the health system [2]. In countries like Nigeria, the prevalence of counterfeit drugs is alarmingly high, despite various regulatory efforts. Uyo Metropolis, a rapidly growing urban area in Akwa Ibom State, Nigeria, is no exception to this growing concern [3].

Nigeria has been identified as one of the countries most affected by the trade in counterfeit drugs due to weak regulatory enforcement, inadequate healthcare infrastructure, and a lack of public awareness [3]. Studies have shown that counterfeit medications are often sold through formal (pharmacies, licensed drugstores) and informal channels (street vendors, unregistered outlets), further complicating efforts to curb their distribution [4]. The sale of counterfeit drugs in Uyo Metropolis is particularly worrisome because of the presence of both urban and peri-urban populations, where the accessibility and affordability of legitimate drugs are major concerns.

In addition to the direct health risks posed by counterfeit drugs, the socio-economic impact of these illicit sales is profound. Counterfeit medicines contribute to the erosion of confidence in the healthcare system, exacerbate the burden on healthcare facilities, and lead to a loss in revenue for legitimate pharmaceutical businesses [6]. These challenges are often compounded by the lack of adequate training for pharmacists and sales personnel, who may unknowingly contribute to the sale of counterfeit drugs. Furthermore, counterfeit drug networks operate with sophisticated methods of deception, including the use of fake packaging, falsified certificates of authenticity, and illegal distribution practices [7].

The regulatory framework designed to combat counterfeit drug sales in Nigeria, including agencies such as the **National Agency for Food and Drug Administration and Control (NAFDAC),** has made significant strides in curbing the problem [8]. However, the widespread nature of counterfeit drug sales in many Nigerian cities suggests that enforcement remains insufficient. There is a pressing need to explore the extent of counterfeit drug sales in Uyo Metropolis specifically, to assess the current state of regulatory practices, and to determine the factors that contribute to the proliferation of counterfeit medicines in the area.

This study investigates the prevalence, characteristics, and sales patterns of counterfeit drugs in Uyo Metropolis. It will also evaluate the knowledge, attitudes, and practices of pharmacists and drug vendors regarding counterfeit drugs, and assess the effectiveness of existing measures to combat counterfeit drug sales [4]. Through this research, the study seeks to provide a clearer picture of the scope of the problem and offer evidence-based recommendations for improving regulatory efforts, public awareness, and consumer safety.

Methods

Research design

This study employed a cross-sectional survey design to investigate the prevalence and patterns of counterfeit drug sales in Uyo Metropolis. The cross-sectional design allows for the collection of data at a single point in time, providing a snapshot of counterfeit drug sales across a variety of pharmacyoutlets in the area.

Study area

The research was conducted in Uyo Metropolis, the capital of Akwa Ibom State in Nigeria. Uyo Metropolis has a growing population and a significant number of formal and informal drug outlets. The study targeted community pharmacies, general drugstores, and informal drug outlets across the metropolis.

Study population

The study targeted 200 drug outlets within Uyo Metropolis, which includes: pharmacies (both independent and chain pharmacies), general drugstores that sell over-the-counter medications, and unregistered or informal drug outlets (e.g., open markets, street vendors). In each of the 200 outlets, the survey targeted pharmacists, pharmacy technicians, and other sales personnel who handle the dispensation of medications and have a direct role in the procurement and sales of drugs.

The study specifically focused on the sale of prescription drugs, over-the-counter medications, and common medications (e.g., pain relievers, antimalarials, antibiotics, and antihypertensives) that are commonly counterfeited. A stratified random sampling technique was employed to select the 200 drug outlets. A random selection was then performed within each stratum to ensure that the sample was representative of all types of drug outlets in Uyo Metropolis.

Sampling of participants

For each selected drug outlet, a convenience sampling method was used to select one respondent—the pharmacist or the sales personnel in charge of drug distribution. The total number of respondents was 200 individuals.

Data collection methods

The research was billed for 6months from April to October 2025. The data collection process involved both structured questionnaires and sales record analysis. A set of two separate structured questionnaires were developed—one for pharmacists and sales personnel (QA), and the other for the analysis of drug sales data (QB).

This questionnaire QA assessed the knowledge, practices, andexperiences of the personnel regarding counterfeit drug detection and prevention. Key areas included knowledge of counterfeit drug characteristics, experience with counterfeit drugs in their outlets, detection methods used (visual inspection, packaging checks, etc.), awareness of regulations and anti-counterfeit measures, and training on counterfeit drug detection. Questionnaire QB focused on understanding the purchasing patterns of consumers and whether counterfeit drugs were being sold in the outlet. Data points included the frequency of counterfeit drugs encountered in sales, types of drugs most commonly suspected to be counterfeit, and methods by consumers to verify drug authenticity.

Finally,a sales record review was conducted to examine the sales patterns and identify suspicious transactions related to counterfeit drugs. Pharmacies and drug outlets were asked to provide anonymized sales data for the past 6 months, including: (a) drug names and brands flagged as counterfeit, (b) the quantity of suspected counterfeit drugs sold, (c) types of drugs most frequently involved in counterfeit transactions, and (d) frequency of consumer complaints about counterfeit drugs.

The researcher analyzed these records to identify trends in the sale of suspiciousor non-standard drugs, helping to triangulate the findings from the questionnaires.

Site visits and observations

A sample of 50 drug outlets was assessed to observe the physical presence of security measures likeholograms, QR codes**,** or tamper-evident packaging. These visits also allowed the observance and assessment ofinventory management practices and how counterfeit drugs might be identified or segregated in real time.

Data analysis

The data analyses were conducted as follows:

Quantitative Data Analysis

Data from the questionnaires and sales records were entered into statistical software SPSS (Version 20, IBM). The following analyses were performed.

Descriptive statistics (frequencies, percentages, and means) were calculated to determine the prevalence of counterfeit drugs, the types of counterfeit drugs encountered, and the sales patterns.Cross-tabulationidentifies relationships between pharmacy characteristics (e.g., size, type, trainings) and the occurrence of counterfeit drug sales.The chi-square test assesses the associations between variables such as the knowledge of pharmacists, sales outlet type, and the frequency of counterfeit drug encounters.

Qualitative data Analysis

Thematic analysis was conducted on the open-ended responses from the questionnaires and any observational data from site visits. Themes such as counterfeit drug characteristics,consumer behavior, detection methods, and regulatory knowledge were identified and analyzed.

Ethical considerations

All participants (pharmacists and sales personnel) were informed about the study's purpose and the voluntary nature of their participation. Written consent was obtained before data collection. The privacy and confidentiality of the respondents was maintained. Personal and outlet identifiers were removed or anonymized in the final dataset.

Ethical approval

The study obtained approval from the University ethical committee (the Institutional Review Board (IRB) of the University of Uyo) to ensure compliance with ethical standards in research involving human participants.

Data availability

Sales records from some outlets may not be available or complete, which could impact the reliability of sales data.

Results

Demographic profile of respondents

Of the 100 pharmacists surveyed, 60% were male, and 40% were female (Table 1). The majority (65%) of pharmacists were aged between 30-45 years, followed by 25% aged 46-60 years, and 10% under 30 years. A significant proportion of pharmacists (70%) had been practicing for more than 5 years, while 15% had between 2-5 years of experience, and 15% had less than 2 years. Most pharmacists (90%) bagged a Bachelor's degree in Pharmacy, while 10% had higher qualifications (MSc, PharmD or PhD.).

Similarly, of the 200 consumers surveyed, 55% were female, and 45% were male. The majority of consumers (50%) were aged 25-40 years, followed by 35% aged 41-60 years, and 15% under 25 years. Most consumers (60%) had at least a secondary school education, 30% had a tertiary education, and 10% had a primary school education or less. Most consumers (50%) were in the middle-income bracket, 30% were in the low-income group, and 20% were in the high-income group (Table 2).

Prevalence of counterfeit drugs in Uyo metropolis

Pharmacists' perspective

Pharmacists (75%) reported encountering counterfeit drugs in their pharmacies within the past year. However, only 45% stated they could identify counterfeit drugs with confidence without external assistance. The drugs most commonly reported as

counterfeit included antimalarials (30%), antibiotics (25%), pain relievers (20%), and antihypertensives (15%). Vitamins and cough syrups were also mentioned, but to a lesser extent (10%).

Pharmacists (60%) indicated they used visual inspection (e.g., checking holograms, and packaging) to detect counterfeit drugs, while 25% used rapid diagnostic tests (RDTs) or spectrometric devices. Only 15% indicated they had access to a pharmaceutical-grade counterfeit detection technology (e.g., scanners or databases for drug verification) (Figure 1).

Consumers (68%) reported being aware of counterfeit drugs, but only 40% knew how to identify counterfeit drugs during purchase. Common methods by consumers to verify authenticity included checking for visible security features like holograms (50%) and asking pharmacists for verification (30%) (Figure 2).

Approximately 20% of consumers reported having unknowingly purchased counterfeit drugs. The most frequently counterfeited medications identified by consumers included antimalarials, antibiotics, and painkillers. Of these, 50% of consumers who reported purchasing counterfeit drugs experienced ineffectiveness or adverse side effects, while 20% experienced health complications related to toxic ingredients. The sourcing of medications by consumers is detailed in Figure 3.

Pharmacists' knowledge and practices on counterfeit drug detection revealed that only 30% of pharmacists reported they received formal training or professional development on detecting counterfeit drugs while 70% stated they learned through self-study or informal training within their pharmacy networks.

Most pharmacists (80%) reported they follow measures to secure the supply chain by purchasing drugs only from authorized distributors. However, 15% admitted purchasing drugs from unverified sources due to cost concerns, and 5% indicated they were unsure about their sources.

Regarding regulatory compliance, 85% of pharmacists were aware of national regulations relating to counterfeit drugs, but only 60% complied consistently with drug verification procedures (e.g., cross-checking batches against regulatory databases). 40% admitted they did not always check for counterfeit drugs due to time constraints or lack of resources.

The frequency of counterfeit drug sales showed that sales records had 12% of all drug sales in the last 6 months flagged as potentially counterfeit. This was based on visual identification, customer complaints, or testing results from local laboratory tests.

The top counterfeit drugs identified included antimalarial drugs (35%), antibiotics (28%), analgesics (18%), and other medications (19%). Pharmacists encounter with counterfeit medicines is summarized in Figure 4.

Pharmacies reported financial losses from counterfeit drugs, with an estimated 8% reduction in overall sales revenue due to returns and unsold stock of potentially counterfeit drugs.

Consumer behaviour towards counterfeit drugs revealed that 45% of consumers indicated that they prioritize price over brand when purchasing medications, and only 35% consistently purchased medications from trusted or well-known pharmacies, while 20% frequented discounted or unbranded drugstores for cost-saving reasons.

Regarding willingness to pay for verification, 60% of consumers expressed willingness to pay a small premium for medications with guaranteed authenticity, such as those with QR codes, holograms, or other anti-counterfeiting measures. However, 40% indicated that price was more important than security features, particularly in lower-income groups.

The observational findings regarding security features revealed that 55% of pharmacies have visible security measures such as holograms, tamper-evident seals, or QR codes on high-risk medications. However, only 30% had advanced counterfeit detection tools like scanners, and fewer than 10% used mobile verification platforms for real-time checking.

In 5% of pharmacies, tampered packaging was identified in a random inspection, suggesting a need for greater vigilance in securing drug stocks.

Table 1: Demographics of Pharmacists respondents in the study

Characteristics	Frequency
Gender	
Male	60
Female	40
Age of respondents (years)	
Under 30	10
30 – 45	53
46-60	25
61 and above	12
Education level	
Bachelor of Pharmacy	63
Masters or PostgraduateDiploma	25
Doctor of Philosophy	12
Years of practice	
Less than 5	55
Greater than 5 but less than 10	15
Greater than 10	30

Table 2: Demographics of consumers' respondents in the study

Characteristics	Frequency	Percentage
Gender		
Male	90	45
Female	110	55
Age of respondents (years)		
Under 25	30	15
25 – 40	80	40
41-60	70	35
61 and above	20	10
Education level		
No formal education	36	18
Primary school	20	10
Secondary school	84	42
Tertiary	60	30

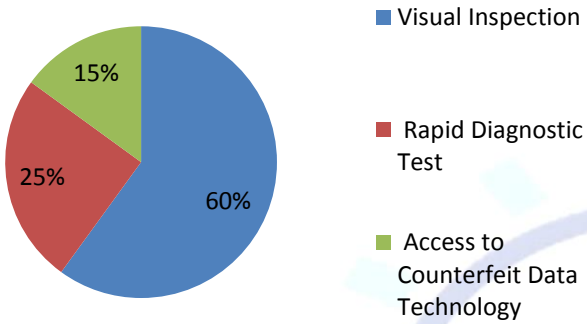

Figure 1: Protocols of Pharmacists respondents for detecting counterfeit drugs

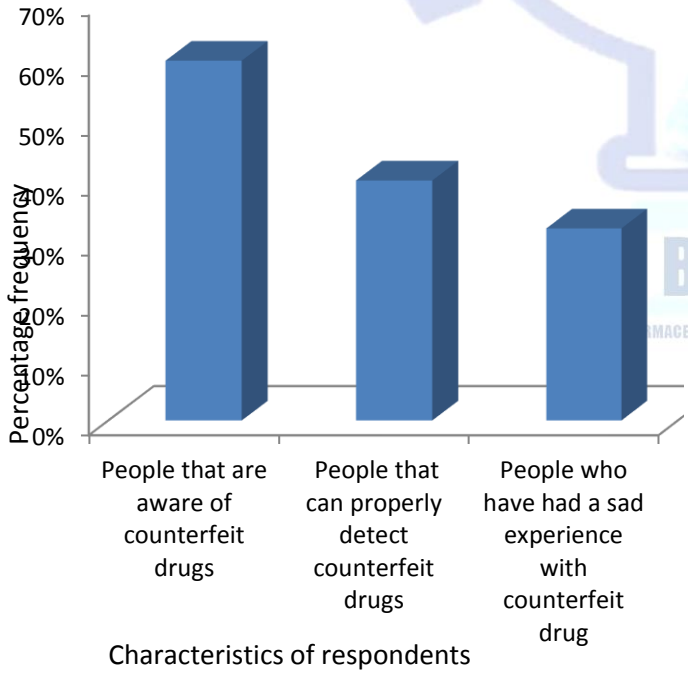

Figure 2: Consumers and their disposition to counterfeit drugs

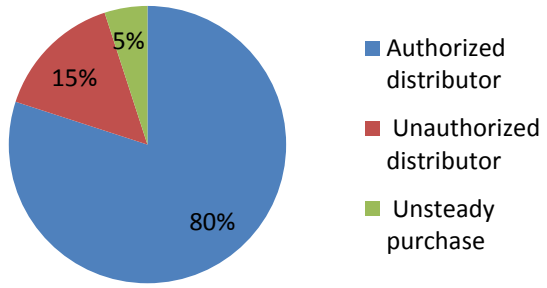

Figure 3: Consumers sourcing of medications

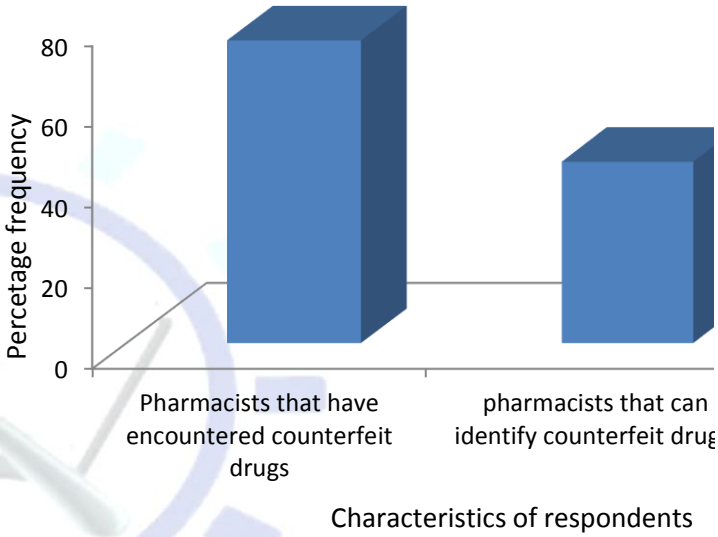

Figure 4: Pharmacists' encounter and self-assessed confidence in spotting out counterfeit drugs

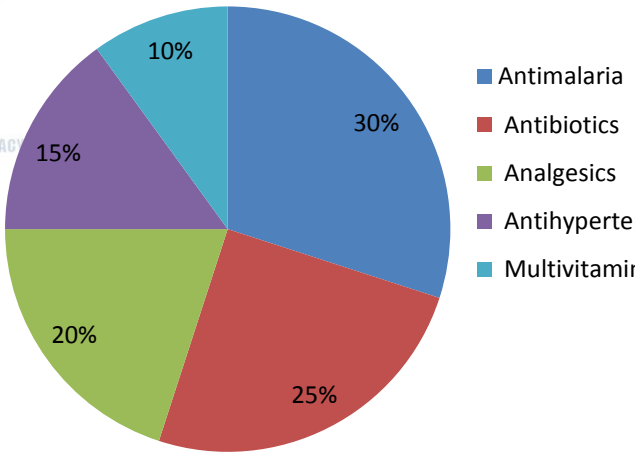

Figure 5: Pharmacists perceived distribution of spotted counterfeit medications

Discussion

The issue of counterfeit drugs is a critical concern for both public health and economic stability in developing countries like Nigeria. This study aimed to investigate the prevalence and patterns of counterfeit drug sales in Uyo Metropolis, with a focus on the knowledge, attitudes, and practices of pharmacists and sales personnel, as well as the regulatory environment. The findings revealed alarming trends in the sale of counterfeit drugs, which have serious implications for patient safety, healthcare quality, and economic stability [9].. 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.

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 JIA handled data analysis and interpretation, and Author AEA 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

The sales pattern of analgesics for pain management in community pharmacies within Uyo metropolis

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ABSTRACT

Analgesics are among the most commonly used medications worldwide, often obtained from community pharmacies without prescriptions. Understanding usage patterns is essential to promote rational use and prevent misuse. This study aimed to examine the patterns of analgesic use among consumers and pharmacists in community pharmacies, focusing on types of analgesics purchased, consumer preferences, influencing factors, and pharmacists' roles in guiding use. A cross-sectional survey was conducted across selected community pharmacies. Data were obtained from 200 pharmacists and 500 consumers using structured questionnaires. Variables collected included demographic characteristics, types of analgesics sold or used, frequency of use, and factors influencing purchase decisions. The majority of consumers (65%) were aged 20–40 years, with females slightly predominating (54%). Paracetamol was the most commonly used analgesic (43%), followed by ibuprofen (15%) and diclofenac (12%). OTC analgesics accounted for 75% of sales, with 65% of consumers practicing self-medication. Cost, accessibility, advertising, and brand reputation were key drivers of consumer choice. Pharmacists reported a high level of engagement in counseling, with 85% routinely advising customers on appropriate analgesic use. Seasonal trends indicated increased purchases during the rainy season, and age-based differences in analgesic preference were observed. Analgesic use in community pharmacies is widespread, primarily driven by self-medication and influenced by socioeconomic and promotional factors. Paracetamol remains the preferred choice due to its affordability and availability. Strengthening pharmacist-led education and implementing stricter regulatory controls could improve analgesic use and minimize associated health risks.

Keywords: Analgesics, Pain management, Pharmacies, Community pharmacy services, Over-the-counter OTC, patient education

Introduction

Pain management is a critical aspect of healthcare, with analgesics playing a central role in alleviating discomfort associated with various medical conditions. Community pharmacies serve as accessible points for the procurement of these medications [1], making it essential to understand sales patterns and consumer behaviors related to analgesic use. This study focuses on Uyo Metropolis, Nigeria, aiming to elucidate the trends in analgesic sales and the factors influencing consumer choices between 2020 and 2024.

Pain is one of the most common reasons people seek medical attention, leading to a significant demand for analgesics in various healthcare settings. Pain management is a vital component of clinical care, and the accessibility of analgesics plays a crucial role in how effectively pain is managed in the community [2]. Community pharmacies, which are often the first point of contact for patients seeking relief, serve as an essential source of medications for managing acute and chronic pain. The sales patterns of analgesics in these pharmacies provide valuable insights into both public health trends and the effectiveness of pain management practices in the local community [3].

In Uyo Metropolis, the capital of Akwa Ibom State in Nigeria, the sale and use of analgesics is influenced by a range of factors, including socio-economic conditions, patient preferences, and the regulatory environment surrounding pharmaceutical distribution. Understanding the sales patterns of analgesics in Uyo's community pharmacies is crucial for identifying gaps in pain management, ensuring the appropriate use of analgesic drugs, and optimizing pharmaceutical services [4]. This study seeks to investigate the sales pattern of analgesics in community pharmacies within Uyo Metropolis, exploring the types of analgesics sold, factors influencing sales trends, and the implications of these patterns for pain management in the region.

Pain is generally categorized into two types: acute and chronic. Acute pain is typically the result of injury or surgery and is often transient, while chronic pain persists over time and can significantly impact the quality of life [5]. The management of pain is essential not only for improving the comfort of individuals but also for facilitating recovery and promoting overall well-being. In clinical practice, analgesics are used to relieve pain, with common categories including non-steroidal anti-inflammatory drugs (NSAIDs), opioids, acetaminophen (paracetamol), and adjuvant analgesics such as antidepressants and anticonvulsants [6].

In the context of Uyo Metropolis, analgesics are widely available in community pharmacies. However, the type of analgesics dispensed and the frequency of sales can vary based on a range of factors, including patient demographics, socio-economic conditions, healthcare access, and public awareness of pain management

in pharmacy practice, while 10% had between 2-5 years, and 12% had less than 2 years of practice.

In the study, 50% of pharmacies were classified as independent, 30% were part of chain pharmacies, and 20% were located in pharmacy shops attached to hospitals or clinics.

Of the 500 consumers surveyed, 58% were female and 42% were male. The study revealed 40% of consumers between 25-35 years, 30% being 36-45 years, 20% within 46-60 years, and 10% were above 60 years.

70% of consumers had at least a secondary school education, 20% had a tertiary education, and 10% had a primary school education or less. Many (45%) of consumers were in the middle-income group, 30% were in high-income groups, and 25% were in low-income brackets.

Analgesic sales trends

Analysis of sales data revealed that OTC analgesics accounted for approximately 75% of total analgesic sales. Paracetamol emerged as the most purchased analgesic, followed by ibuprofen and diclofenac. There was a notable increase in the sales of natural and herbal analgesics, reflecting a growing consumer preference for alternative pain management options (Figure.

Factors influencing consumer choices

The study identified several factors influencing consumer choices:

Pharmacies that engaged in advertising experienced increased consumer patronage. Consumers reported that advertisements enhanced their perception of product quality and influenced their choice of purchase location. The study corroborates findings from previous research indicating that advertising positively influences consumer behavior in the pharmaceutical sector. Pharmacies that invested in advertising reported higher sales volumes and enhanced customer loyalty. Consumers preferred pharmacies that were easily accessible and offered extended operating hours. Cost considerations significantly impacted consumer choices, with a preference for affordable generic options.

Types of pain relievers sold

Paracetamol (43%) was the most commonly sold pain reliever, followed by ibuprofen (15%) and diclofenac (12%). Opioid-based pain relievers (e.g., tramadol) were sold in smaller quantities, accounting for approximately 7% of the total pain reliever sales. Topical analgesics (creams, gels) made up around 5% of sales (Figure 1).

Frequency and pattern of sales

On average, participating pharmacies reported selling between 200 to 500 packs of pain relievers per month, with higher sales volumes for paracetamol and ibuprofen were recorded. Sales of pain relievers showed some seasonal variation. The highest sales occurred during the rainy season (increased incidence of common colds and musculoskeletal pain), and the lowest sales during the dry season (fewer health-related complaints).

The group (18-35 years) accounted for 40% of total pain reliever sales, with paracetamol was the most commonly purchased product. Middle-aged adults (36-60 years)accounted for 35% of sales, purchasing a wider range of pain relievers, with a preference for ibuprofen and diclofenac for musculoskeletal pain.

The elderly (i.e., 60+ years) consumers made up about 25% of sales, mostly purchasing paracetamol and topical analgesics for chronic pain and arthritis. Consumers (50%) reported relying on pharmacists for advice on pain management. Physicians were the second most common source (30%), while 20% of consumers relied on internet-based resources or family and friends for guidance. Consumers (65%) indicated that they self-medicate for mild to moderate pain without a prescription. Paracetamol was the most commonly used medication for self-medication (70%), followed by ibuprofen (20%) and diclofenac (10%).

Furthermore, consumers (35%) indicated that they consulted a healthcare professional (pharmacist or doctor) before using a pain reliever, especially for chronic pain or more severe conditions. Consumers (60%) cited cost as a primary factor influencing their choice of pain reliever, with paracetamol being the most affordable option. Furthermore, 25% of consumers chose pain relievers based on brand reputation, while 15% prioritized product packaging (e.g., holograms, seals for authenticity).

Consumers (50%) reported using pain relievers on anoccasional basis(e.g., for headaches, menstrual pain, or occasional musculoskeletal pain). Consumers (20%) used pain relievers frequently (e.g., for chronic conditions like arthritis or migraines), with a preference for ibuprofen ordiclofenac. Lastly, 10% of consumers with chronic pain conditions reported usingopioid-based pain relievers(e.g.,tramadol), although these were less commonly dispensed in pharmacies.

Pharmacists (85%) indicated that they routinely provide counseling on the appropriate use of pain relievers, emphasizing the correct dosage and potential side effects.

Self-Medication Guidance: 90% of pharmacists reported advising consumers against long-term self-medication without professional supervision, particularly for pain relievers like diclofenacandibuprofen due to their potential side effects.

The majority (80%) of pain relievers sold wereover-the-counter (OTC)products. Only 20% of sales involvedprescription-only medications, mainlyopioidsorstronger analgesicsfor more severe or chronic pain. Pharmacists frequently referred consumers todoctorsfor stronger medications or cases of persistent pain (50% of cases), especially formusculoskeletal pain, joint pain, andheadaches.

Most pharmacies (90%) reported having aregular stockof commonly used pain relievers likeparacetamolandibuprofen. Fewer pharmacies (60%) stockeddiclofenacoropioid-based medicationsdue toregulatory restrictionsandstorage requirements. Pharmacists (70%) reported thatgeneric brandsof pain relievers were sold at a higher volume thanbrand-name drugsdue to cost concerns.

Consumer satisfaction

Consumers (75%) reported being satisfied with the pain relievers they purchased, particularly paracetamol for mild pain and ibuprofen for moderate pain. However, 20% of consumers were dissatisfied with pain relief for chronic or severe pain and reported inconsistent results with their current pain relievers, prompting some to seek stronger alternatives.

A number of consumers (15%) reported experiencing side effects from pain relievers, including stomach upset (ibuprofen), and drowsiness (opioids). [7]. Additionally, the regulatory environment surrounding the sale of analgesics—particularly those with potential for misuse, such as opioids—can significantly influence sales trends.

Community pharmacies are an integral part of the healthcare system, particularly in resource-limited settings where access to hospitals and clinics may be constrained. In Nigeria, community pharmacies are one of the most accessible sources of medication, and they provide an essential service for the management of common ailments, including pain [8]. Pharmacists in these settings are not only dispensers of medications but also play a critical role in counseling patients on the appropriate use of analgesics, potential side effects, and alternative pain management options.

The role of community pharmacies in pain management is particularly significant given the increasing burden of chronic pain conditions such as arthritis, back pain, and neuropathic pain. In urban centers like Uyo, where population density is high and healthcare infrastructure is developing, pharmacies often serve as the primary source of analgesics for both acute and chronic pain conditions [9].

The sales pattern of analgesics in community pharmacies is influenced by multiple factors. Patient-related factors such as age, gender, income level, and health literacy can affect the demand for analgesics [10]. For instance, elderly patients, who are more likely to experience chronic pain, may have a higher demand for certain analgesics, such as NSAIDs and opioids [11]. Similarly, socio-economic factors such as income levels, access to healthcare, and the affordability of medications also play a role in shaping sales patterns [12]

The availability and cost of analgesics can also be influenced by supply chain dynamics and government regulations. For example, restrictions on the sale of opioids due to concerns about misuse and addiction can result in fluctuations in the types of analgesics that are sold in pharmacies [9]. The presence or absence of over-the-counter analgesics and the reliance on prescription-only drugs also affect sales patterns. Additionally, local healthcare policies, including the promotion of generic medications, may encourage the sale of certain types of analgesics over others [13].

Uyo Metropolis, the capital city of Akwa Ibom State, is located in southeastern Nigeria. The city has witnessed rapid urbanization and population growth in recent years, leading to increased demand for healthcare services, including pain management [14]. With a population that is diverse in age, socio-economic status, and health needs, Uyo presents a unique setting for studying the sales patterns of analgesics in community pharmacies.

The healthcare infrastructure in Uyo is gradually improving, with both public and private healthcare facilities providing a range of services. However, like many other parts of Nigeria, there are challenges related to access, affordability, and quality of care. These challenges make community pharmacies a critical component of the healthcare delivery system. Understanding the sales trends of analgesics in Uyo's community pharmacies can provide valuable insights into the local demand for pain management and help identify areas where improvements in healthcare access and education are needed [15].

The rationale for this research stems from the need to understand how analgesics are dispensed in community pharmacies and the broader implications for pain management in the local community. By analyzing sales trends, the study can offer recommendations for improving the availability and appropriate use of analgesics, e 7nsuring that patients receive effective and safe pain management.

Pharmacists (85%) indicated that they routinely provide counseling on the appropriate use of pain relievers, emphasizing the correct dosage and potential side effects.

Self-Medication Guidance: 90% of pharmacists reported advising consumers against long-term self-medication without professional supervision, particularly for pain relievers like diclofenac and ibuprofen due to their potential side effects.

Methods

Research design

A cross-sectional survey design was employed, targeting community pharmacies and consumers within Uyo Metropolis. Data collection involved structured questionnaires administered to pharmacists and consumers, alongside the analysis of sales records from participating pharmacies.

Study population

The study targeted pharmacists working in community pharmacies within Uyo Metropolis. These pharmacists were selected as they directly interact with consumers, have access to medications, and are responsible for ensuring the authenticity of drugs dispensed to patients. The second target group was consumers who purchase medications from community pharmacies in the metropolis. This group included individuals from different age groups, gender, and socio-economic backgrounds, ensuring a diverse representation of the general public.

Sampling method

A stratified random sampling technique was used to select community pharmacies within Uyo Metropolis. Pharmacies were categorized based on their location (urban, suburban) and size (small, medium, large). From each category, a random selection of pharmacies was made to participate in the study. Consumers were selected using convenience sampling at the time of their visit to participating pharmacies.

Inclusion criteria

For consumers, individuals who had recently purchased over-the-counter or prescription medications in the study site were eligible to participate in the study.

Data collection

The data collection process involved structured questionnaires, sales records analysis, and observational data. Two sets of structured questionnaires were developed and administered to pharmacists and consumers, respectively. The pharmacists' questionnaire (PQ) included sections on their knowledge of counterfeit drugs, practices for detecting counterfeit medications, awareness of regulatory measures, and training on counterfeit detection. It also included questions on the extent to which counterfeit

The majority (80%) of pain relievers sold were over-the-counter (OTC) products. Only 20% of sales involved prescription-only medications, mainly opioids or stronger analgesics for more severe or chronic pain. Pharmacists frequently referred consumers to doctors for stronger medications or cases of persistent pain (50% of cases), especially for musculoskeletal pain, joint pain, and headaches. *Most pharmacies (90%) reported having a regular stock of commonly used pain relievers like paracetamol and ibuprofen. Fewer pharmacies (60%) stocked diclofenac or opioid-based medications due to regulatory restrictions and storage requirements. Pharmacists (70%) reported that generic brands of pain relievers were sold at a higher volume than brand-name drugs due to cost concerns.*

Consumer satisfaction

Consumers (75%) reported being satisfied with the pain relievers they purchased, particularly paracetamol for mild pain and ibuprofen for moderate pain. However, 20% of consumers were dissatisfied with pain relief for chronic or severe pain and reported inconsistent results with their current pain relievers, prompting some to seek stronger alternatives.

A number of consumers (15%) reported experiencing side effects from pain relievers, including stomach upset (ibuprofen), and drowsiness (opioids).

Table 1: Demographics of respondents (pharmacists) in the study

Characteristics	Number	Percentage Occurrence
Gender		
Male	86	43
Female	114	57
Age		
<30	36	18
30-45	78	39
46-60	50	25
>60		
Years of experience		
<2 years	24	12
2-5 years	20	10
>5 years	156	78

Table 2: Demographics of respondents (Clients) in the study

Characteristics	Number	Percentage Occurrence
Gender		
Male	210	42
Female	290	58
Age		
25-35	190	38
36-45	150	30
46-60	110	22
>60	50	10
Education		
Primary	20	10
Secondary	140	70
Tertiary	40	20
Income level		
Low	125	25
Middle	225	45
High	150	30

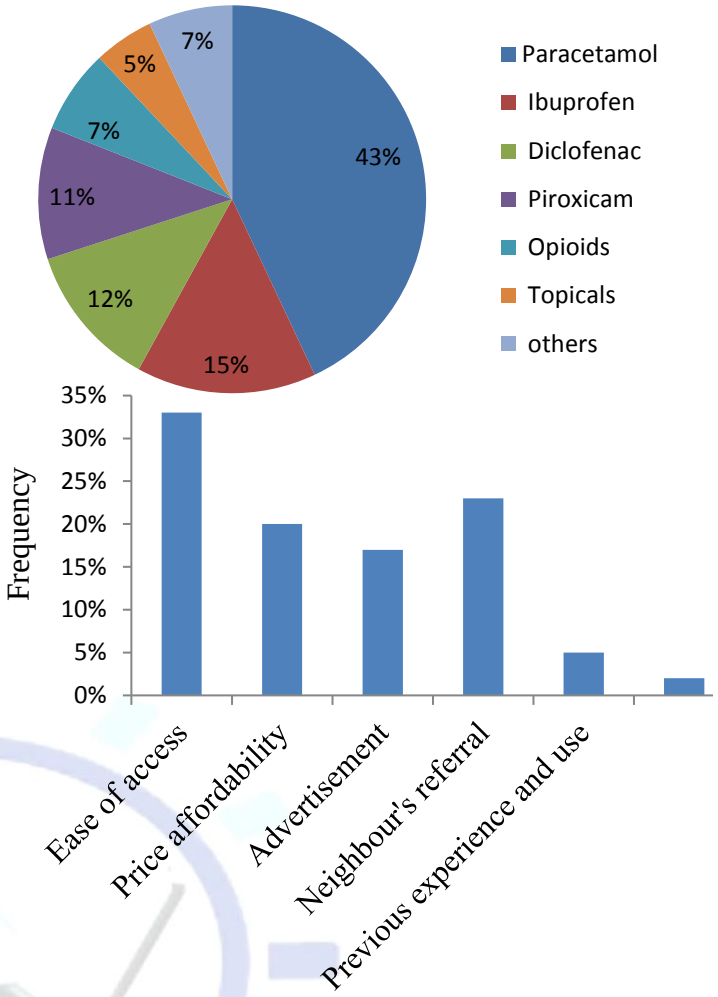

Figure 2: Reasons for use of analgesics by respondents (consumers)

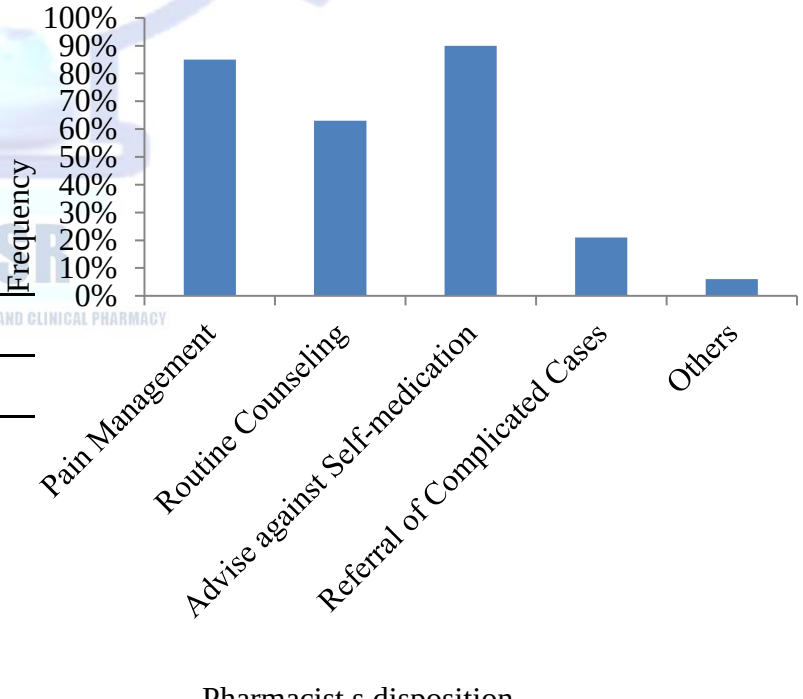

Figure 3: Disposition to use/recommending of analgesics by pharmacist respondents

Discussion

The study provides valuable insights into the pattern of analgesic use in community pharmacy settings, revealing significant trends in consumer behavior, pharmacy operations, and pharmacist involvement. The findings shed light on demographic distributions, sales patterns, and factors influencing consumer choices, with important implications for public health policy, pharmacy practice, and patient education.

A total of 500 consumers participated in the study, with the majority (65%) aged between 20 and 40 years, and a slight female predominance (54%) (Table 1). This is reflective of a demographic that is generally more health-conscious, active, and likely to engage in self-care practices such as self-medication. It also aligns with global patterns where women are more likely than men to seek healthcare services and purchase over-the-counter (OTC) medications, including analgesics [16].

Among pharmacists, 43% were male and 57% female, with most (78%) having over five years of experience. This indicates a relatively experienced workforce, which is encouraging from a patient safety perspective, especially given the risks associated with improper analgesic use. The age distribution of pharmacists, with a significant portion (39%) aged between 30 and 45, suggests a mature professional cohort that may influence responsible dispensing practices and patient counseling [17].

The data indicate that 50% of the surveyed pharmacies were independent, while 30% belonged to pharmacy chains, and 20% were located in or near hospitals. This distribution suggests that independent pharmacies play a dominant role in community healthcare delivery. It also reflects the potential for variation in business models, marketing strategies, and customer engagement approaches, which may influence analgesic sales patterns [18].

Ease of access and extended operating hours were reported as key factors affecting consumer choice, emphasizing the need for pharmacies to consider convenience as part of their service delivery. With many consumers valuing availability and proximity, pharmacies that optimize these aspects may enjoy increased patronage.

The study revealed that OTC analgesics accounted for 75% of total analgesic sales, with paracetamol being the most commonly purchased (43%), followed by ibuprofen (15%) and diclofenac (12%). The dominance of paracetamol is unsurprising, given its wide availability, affordability, and perceived safety profile. These findings echo global trends and reflect paracetamol's status as a first-line treatment for mild to moderate pain [19].

Opioid-based pain relievers (e.g., tramadol) accounted for a small portion (7%) of total analgesic sales, likely due to regulatory restrictions and concerns around abuse and dependence. Topical analgesics also constituted a modest proportion of sales (5%), often favored by older adults with localized pain conditions [20].

Sales data revealed a seasonal pattern, with higher sales volumes during the rainy season, possibly due to increased prevalence of colds, flu, and musculoskeletal complaints. Such variations suggest that environmental factors may influence consumer demand and should be taken into account in inventory planning and public health messaging [21].

Age-based consumption trends showed that the 18–35 age group accounted for 40% of total pain reliever sales, favoring paracetamol for conditions like headaches, menstrual pain, and general discomfort. Middle-aged consumers (36–60 years) showed more diverse preferences, often choosing ibuprofen and diclofenac for musculoskeletal and inflammatory pain [22]. The elderly (60+ years) accounted for 25% of sales, with a higher reliance on paracetamol and topical analgesics, likely due to chronic conditions like arthritis and concerns about adverse effects associated with NSAIDs.

Several factors influenced analgesic selection. Cost emerged as a major determinant, with paracetamol preferred for its affordability. This underscores the socioeconomic considerations that affect healthcare decisions in low- and middle-income populations. About 45% of consumers were from middle-income groups, with 25% in low-income categories, further reinforcing the importance of cost-effective treatment options [23].

Advertising also played a substantial role, with consumers reporting that it enhanced their perceptions of product quality and influenced their choice of pharmacy. Pharmacies that invested in promotional strategies reportedly experienced higher patronage and sales volumes. This finding supports prior research on the role of advertising in shaping pharmaceutical consumer behavior and suggests that strategic marketing may be beneficial for community pharmacies.

Additional factors included brand reputation (25%) and product packaging/authenticity features (15%), indicating that perceived quality and safety features are crucial in consumer decision-making [24].

The study found that 65% of consumers practiced self-medication for mild to moderate pain, with paracetamol (70%) being the most used, followed by ibuprofen (20%) and diclofenac (10%). This reflects both the accessibility of these medications and the common belief that they are safe for unsupervised use. However, long-term or inappropriate use of NSAIDs can lead to serious adverse effects, including gastrointestinal complications, kidney damage, and

cardiovascular events [25].

Only 35% of consumers sought professional advice before using pain relievers, mainly for chronic or severe pain. Pharmacists were the most consulted healthcare providers (50%), ahead of physicians (30%) and informal sources like the internet or friends (20%). This highlights the critical role of pharmacists in public health education and the need for continued efforts to ensure responsible medication use.

Encouragingly, 85% of pharmacists reported providing counseling on appropriate analgesic use, and 90% cautioned against long-term self-medication, particularly with NSAIDs like ibuprofen and diclofenac. This reflects a strong commitment to promoting safe medication practices and reducing the risk of adverse drug events. However, the gap between consumer practices and pharmacist advice indicates a need for enhanced communication strategies, public awareness campaigns, and possibly regulatory measures to promote appropriate analgesic use [26].

The findings underscore the importance of community pharmacists in managing pain and guiding medication use. Given the high prevalence of self-medication and reliance on OTC analgesics, regulatory bodies should consider policies that support pharmacist-led interventions, including medication therapy management and public education initiatives.

Additionally, efforts should be made to standardize the labeling, pricing, and promotion of OTC analgesics to reduce misinformation and prevent misuse [27]. The increasing trend toward herbal alternatives also warrants regulatory attention to ensure product safety and efficacy.

Conclusion

This study highlights significant patterns in analgesic use across community pharmacies, influenced by demographic, economic, and behavioral factors. Paracetamol remains the most widely used analgesic, while self-medication is prevalent, particularly among younger adults. Pharmacists play a vital role in guiding safe use, yet more robust public education and regulatory oversight are needed to optimize pain management practices and safeguard public health.

Ethical Consideration

Data availability

All authors contributed to the conception and design of the study. [Insert Author Name(s)] collected and analyzed the data. [Insert Author Name(s)] drafted the manuscript. All authors critically reviewed the content and approved the final version for submission.

Conflict of interest

The authors declare that they have no conflicts of interest relevant to the content of this article.

Compliance with ethical guidelines

This study was conducted in accordance with the ethical standards set forth in the Declaration of Helsinki and the guidelines of the University of Uyo Institutional Review Board. Ethical approval for this research was obtained from the institution, and informed consent was obtained from all participants involved in the study.

Authors' contributions

SOA conceptualized the study, designed the methodology, and was responsible for data analysis and interpretation. RYI and PJE assisted with data collection, performed statistical analysis, and contributed to the manuscript draft. SOA reviewed the manuscript and provided critical revisions. All authors read and approved the final manuscript.

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GUIDE TO AUTHORS

Standardization of drug therapy problems (DTPs) interventions in pharmaceutical care: a pathway for enhancing patient outcomes

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ABSTRACT

Pharmaceutical care in Nigeria's hospital and community settings has become a vital component of healthcare delivery. However, the absence of standardized protocols has led to inconsistent practices across institutions and regions. This review examines pharmacists' knowledge, attitudes, practices, and behaviors in delivering pharmaceutical care, with a focus on intra- and inter-professional collaboration. It also explores how lifestyle factors influence pharmacokinetics, pharmacodynamics, and biopharmaceutics, affecting therapeutic outcomes.A literature search covering publications from 2000 to 2025 was conducted using databases such as Google Scholar, PubMed, Web of Science, Embase, and Scopus. Keywords included "pharmaceutical care," "healthcare collaboration," "standardized protocols," "drug therapy problems," and "variability in practice."Findings suggest that pharmaceutical care practices in Nigeria are often shaped by informal norms, training differences, and individual experiences, rather than structured guidelines. This results in variability in care quality and teamwork efficiency. Inter-professional relationships, particularly communication and collaboration between pharmacists and other healthcare professionals, play a critical role in care outcomes.Although pharmacists are generally committed to patient welfare, factors such as limited continuing education, resource constraints, and systemic challenges undermine optimal care delivery.The review advocates for the development and implementation of standardized, evidence-based pharmaceutical care protocols. It emphasizes the need for enhanced professional training, improved communication, and stronger interdisciplinary collaboration to ensure consistent, high-quality care across the healthcare system in Nigeria.

Keywords: Pharmaceutical care, Healthcare collaboration, Standardized protocols, Inter-professional relationships, Nigeria healthcare system

Introduction

Drug therapy problems (DTPs) are a critical focus in pharmaceutical care and represent a significant area of pharmacist intervention aimed at improving the therapeutic outcomes for patients and reducing the harm associated with medications [1]. DTPs arise when there are issues related to the appropriateness, effectiveness, safety, or adherence to prescribed drug regimens. Addressing these problems can significantly enhance patient safety, treatment effectiveness, and healthcare quality [2]. Pharmacists play a crucial role in identifying, assessing, and resolving DTPs through direct interaction with patients and other healthcare providers. This paper discusses the importance of DTP identification and resolution, the varying approaches for addressing DTPs in different healthcare settings, and the need for standardization in the delivery of pharmaceutical care to ensure consistent, high-quality patient care [3].

Methods

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 pharmacists' knowledge, attitudes, behaviors, and practices, with a specific focus on the impact of standardized protocols, interprofessional collaboration, and lifestyle-related pharmacological factors on therapeutic outcomes.

Literature search strategy

A comprehensive literature search was conducted across five electronic databases: Google Scholar, PubMed, Web of Science, Embase, and Scopus. The search covered a 25-year period from January 2000 to February 2025. Relevant publications were identified using combinations of keywords and Boolean operators, including:"pharmaceutical care", "healthcare collaboration", "standardized protocols", "drug therapy problems", "variability in practice", "pharmacists in Nigeria", "pharmacokinetics and lifestyle", and "inter-professional collaboration"

Inclusion and Exclusion Criteria

To ensure relevance and quality, articles were selected based on the following criteria: studies conducted in Nigeria or involving Nigerian healthcare professionals, research articles, reviews, policy papers, and reports addressing pharmaceutical care practices, healthcare collaboration, or patient-centered care and publications written in English.

Articles were excluded if they focused solely on clinical trials of specific medications without reference to pharmaceutical care models; not peer-reviewed or lacked sufficient methodological detail; and if duplicated publications or abstracts without full texts.

Data Extraction and Analysis

Data were extracted using a structured template

unnecessary drug, and other systematic and standardized protocols [24].

The resolution or intervention similarly requires a format of protocol that are consistent and homogenous. In most cases, the resolution outcomes of the DTP will also need a predefined and standardized approach. The outcome of the intervention (accepted as observed, requires a change, maintained and dispersed as previously written) is expected to pass through a regimented protocol, for finality [25].

The process of reporting of the observed intervention before treating the patient is somewhat of a controversial issue. It is assumed that the prescriber must give his consent to the superiority of the argument presented in the intervention. It appears sometimes that no matter how superior and valid the point in the intervention stands, the patient is assertively the prescriber's patient. In a standardized practice in all settings, the protocol for the clarification and resolution must be established and standardized [26].

The role of standardization in pharmaceutical care

The verb "standardized" refers to the process of making products, services, or rules conform to a particular model or set of guidelines. In the context of pharmaceutical care, standardization involves the development and implementation of consistent protocols, practices, and technologies to ensure that all patients receive high-quality, evidence-based care (American Society of Health-System Pharmacists, 1999).

Standardization in pharmaceutical care can take many forms, from uniform medication therapy management protocols to standardized drug formularies. The primary goal of standardization is to reduce variation in the delivery of care, ensuring that all patients receive the same level of quality regardless of the healthcare setting. This approach not only promotes consistency but also improves patient safety by minimizing the risk of medication errors and DTPs [27].

Standardization is important in the context of DTP resolution. By adopting standardized protocols for assessing and managing DTPs, healthcare organizations can ensure that pharmacists approach patient care in a systematic, evidence-based manner. For example, use of standardized medication review templates can help pharmacists identify common DTPs, such as drug-drug interactions or dosing errors, and take appropriate action to address them. Similarly, standardized training programs for pharmacists can ensure that all professionals are equipped with the knowledge and skills needed to manage complex drug therapy issues [28].

The benefits and challenges of standardizing pharmaceutical care

There are numerous benefits to standardizing pharmaceutical care, particularly in addressing DTPs. One of the key advantages is that standardization helps reduce ambiguity and guesswork in clinical decision-making. When pharmacists follow well-established protocols, the likelihood of errors decreases, and the consistency of care improves. This can lead to better therapeutic outcomes for patients and greater satisfaction with the healthcare system.

Moreover, standardized practices help streamline workflows, increase productivity, and improve resource allocation [29]. In a busy hospital or community pharmacy, standardized processes allow pharmacists to focus on delivering care rather than passing time for determining the best course of action for each patient. This not only saves time but also ensures that pharmacists' expertise is applied consistently across all patients.

However, the process of standardization is not without its challenges. One of the primary obstacles is the variation in healthcare settings, where differences in resources, patient populations, and local regulations may make it difficult to implement a universal standard. For instance, what works in a large, well-funded hospital may not be feasible in a rural community pharmacy with limited resources. Additionally, resistance to change among healthcare professionals can be a significant barrier to successful implementation of standardized practices [30].

Despite these challenges, the movement toward standardization in pharmaceutical care is gaining momentum globally. Standardized care frameworks have been shown to improve patient outcomes in various settings, and the adoption of such frameworks by pharmacy organizations is crucial to ensuring that patients receive safe, effective, and high-quality care.

The identification and resolution of drug therapy problems (DTPs) are essential components of pharmaceutical care that can significantly improve patient outcomes and reduce the harm associated with medications. Pharmacists play a central role in this process by reviewing prescriptions, assessing patients' drug regimens, and intervening to resolve any identified issues. However, the variability in the delivery of pharmaceutical care across different healthcare settings underscores the need for standardization in the approach to DTP management.

Standardization offers a promising solution to ensuring consistency and quality in pharmaceutical care. By developing and implementing standardized protocols, healthcare organizations can reduce the risk of DTPs, enhance patient safety, and improve overall healthcare outcomes. While there are challenges to implementing standardized practices, the benefits of a unified approach to pharmaceutical care are clear. Standardization not only reduces variation in clinical decision-making but also promotes efficiency, improves patient satisfaction, and enhances the overall quality of care delivered [31].

The future of pharmaceutical care lies in the continued development of standardized practices that can be adapted to diverse healthcare settings. As pharmaceutical care continues to evolve, the need for robust, evidence-based protocols that guide the identification and resolution of DTPs will be essential to improving patient care globally.

Pharmaceutical care functions

The standardized system should include core functions such as collecting and organizing patient-specific information alongside determining the presence of medication-therapy problems, summarizing patients' healthcare needs, specifying pharmacotherapeutic goals, designing a pharmacotherapy regimen, designing a pharmacotherapy regimen and corresponding monitoring in collaboration with the patient and other health professionals [32]. *Initiating the pharmacotherapy regimen and monitoring plan*

The above was adapted from the pharmacotherapy series of the ASHP clinical skills programme and the final report of the ASHP model for Pharmacy Practice Research Learning Demonstration Project [33].

The determination of presence of DTP and subsequent conclusion is expected of medication, disease, laboratory test, and patient-specific information. With these in mind, the prescriptions for patients should be assessed for medication-therapy problems systematically under the headings of scrutiny such as: Are there any medical induction for this drug? Is there any drug prescribed? Is this drug appropriately prescribed for a medical condition? Are these medication dose, dosage form, schedule, route of administration, methods of administration appropriate? Any therapeutic duplication? Any there allergic reactions to the medications? Are there any possible actual and potential adverse drug events? Any actual and potential clinically significant drug-drug, drug nutrient and drug-laboratory test interactions?; Any possible interference with medical therapy by social or recreational drug use? Is there any problem arising from the financial impact of medication therapy on patients? Any possible reason for not receiving the full benefit of prescribed medication therapy?

Posing these "Any" questions will require careful structural arrangements and standardized protocols for probing, receiving, processing and taking necessary action toward maximizing patients' benefit [34]. Taking necessary action in the event of intervention also requires a standardized approach. Questions such as "do I meet the prescriber? Can I change the prescription to meet appropriate patient's need?

Documenting of pharmacist's intervention has to be standardized. A documentation protocol needs to be developed, if necessary by the pharmacists' regulatory

council and other stakeholders and promoted as a tool for effective pharmaceutical care in the various settings. The importance of pharmacists' checklist and worksheet in patients' folders alongside nurses' and physicians' entries cannot be underestimated. A curriculum that emphasizes a standardized and harmonized protocol in this regard is belated in the country. The curriculum should specify on the worksheet a summarized patient's healthcare need, the specific pharmacotherapeutic goals, and desired outcome [35].

Collecting and organizing pertinent patent-specific information will help form a database for the practice and prevent, detect, and resolve patient's medication-related problems to make appropriate medication-therapy recommendations [36]. When the database is not available in any setting, what kind of impute can any pharmacist make that can reasonably add to the value of care? Demographic e.g. name, address, date of birth, sex, religion, occupation, medical details (weight and height, acute and chronic medical problems, current symptoms, vital signs and other monitoring information, allergies and intolerances, past medical history) laboratory information, diagnostic and surgical procedures, medication therapy (prescribed medications, non-prescription medications, medication used prior admission, home remedies and other types of health products, medication allergies and intolerances and other concerns [37]

The manner of systematically collecting the information, storing the data, and retrieving it for pharmaceutical care judgment is expected to be standardized in the various care settings. It is believed that the homogeneity or similarity of care practice in different settings will promote the image of the profession. In developed settings, the record system is favoured by the constant electricity supply. Electronic 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.

capturing: study type, setting (hospital or community), study population, key findings related to pharmaceutical care practices, collaboration, and system-level challenges. Attention was also paid to discussions on lifestyle influences on pharmacokinetics and pharmacodynamics. Thematic analysis was employed to identify recurring patterns and critical gaps across the literature.

Quality Assessment

The methodological quality of included studies was evaluated using appropriate tools depending on study design (e.g., CASP checklists for qualitative studies, STROBE for observational studies). Only studies meeting minimum quality thresholds were included in the synthesis.

Discussion

Pharmaceutical care and drug therapy problems (DTPs)

Pharmaceutical care is a patient-centered approach to pharmacy practice that focuses on optimizing the use of medications to achieve desired therapeutic outcomes [4]. One of the primary goals of pharmaceutical care is to identify and resolve DTPs that may affect patient safety and treatment outcomes. DTPs can manifest in various forms, including medication errors, inappropriate drug choices, dosage issues, or lack of adherence to prescribed regimens. According to the American Society of Health-System Pharmacists (ASHP), DTPs can be categorized into several key areas: drug effectiveness, drug safety, drug interactions, and issues related to patient compliance or adherence [5].

Pharmacists are uniquely positioned to intervene in these issues through direct medication therapy management (MTM). MTM is a comprehensive, patient-specific service designed to optimize therapeutic outcomes by assessing the drug therapy regimen, identifying any DTPs, and making the necessary recommendations for resolution [6]. The pharmacist's role in identifying and resolving DTPs can prevent adverse drug events (ADEs) and medication-related problems, thereby reducing healthcare costs, and improving patient outcomes (Chisholm-Burns et al., 2010) [7].

The pharmacist's role in identifying and resolving DTPs

Pharmacists influence healthcare outcomes positively by scrutinizing prescriptions, identifying DTPs, and collaborating with other healthcare professionals to resolve these issues. DTPs can vary widely in terms of their clinical significance, and their severity must be assessed to determine the likelihood of harm to the patient [10]. In a hospital setting, DTPs may be related to complex medication regimens, polypharmacy, or patients with multiple co-morbidities. In ambulatory and community care settings, DTPs may involve issues

such as medication non-adherence, lack of proper counseling, or drug interactions due to self-medication [11].

The pharmacist's role in the identification and resolution of DTPs typically involves several stages, including: Prescription Review - this is the process of reviewing a patient's medication orders to identify potential problems related to drug selection, dosing, or duration of therapy; Patient Assessment- Pharmacists assess the patient's clinical status, medication history, and adherence to prescribed therapies; Risk Assessment- this involves evaluating the potential risks associated with identified DTPs, including the severity of the problem and the likelihood of harm to the patient; Intervention and Communication-Pharmacists collaborate with other healthcare professionals to make recommendations and resolve identified DTPs. Effective communication ensures that resolution of these issues leads to improved patient outcomes [12].

Approaches to delivering pharmaceutical care

Pharmaceutical care can be delivered through different methods depending on the setting and patient needs [13]. The traditional face-to-face consultation remains the most common approach, particularly in hospital and community pharmacy settings. However, technological advancements have enabled pharmacists to provide care through telehealth and virtual consultations, allowing greater accessibility and flexibility for patients, especially in remote areas or for those with mobility issues [14].

Each method of delivery comes with its own set of challenges and benefits. Face-to-face consultations provide an opportunity for in-depth, personalized patient interactions, allowing pharmacists to address concerns directly and monitor patient responses. However, this approach may not always be feasible, especially in under-resourced areas or during healthcare system strain, such as the COVID-19 pandemic [15].

Telehealth and virtual consultations have become increasingly popular in recent years, offering a convenient alternative for patients to consult with pharmacists remotely. While these methods give the advantage of accessibility and convenience, they may limit the ability to perform physical assessments or offer hands-on counseling. Despite these limitations, telehealth has proven effective in managing DTPs, particularly in ambulatory care settings, where patients can be monitored through regular check-ins and medication reviews [16].

It is essential to implement systematic processes for reviewing patient care, regardless of the method used. Whether in person, via telephone, or virtual platforms, the quality of the pharmaceutical care provided can vary significantly if no strategic plan or quality control measures are in place [17]. This is where the concept of

standardization comes into play.

Quality and productivity

In cases where there are no set guidelines for handling a task and any manager pulls in a group of random people from the street, set them up. It works and expects to get a

fantastic result. At best, the output looks like an uncoordinated and chaotic effort which consists of discharge of duties on a daily, weekly, monthly, or yearly basis to ensure smooth running. If the processes undertaken are not standardized, then there will be some measure of chaos. Every profession therefore requires rules that define the scope, quality, and processes followed. The rules and "modus operandi" in pharmaceutical care delivery need to be standardized to have visibility over ensuring quality [18-19].

Process standardization

This fundamentally describes the establishment of a set of rules governing how people in a setting are expected to complete a given task. This can be applied to any task; even answering a phone call, and taking down a client's information. Already the content and functions a pharmacist performs are well understood, the primary concern now is the method that will foster consistency in the provision of pharmaceutical care and support continuity of care both within a practice setting (e.g. pharmacists on different work shifts) and among practice setting (e.g. on discharge to home or ambulatory care). The basic issue here is what the sequence in the protocol is and for each step how this proceeds [20].

Variability in practice

Nature and style of practice by third-year post-graduation pharmacists in hospital or community as a fully registered professional (i.e. first year and second year being internship and national youth service years, respectively) tell a lot about variability in service delivery [21-22]. He is sometimes not under any senior or mentor, so he is believed to be able to discharge duties based on his undergraduate training and the experience gathered during the 2-years postgraduate life. Different strokes for different folks exist as some persons have the first year post-graduation experience in the academic or hospital or community setting while the second year in another of these and finally settles for a completely different area of practice, not by design but fate. In all these sway areas, it suffices to state that no fundamental standardized system exists. For example, in a hospital setting e.g. tertiary institution and secondary health facility, the standard of care is not homogenous, approaches to care of clients vary widely most likely depending on the situation facility, and where a strongly willed mentor exists, the personality comes into play. A standardized professional care approach is being advocated that transcends all of these variable characters [23]. being the immediate necessary action (e.g., the addition of another drug, rectification of incomplete prescription, change of drug or dosage discontinuation of a particular offending drug, removal of an unnecessary drug, and other systematic and standardized protocols [24].

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Posing these "Any" questions will require careful structural arrangements and standardized protocols for probing, receiving, processing and taking necessary action toward maximizing patients' benefit [34]. Taking necessary action in the event of intervention also requires a standardized approach. Questions such as "do I meet the prescriber? Can I change the prescription to meet appropriate patient's need? Documenting of pharmacist's intervention has to be standardized. A documentation protocol needs to be developed, if necessary by the pharmacists' regulatory council and other stakeholders and promoted as a tool for effective pharmaceutical care in the various settings. The importance of pharmacists' checklist and worksheet in patients' folders alongside nurses' and physicians' entries cannot be underestimated. A curriculum that emphasizes a standardized and harmonized protocol in this regard is belated in the country. The curriculum should specify on the worksheet a summarized patient's healthcare need, the specific pharmacotherapeutic goals, and desired outcome [35].

Collecting and organizing pertinent patent-specific information will help form a database for the practice and prevent, detect, and resolve patient's medication-related problems to make appropriate medication-therapy recommendations [36]. When the database is not available in any setting, what kind of impute can any pharmacist make that can reasonably add to the value of care? Demographic e.g. name, address, date of birth, sex, religion, occupation, medical details (weight and height, acute and chronic medical problems, current symptoms, vital signs and other monitoring information, allergies and intolerances, past medical history) laboratory information, diagnostic and surgical procedures, medication therapy (prescribed medications, non-prescription medications, medication used prior admission, home remedies and other types of health products, medication allergies and intolerances and other concerns [37]

The manner of systematically collecting the information, storing the data, and retrieving it for pharmaceutical care judgment is expected to be standardized in the various care settings. It is believed that the homogeneity or similarity of care practice in different settings will promote the image of the profession. In developed settings, the record system is favoured by the constant electricity supply. Electronic 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.

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 JIA handled data analysis and interpretation, and Author AEA contributed to the drafting and revising of the manuscript. All authors reviewed and approved the final version of the manuscript.

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