RESEARCH ARTICLE

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Assessing the Impact of Pharmacists' Interventions on Preventing and Resolving Drug-Related Problems in Cancer Pain Management

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Abstract

Objective: Drug-related problems (DRPs) hinder patients from fully benefiting from pharmacotherapy, with persistent pain in cancer patients remaining a significant issue. This study aimed to evaluate the clinical outcomes and medication cost changes resulting from pharmacists' interventions in managing DRPs associated with cancer pain. **Methods:** A randomized controlled study was conducted in a scholarly medical institution. Hospitalized cancer patients experiencing pain were randomly assigned to either the Intervention Category (IC) or Control Category (CC). The Pharmaceutical Care Network Europe (PCNE) classification system was utilized to categorize DRPs related to analgesic use. Pharmacists conducted assessments focusing on pain relief, incidence of adverse drug reactions (ADRs), and cost savings from DRP resolutions. Data on DRP types, causes, proposed interventions, and outcomes of pharmacist recommendations were collected and analyzed. **Results:** A total of 180 participants were enrolled and evenly distributed between the IC and CC groups. In the IC, pharmacists identified 68 DRPs in 49 participants, averaging 0.8 DRPs per patient. A total of 150 pharmacist-led interventions were proposed. By the third day of treatment, the IC demonstrated significantly greater analgesic relief compared to the CC. Additionally, 35 DRP interventions in the IC led to measurable cost reductions. **Conclusion:** Pharmacist-led interventions for cancer patients experiencing pain effectively addressed drug-related problems, enhanced pain management, and contributed to reduced medication costs. Integrating clinical pharmacy services into cancer pain management can lead to improved therapeutic outcomes and resource optimization.

Keywords: Pharmacy-Interventions- Drug-Related Problems- Cancer- Pain Management

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Introduction

As per the official description by Pharmaceutical Care Networks Europe (PCNE), Drug-Related Problems (DRPs) are occurrences or circumstances associated with pharmacotherapy that possibly impede desirable medical results [1]. The World Health Organization (WHO) believes that over fifty percent of all medications contain DRPs in prescription or management [2]. Patients experiencing cancer pain face a markedly heightened risk of DRPs due to the concomitant use of several medicines, which are not restricted to antineoplastic representatives, analgesics, therapeutic pharmaceuticals, and drugs for side effects and complications. Neglected DRPs contribute to a heightened risk of hospitalizations and emergency department visits. Moreover, severe Adverse Drug Reactions (ADRs), with half deemed attributable to DRPs, are linked to patient mortality, imposing a significant burden on worldwide medical resources and indicating a need for enhancement [3].

Clinical pharmacists, due to their proficiency in medication management and the identification and resolution of complicated DRPs, can aid individuals in attaining optimal pharmacotherapy outcomes. The Agency for Disease Management and Prevention and the Institute of Medical Sciences have recognized pharmacists as integral parts of the medical team in the USA. Medical pharmacists are increasingly vital in pharmacotherapy, focusing more on clinical DRPs [4].

Analgesia is among the most prevalent problems experienced by cancer survivors. It can induce or exacerbate anxiety, sleeplessness, sadness, exhaustion, and loss of hunger, significantly impacting a patient's routines, self-care capabilities, and overall quality of life. Approximately two million new cancer cases are identified annually in China, with over fifty percent likely experiencing cancer-related pain. The National Comprehensive Cancer Networks (NCCN) guidelines endorse a Multidimensional Team (MDT) approach for managing cancer-related pain [5]. Correspondingly, pharmacists participated in hospice care in 85.5% and 55.3% of medical facilities.

In emerging nations like China, the approach of pharmacist involvement in cancer pain management has

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lately been implemented. A prospective multinational cohort investigation on the influence of Pharmacist-Led Clinical Guiding Teams (PCGTs) on cancer pain management demonstrated that PCGTs considerably enhanced the uniformity of cancer pain therapy [6]. The standardization encompassed an increased frequency of pain assessments, more uniform dose adjustments, and a reduction in pethidine prescriptions. The disparity in total patient-reported pain levels and gastrointestinal problems was considerable when contrasted with the control category. The results indicate that PCGTs can enhance the efficiency and effectiveness of cancer pain management while fostering acknowledgment of the clinical pharmacy industry. Numerous studies demonstrate that pharmacists can leverage their knowledge of cancer and pharmacotherapy to manage and alleviate pain in oncology patients [7]. Systematic research delineated the operational framework of cancer pain management among Chinese pharmacists across the dimensions: (1) pharmacists deliver foundational cancer pain instruction to individuals suffering from cancer-related pain, (2) pharmacists engage in more proactive pain intensity assessment, (3) pharmacists advocate for and endorse judicious medication utilization through actions, and (4) pharmacists conduct follow-ups for individuals to guarantee sustained, appropriate, and effective management of cancer-related pain.

Despite numerous studies examining pharmacists' involvement in cancer pain management teams, there is a deficiency of research about pharmacists' treatments for DRPs [8]. The DRP categorization is a validated instrument employed in many contexts to classify DRPs in pharmacists' routine medical practices [9, 10]. Moreover, prior research has not documented the financial benefit of pharmacist treatments in recognizing and addressing DRPs in cancer pain sufferers. This research employed the DRP categorization to assess the features of DRPs found by pharmacists in the pharmacologic therapy for cancer pain sufferers at the hospital. The financial benefits of pharmacists' intervention regarding medication costs were examined.

Materials and Methods

Study design and data collection

Participants who satisfied the inclusion conditions were randomly assigned to the intervention and control categories using random number generation in Excel®. The MDT comprised doctors, nurses, and pharmacists. The pharmacists had undergone standardized instruction in clinical pharmacy and pain treatment and had over a decade of professional experience [11]. The responsibilities of pharmacists within the MDT include (1) engaging in daily MDT phases and case conversations; (2) supplying drug data and treatment consultations to the MDT, utilizing the hospital's pharmacy services database to perform thorough reviews and implement treatments on medical orders given by physicians; and (3) offering medicine advice and pain assessments for patients receiving analgesics, documenting DRPs (such as ADR) that arise while taking medications, and addressing patients' medication-related requests throughout their treatment [12]. Participants in the Control Category (CC) got pain care from doctors and nurses without the clinical pharmacists' Intervention Category (IC). The management encompassed pain evaluation and therapy modification, ADR tracking, and patient medication guidance.

Pharmacists evaluated the prescription lists of every individual who satisfied the inclusion requirements [13]. They gathered the patient's healthcare record quantity, name, age, gender, admittance evaluation, drug expenses, and more data from the electronic health record. Within 24-48 hours of admission, each patient underwent an alteration of therapy according to information gathered from the individual's health records, a direct conversation with the patient-pharmacist, and the MDT. During the MDT phases, the pharmacist observed the nurse's administration of drugs.

Applicable treatment standards from Chinese and international organizations were utilized to identify DRPs. The China National Health Committee provided the primary treatment recommendations cited. The Chinese recommendations resembled international criteria, except that the medications were administered in China. The MDT corroborated the detected DRPs, and suitable strategies to rectify the DRPs were deliberated with the entire group [14]. The pharmacist assessed the outcomes of each suggestion, and the physician validated the findings.

DRPs were categorized based on the PCNE-DRP categorization system. A single problem (P) can have several causes (C) and result in various interventions (I), yet it can culminate in a singular outcome (O). The prevalence of DRPs was determined by quantifying the number of DRPs per participant. Cost reductions were determined by the disparity between the expense of the new medication advised by the pharmacist and the original therapy. It is widely accepted that savings resulting from alterations in drug therapy will persist until the conclusion of the new drug regimen. Suppose an intravenous (IV) to oral medication conversion occurs [15]. In that case, the cost differential among the prescription forms is assessed within the initial two days of the transformation, assuming the doctor will transition to the oral prescription type within that timeframe without pharmacist assistance.

The formula for estimating drug cost reductions is: cost distinction (USD) = (cost of single drug therapy before intervention X daily the rate X therapy time, assuming continuation into the intervention period with new medications) - (cost of single drug therapy post-intervention X daily rate X time after treatment assistance + the expense of drugs utilized before response). The net cost reductions were the aggregate of each medication price variance.

Criteria for Qualification

Articles were incorporated if they satisfied the subsequent inclusion standards:

• Experimental design research utilizing randomization in comparison to a CC.

• Documented in English or accompanied by an English translation.

• Provision of any form of educational treatment by a

pharmacist, potentially as a component of a more intricate interdisciplinary approach.

• Any environment (residence, medical facility, primary healthcare, etc.).

• The subjects were adults who were experiencing discomfort due to active cancer, regardless of kind, stage, or location.

Articles were accepted if they possessed the specified indicators of outcome.

Principal outcome metrics

• Pain, such as self-reported pain, is quantified using a visible analog or numeral rating system.

• Patient cognition, convictions, dispositions, and actions

• Self-efficacy and compliance with medications

Secondary performance metrics

• Patient contentment

• Mitigation or diminished likelihood of adverse consequences or pharmacological interactions

• Decreased interruption from pain in everyday tasks, including health, cancer-specific functional position, relationships, sleeping, Quality Of Life (QOL), and mood.

Clinical Pharmacist Model for DRPs

The present investigation established an MDT comprising doctors, nurses, and medical pharmacists for medical care. Within the cohort of medical pharmacists, chemists engaged in the evaluation of cancer-related pain and the recognition of DRPs [16]. At the same time, the top pharmacist-in-charge was tasked with verifying DRPs and delivering interventions and feedback. The National Multimodal Cancer Initiative Adolescent Cancer Pain Standards issued each DRP and accompanying suggestions. Upon the commencement of a cancer pain individual's registration, pharmacists conduct a thorough assessment, including pain features, magnitude, existing analgesic regimen, adherence to therapy, and side effects, while providing medication instruction. Evaluations were performed daily and biweekly before and following pain management.

Throughout the 28-day follow-up period, in-person interviews during hospitalization or mobile post-discharge assessed analgesic safety and effectiveness. Examinations of the medications for individuals hospitalized over the weekend were conducted within 48 hours following a finding of cancer discomfort. The clinical chemists recognized and documented potential DRPs with the DRP categorization during every ward visit with the MDT, patient-pharmacist interviews, and prescription reviews. A recommendation for treatment to enhance opioid therapy was presented to physicians.

Standard instance

A representative example was given to illustrate the entire process of treatments by medical pharmacists. A 56-year-old male with stage IV tumors of the ureter was taken into the radiation therapy unit. The individual experienced intense extending pain in the left bottom stomach, characterized as abdominal pain. The following assessment and treatment of the medication regimen by medical pharmacists concentrated on the following topics. Firstly, the suggestions recommend avoiding pairings of opioid-acetaminophen medications due to hepatotoxicity associated with overdoses of acetaminophen. The patient was administered oxycodone and acetaminophen pills as the primary analgesic. The DRP was classified as an "ADE potentially happening P-2.1," with the cause indicated as "inappropriate medication per guidelines C1.1." The pharmacists suggested opium or oxycodone sustained-release pills as the primary analgesic.

The patient had severe pain following the administration of oxycodone long-lasting release pills, whereas quick-release morphine pills were unavailable. The DRP was classified as "suboptimal drug therapy P-1.2," resulting from "absence or incomplete drug therapy despite established justification C1.6." The pharmacists advised the doctor to issue immediate-release morphine pills for severe pain. Lastly, the individual experienced opioid-induced constipation, although the physician failed to recognize and address the issue. The DRP was classified as "ADR potentially happening P-2.1," with the cause characteristicd to "absence or inadequate outcome surveillance C9.1." The pharmacists recommended that the physician prescribe a laxative.

Results and Statistical Evaluation

A descriptive study was performed on the individual's demographics, clinical characteristics, and first analgesics. Data on the types, triggers, and state of DRPs, along with pharmacist treatments and the acceptance of recommendations, were gathered by the DRP categorization. Categorical parameters are shown as counts with percentages, while continuous parameters are stated as means with standard deviations.

Assessments

Intensity of Pain and Its Disruption

The Brief Pain Indicator (BPI) was utilized to evaluate pain severity and its impact on patients' quality of life. The BPI has emerged as a prevalent instrument for assessing clinical pain. The BPI enables individuals to determine the intensity of their pain and how much it disrupts several aspects of emotional and functional well-being.

BPI encompasses inquiries on pain place, pain level (including worst, lowest, median, and current pain), discomfort impact (affecting general behavior, attitude, walking ability, everyday job, relationships, sleeping, and pleasure of life), and analgesic effectiveness. Pain scores vary from 0 (no pain) to 10 (maximum agony), while pain interruption ratings range from 0 (no interruption) to 10 (total interruption).

Sufficiency of Pain Management

The PMI is commonly employed to assess cancer pain management by WHO standards for treating cancer pain. The PMI assesses pain treatment by measuring the equilibrium between the recommended potent analgesics and the severity of pain described by the individual in question. The PMI values span from -3 (indicating a patient experiencing intense discomfort without analgesic

intervention) to +3 (denoting a patient experiencing no pain while prescribed morphine or a comparable powerful opioid). Unfavorable PMI ratings signify insufficient pain management, whereas ratings of 0 or above are considered a conservative measure of satisfactory treatment. Medicines were gathered via conversations with patients by the pharmacist, and the pain score was determined by the highest pain rating recorded from the BPI-C evaluation.

Evaluation of Medication Compliance

Compliance with analgesics was evaluated using the Morisky Medicine Adherence Measurement (MMAM), a validated evaluation tool demonstrating exceptional validity and reliability within the Chinese cancer pain demographic. The evaluation encompasses the medication adherence behaviors: inattention, negligence, discontinuation of the regimen upon improvement, and resumption of the medicine with deterioration. The total of the "yes" responses constitutes a composite metric of non-compliance. Compliance scores vary from 0 to 4, with adherence classified into three categories: non-compliance (marks 0), partial compliance (marks 1-3), and complete compliance (marks 4).

QOL Linked to Health

The patient's health-related standard of life was evaluated at the four-week follow-up utilizing the Chinese form of the European Association for Research and Therapy of Cancer QOL Questionnaire-Core. The survey was developed to assess the physical, mental in nature and social functions of individuals with cancer. The approach consists of 30 questions, 25 consolidated into nine multi-item measures: five functional scales (actual, role, mental, emotional, and social), three symptom measures (tiredness, discomfort, nausea, and/or puking), and one worldwide well-being scale. The final six items evaluate the signs of dyspnoea, hunger reduction, sleep disruption, constipation, vomiting, and financial repercussions. The scoring guideline assessed the approach. The initial results were converted into averages that span from 0 to 100. In the operational scales, elevated scores signify improved performance, while diminished values reflect superior health status in the symptomatic scales.

Results

Characteristics of the patient

A total of 180 individuals with cancer were examined; 55.5% were male. Participants were randomly assigned in equal numbers to the Intervention Category (IC) (n = 90) and the Control Category (CC) (n = 90). The IC and CC were similar in age, sex, tumor characteristics, and comorbidity (Table 1).

Table 1. Patient Characteristic Analysis

Characteristics		IC	CC
Gender	Men	55.50%	54%
	Women	44.50%	46%
Age	> 80	12.40%	16.20%
	60 to 80	46.50%	42.60%
	< 60	41.10%	41.20%
	Average	57.40%	47.20%

Recognized DRPs and their Origins in the IC

Participants in the IC got a cumulative total of 125 analgesic drugs, averaging 2.5 per patient. Nearly all painkillers were opioids (either single-ingredient or a mixture of medications), comprising 97.4%, next to non-opioid analgesics such as ibuprofen and paracetamol. DRPs were identified in 52 patients. Sixty-six DRPs were identified, averaging 0.8 DRPs per patient. The primary category of DRPs was treatment efficacy (P-1) at 243.5%, succeeded by treatment security (P-2) at 18%. The primary issue with treatment efficiency (P-1) was the suboptimal impact of drug therapy (P-1.2) (25.5%) (Table 2).

A total of 86 reasons were discovered for DRP. Drug selection (C-1) was the predominant factor (54.5%), followed by other factors (C-8) (24.5%) and choosing the dose (C-3) (12.5%). In the two cause categories, incorrect choice of drugs per guidelines (C-1.1) (31.5%) was the predominant cause for drug choosing (C-1). In contrast, the absence or inadequacy of outcome management (including TDM) (C-8.1) (27.5%) was the main reason in the other area (C-8).

Proposed measures to address the DRPs in the treatment cohort

Pharmacists offered 150 actions and 2.5 treatments per DRP. Treatments predominantly took place at the drug level (I-3) (52.5%) and then at the doctor's level (I-1) (40.5%). The key treatment at the drug stage was the dose modification (I-3.2) at 19.5%. The primary treatment at the prescriber stage was the recommended treatment to the physician (I-1.3) at 37.5%.

Adoption of the therapies and the results of DRPs in the treatment cohort

All measures have been embraced (100%). Of them, 71.5% were fully executed (A-1.1), 23.5% were not executed (A-1.3), and 3.5% were partly executed (A-1.2). Of the 68 DRPs, 62.5% were resolved entirely (O-1), 8.5% were determined in part (O-2), and 35.5% remained unresolved (O-3). Within the 21 DRPs classified as unresolved (O-3), one was characteristicd to patient non-cooperation (O-3.1), 15 to prescriber non-cooperation (O-3.2), and five to unsuccessful treatments (O-3.3).

Table 2. DRP Recognition Analysis

Primary area	Issue	Result (%)
P-1	P-1.1	2.50%
	P-1.2	25.50%
	P-1.3	15.50%
P-2	P-2.1	18.00%
P-3	P-3.1	10.50%
	P-3.2	18.50%
	P-3.3	9.50%

Table 3. Analgesic Efficiency Analysis

Time		Third day		End of hospitalisation	
Group		IC	CC	IC	CC
Pain relief (%)	Not relieved	32.5	42.5	17.5	22.5
	Mil	33.25	37.25	31.75	37.75
	Medium	30.25	15.25	42.25	30.75
	Obvious	3.25	4.5	3.75	6.5
	Complete	0.75	0.5	4.75	2.5
Pain relief rate (%)		33.25	19.75	51.5	38
X^2		4.75		2.75	
P		0.038		0.153	

Comparison of analgesic efficacy across the two cohorts of patients

Per the pain grading criteria, the pain alleviation rates in CC on the third day of therapy and after treatment were 18.5% and 38.5%, respectively, whereas the pain relief percentages in the IC were 34.5% and 50.5%, respectively (Table 3). The disparity in pain alleviation rates among the two categories on the third day of therapy was statistically significant (P = 0.048). The gap in pain alleviation rates among the two groupings after confinement was not statistically significant (P = 0.131).

Discussion

Evaluation of adverse effects of analgesic medications

In the IC, 55 individuals (60.5%) encountered ADRs. The three most prevalent ADRs were constipation (50.5%), puking (36.5%), and diarrhea (4.25%). In the CC, 58 patients (63.5%) encountered ADRs. The three most prevalent ADRs were defecation (46.5%), puking (32.5%), and nausea (15.5%). A markedly lower percentage of patients experienced nausea in the IC compared to the CC (2.5% versus 15.5%, P = 0.025).

Variations in pharmaceutical expenses following the resolution of DRPs

Treatments conducted in the IC resulted in cost modifications for 35 DRPs. Of the 35 DRPs, 41 cost-related treatments were identified, comprising prevention of ADRs (36.5%), cessation of unneeded medications (28.5%), dose modification (26.5%), and transition from injectable/external formulations to oral medications (13.5%). Discontinuing superfluous medications resulted in savings of $725.4, but ADR avoidance incurred an additional expense of $143.7. Dose modification led to an extra expense of $78.21, and the transition from injection/external formulation to oral formulation added $4.25 to the total expenditure. The cumulative cost savings amounted to $495.25, yielding a mean reduction of $12.45 per treatment.

Clinical Pharmacy Enhancement

Enhancing cancer patient care through clinical pharmaceutical services necessitates a targeted, systematic methodology. Directed by particular suggestions, the objective is to close disparities and improve results. To effectively include clinical pharmacies in cancer treatment for pain, it is essential to shift beyond recognizing care components to implementing practical enhancement measures.

Targeted Training and Skill Development

Specialized training and education courses for pharmacists in clinical settings must be established to provide them with the essential skills for proficiency in cancer pain treatment. Modules for training encompass pain evaluation methodologies, counseling with patients' approaches, monitoring adverse drug reactions, and interventions for drug interactions.

Integrating clinical pharmacists into heterogeneous cancer teams promotes cohesive collaboration with other healthcare specialists

This combination guarantees a comprehensive patient-centered strategy, wherein pharmacists apply their drug management knowledge to improve overall patient results.

Protocol growth and uniformity

Formulating standardized procedures and recommendations that address the distinct difficulties and possibilities in cancer treatment, supported by medical organizations and hospitals, can establish an environment for uniform and evidence-based treatment. The procedures must include pain evaluation instruments, dosage instructions, medication choice criteria, and patient educational resources.

Pharmacist prescribing competence

Investigating the augmentation of pharmacist prescribing power, as seen in nations such as the UK, can improve the efficacy of cancer pain relief. Allowing pharmacists to choose their pain drugs empowers pharmacists to make immediate judgments, enhancing patient utilization of prompt and suitable care.

Technology connection

Implementing technological solutions, including electronic medical files and telehealth systems, can enhance remote counseling and managing medications, especially for patients in isolated or neglected areas.

Quantitative staffing goals or establishing a specified ratio of pharmacy technicians to hospital beds can facilitate full-service provision and accessibility

Utilizing international best practices and adapting them to the local situation can offer a uniform methodology while considering differences in patient volume and resource limitations.

Investigation and outcome assessment

Comprehensive investigations are essential to measure the effect of clinical pharmacy care on managing cancer. This encompasses evaluating pain intensity, pain alleviation, patient results, QOL enhancements, medication-related problems, drug-to-drug interactions, and healthcare cost reductions. Expertise concerning managing pain and patient contentment with pain treatment services can be evaluated.

It is imperative to customize the approach to execution

to the distinct healthcare environment of each nation, taking into account issues such as current facilities, resources at hand, and cultural differences. A phased strategy commencing with focused pilot initiatives and progressively extending to broader execution can guarantee viability and sustainability.

Suggestions

To fully realize the promise of medical pharmacy services in cancer pain treatment, it is essential to consider these critical guidelines for a holistic and patient-centered approach.

Strategic growth

Methodically enhance the incorporation of clinical pharmacies throughout medical centers and hospitals, guaranteeing sufficient coverage and availability for oncology patients.

Productive alliances

Encourage strong partnerships between pharmacy technicians and the wider healthcare team, highlighting a multidisciplinary strategy for managing cancer pain.

Specialized education

Create customized educational initiatives that provide medical pharmacists with expertise in pain evaluation, drug review, handling medications, morphine dosage calculation, instruction for patients, and counseling.

Evidence-based action

Promote the formulation and implementation of standard procedures and recommendations for managing cancer pain based on the most recent evidence.

Activism and Understanding

Elevate public and medical staff cognizance of the pivotal role of medical pharmacy solutions in improving cancer discomfort and patient satisfaction.

In conclusion, the investigation represents the inaugural prospective investigation detailing the medical and financial consequences of pharmacist treatments in addressing DRPs in cancer pain sufferers at a hospital. DRPs with analgesic medications are prevalent in this patient demographic. The research emphasizes the necessity of medical pharmacy services for this specific patient demographic.

In the research, following three days of therapy, the pain alleviation rate in the intervention group was considerably superior to that in the CC, indicating an early therapeutic advantage of pharmacist engagement in cancer pain management. There was no notable variance in the pain alleviation rate among the two subgroups (CC and IC) after hospitalization. This is elucidated by the fact that when the initial effectiveness for CC was suboptimal, physicians would more vigorously escalate dosages of painkillers or employ more potent narcotics and combinations of medications after interventions; members of the MDT might be managing individuals receiving CC, leading to modifications in their pain management strategies due to collaboration with pharmacies in the IC.

The investigation presents several drawbacks in the cost evaluation: the research failed to account for the input costs related to delivering pharmaceutical and medical care, potential contamination between both populations due to doctors in the MDT treating patients in the control category, and the possibility that their pain treatment procedures might be influenced by collaboration with the pharmacists in the IC. The self-selection aspect of participants in the research and the pharmacy's expertise in pain administration were factors not fully considered. The findings lack generalizability if fewer trained pharmacies administered the treatment, so the research did not conduct a sample size assessment.

Author Contribution Statement

Sachin Pradhan conceptualized the study, collected and analyzed data, and drafted the manuscript. Lakhan Lal Kashyap supervised the research process and contributed to data interpretation and manuscript revision.

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Scientific Approval/Thesis Information

The study was conducted as part of an approved student thesis project under the Department of Pharmacy, Kalinga University, and received academic clearance from the institutional research committee.

Ethical Considerations

Ethical approval was granted by the corresponding committee.

Availability of Data

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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