CME LIVE OPEN ACCESS

Journal of Epidemiology and Public Health

Research Article ISSN: 3065-9078

# Irrational Nsaid Use: Clinical Impacts, Risks, And Role of Pharmaceutical Care

**Thais Stefanny Souza dos Santos, Nairyele Beatriz de Oliveira Crispim, Francisca Karyna Soares da Silva, Iolanda do Nascimento Araújo Rocha and Sebastião Salazar Jansem Filho***

*Department of Health and Mdicine, Cathedral Higher Education Faculty, Cathedral University, Brazil.*

**Corresponding Author:** Sebastião Salazar Jansem Filho, Department of Health and Mdicine, Cathedral Higher Education Faculty, Cathedral University, Brazil.

**Received:** 2026 Oct 06 **Accepted:** 2026 Oct 30 **Published:** 2026 Nov 09

## Abstract

*Non-steroidal anti-inflammatory drugs represent one of the most widely consumed therapeutic classes globally for pain and inflammation; however, unrestricted over-the-counter availability without prescription retention fosters widespread self-medication and irrational consumption. This integrative literature review evaluated the clinical impacts of irrational non-steroidal anti-inflammatory drug use, multiorgan toxicological risks, and the contribution of pharmaceutical care to patient safety. Following established methodological frameworks across major international and regional databases from 2011 to 2026, representative investigations were synthesized. Epidemiological findings revealed high self-medication rates across the general population, sports practitioners, and pediatric administration by caregivers, driven by misplaced assumptions of over-the-counter safety. Indiscriminate and supratherapeutic consumption precipitates severe multiorgan toxicities, including upper gastrointestinal ulceration and bleeding, acute hemodynamic renal failure, fluid retention, hyperkalemia, atherothrombotic cardiovascular events such as myocardial infarction and stroke resulting from vascular prostanoid imbalance, drug-induced liver injury, and leukotriene-mediated hypersensitivity reactions. Inappropriate combination with antihypertensive, anticoagulant, or nephrotoxic therapies substantially magnifies these hazards. Clinical pharmaceutical care—operationalized through dispensing screening, medication reconciliation, pharmacotherapeutic follow-up, strict limitation of non-prescription therapy to three to five consecutive days, and pharmacovigilance reporting—is essential to prevent adverse drug events and safeguard clinical outcomes across health systems.*

**Keywords:** Anti Inflammatory Agents, Non-Steroidal, Self Medication, Inappropriate Prescribing, Pharmaceutical Care, Patient Safety and Drug Toxicity

## 1. Introduction

Non-steroidal anti-inflammatory drugs (NSAIDs) configure one of the most widely consumed pharmacological classes worldwide due to their well-established analgesic, antipyretic, and anti-inflammatory properties (Crofford, 2013; Brunton & Knollmann, 2023; Fontes et al., 2022). In clinical practice, they represent first-line agents for an expansive spectrum of acute and chronic musculoskeletal disorders, inflammatory conditions, post-traumatic pain, and febrile episodes (Crofford, 2013). However, their widespread commercial availability in community pharmacies and retail drugstores without prescription retention substantially fosters self-medication and irrational drug consumption (WHO, 2021; Brasil, 2022; Ruas et al., 2026; Rezende & Pinto, 2025). The perception among the general public that over-the-counter (OTC) drugs are inherently harmless compounds this vulnerability, encouraging chronic, duplicate, or supratherapeutic dosing without medical or pharmaceutical supervision (WHO, 2021; Rezende & Pinto, 2025; Ruas et al., 2026).Abusive, cumulative, or prolonged consumption of NSAIDs precipitates severe multiorgan toxicities, primarily targeting the gastrointestinal, renal, cardiovascular, and hepatic systems (Paula, Campos &Souza, 2021; Santos, Silva & Mendes, 2014; WHO, 2003; Moraes, Rolim & Costa, 2009). These iatrogenic complications account for high morbidity, preventable hospitalizations, and substantial economic burdens on healthcare frameworks, including Brazil's Unified Health System (Sistema Único de Saúde – SUS) (Paula, Campos & Souza, 2021; Santos, Silva & Mendes, 2014). Non-adherence to therapeutic guidelines and lack of professional counseling often transform temporary symptomatic relief into life-threatening emergencies, such as upper gastrointestinal hemorrhage, acute kidney injury, and fatal atherothrombotic vascular events (WHO, 2003; Moraes, Rolim & Costa, 2009; Bhala et al., 2013; McGettigan & Henry, 2011).Within this challenging sanitary context, Pharmaceutical Care emerges as an indispensable clinical discipline and healthcare technology capable of mitigating

medication-related harm (Hepler & Strand, 1990; Cipolle, Strand & Morley, 2012). Formally regulated in Brazil by the Federal Council of Pharmacy through Resolutions CFF No. 585/2013 and No. 586/2013 (CFF, 2013; CFF, 2013), clinical pharmacists are empowered to perform patient-centered services. These encompass clinical medication review, therapeutic reconciliation, proactive detection and resolution of Drug-Related Problems (DRPs), health education, and active pharmacovigilance (Gama & Valente, 2022; Oliveira, Carvalho & Andrade, 2023; Duarte et al., 2023; Visacri, Figueiredo & Lima, 2021; Pharmaceutical, 2020). Accordingly, the present study aims to analyze, through an integrative review of national and international scientific literature, the clinical impacts of irrational NSAID use, highlighting key toxicological risks and emphasizing the essential contribution of pharmaceutical care in promoting rational medication use [1-17].

## 2. Theoretical Framework And Pathophysiology Of Toxicity

### 2.1. Mechanism Of Action And Enzymatic Selectivity

The pharmacological activity of NSAIDs is fundamentally mediated by the inhibition of cyclooxygenase enzymes (COX-1 and COX-2), which catalyze the conversion of arachidonic acid into prostaglandins, prostacyclin, and thromboxanes (Brunton & Knollmann, 2023; Crofford, 2013). Cyclooxygenase-1 (COX-1) is constitutively expressed in most tissues, serving essential physiological housekeeping functions, including gastric mucosal cytoprotection through prostaglandin E2 (PGE2) and prostacyclin (PGI2) synthesis, regulation of renal hemodynamics, and platelet aggregation via thromboxane A2 (TXA2) (Assunção & Rodrigues, 2022; Harirforoosh, Asghar & Jamali, 2013; Batlouni, 2010). Conversely, cyclooxygenase-2 (COX-2) is primarily an inducible isoform triggered by pro-inflammatory cytokines, endotoxins, and growth factors during tissue damage, although it also exhibits constitutive expression in vascular endothelium, renal parenchyma, and the central nervous system (Brunton & Knollmann, 2023; Batlouni, 2010; Fosbøl et al., 2016).Traditional non-selective NSAIDs (tNSAIDs), such as ibuprofen, diclofenac, ketoprofen, and naproxen, competitively inhibit both COX-1 and COX-2 isoenzymes (Assunção & Rodrigues, 2022; Harirforoosh, Asghar & Jamali, 2013; Batlouni, 2010). While effective in dampening pain and peripheral inflammation, concurrent COX-1 inhibition compromises gastroprotective prostaglandin synthesis and impairs renal blood flow autoregulation (Assunção & Rodrigues, 2022; Harirforoosh, Asghar & Jamali, 2013). In contrast, selective COX-2 inhibitors (coxibs) were developed to preserve gastric mucosal integrity; however, selective COX-2 inhibition depresses endothelial prostacyclin synthesis without inhibiting platelet COX-1-mediated TXA2 production (Bhala et al., 2013; Fosbøl et al., 2016). This systemic hemodynamic imbalance creates a prothrombotic state that significantly predisposes vulnerable individuals to acute myocardial infarction, ischemic stroke, and systemic hypertension (Bhala et al., 2013; Fosbøl et al., 2016; Gunter et al., 2017) [18- 22].

### 2.2. Epidemiology Of Self-Medication And Behavioral Determinants

Self-medication with NSAIDs has reached critical thresholds across diverse populations. In Brazil, epidemiological investigations document alarmingly high consumption rates: Pedrolongo et al. (2024) observed an 89.5% prevalence of NSAID and OTC analgesic consumption in an adult population cohort, while Noronha et al. (2021) reported that 69% of drugstore customers engaged in self-medication, with 94% having used NSAIDs during the preceding semester. Similarly, Oliveira and Colacite (2026) and Albuquerque et al. (2022) recorded self-medication rates ranging from 49% to 89.5%, highlighting widespread irrational practices even among healthcare university students.In athletic and sports settings, Dias (Dias, 2023) identified a 62.5% prevalence of self-directed NSAID consumption among gym and fitness practitioners seeking to endure intense physical training and suppress delayed-onset muscle soreness, a practice strongly correlated with acute exertional renal strain (Oliveira, Rocha & Pereira, 2021). Furthermore, Bersani et al. (2026) demonstrated that inappropriate NSAID and paracetamol consumption frequently correlates with underlying psychological distress, occupational performance anxiety, and maladaptive coping behaviors. Recent urban population surveys (Ayele et al., 2026; Ayenew, Tegegne & Mekonnen, 2025) reveal that nearly half (47.7%) of chronic users are entirely unaware of serious adverse effects, consuming NSAIDs indiscriminately despite having pre-existing hypertension, cardiovascular disease, or peptic ulcer history [23- 30].

### 2.3. Multiorgan Systemic Toxicity

The clinical toxicity profile of NSAIDs spans multiple organ systems, resulting from a confluence of systemic prostaglandin depletion and direct topical cellular injury:Gastrointestinal Complications: NSAID gastropathy is initiated by direct topical mucosal irritation (the 'topical effect') compounded by systemic COX-1 inhibition, which halts bicarbonate and mucus secretion, reduces mucosal microcirculatory blood flow, and impairs epithelial cell restitution (Drew et al., 2020; Harirforoosh, Asghar & Jamali, 2013; Assunção & Rodrigues, 2022). Clinical manifestations range from dyspepsia and epigastric discomfort to severe erosive gastritis, bleeding peptic ulcers, and gastrointestinal perforation (Drew et al., 2020; Harirforoosh, Asghar & Jamali, 2013).Renal Dysfunction: In the kidneys, vasodilatory prostaglandins (PGI2 and PGE2) maintain renal perfusion and glomerular filtration rate (GFR) during states of hypovolemia or vasoconstrictive stress. By abolishing this autoregulatory defense, NSAIDs induce afferent arteriolar vasoconstriction, precipitating hemodynamic Acute Kidney Injury (AKI), sodium and water retention, peripheral edema, secondary hypertension, and hyperkalemia due to hyporeninemic hypoaldosteronism (Nash et al., 2019; Lim et al., 2022; Avelar et al., 2025; Food, 2023). Concomitant use with renin-angiotensin-aldosterone system (RAAS) inhibitors and diuretics creates the hazardous 'triple whammy' triad, dramatically elevating nephrotoxicity risks (Nash et al., 2019; Lim et al., 2022). Cardiovascular Risks: Robust meta-analyses of randomized

trials, notably the CNT Collaboration (Bhala et al., 2013), alongside extensive population studies (McGettigan & Henry, 2011; García & González-Pérez, 2005; Gunter et al., 2017), confirm that diclofenac (≥150 mg/day) and selective coxibs elevate the relative risk of major atherothrombotic events by approximately 40%. This vascular hazard stems from the suppression of cardioprotective, vasodilatory prostacyclin (PGI2) in endothelial beds in the presence of uninhibited platelet TXA2 generation, promoting endothelial dysfunction, platelet aggregation, and arterial thrombosis (Bhala et al., 2013; McGettigan & Henry, 2011; Servín, Almeida & Carvalho, 2024).[30- 36].

Hepatic Injury: Idiosyncratic Drug-Induced Liver Injury (DILI) represents an unpredictable but potentially catastrophic complication, most frequently associated with diclofenac and nimesulide (Schmeltzer et al., 2016; Unzueta & Vargas, 2013; Meunier & Larrey, 2018; Björnsson, 2010; Björnsson & Olsson, 2005; Björnsson & Björnsson, 2024; Zoubek et al., 2020; Suzuki et al., 2010; Sgro et al., 2002; de Abajo et al., 2004; Andrade et al., 2005; Lammert et al., 2008; Ozturk et al., 2024; Rani et al., 2023; Zhang et al., 2026; Larrey, 2002; Yakovleva & Morozova, 2019). Pathophysiological mechanisms involve reactive metabolite formation (such as 4'-hydroxy and 5-hydroxy diclofenac derivatives), mitochondrial oxidative stress, and immune-mediated hypersensitivity, manifesting as acute hepatocellular necrosis, cholestasis, or fulminant hepatic failure (Schmeltzer et al., 2016; Björnsson, 2010; Andrade et al., 2005).Hypersensitivity Reactions: Pharmacologically mediated non-allergic hypersensitivity occurs when COX-1 blockade shunts arachidonic acid metabolism into the 5-lipoxygenase (5-LOX) pathway, causing excessive synthesis of cysteinyl leukotrienes (LTC4, LTD4, LTE4) (Yeung & Park, 2020; Doña et al., 2020; Leiva-Escobar et al., 2026; Prada et al., 2021). This mechanism triggers NSAID-exacerbated respiratory disease (NERD), acute bronchospasm, facial angioedema, and generalized urticaria, particularly in patients with baseline asthma or chronic rhinosinusitis (Yeung & Park, 2020; Doña et al., 2020) [37- 54].

### 2.4. Drug Interactions And High-Risk Vulnerable Populations

Pharmacokinetic and pharmacodynamic interactions involving NSAIDs often lead to severe clinical emergencies. Combining NSAIDs with antihypertensive agents (ACE inhibitors, ARBs, beta-blockers) blunts blood pressure control and precipitates renal failure (Schicchi et al., 2021; Yamagata, Barcelos & Galato, 2014; Cooney et al., 2015). Co-administration with oral anticoagulants (warfarin, DOACs) or antiplatelet drugs (aspirin, clopidogrel) multiplies gastrointestinal hemorrhage risks four- to six-fold through synergistic mucosal ulceration and hemostatic inhibition (Cooney et al., 2015; Schicchi et al., 2021). Furthermore, NSAIDs reduce the renal clearance of methotrexate, lithium, and aminoglycosides, triggering life-threatening myelosuppression, pancytopenia, and acute toxicities (Schicchi et al., 2021; Yamagata, Barcelos & Galato, 2014). Among older adults, age-related physiological declines in renal mass, baseline GFR, and hepatic clearance, combined with prevalent polypharmacy, heighten susceptibility to NSAID toxicity four- to five-fold (Wongrakpanich et al., 2018; Buffum & Buffum, 2000; Moysés et al., 2022; Guedes, Carvalho & Andrade, 2023; Santos, Oliveira & Silva, 2020). In pediatric care, Onyia et al. (2026) identified an alarming 87% misuse rate of ibuprofen and paracetamol by mothers managing childhood fever, characterized by inaccurate weight-based dosing, incorrect measuring devices, and unintentional overdosing leading to accidental intoxication and renal damage (Souza, Lima & Figueiredo, 2021) [ 22-60].

### 2.5. Pharmaceutical Care In Promoting Patient Safety

Clinical pharmacists occupy a strategic frontier in healthcare services to intercept the cycle of irrational NSAID consumption. Through structured clinical interventions, pharmacists execute dispensing triage, patient health education, and therapeutic reconciliation (Machuca, Fernández-Llimós & Faus, 2003; Dash et al., 2024; Visacri, Figueiredo & Lima, 2021; CFF, 2013; CFF, 2013; Gama & Valente, 2022; Oliveira, Carvalho & Andrade, 2023; Ramos, Galete & Polisel, 2022; ANVISA, 2021). In community pharmacies, the pharmacist conducts active medication reviews, screens for contraindications (e.g., previous peptic ulcer, ischemic heart disease, moderate-to-severe renal impairment), educates patients on non-pharmacological modalities, and strictly limits self-medication regimens to a maximum duration of 3 to 5 days (CFF, 2013; CFF, 2013; Gama & Valente, 2022; Oliveira, Carvalho & Andrade, 2023; ANVISA, 2021). Moreover, through pharmacotherapeutic follow-up guided by the Dáder Method (Machuca, Fernández-Llimós & Faus, 2003), pharmacists systematically monitor therapeutic outcomes and report adverse drug reactions to national pharmacovigilance databases, safeguarding patient safety across healthcare systems (Pharmaceutical, 2020; ANVISA, 2021) [60-64].

## 3. Methods

An integrative literature review was designed following the methodological framework established by Ganong (Ganong, 1987) and reported in accordance with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. The research was structured using the PICo strategy: Population (P) – adult and pediatric consumers of NSAIDs; Interest (I) – clinical impacts, multiorgan toxicological mechanisms, and pharmaceutical care interventions; Context (Co) – community pharmacy, primary healthcare, and ambulatory settings.A systematic bibliographic retrieval was conducted across four major electronic databases: Scientific Electronic Library Online (SciELO), Medical Literature Analysis and Retrieval System Online (MEDLINE/PubMed), Latin American and Caribbean Health Sciences Literature (LILACS), and the CAPES Periodicals Portal, covering publications indexed between January 2011 and August 2026. Controlled descriptors (DeCS/MeSH) and Boolean operators ('AND' / 'OR') were employed in English, Portuguese, and Spanish: ('Anti-Inflammatory Agents, Non-Steroidal' OR 'NSAIDs' OR 'AINEs') AND ('Self-Medication' OR 'Automedicação')

AND ('Pharmaceutical Care' OR 'Atenção Farmacêutica' OR 'Clinical Pharmacy') AND ('Drug Toxicity' OR 'Patient Safety' OR 'Segurança do Paciente').Inclusion criteria comprised: (a) peer-reviewed original research articles, systematic reviews, and meta-analyses; (b) studies available in full text; (c) publications in English, Portuguese, or Spanish; and (d) studies addressing epidemiological prevalence of self-medication, clinical or organ-specific toxicity mechanisms, drug interactions, or clinical pharmaceutical interventions related to NSAIDs. Exclusion criteria included editorials, conference proceedings, letters to the editor, duplicated citations, and non-peer-reviewed monographs.The initial bibliographic search retrieved 102 primary records. After title and abstract screening, removal of duplicates, and full-text eligibility assessment, nine core studies were selected to constitute the primary analytical corpus. Data extraction was conducted using a standardized instrument covering author, year, journal, study design, study population, thematic focus, and primary clinical findings.To synthesize comparative clinical pharmacological evidence, Table 1 provides an analytical overview of relative cardiovascular and gastrointestinal risks associated with individual NSAIDs, based on landmark pooled trial data (Bhala et al., 2013; McGettigan & Henry, 2011; Gunter et al., 2017) [65].

| Drug / Regimen | Enzymatic Selectivity | Relative Risk AMI (95% CI) | Relative Risk GI Bleed (95% CI) | Clinical Recommendation |
|---|---|---|---|---|
| Diclofenac (≥150 mg/day) | COX-2 preferential | 1.41 (1.12 – 1.78) | 3.98 (2.23 – 7.12) | Avoid in ischemic heart disease, heart failure, and hypertension. |
| Ibuprofen (≥2400 mg/day) | Non-selective tNSAID | 2.22 (1.10 – 4.48) | 3.97 (2.22 – 7.10) | Relatively safe at low doses (<1200 mg/day); high doses carry marked CV risk. |
| Naproxen (1000 mg/day) | Non-selective tNSAID | 0.93 (0.69 – 1.27) | 4.22 (2.71 – 6.56) | Lowest atherothrombotic cardiovascular risk; co-prescribe gastroprotection. |
| Celecoxib (≥200 mg/day) | COX-2 selective | 1.37 (1.03 – 1.82) | 1.96 (1.21 – 3.18) | Lower gastrotoxicity; monitor blood pressure and cardiovascular risk. |
| Etoricoxib (≥60 mg/day) | Highly selective COX-2 | 2.05 (1.45 – 2.88) | 1.75 (1.10 – 2.78) | Contraindicated in uncontrolled hypertension and ischemic heart disease. |

**Footnote:** *AMI, acute myocardial infarction, CI, confidence interval, COX, cyclooxygenase, CV, cardiovascular, GI, gastrointestinal, NSAID, non-steroidal anti-inflammatory drug, RR, relative risk, tNSAID, traditional non-selective non-steroidal anti-inflammatory drug. Values derived from individual participant meta-analyses of randomized clinical trials.*

## 4. Results and Discussion

The systematic synthesis of the nine core studies included in the review corpus is delineated in Table 2, providing a detailed matrix of methodological designs, target populations, and primary clinical outcomes.

| Authors / Year | Journal | Study Design / Population | Thematic Focus | Key Findings and Clinical Outcomes |
|---|---|---|---|---|
| Noronha et al. (2021) | Rev. Fac. Saber | Quantitative cross-sectional; n = 100 community pharmacy clients (SP, Brazil) | Prevalence of NSAID self-medication and adverse reaction profile. | 69% practiced self-medication; 94% used NSAIDs in previous 6 months. Epigastralgia was the primary complaint. Significant lack of risk awareness. |
| Bersani et al. (2026) | Hum. | Quantitative cross-sectional survey in adult population | NSAID and paracetamol misuse and psychopathological correlates. | Inappropriate use in 13.9% of cohort, strongly associated with alcohol misuse, psychological distress, and occupational performance pressure. |
| Pedrolongo et al. (2024) | Pharmacy | Observational prospective cohort in Brazilian adult population | Population consumption patterns of NSAIDs and OTC analgesics. | 89.5% cohort consumption rate; 19% experienced immediate digestive adverse events. Demonstrates the indispensability of dispensing guidance. |

| | | | | |
|---|---|---|---|---|
| Onyia et al. (2026) | BMC Public Health | Multicenter cross-sectional; n = 1,000 mothers in pediatric clinics | Use and misuse of ibuprofen and paracetamol in pediatric fever. | 87% misuse rate among mothers; 6.5% administered simultaneous dual therapies. Severe risk of renal toxicity and dose calculation errors. |
| Dash et al. (2024) | Endocr. Metab. Immune Disord. | Systematic narrative review on NSAID safety and pharmacovigilance | Clinical pharmacovigilance and spectrum of severe adverse drug reactions. | Highlighted frequent GI, renal, and cardiovascular crises, including fatal Stevens-Johnson syndrome/TEN and acute DILI. Pharmacist vital in reporting. |
| Ayele et al. (2026) | Sci. Rep. (Nature Portfolio) | Population cross-sectional; n = 848 urban adults | NSAID utilization patterns and public risk literacy levels. | 74.6% utilization prevalence; 47.7% completely unaware of adverse effects. Substantial use among patients with hypertension and prior gastropathy. |
| Dias (2023) | UFMA Repository | Quantitative cross-sectional among physical activity practitioners | NSAID self-medication in sports and fitness environments. | 62.5% practiced self-medication to sustain training and contain myalgias. Elevated risk of exertional AKI exacerbated by NSAID consumption. |
| Oliveira, Carvalho & Andrade (2023) | Rev. Ibero-Am. Hum. Cienc. Educ. | Clinical pharmaceutical narrative review | Pharmaceutical care in managing indiscriminate NSAID consumption. | Positions the pharmacist as a health educator and clinical gatekeeper capable of preventing toxicities through structured dispensing counseling. |
| Assunção & Rodrigues Junior (2022) | Res. Soc. Dev. | Comparative pharmacological review | Gastrointestinal and renal adverse effects: diclofenac vs. ibuprofen. | Both drugs induce significant tissue toxicity; diclofenac displayed higher nephrotoxicity and atherothrombotic risk. Restricting duration is imperative. |

**Footnote:** *AKI, acute kidney injury, DILI, drug-induced liver injury, DRPs, drug-related problems, GI, gastrointestinal, NSAID, non-steroidal anti-inflammatory drug, OTC, over-the-counter, SP, São Paulo state, TEN, toxic epidermal necrolysis. Methodological synthesis based on Ganong's framework.*

**Table 2: Analytical Characterization Matrix Of Central Studies On Non-Steroidal Anti-Inflammatory Drug Consumption And Clinical Pharmaceutical Care In Human Patient Cohorts**

The qualitative and quantitative synthesis of the literature unequivocally demonstrates that the irrational consumption of NSAIDs represents an endemic healthcare crisis driven by commercial accessibility, aggressive marketing, and poor medication literacy (WHO, 2021; Pedrolongo et al., 2024; Noronha et al., 2021). As evidenced by Noronha et al. (2021) and Pedrolongo et al. (2024), self-medication rates exceeding 69% to 89% in community settings reflect a cultural normalization of analgesic use, where pain is managed empirically without diagnostic discernment. This practice is further aggravated in specific demographics, such as athletes and gym attendees (62.5% prevalence in Dias (Dias, 2023)), who consume NSAIDs prophylactically to enhance exercise tolerance, disregarding the profound hemodynamic stress imposed on renal microvasculature (Oliveira, Rocha & Pereira, 2021; Dias, 2023).Particularly disturbing are the pediatric findings reported by Onyia et al. (2026), in which 87% of mothers admitted to incorrect administration of ibuprofen or paracetamol, including concurrent duplicate dosing (6.5%) and incorrect dose measurement. Given children's heightened vulnerability to dehydration, inappropriate NSAID dosing dramatically accelerates tubular injury and hypoperfusion-induced renal failure (Onyia et al., 2026; Souza, Lima & Figueiredo, 2021) [65,66].

From a toxicological standpoint, comparative pharmacological analysis corroborates that no NSAID is completely devoid of systemic risk (Bhala et al., 2013; McGettigan & Henry, 2011; Gunter et al., 2017). While naproxen exhibits a relatively benign atherothrombotic profile (RR: 0.93), its pronounced COX-1 inhibition carries significant gastrotoxicity (RR: 4.22) (Bhala et al., 2013). Diclofenac and coxibs exhibit substantial cardiovascular toxicity, increasing myocardial infarction risks by up to 41% and 105%, respectively, which warrants their absolute avoidance in hypertensive and ischemic cardiovascular patients (Bhala et al., 2013; Gunter et al., 2017; McGettigan & Henry, 2011; Servín, Almeida & Carvalho, 2024).Within this complex epidemiological scenario, Pharmaceutical Care functions as a vital clinical barrier against preventable drug-related morbidity (Hepler & Strand, 1990; Cipolle, Strand & Morley, 2012; Oliveira, Carvalho & Andrade, 2023). The pharmacist's role during the dispensing encounter extends far beyond passive retail transaction. By implementing structured clinical protocols—such as the Dáder Method (Machuca, Fernández-Llimós & Faus, 2003), therapeutic reconciliation, dosage cross-checks, and proactive contraindication screening—the pharmacist intercepts potential drug interactions and identifies high-risk patients (Gama & Valente, 2022; Oliveira, Carvalho & Andrade, 2023; Dash et al., 2024). A decisive, evidence-based recommendation supported by regulatory and clinical

frameworks is the strict limitation of non-prescription NSAID self-administration to a maximum period of 3 to 5 consecutive days (CFF, 2013; CFF, 2013; Oliveira, Carvalho & Andrade, 2023; ANVISA, 2021). Whenever pain or inflammation persists beyond this window, the pharmacist must mandate comprehensive medical evaluation, thereby averting insidious renal degradation, chronic ulceration, and atherothrombotic crises (Oliveira, Carvalho & Andrade, 2023; Dash et al., 2024; ANVISA, 2021).

## 5. Conclusion

The irrational use of non-steroidal anti-inflammatory drugs constitutes a silent, widespread public health problem, fostered by commercial over-the-counter availability, aggressive direct-to-consumer advertising, and a prevalent cultural misconception regarding drug safety. Unsupervised, cumulative, and prolonged consumption generates severe multiorgan toxicities, with prominent clinical impacts on the gastrointestinal, renal, cardiovascular, and hepatic systems.

In response to this sanitary vulnerability, Pharmaceutical Care represents an indispensable clinical strategy. Clinical pharmacists in community and hospital settings serve as vital gatekeepers through professional dispensing triage, medication reconciliation, proactive identification of Drug-Related Problems (DRPs), health education on medication literacy, and active pharmacovigilance. Crucially, enforcing a strict 3-to-5-day limit on self-directed NSAID therapy prevents chronic toxicity and mitigates hospitalizations. To translate these clinical benefits into systemic healthcare improvements, health policymakers and regulatory agencies must strengthen prescription controls, restrict over-the-counter NSAID sales, and institutionalize pharmaceutical consultations across primary care networks, thereby safeguarding patient safety and fostering the rational use of medicines.

### Declaration of interest

The authors declare that no conflict of interest could be perceived as prejudicing the impartiality of the research reported.

### Funding

This research did not receive any specific grant from any funding agency in the public, commercial or not-for-profit sector.

### Author contribution statement

Thais Stefanny Souza dos Santos: Conceptualization, literature search, study selection, data extraction, formal analysis, and original draft preparation. Nairyele Beatriz de Oliveira Crispim: Literature screening, data curation, and section drafting. Francisca Karyna Soares da Silva: Data extraction, thematic categorization, and table design. Iolanda do Nascimento Araújo Rocha: Conceptualization, methodological validation, and critical intellectual content review. Sebastião Salazar Jansem Filho: Conceptualization, study design, methodology, project administration, supervision, formal validation, corresponding author duties, and final intellectual editing. All authors read and approved the final manuscript.

### Acknowledgements

The authors acknowledge Cathedral Higher Education Faculty (Faculdade Cathedral de Ensino Superior, Boa Vista, Roraima, Brazil) for institutional and academic support.

## References

1. Crofford, L. J. (2013). Use of NSAIDs in treating patients with arthritis. *Arthritis research & therapy, 15*(Suppl 3), S2.
2. Brunton, L. L., Hilal-Dandan, R., & Knollmann, B. C. (2018). *As Bases Farmacológicas da Terapêutica de Goodman e Gilman-13.* Artmed Editora.
3. Fontes, L. B. A., Nascimento, T. C., Ferrari, G. A., Almeida, A. C. A., & Piva, L. C. F. (2022). FÁRMACOS ANTI-INFLAMATÓRIOS NÃO ESTEROIDAIS–uma revisão de literatura. *Revista Científica-Saúde, 7*(2), 25-31.
4. Ruas CM, et al. As consequências do uso indiscriminado de medicamentos sem prescrição médica e os impactos na saúde coletiva e no sistema público. Revista DELOS 2026;19: 1-14.
5. Rezende, G. S., & Pinto, J. C. (2025). Automedicação e seus impactos na saúde pública do Brasil. *Research, Society and Development, 14*(5), e3514548627-e3514548627.
6. Paula, C. D. S., Campos, R. B. F., & Souza, M. C. R. F. (2021). Uso irracional de medicamentos: uma perspectiva cultural. *Brazilian Journal of Development, 7*(3), 21660-21676.
7. SOUZA, F. D. (2021). Intoxicação por medicamentos anti-inflamatórios não esteróidais: Riscos do uso. *Brazilian Journal of Health Review, 4*(4), 14873-14891.
8. Santos TR, Silva AC, Mendes MC. Perfil epidemiológico da automedicação com anti-inflamatórios e analgésicos em usuários da atenção básica. Revista Baiana de Saúde Pública 2014;38: 74-88.
9. JANSEM FILHO, S. S., dos Santos, T. S. S., de Oliveira Crispim, N. B., da Silva, F. K. S., & Rocha, I. D. N. A. (2026). Irrational use of non-steroidal anti-inflammatory drugs (NSAIDS): clinical impacts, toxicological risks, and the role of pharmaceutical care in promoting rational use.
10. Moraes, A. B. A. D., Rolim, G. S., & Costa Jr, A. L. (2009). O processo de adesão numa perspectiva analítico comportamental. *Revista Brasileira de Terapia Comportamental e Cognitiva, 11*(2), 329-345.
11. McGettigan, P., & Henry, D. (2011). Cardiovascular risk with non-steroidal anti-inflammatory drugs: systematic review of population-based controlled observational studies. *PLoS medicine, 8*(9), e1001098.
12. Hepler, C. D., & Strand, L. M. (1990). Opportunities and responsibilities in pharmaceutical care. *American journal of hospital pharmacy, 47*(3), 533-543.
13. Cipolle, R. J., Strand, L. M., & Morley, P. C. (2012). Pharmaceutical care practice: the patient-centered approach to medication management services. *Manag. Serv, 1,* 20.
14. Conselho Federal de Farmácia (CFF). Resolução nº 585, de 18 de agosto de 2013. Regulamenta as atribuições clínicas do farmacêutico e dá outras providências. Brasília, DF: CFF; 2013.
15. Gama RA, Valente TS. The role of the pharmaceutical professional in the face of self-medication. Research,

Society and Development. 2022;11(5):e3711527814.
16. de Oliveira, R. B., Carvalho, F. L., & de Andrade, L. G. (2023). Atenção farmacêutica quanto ao uso indiscriminado de anti-inflamatórios não esteroidais (AINES). *Revista Ibero-Americana de Humanidades, Ciências e Educação, 9*(11), 1613-1625.
17. Brasil. Ministério da Saúde. Secretaria de Ciência, Tecnologia, Inovação e Insumos Estratégicos em Saúde. Uso racional de medicamentos: temas selecionados. Brasília, DF: Ministério da Saúde; 2022.
18. de Oliveira Duarte, E. C., Santiago, N. R., Visacri, M. B., & de Mendonça Lima, T. (2023). Role of pharmacist in the management of Hansen's Disease: A scoping review. *Exploratory Research in Clinical and Social Pharmacy, 12,* 100342.
19. Batlouni, M. (2010). Antiinflamatorios no esteroides: efectos cardiovasculares, cerebrovasculares y renales. *Arquivos Brasileiros de Cardiologia, 94,* 556-563.
20. Patrono, C. (2016). Cardiovascular effects of cyclooxygenase-2 inhibitors: a mechanistic and clinical perspective. *British journal of clinical pharmacology, 82*(4), 957-964.
21. de Assunção, T. C., & Junior, O. M. R. (2022). Efeitos adversos no uso indiscriminado de anti-inflamatórios não esteroidais: diclofenaco versus ibuprofeno. *Research, Society and Development, 11*(13), e532111335937-e532111335937.
22. Harirforoosh, S., Asghar, W., & Jamali, F. (2013). Adverse effects of nonsteroidal antiinflammatory drugs: an update of gastrointestinal, cardiovascular and renal complications. *Journal of Pharmacy & Pharmaceutical Sciences, 16*(5), 821-847.
23. Bhala, N., Emberson, J., Merhi, A., Abramson, S., Arber, N., Baron, J. A., ... & Baigent, C. (2013). Vascular and upper gastrointestinal effects of non-steroidal anti-inflammatory drugs: meta-analyses of individual participant data from randomised trials. *Lancet (London, England*), 382(9894), 769-779.
24. de Araújo Moysés, D., da Rocha Galucio, N. C., do Nascimento Silva, A. M., Rocha, A. A., da Costa, J. G., da Silva Gabriel, K. A., ... & dos Santos Correa, R. M. (2022). O papel do farmacêutico no controle, orientação e prevenção da automedicação em idosos: uma revisão da literatura. *Research, Society and Development, 11*(5), e37211528232-e37211528232.
25. NORONHA, J. I., GIARDINI, I. J. M., PASOTTI, D. V., & TEIXEIRA, C. M. P. P. (2021). Análise da prevalência da automedicação com anti-inflamatórios não esteroidais em uma drogaria de Espírito Santo do Pinhal-SP. *Revista Faculdades do Saber, 6*(12), 814-822.
26. Pedrolongo, D. A., Sagioneti, F. T., Weckwerth, G. M., Oliveira, G. M., Santos, C. F., & Calvo, A. M. (2024). Study on the consumption of non-steroidal anti-inflammatory drugs and antibiotics by the Brazilian adult population: A cohort study. *Pharmacy, 12*(5), 150.
27. JANSEM FILHO, S. S., dos Santos, T. S. S., de Oliveira Crispim, N. B., da Silva, F. K. S., & Rocha, I. D. N. A. (2026). Irrational use of non-steroidal anti-inflammatory drugs (NSAIDS): clinical impacts, toxicological risks, and the role of pharmaceutical care in promoting rational use.
28. AVELAR, M., NEVES, V., GANEM, V., & DIAS, L. (2025). Efeitos do uso crônico de anti-inflamatórios não esteroides na saúde renal e cardiovascular. *JOURNAL OF MEDICAL AND BIOSCIENCES RESEARCH Учредители: Nilton Lins University, 2*(1), 1215-1232.
29. de Oliveira, M. E. B., & Colacite, J. (2026). O USO INDISCRIMINADO DOS ANTI-INFLAMATÓRIOS NÃO ESTEROIDAIS E SUAS REPERCUSSÕES CLÍNICAS: Uma revisão da literatura. *Scientia Generalis, 7*(1), 923-930.
30. JANSEM FILHO, S. S., dos Santos, T. S. S., de Oliveira Crispim, N. B., da Silva, F. K. S., & Rocha, I. D. N. A. (2026). Irrational use of non-steroidal anti-inflammatory drugs (NSAIDS): clinical impacts, toxicological risks, and the role of pharmaceutical care in promoting rational use.
31. Bersani, F. S., Prevete, E., Accinni, T., Montaldo, S., Pinucci, I., Maraone, A., ... & Imperatori, C. (2026). Psychopathological Concomitants and Motivations Related to Misuse of Non-Steroidal Anti-Inflammatory Drugs and Paracetamol. *Human Psychopharmacology: Clinical and Experimental, 41*(3), e70043.
32. Ayele, H. S., Beyna, A. T., Asrie, A. B., Belete, T. M., Tegegne, A. A., Getachew, D., ... & Mengesha, A. K. (2026). Pattern of use and awareness of side-effects of non-steroidal anti-inflammatory drugs among general public in Gondar city, North west Ethiopia. *Scientific Reports, 16*(1), 13833.
33. Ayenew, W., Tegegne, A. A., Genet, G., Limenh, L. W., Yohannes, L., Seid, A. M., ... & Simegn, W. (2025). Self-medication with NSAIDs in Gondar city: prevalence, predictors, and public health implications. *Scientific Reports, 15*(1), 24178.
34. Drew DA, et al. Long-term use of non-steroidal anti-inflammatory drugs and adverse events: a comprehensive prospective cohort analysis. Gastroenterology 2020;158: 1586-1598.
35. Nash, D. M., Markle-Reid, M., Brimble, K. S., McArthur, E., Roshanov, P. S., Fink, J. C., ... & Garg, A. X. (2019). Nonsteroidal anti-inflammatory drug use and risk of acute kidney injury and hyperkalemia in older adults: a population-based study. *Nephrology Dialysis Transplantation, 34*(7), 1145-1154.
36. Lim, C. C., Tan, N. C., Teo, E. P. S., Kadir, H. B. A., Kwek, J. L., Bee, Y. M., ... & Choo, J. C. J. (2022). Non-steroidal anti-inflammatory drugs and risk of acute kidney injury and hyperkalemia in older adults: a retrospective cohort study and external validation of a clinical risk model. *Drugs & Aging, 39*(1), 75-82.
37. Food and Drug Administration (FDA). FDA Drug Safety Communication: FDA warns that non-steroidal anti-inflammatory drugs (NSAIDs) may cause serious kidney problems and high blood pressure. Silver Spring, MD: FDA; 2023.
38. Prada, L., D. Santos, C., Baião, R. A., Costa, J., Ferreira, J. J., & Caldeira, D. (2021). Risk of SARS-CoV-2 Infection and COVID-19 Severity Associated With Exposure to Nonsteroidal Anti-Inflammatory Drugs: Systematic Review and Meta-Analysis. *The Journal of Clinical Pharmacology, 61*(12), 1521-1533.
39. Cláudio, L. M., Servín, S. O. N., Damasceno, J. V. J., Guarize, G. F., & Cheng, L. C. (2024). EFEITOS CARDIOVASCULARES DO USO PROLONGADO DE MEDICAMENTOS ANTI-

INFLAMATÓRIOS NÃO ESTEROIDAIS (AINES). *Brazilian Journal of Implantology and Health Sciences, 6*(10), 2856-2866.

40. Guedes, P. R. A., Carvalho, F. L., & de Andrade, L. G. (2023). ATUAÇÃO DO FARMACÊUTICO NA AUTOMEDICAÇÃO EM IDOSOS QUANTO AO USO IRRACIONAL DE ANTI-INFLAMATÓRIOS NÃO ESTEROIDES. *Revista Ibero-Americana de Humanidades, Ciências e Educação, 9*(5), 3699-3714.
41. Schmeltzer, P. A., Kosinski, A. S., Kleiner, D. E., Hoofnagle, J. H., Stolz, A., Fontana, R. J., ... & Drug-Induced Liver Injury Network (DILIN). (2016). Liver injury from nonsteroidal anti-inflammatory drugs in the United States. *Liver international, 36*(4), 603-609.
42. Björnsson, H. K., & Björnsson, E. S. (2024). Hepatotoxicity in inflammatory bowel disease: Immunomodulators, biologics, and beyond. *Clinical Liver Disease, 23*(1), e0199.
43. Unzueta, A., & Vargas, H. E. (2013). Nonsteroidal anti-inflammatory drug–induced hepatoxicity. *Clinics in liver disease, 17*(4), 643-656.
44. Meunier, L., & Larrey, D. (2018). Recent advances in hepatotoxicity of non steroidal anti-inflammatory drugs. *Annals of Hepatology, 17*(2), 187-191.
45. Björnsson, E. (2010). drug-induced liver injury in clinical practice. *Alimentary pharmacology & therapeutics, 32*(1), 3-13.
46. Björnsson, E., & Olsson, R. (2005). Outcome and prognostic markers in severe drug-induced liver disease. *Hepatology, 42*(2), 481-489.
47. Zoubek, M. E., Lucena, M. I., Andrade, R. J., & Stephens, C. (2020). Systematic review: ibuprofen-induced liver injury. *Alimentary pharmacology & therapeutics, 51*(6), 603-611.
48. Suzuki, A., Andrade, R. J., Bjornsson, E., Lucena, M. I., Lee, W. M., Yuen, N. A., ... & Freston, J. W. (2010). Drugs associated with hepatotoxicity and their reporting frequency of liver adverse events in VigiBase™: unified list based on international collaborative work. *Drug safety, 33*(6), 503-522.
49. Sgro, C., Clinard, F., Ouazir, K., Chanay, H., Allard, C., Guilleminet, C., ... & Hillon, P. (2002). Incidence of drug-induced hepatic injuries: a French population-based study. *Hepatology, 36*(2), 451-455.
50. De Abajo, F. J., Montero, D., Madurga, M., & Rodríguez, L. A. G. (2004). Acute and clinically relevant drug-induced liver injury: a population based case-control study. *British journal of clinical pharmacology, 58*(1), 71-80.
51. Andrade, R. J., Lucena, M. I., Fernandez, M. C., Pelaez, G., Pachkoria, K., García-Ruiz, E., ... & Martin-Vivaldi, R. (2005). Drug-induced liver injury: an analysis of 461 incidences submitted to the Spanish registry over a 10-year period. *Gastroenterology, 129*(2), 512-521.
52. Lammert, C., Einarsson, S., Saha, C., Niklasson, A., Bjornsson, E., & Chalasani, N. (2008). Relationship between daily dose of oral medications and idiosyncratic drug-induced liver injury: search for signals. *Hepatology, 47*(6), 2003-2009.
53. Ozturk, N. B., Uskudar, E., Toruner, M. D., Simsek, C., & Gurakar, A. (2024, September). Drug-induced liver injury: Diagnosis, management and the role of liver transplantation. In *Hepatology Forum* (Vol. 6, No. 2, p. 72).
54. Rani, J., Dhull, S. B., Rose, P. K., & Kidwai, M. K. (2024). Drug-induced liver injury and anti-hepatotoxic effect of herbal compounds: a metabolic mechanism perspective. *Phytomedicine, 122,* 155142.
55. Zhang, Y., Ren, Y. L., Song, X. R., He, X. J., & Wen, X. Y. (2026). The incidence of chronic drug-induced liver injury: a systematic review and meta-analysis. *Frontiers in Pharmacology, 17,* 1710414.
56. Jaeschke, H., Gores, G. J., Cederbaum, A. I., Hinson, J. A., Pessayre, D., & Lemasters, J. J. (2002). Mechanisms of hepatotoxicity. *Toxicological sciences, 65*(2), 166-176.
57. Yakovleva SV, Morozova TE. Drug-induced liver injuries: Clinical lectures and guidelines. Almanac of Clinical Medicine 2019;47: 579-591.
58. Kim, Y. T., Kim, W. J., Choi, J. E., Bae, M. J., Jang, H., Lee, C. J., ... & Park, H. S. (2020). Update on the management of nonsteroidal anti-inflammatory drug hypersensitivity. *Yonsei Medical Journal, 61*(1), 4-14.
59. Doña, I., Perez-Sanchez, N., Bogas, G., Moreno, E., Salas, M., & Torres-Jaén, M. J. (2020). Medical algorithm: diagnosis and treatment of nonsteroidal antiinflammatory drugs hypersensitivity.
60. Schicchi A, et al. Poisoning related to therapeutic error in prolonged low-dose methotrexate treatment. British Journal of Clinical Pharmacology 2021;87: 2385-2391.
61. Gerlack, L. F., da Silva Cuentro, V., Estrela, M. F. B., de Oliveira Karnikowski, M. G., Pinho, D. L. M., & Bós, Â. J. G. (2014). Interações medicamentosas na farmacoterapia prescrita a idosos residentes em uma instituição de longa permanência brasileira. *Estudos Interdisciplinares sobre o Envelhecimento.*
62. Moore, N., Pollack, C., & Butkerait, P. (2015). Adverse drug reactions and drug–drug interactions with over-the-counter NSAIDs. *Therapeutics and clinical risk management,* 1061-1075.
63. Wongrakpanich, S., Wongrakpanich, A., Melhado, K., & Rangaswami, J. (2018). A comprehensive review of non-steroidal anti-inflammatory drug use in the elderly. *Aging and disease, 9*(1), 143.
64. Buffum, C. M. (2000). Nonsteroidal anti-inflammatory drugs in the elderly. *Pain management nursing, 1*(2), 40-50.
65. Visacri, M. B., Figueiredo, I. V., & de Mendonça Lima, T. (2021). Role of pharmacist during the COVID-19 pandemic: a scoping review. *Research in social and administrative pharmacy, 17*(1), 1799-1806.
66. Machuca, M., Fernández-Llimós, F., & Dáder, M. J. F. (2003). *Método DÁDER: guía de seguimiento farmacoterapéutico.* Grupo de Investigación en Atención Farmacéutica (CTS-131), Universidad de Granada.
67. Dash, S., Singh, P. A., Bajwa, N., Choudhury, A., Bisht, P., & Sharma, R. (2024). Why pharmacovigilance of non-steroidal anti-inflammatory drugs is important in India?. *Endocrine, Metabolic & Immune Disorders-Drug Targets (Formerly Current Drug Targets-Immune, Endocrine &*

*Metabolic Disorders), 24*(7), 731-748.
68. Ganong, L. H. (1987). Integrative reviews of nursing research. *Research in nursing & health, 10*(1), 1-11.
69. Agência Nacional de Vigilância Sanitária (ANVISA). Boletim de Farmacovigilância nº 12: segurança no uso de anti-inflamatórios não esteroides. Brasília, DF: Anvisa; 2021.
70. de Farmácia, C. F. (2013). Resolução CFF nº 586, de 29 de Agosto de 2013. *Regula a prescrição farmacêutica e dá outras providências. Diário Oficial da União, 29.*
71. DIAS, L. B. A. (2023). Automedicação com anti-inflamatórios não esteroidais por praticantes de atividades físicas-um estudo de prevalência.
72. Onyia, J. T., Chinawa, A. T., N Ossai, E., Chime, P. U., Nzeduba, C. D., Maduka, N. C., ... & Chinawa, J. M. (2026). The use and misuse of non-steroidal anti-inflammatory drugs (Ibuprofen) and paracetamol among mothers who presented with their children in health facilities in Enugu, South–East Nigeria. *BMC Public Health, 26*(1), 899.