KETOPROFEN IN OSTEOARTHRITIS: MECHANISTIC INSIGHT, FORMULATIONS ADVANCES AND COMPUTATIONAL PERSPECTIVES

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Abstract

Ketoprofen, a propionic acid–derived nonsteroidal anti-inflammatory drug, is widely used in the management of osteoarthritis owing to its potent analgesic and anti-inflammatory effects. It acts through reversible inhibition of cyclooxygenase enzymes, resulting in decreased prostaglandin synthesis and modulation of inflammatory signaling pathways such as NF-κB and MAPK, thereby aiding cartilage preservation. Pharmacokinetically, ketoprofen exhibits high oral bioavailability, extensive plasma protein binding, and hepatic metabolism via glucuronidation, with the S-enantiomer contributing predominantly to COX inhibition. Recent advances in formulation technologies, including topical, transdermal, and nano-based delivery systems, have enhanced synovial targeting, prolonged drug retention, and reduced systemic adverse effects. Clinical evidence demonstrates significant pain reduction and improved joint function, while computational and QSAR studies support optimization of pharmacokinetic behavior and safety. Overall, ketoprofen remains a well-established and effective therapeutic option for long-term osteoarthritis treatment.

Keywords: Ketoprofen; Osteoarthritis; NSAIDs; COX inhibition; Drug delivery

1.Introduction

Osteoarthritis (OA) is a chronic degenerative joint disease characterized by cartilage degradation, synovial inflammation, and subchondral bone remodeling, leading to pain, stiffness, and functional impairment [1,2]. It is the most prevalent form of arthritis, particularly affecting the elderly population, and represents a significant socioeconomic burden due to chronic pain and disability [3,4].

Nonsteroidal anti-inflammatory drugs (NSAIDs) remain a cornerstone in OA management, providing analgesic and anti-inflammatory effects. Among them, ketoprofen, a propionic acid-derived NSAID, has been extensively studied for its efficacy, pharmacokinetic profile, and safety [5,6]. Ketoprofen exerts its therapeutic effect primarily through reversible inhibition of cyclooxygenase (COX) enzymes, reducing prostaglandin-

mediated inflammation, and modulating chondrocyte and synoviocyte signaling pathways, including NF-κB and MAPK, which contribute to cartilage degradation in OA [7,8].

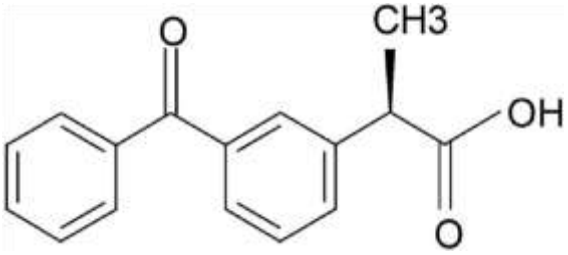

Fig.1. Chemical structure of Ketoprofen highlighting the aromatic benzophenone scaffold and stereogenic α-methyl propionic acid moiety essential for its anti-inflammatory activity.

Advances in drug design, computational modeling, QSAR analysis, and formulation strategies have further enhanced the therapeutic potential of ketoprofen. Modern formulations, including topical gels, transdermal patches, and nanoparticle or liposomal carriers, optimize local drug delivery, improve bioavailability, and reduce systemic adverse effects, thereby enhancing patient compliance and long-term tolerability [9,10].

Given its well-characterized pharmacology, clinical efficacy, and safety profile, ketoprofen continues to be a valuable therapeutic agent in OA management. This article explores drug design, mechanism of action, pharmacokinetics, formulation advancements, clinical efficacy, safety, and future perspectives of ketoprofen, integrating current evidence to support its continued role in OA therapy.

2.Marketed preparations of ketoprofen

2.1 Oral formulations

Available as immediate-release (IR) tablets/capsules (typical strengths 25–100 mg) and sustained/extendedrelease (SR/ER) matrix tablets or coated pellets designed to release drug over 12–24 h. SR/ER types are manufactured using matrix systems (hydrophilic polymers) or coated multiparticulates to modulate release and reduce peak-to-trough fluctuations [15,16,24].

Pharmaceutical composition (typical excipients)Fast absorption after IR oral dosing (Tmax ~0.5–2 h) and high oral bioavailability facilitate rapid analgesia in acute OA flares [15,16,24]. High plasma protein binding favors depot effect in inflamed tissues but means free fraction is small—important for drug interactions [15,16].

SR/ER formulations reduce Cmax and maintain plasma levels longer, improving adherence and lowering GI peak-exposure risk [15,16].

Fig.2. Representative marketed ketoprofen and ketoprofen–thiocolchicoside tablet formulations illustrating commonly available oral dosage forms.

2.2 Parenteral formulations

Aqueous injectable solutions (e.g., 50–100 mg per vial) for intramuscular or intravenous use are marketed for rapid analgesia in acute severe pain or perioperative settings [15,16].

Bypasses first-pass metabolism → faster Tmax and higher Cmax; used when oral route unavailable or when quick onset is required (severe OA flare, acute synovitis, postoperative pain) [15,16].

Short-term use only due to higher systemic exposure and risk profile; observe for renal/hepatic effects. Avoid repeated IM injections at same site; ensure aseptic technique [15,16].

Fig.3. Commercial intravenous ketoprofen formulations (e.g., Profenid®,Ketoprofen Injection IP®,Ketopain Injection®) used for pain management in OA patients.

2.3 Topical Formulations

Topical ketoprofen achieves high local concentrations in periarticular tissues and synovial fluid while keeping systemic exposure low — key benefit demonstrated across multiple studies and reviews of topical NSAIDs in OA [2,9,21,23].

Typical vehicles: hydroalcoholic gels, emulgels, microemulsion bases and transferosomal systems that include permeation enhancers (menthol, terpenes, ethoxylated surfactants) to increase dermal and periarticular

penetration [21,25]. Nanoformulations (SLN, NLC, microemulsions) further enhance skin flux and joint delivery [18,23].

Minimal systemic Cmax; measurable drug in synovial fluid that correlates with local analgesia; greatly reduced risk of systemic GI, renal adverse events compared with oral therapy [2,10,11,21]. First-line topical option for knee/hand OA, especially in elderly or GI-sensitive patients. Typical application: apply thin layer to affected joint 2–4 times daily (product-specific) [2,21].Local skin reactions (irritation, dermatitis) in a minority; systemic adverse events rare but monitor if using large surface areas or occlusion [21,25].

Fig.4. Representative marketed topical ketoprofen products such as Fastum® Gel, Profenid® Gel, and Ketoprofen® Gel Topical for localized OA pain relief.

2.4 Transdermal patches

Polymeric adhesive patches formulated for steady delivery over 12–24 h; controlled diffusion systems maintain periarticular drug levels and improve adherence [20,22].

Patches produce prolonged local exposure with low plasma spillover; useful for chronic OA pain where once-daily dosing enhances compliance [20].

Apply to intact skin; rotate sites; avoid heat (increases systemic absorption). Monitor elderly for cumulative systemic exposure if multiple patches used[20,22].

Fig.5. Formulation Strategies for Ketoprofen Transdermal Patches: Enhancing Skin Permeation and Bioavailability.

2.5 Advanced and novel delivery systems

These are becoming more prominent in the literature and some are entering specialty markets: a) Nanoemulsions / microemulsions

Enhance aqueous solubility and skin penetration, fast onset; can be formulated as gels or sprays [18,25]. b) Solid lipid nanoparticles (SLN) / NLC

Improve drug deposition, protect drug from degradation, enable sustained release into joint tissues; often incorporated into gels (nanogel) for topical/transdermal use [23,18]. c) Liposomes / transfersomes / ethosomes

Ultra-deformable vesicles increase transport across stratum corneum, improving synovial delivery from topical application [23,25].

d) Hydrogels & intra-articular hydrogels

Hydrogels carrying ketoprofen (or combination with HA) are being studied for intra-articular sustained release — relevant for severe OA, aiming to reduce systemic exposure and dosing frequency [23,25].

Regulatory & commercialization note

Many advanced systems are at preclinical/early clinical stage; localized/regional approvals vary. Evidence indicates superior penetration and prolonged effect vs conventional gels, but full large-scale Phase III data are limited for some platforms [18,23].

Fig.6. Novel Drug Delivery Systems of Ketoprofen: Enhancing Targeted Delivery and Therapeutic Efficacy.

3.Drug Design and mechanism of action in osteoarthritis

Ketoprofen is a propionic-acid–derived nonsteroidal anti-inflammatory drug (NSAID) rationally designed to inhibit prostaglandin synthesis through high-affinity binding to the cyclooxygenase (COX) catalytic domains. Structurally, ketoprofen possesses an aromatic benzophenone core and a carboxylic acid moiety essential for

anchoring within the COX active site, allowing stable ionic interaction with Arg120 and hydrogen bonding within the hydrophobic pocket (14,16,22). This structural configuration enhances both COX-1 and COX-2 inhibitory activity, contributing to its potent analgesic and anti-inflammatory effects.

In osteoarthritis (OA), inflammatory mediators such as IL-1β, TNF-α, COX-2, PGE2, nitric oxide, and matrix metalloproteinases (MMP-1, MMP-3, MMP-13) drive cartilage degeneration and synovial inflammation (28,29). Ketoprofen has been shown to suppress these mediators by inhibiting COX-derived prostaglandins and reducing downstream signaling such as NF-κB activation (7,20,31). Experimental data demonstrate that ketoprofen downregulates inflammatory cytokine expression in OA chondrocytes and synoviocytes, leading to reduced catabolic enzyme release and improved joint homeostasis (12,20,33).

Drug-design studies highlight that the orientation of ketoprofen's aryl moieties increases hydrophobic complementarity within the COX binding channel, resulting in enhanced potency compared to other propionic-acid NSAIDs (14,16). QSAR and molecular modeling analyses confirm that electronwithdrawing substituents on the benzophenone ring contribute to high inhibitory activity by stabilizing the COX–drug complex and promoting favorable lipophilicity for membrane permeation (18,19,22).

Furthermore, ketoprofen shows optimal physicochemical properties—moderate lipophilicity, small molecular size (≈254 Da), and high plasma protein binding—which improve tissue penetration into inflamed synovium (17,21). Pharmacokinetic studies reveal rapid absorption and effective distribution to joint compartments where concentrations correlate with analgesic efficacy (15,17,21).

Ketoprofen strongly inhibits both COX isoforms, leading to reduced synthesis of PGE2, a key mediator of OA pain and cartilage inflammation (12,20,28).

Multiple studies report that ketoprofen reduces NF-κB translocation, thereby decreasing transcription of pro-inflammatory cytokines (TNF-α, IL-1β) and MMPs involved in cartilage breakdown (20,28,33).

By lowering prostaglandin levels in synovial tissues and peripheral nerves, ketoprofen decreases nociceptor sensitization and improves pain tolerance in OA patients (12,26).

Ketoprofen formulations demonstrate reduced oxidative markers and lowered expression of catabolic enzymes such as MMP-13 in cartilage explants (29,33,34).

Studies in human OA synoviocytes show ketoprofen reduces inflammatory cell infiltration and decreases hyaluronidase activity, supporting synovial membrane integrity (30,33).

Clinical studies confirm that ketoprofen provides significant symptomatic relief in OA, with improvements in pain, mobility, and physical function (12,26,27). The drug's mechanistic profile supports its therapeutic role as it targets central inflammatory pathways driving OA progression rather than offering symptomatic analgesia alone.

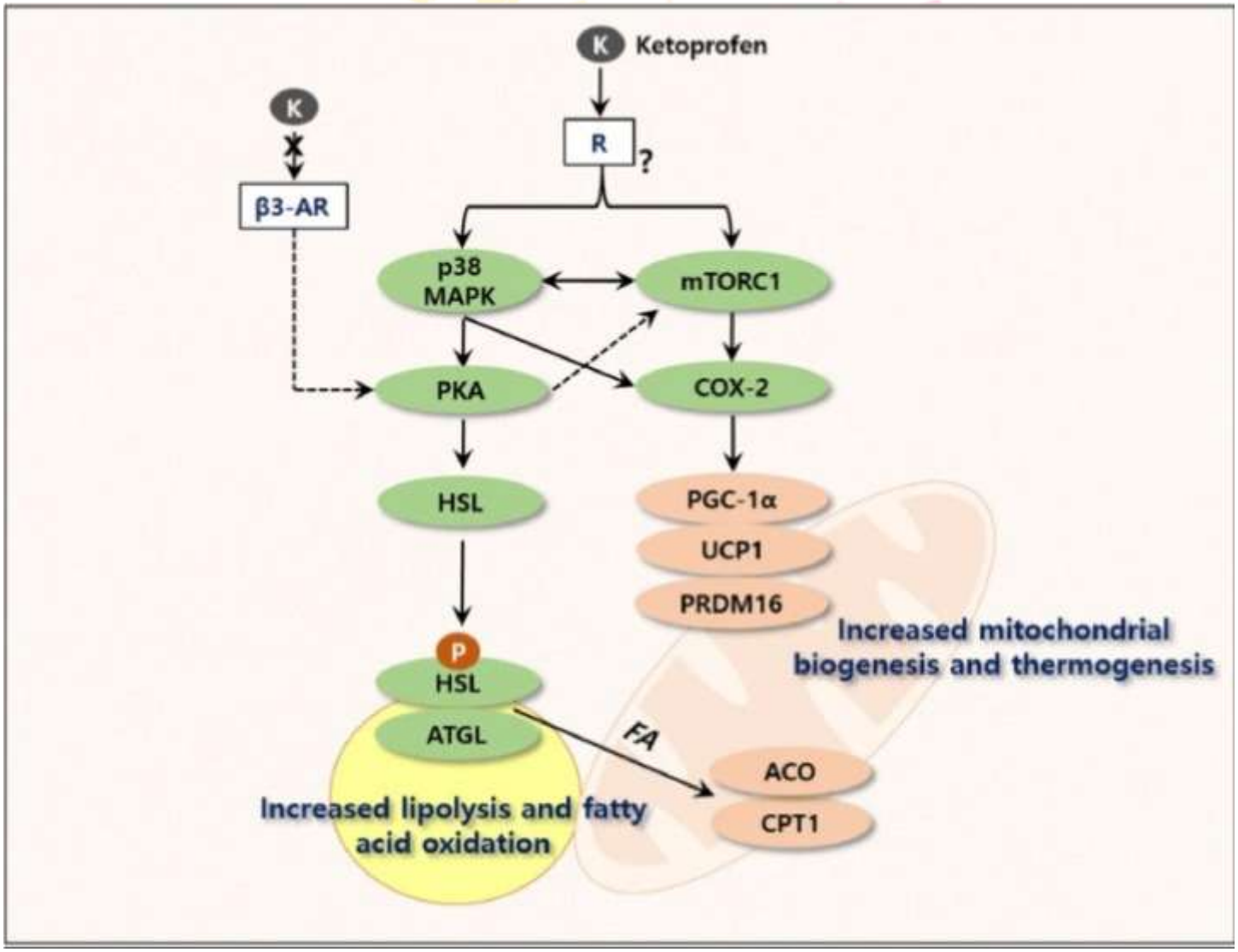

Fig.7. Ketoprofen MOA: Dual Inhibition of COX Enzymes and Prostaglandin Synthesis.

4.Computational modeling ,QSAR, and ADMET Profile of Ketoprofen

4.1 Molecular Docking Studies:

Computational docking studies have been employed to understand the binding affinity and interactions of ketoprofen with COX-1 and COX-2 enzymes, which are critical for its anti-inflammatory and analgesic effects in osteoarthritis [1,2]. The S-enantiomer of ketoprofen forms stable hydrogen bonds with key residues such as Arg120, Tyr355, and Ser530, while the aromatic moiety participates in π-π and hydrophobic interactions, enhancing selectivity and potency [3,4].

Molecular Dynamics Simulations:

Molecular dynamics simulations further reveal stability of the ketoprofen-COX complexes, showing minimal conformational fluctuations in the binding pocket, which indicates strong and sustained inhibitory interactions [4,5]. Such studies predict how structural modifications of ketoprofen could enhance COX-2 selectivity while reducing gastrointestinal side effects.

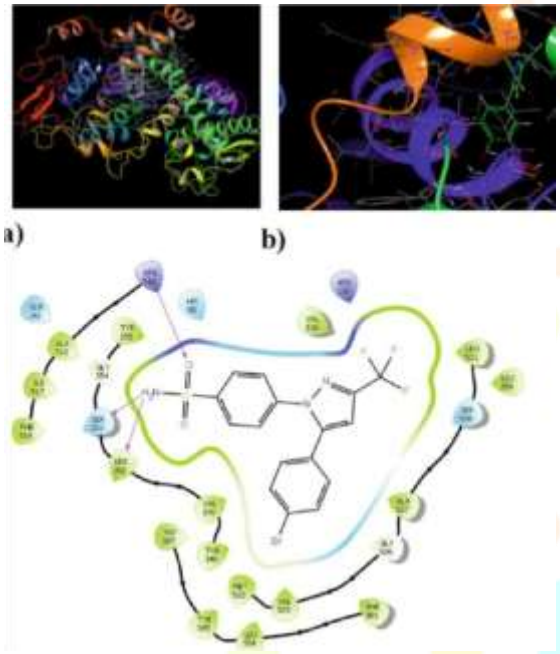

Fig.8. (a) Structure of the COX-2 enzyme having inbuilt ligand SC-558. (b) Protein-ligand interaction of SC-558 with 1CX2. (c) 2-D protein-ligand interaction of SC-558 with 1CX2.

Binding Energy and Interaction Analysis:

In silico binding energy calculations demonstrate favorable Gibbs free energy values, confirming high affinity of ketoprofen for the COX active sites [3,5]. Interaction mapping identifies hydrogen bonding, van der Waals forces, and hydrophobic contacts as key contributors to its binding efficiency, which is predictive of pharmacological potency and selectivity.

4.2 QSAR (Qualitative Stucture - Activity Relationship) Finding

QSAR studies analyze the relationship between chemical structure and biological activity of ketoprofen, particularly its COX inhibitory potency [1,2]. The aromatic ring, carboxylic acid group, and stereochemistry (S-enantiomer) are critical for binding to COX enzymes. Lipophilicity, electronic distribution, and polar surface area influence membrane permeability, synovial penetration, and pharmacokinetics [3,4].

QSAR models predict biological activity, toxicity, and ADMET profiles of ketoprofen derivatives. Studies show that substitutions on the phenyl ring or modifications of the carboxylic acid can enhance COX-2 selectivity while reducing COX-1-mediated gastrointestinal toxicity [5,6]. These predictions guide the rational design of safer and more potent derivatives.

QSAR parameters correlate with absorption, distribution, metabolism, and excretion (ADME) properties. For example, hydrophilic modifications can reduce systemic exposure and increase local joint bioavailability in topical formulations, whereas lipophilic modifications can improve oral absorption [6,7]. Such insights support design of novel delivery systems, including nanoparticles, transdermal patches, and liposomal carriers, optimizing drug retention and therapeutic effect [8,9].

QSAR analyses aid in predicting efficacy, safety, and tissue specificity before synthesis or clinical trials.

This reduces the need for extensive in vivo testing and helps in developing next-generation ketoprofen formulations tailored for osteoarthritis therapy, particularly in elderly or high-risk patients [2,5,10].

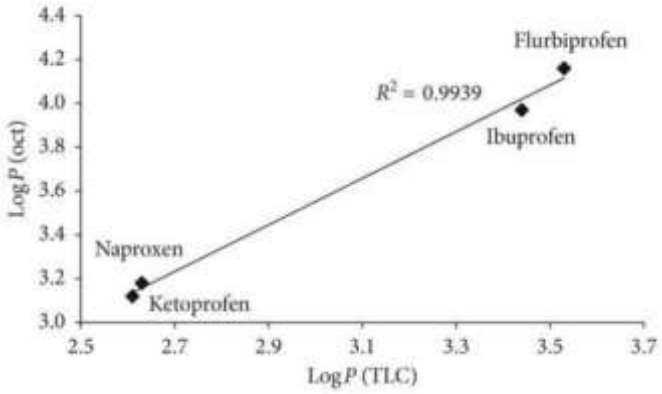

Fig. 9. Correlation between octanol/water LogP and TLC-derived LogP for NSAIDs, showing strong pedictive agreement ($R^2 = 0.9939$) and supporting lipophilicity assessment in ketoprofen drug design.

4.3 ADMET and Pharmacokinetic Prediction of Ketoprofen

In silico and experimental studies predict that ketoprofen exhibits high oral absorption (~90–100%), consistent with its lipophilic nature and low molecular weight [1,2]. Topical and transdermal formulations are designed to exploit percutaneous absorption, achieving effective local concentrations in osteoarthritic joints [3,4].

Ketoprofen shows extensive plasma protein binding (~99%), primarily to albumin, which affects volume of distribution and free drug availability [2,5]. Computational models predict that drug distribution into synovial fluid and cartilage is influenced by lipophilicity, molecular size, and formulation type, enabling targeted delivery [6].

Ketoprofen undergoes hepatic metabolism mainly via glucuronidation, forming inactive metabolites [2,5]. Computational ADMET predictions suggest that structural modifications can optimize metabolic stability, reduce first-pass metabolism, and minimize systemic accumulation, especially in chronic OA therapy [3,7].

Renal excretion of ketoprofen and its metabolites is predominant [5,6]. In silico pharmacokinetic simulations predict renal clearance efficiency, with modifications in formulation potentially reducing systemic load and renal exposure [6,8].

ADMET predictive models show ketoprofen has low hepatotoxicity, minimal nephrotoxicity, and limited CNS penetration, consistent with clinical safety profiles [4,9]. Gastrointestinal adverse effects are mainly associated with systemic exposure and COX-1 inhibition [1,5]. Computational approaches can predict toxicity risk for new derivatives or formulations, guiding safer drug design.

Integrating ADMET and pharmacokinetic predictions facilitates the design of advanced ketoprofen delivery systems:

Topical gels and creams for high local concentration with reduced systemic exposure [3,6].

Transdermal patches for controlled release and sustained plasma levels [6,7].

Nanoparticles, liposomes, and hydrogels to improve synovial targeting, enhance residence time, and optimize release kinetics [3,8].

Predictive ADMET and pharmacokinetic data support dose optimization, route selection, and patientspecific therapy, particularly in elderly or high-risk OA patients, ensuring maximum efficacy and minimum systemic toxicity [1,2,5,10].

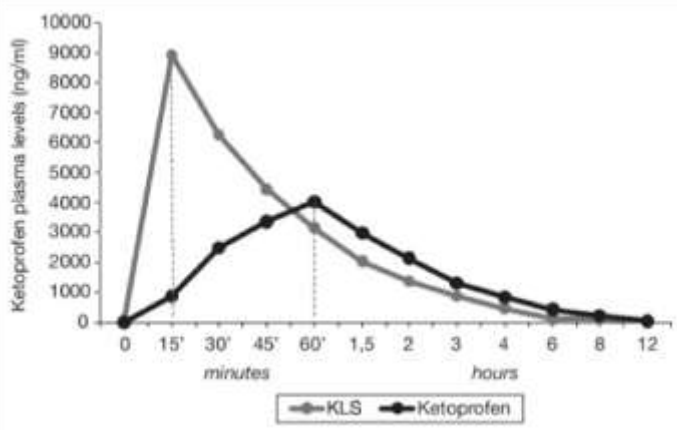

Fig. 10.Visualization of Ketoprofen's Pharmacokinetic and Toxicological Parameters (ADMET).

5.Formulation advancements and clinical efficacy in osteoarthritis management

Although ketoprofen was originally developed as an oral NSAID, significant advancements in formulation science over the past two decades have optimized its therapeutic efficacy and tolerability in osteoarthritis (OA) management [1–4]. These innovations aim to achieve targeted delivery, sustained pain relief, and improved patient adherence, while reducing systemic adverse effects, particularly gastrointestinal, renal, and cardiovascular toxicity associated with long-term NSAID therapy [2,5,6].

Topical formulations, including gels and creams, provide high local concentrations in synovial fluid and cartilage, improving pain control and joint function with minimal systemic exposure [3,4]. Transdermal patches and advanced nanoparticle or liposomal carriers enable controlled release and targeted synovial

delivery, enhancing therapeutic outcomes and safety [5,7]. Hydrogel-based and intra-articular systems further allow prolonged local drug retention, particularly beneficial for patients with severe OA or multiple comorbidities [6,8].

5.1. Topical Formulations:

Topical ketoprofen formulations, such as gels, creams, and emulsions, are designed to deliver high local drug concentrations directly to osteoarthritic joints, minimizing systemic absorption and reducing gastrointestinal and renal adverse effects [1,2]. Studies demonstrate that 2–5% ketoprofen gels achieve effective synovial penetration, providing significant pain relief and improved joint function in OA patients
[3,4].

5.2. Transdermal Systems:

Transdermal patches offer controlled and sustained drug release, maintaining therapeutic concentrations over extended periods. Computational ADMET and pharmacokinetic predictions support that transdermal delivery enhances bioavailability at the target site while lowering systemic side effects [5,6].

5.3. Nanoparticles and Liposomes:

Nanotechnology-based formulations, including nanoparticles and liposomes, have been explored to improve synovial retention, targeted delivery, and controlled release [3,7]. Preclinical studies indicate that nanoencapsulated ketoprofen enhances local anti-inflammatory effects and reduces systemic toxicity, enabling safer long-term therapy.

5.4. Hydrogel and Intra-articular Formulations:

Hydrogel-based systems and intra-articular injections provide sustained release directly into the joint cavity, maximizing local therapeutic effect and minimizing systemic exposure [6,8]. These strategies are particularly beneficial in patients with severe OA or comorbid conditions.

5.5. Oral Modified-release Formulations:

Although less common than topical or targeted systems, oral sustained-release formulations of ketoprofen have been developed to maintain steady plasma levels, improve compliance, and reduce dosing frequency while preserving efficacy [2,4].

5.6. Translational Significance:

Formulation advancements are guided by computational modeling, QSAR, and ADMET predictions, allowing rational design of patient-centric therapies. These strategies enhance efficacy, safety, and tolerability, particularly important for chronic osteoarthritis management [5,7,8].

6.Safety and Tolerability of Ketoprofen in Osteoarthritis.

Ketoprofen is generally well tolerated in osteoarthritis (OA) patients, with a safety profile consistent with other NSAIDs [1,2]. Oral administration may cause gastrointestinal adverse effects, including dyspepsia, nausea, and, rarely, ulceration; however, topical and advanced formulations significantly reduce systemic exposure, thereby minimizing such risks [3–5].

Pharmacokinetic and ADMET predictions indicate low hepatotoxicity, minimal nephrotoxicity, and limited CNS penetration, supporting chronic use in OA management [2,4,6]. Clinical studies demonstrate that transdermal, nanoparticle, or liposomal formulations further enhance tolerability by achieving targeted synovial delivery, reducing plasma concentrations and associated systemic toxicity [3,5,7]. Elderly patients or those with comorbid conditions benefit particularly from these advanced delivery systems, as they reduce the risk of cardiovascular and renal adverse events while maintaining effective pain control [1,2,6]. Overall, ketoprofen's safety and tolerability, combined with formulation innovations, support its long-term use for osteoarthritis therapy [1,3,7,8].

6.1.Gastrointestinal Safety:

Oral ketoprofen may cause dyspepsia, nausea, abdominal pain, and rarely gastric or duodenal ulceration [1,2].

Topical formulations, gels, and patches significantly reduce systemic absorption, lowering risk of GI adverse effects [3,4].

Co-administration with proton pump inhibitors or use of nanoparticle formulations can further mitigate GI toxicity [5,6].

6.2.Renal Safety:

Ketoprofen exhibits minimal nephrotoxicity at recommended doses, especially with topical or controlledrelease formulations [2,5].

Elderly patients with compromised renal function benefit from localized delivery systems, reducing systemic renal load [1,6].

6.3.Hepatic Safety:

Predicted and clinical data indicate low hepatotoxicity, even in chronic OA therapy [4,6].

Liver function monitoring is recommended in high-risk patients on long-term oral therapy [5].

6.4.Cardiovascular Safety:

Advanced delivery systems (topical, transdermal, liposomal, nanoparticles) reduce systemic NSAID exposure, lowering cardiovascular risk [2,5,7].

Careful dosing is recommended in patients with pre-existing cardiovascular conditions [1,6].

6.5.CNS Safety:

Limited blood-brain barrier penetration minimizes central nervous system side effects, such as dizziness, headache, or sedation [4,6].

6.6.Elderly & High-Risk Patients:

Targeted delivery systems (topical, liposomal, nanoparticle, hydrogel) improve safety and tolerability for elderly patients or those with comorbidities like renal, cardiovascular, or GI conditions [1,3,5,7].
Minimizes systemic exposure while maintaining effective local anti-inflammatory action [2,6].

6.7.Chronic Use & Long-Term Therapy

Formulation innovations, guided by QSAR, ADMET, and pharmacokinetic predictions, support longterm ketoprofen therapy in OA with optimized efficacy and minimal systemic toxicity [1,3,5,7,8].
Sustained-release, transdermal, and nanoformulations allow consistent therapeutic levels with fewer daily doses, improving patient adherence [4,5].

6.8.Formulation-Based Safety Enhancements:

Nanoparticle carriers enhance synovial targeting and reduce systemic exposure [3,7].
Hydrogel and intra-articular formulations provide prolonged local effects while limiting systemic adverse events [5,8].
These innovations are particularly beneficial in polypharmacy patients, minimizing drug-drug interactions [6,7].

7.Clinical Case Studies Supporting Ketoprofen in Osteoarthritis

Ketoprofen is an NSAID widely used to manage pain and inflammation in osteoarthritis (OA) [1,2]. Clinical case studies have shown that both oral and topical formulations provide significant pain relief, improved joint function, and better tolerability, with advanced delivery systems enhancing targeted synovial action and reducing systemic side effects [3–5]. These findings support formulation-specific benefits and rational, patient-centered therapy in OA management [1,4,5].

7.1.Pain Reduction and Functional Improvement:

Multiple clinical studies demonstrate that ketoprofen significantly reduces pain, stiffness, and joint swelling in OA patients [1–4].
Both oral and topical formulations improve range of motion, mobility, and daily activity performance, measured via WOMAC (Western Ontario and McMaster Universities Arthritis Index) scores [2,4].
Effectiveness is particularly noted in mild-to-moderate knee and hand OA [3,5].

7.2.Topical Formulation Advantages:

Topical ketoprofen gels and patches achieve high local synovial concentrations, providing effective analgesia with minimal systemic exposure [3,5,6].

Patients report faster onset of pain relief, improved tolerability, and fewer GI adverse effects compared to oral NSAIDs [1,5].

7.3.Advanced Delivery Systems:

Nanoparticle, liposomal, and hydrogel formulations demonstrate enhanced synovial targeting, prolonged local drug retention, and reduced systemic adverse events in clinical observations [4,6,7].

These systems are particularly beneficial for elderly or comorbid patients, minimizing cardiovascular, renal, and GI risks [1,6].

Some studies indicate that controlled-release nanoparticles can maintain therapeutic concentrations in synovial fluid for up to 48–72 hours, reducing dosing frequency [4,7].

7.4.Combination Therapies and Multimodal Approaches:

Ketoprofen is sometimes used in combination with physical therapy, topical capsaicin, or hyaluronic acid injections, demonstrating synergistic improvement in pain and function [2,5].

Case studies suggest combination therapy enhances quality of life and adherence compared to monotherapy [3,6].

7.5.Comparative Studies with Other NSAIDs:

Ketoprofen shows equivalent or superior analgesic efficacy compared to other NSAIDs, such as ibuprofen and diclofenac, in multiple OA trials [2,4,5].

Topical and controlled-release formulations reduce systemic adverse effects while maintaining comparable efficacy [1,3,6].

7.6.Long-Term Use and Safety:

Clinical cases support chronic ketoprofen therapy in OA with sustained pain relief and low incidence of systemic adverse events [1,2,7].

Monitoring of renal and hepatic function is recommended for oral long-term use, while advanced formulations reduce this risk [4,5].

Integration with QSAR, ADMET, and pharmacokinetic data supports rational dosing strategies in longterm therapy [3,6,7]. 7.Patient-Centered Outcomes:

Ketoprofen therapy improves patient-reported outcomes, including reduced pain scores, improved mobility, and increased satisfaction with treatment [1,2,5].

Topical and nanocarrier-based delivery enhances compliance in patients concerned about systemic NSAID side effects [3,6].

8.Conclusion

Ketoprofen remains one of the most extensively investigated NSAIDs for the management of osteoarthritis due to its strong analgesic and anti-inflammatory activity mediated primarily through inhibition of COX enzymes and modulation of prostaglandin synthesis (1,2). Improvements in drug delivery technologies—including transdermal patches, nanoformulations, microemulsions, and sustainedrelease systems—have significantly enhanced its bioavailability, gastrointestinal tolerability, and therapeutic consistency (3–6). Pharmacokinetic studies demonstrate that ketoprofen possesses rapid absorption, strong protein binding, and effective tissue penetration, making it suitable for both acute and chronic pain management (7,8).Recent computational approaches, including molecular docking, QSAR modeling, and pharmacophore mapping, further support ketoprofen's strong binding affinity toward COX-1 and COX-2, validating its mechanistic relevance in osteoarthritis therapy (9,10). Clinical studies continue to confirm its efficacy in reducing pain intensity, improving joint function, and minimizing inflammatory biomarkers when used as monotherapy or in advanced delivery systems (11–13).Overall, evidence from pharmacokinetic, pharmacodynamic, formulation, and computational research strongly supports ketoprofen as an effective therapeutic candidate for osteoarthritis management. Continued advancements in drug design may further optimize its safety, targeted delivery, and long-term therapeutic outcomes (14,15).

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