Submitted: 03 April, 2025 Accepted: 20 May, 2025 Published: 08 June, 2025 DOI:10.22514/sv.2025.078

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REVIEW

Acute pain management: the role of multimodal analgesia with a focus on dexketoprofen and tramadol hydrochloride fixed-dose combination in acute low back pain

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Abstract

Acute pain, such as moderate to severe low back pain, significantly impacts quality of life and is a leading cause of disability. Traditional pain management, often reliant on opioids, is facing scrutiny due to concerns about side effects, dependency and misuse. Multimodal analgesia, which combines different analgesics targeting various pain pathways, has emerged as a safer alternative to minimize opioid use. This narrative review focuses on the combination of dexketoprofen trometamol (a nonsteroidal anti-inflammatory drug) and tramadol hydrochloride (a centrally acting analgesic), which together target both peripheral and central pain mechanisms. Particular attention is given to the pharmacological properties of these agents and the results of key clinical trials, especially the Dexketoprofen TrometAmol aNd Tramadol HydrochloridE (DANTE) study. The DANTE study, a Phase IV clinical trial, demonstrated that the fixed-dose combination of dexketoprofen and tramadol significantly reduced pain intensity and improved functional outcomes in patients with acute low back pain. Furthermore, the combination showed a favorable safety profile comparable to that of single-agent treatments, with mild and manageable adverse events. This evidence suggests that the dexketoprofen–tramadol combination offers a more effective and well-tolerated alternative to traditional pain management strategies. By targeting multiple pain pathways simultaneously, this multimodal approach can enhance analgesic efficacy while reducing opioid reliance, representing a promising advance in the management of acute pain.

Keywords

Acute pain; Multimodal analgesia; Dexketoprofen; Tramadol; Low back pain; DANTE study; Pain management; Pharmacological treatment

1. Introduction

Acute pain is a significant clinical concern that can profoundly impact quality of life, leading to both physical discomfort and emotional distress [1]. It is typically defined as pain that arises suddenly in response to injury, surgery or illness and is usually of short duration, although it can vary in intensity from mild to severe [2]. Among the most common forms of acute pain, low back pain (LBP) stands out due to its high prevalence—affecting up to 80% of individuals at some point in their lives [3]. LBP is a leading cause of disability globally and poses a substantial burden on healthcare systems and workforce productivity [4]. As such, effective management of acute pain is essential, not only to alleviate immediate suffering but also to prevent long-term functional impairment [5]. Moderate to severe acute pain, particularly in conditions such as LBP, presents a therapeutic challenge. Conventional treatment often relies on opioids, which, while effective, are associated with significant drawbacks, including the risk of dependence, abuse and adverse effects [6]. The opioid crisis has underscored the urgent need for alternative approaches that provide effective pain control without the associated risks [7]. In this context, multimodal analgesia has emerged as a valuable strategy. By combining drugs with complementary mechanisms of action, this approach seeks to enhance analgesic efficacy while reducing reliance on opioids [8, 9]. Evidence suggests that multimodal regimens frequently outperform monotherapies in terms of both effectiveness and safety, particularly for moderate to severe pain [10]. This review focuses on one such multimodal combination: dexketoprofen trometamol, a fast-acting nonsteroidal anti-inflammatory drug (NSAID), and tramadol hydrochloride, a centrally acting analgesic with both

opioid and non-opioid properties. In addition, it provides further insights into the "Dexketoprofen Trometamol and Tramadol Hydrochloride Fixed-Dose Combination in Moderate to Severe Acute Low Back Pain: A Phase IV, Randomized, Parallel Group, Placebo, Active-Controlled Study (DANTE)" [11], which evaluated the efficacy and safety of this fixed-dose combination in patients with acute LBP. The findings underscore the clinical potential of this regimen within a multimodal framework, offering significant pain relief while potentially reducing the risks associated with higher-dose opioid therapy.

2. Methods

A narrative review approach was employed to capture the scope of literature on acute pain, multimodal analgesia, and LBP, following Scale for the Assessment of Narrative Review Articles (SANRA) guidelines for methodological transparency [12]. Although less rigid than a systematic review, applying quality criteria enhances the reliability of the synthesis. A search was conducted in PubMed, Scopus and Web of Science using keywords such as "acute pain", "low-back pain", "multimodal analgesia" and "tramadol-dexketoprofen", with Boolean operators (AND/OR). The exact search strings used were: PubMed: "acute pain" (Title/Abstract) OR "low back pain" (Title/Abstract) AND ("multimodal analgesia" (Title/Abstract)) AND ("tramadol-dexketoprofen" (Title/Abstract)); Scopus: TITLE-ABS-KEY ("acute pain" OR "low back pain") AND TITLE-ABS-KEY ("multimodal analgesia") AND TITLE-ABS-KEY ("tramadol-dexketoprofen"); Web of Science: TS = ("acute pain" OR "low back pain") AND TS = ("multimodal analgesia") AND TS = ("tramadol-dexketoprofen"). The inclusion and exclusion criteria are summarized in Table 1.

Using the SANRA scale ensured clarity regarding rationale, objectives, search processes and critical discussions [12]. Key information on retrieved studies, including study characteristics, methodological quality and outcomes relevant to acute pain and multimodal analgesia, was collected using a standardized form. Particular attention was paid to combined tramadol–dexketoprofen use. We did not perform a systematic review due to the significant heterogeneity among the included studies—particularly regarding inclusion criteria, outcome measures, and timing of evaluations—which made quantitative synthesis unfeasible; therefore, we opted for a narrative synthesis approach to more accurately reflect and interpret the available evidence. A total of 124 articles were retrieved. After screening titles and abstracts, 121 were considered potentially relevant. Following full-text evaluation, 38 studies met the inclusion criteria and were included in the final synthesis. The selection process is visually summarized in Fig. 1 (PRISMA-style flow diagram).

Data were organized into themes, including:

(1) Acute pain and its impact
(2) Multimodal analgesia in acute pain management
(3) Key pharmacological agents in multimodal analgesia
(4) DANTE study insights
(5) Mechanisms and synergy of dexketoprofen and tramadol
(6) Clinical implications and opioid-sparing strategies
(7) Future directions in acute pain management

3. Acute pain and its impact

Acute pain arises from injury or tissue damage and typically resolves once the underlying cause is addressed. Unlike chronic pain, it is generally short-lived and serves a protective function, warning against further harm [13]. Post-surgical, trauma-induced or musculoskeletal acute pain may vary by etiology but shares the potential to disrupt daily function and mental well-being [14]. In the very large majority of cases, it has an inflammatory process at the base [15–17].

3.1 Central and peripheral mechanisms

Nociceptive pain is mediated by peripheral nociceptors responding to tissue damage, while neuropathic pain stems from injury to the nervous system itself [18]. Central sensitization, wherein the spinal cord and brain amplify pain signals, can transition acute pain to chronic [19]. Addressing both peripheral and central pathways is vital for optimal relief and prevention of chronicity, highlighting the importance of multimodal approaches [20].

3.2 Acute low back pain

Acute LBP is a leading cause of disability, with up to 80% of adults experiencing it at some point [21]. It often arises from muscle strains, ligament sprains, or disc issues and disproportionately affects individuals aged 30 to 50 [22]. Acute LBP imposes a heavy societal burden, reflected in work absenteeism, healthcare costs, and potential progression to chronic pain [4, 23]. Mechanical factors (*e.g.*, disc herniation) and inflammatory processes can compress or irritate spinal nerves, while psychological elements (*e.g.*, fear-avoidance behaviors) exacerbate pain and hinder recovery [24]. Addressing these

TABLE 1. Inclusion and exclusion criteria for selecting article for this narrative review.

Inclusion Criteria	Exclusion Criteria
Articles published in English (2000–2025)	Non-English articles
Studies involving acute LBP managed with multimodal analgesia	Studies not related to acute LBP or multimodal analgesia
Original research, reviews and meta-analyses	Commentaries and editorials (unless theoretically relevant)
Focus on pharmacological strategies, especially tramadol-dexketoprofen	Studies lacking therapeutic focus or unrelated pharmacological agents

LBP: low back pain.

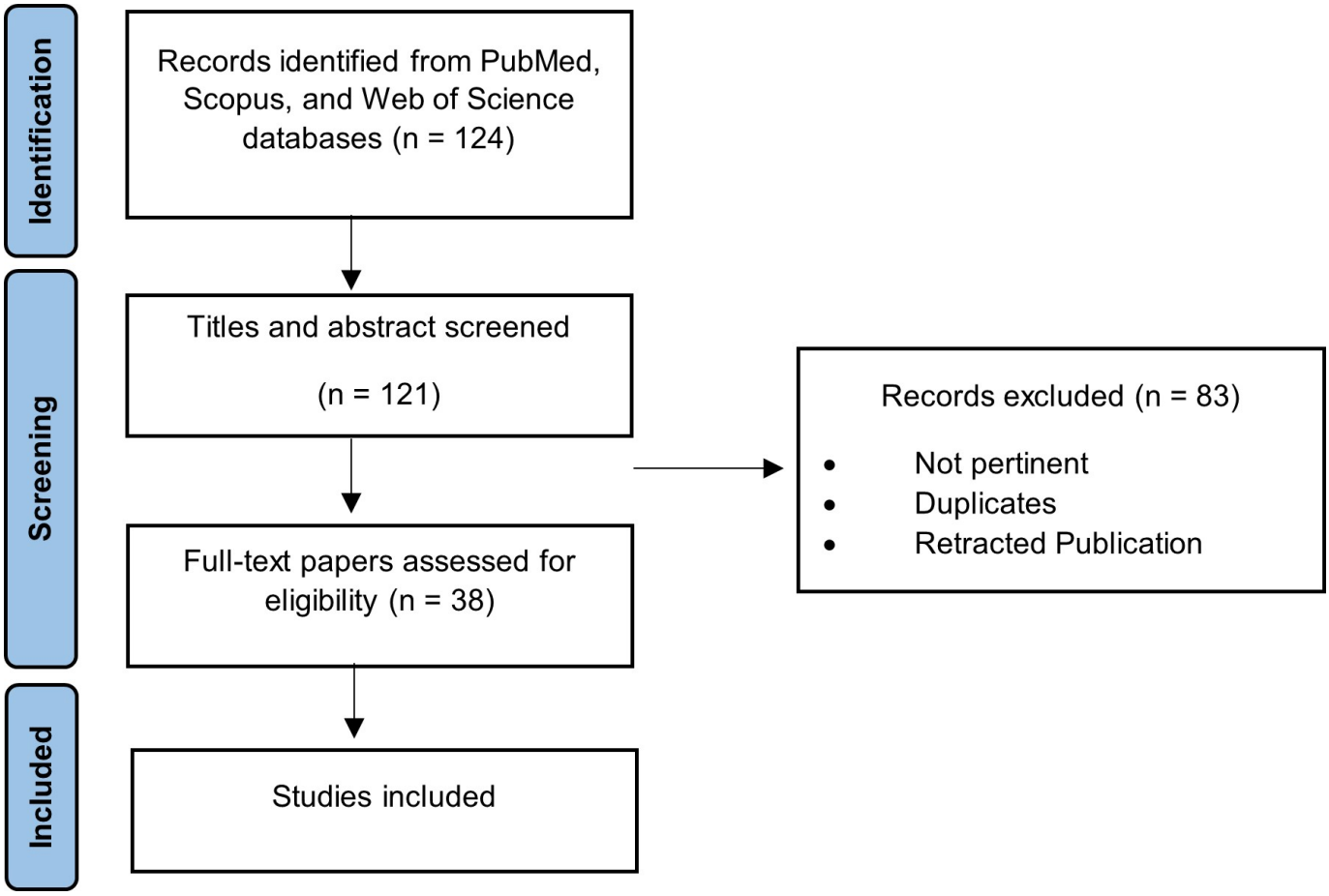

FIGURE 1. Literature search and selection flowchart.

multidimensional factors is crucial for successful LBP treatment and preventing long-term disability. Age, occupation and lifestyle (*e.g.*, prolonged sitting, heavy lifting) are significant risk factors [25]. Additional contributors include obesity, smoking, poor posture and psychosocial stressors [26]. Recognizing these factors is essential in devising comprehensive management plans.

4. Multimodal analgesia in acute pain management

Multimodal analgesia involves combining different classes of analgesic agents to target various pain mechanisms at both peripheral and central levels. By leveraging synergistic effects, this approach aims to optimize pain relief while minimizing the adverse effects often associated with single-agent therapy. The modern emphasis on multimodal strategies arose in part from the opioid crisis, underscoring the need for alternatives that reduce opioid misuse and dependence [27, 28]. When drugs acting on distinct pathways are used together, the overall effect can exceed what any one agent could achieve alone [29].

4.1 Benefits of multimodal analgesia

4.1.1 Enhanced pain control

Combining analgesics that act on different pain pathways often produces better relief for moderate to severe pain compared to monotherapy [30].

4.1.2 Reduced opioid use

Opioid analgesics carry significant risks, including sedation, respiratory depression and misuse potential [31]. Multimodal approaches can lower the required opioid dose, decreasing these risks while maintaining adequate pain control [32].

4.1.3 Targeting peripheral and central pathways

Pain can involve both peripheral tissue injury and central sensitization. By addressing both, multimodal therapy not only improves pain intensity but also helps restore function [33].

4.2 Common components of multimodal analgesia

4.2.1 Nonsteroidal anti-inflammatory drugs (NSAIDs)

Drugs like ibuprofen, diclofenac or dexketoprofen reduce inflammation by inhibiting cyclooxygenase (COX) enzymes, making them effective for nociceptive pain [34].

4.2.2 Paracetamol

Effective for mild to moderate pain, often combined with NSAIDs or opioids to boost analgesia and reduce opioid consumption [35].

4.2.3 Opioids

Still used for acute severe pain, but multimodal regimens aim to minimize their dosage to lessen dependence and side effects [36].

4.2.4 Gabapentinoids (gabapentin, pregabalin)

These modulate central pain pathways, and are especially useful for neuropathic or mixed pain [37].

4.2.5 Local anesthetics (lidocaine, bupivacaine)

Often used in regional blocks, providing localized pain relief with fewer systemic effects [38].

4.2.6 Corticosteroids

Reduce inflammation and can be helpful for musculoskeletal or radicular pain [39].

4.2.7 Adjuvant Therapies

Adjuvants such as antidepressants (*e.g.*, Serotonin and norepinephrine reuptake inhibitors (SNRIs)) and anticonvulsants also play roles in certain acute or chronic pain contexts [18].

By combining these agents, multimodal regimens typically improve patient outcomes, reduce adverse effects and lower opioid consumption [40, 41].

5. Key pharmacological agents in multimodal analgesia

5.1 Dexketoprofen trometamol

Dexketoprofen trometamol is a potent NSAID, the active enantiomer of ketoprofen, with rapid absorption and high bioavailability. It selectively inhibits COX-1, reducing the production of pro-inflammatory prostaglandins and exerting anti-inflammatory, analgesic and antipyretic effects [42, 43]. Compared to non-selective NSAIDs, dexketoprofen salt often has fewer gastrointestinal side effects [44]. A randomized controlled trial showed dexketoprofen effectively manages acute musculoskeletal pain, post-surgical pain and especially acute LBP [45]. Its rapid onset and short half-life make it particularly suitable for acute pain scenarios. European guidelines endorse dexketoprofen for moderate to severe pain, noting its favorable safety profile and efficacy in acute conditions [46].

5.2 Tramadol hydrochloride

Tramadol is a centrally acting analgesic that exerts both opioid and non-opioid effects. It acts as a weak agonist at μ-opioid receptors and inhibits the reuptake of serotonin and norepinephrine, thereby modulating pain transmission at the level of the spinal cord [47]. Common side effects include nausea, dizziness and constipation [48]. However, tramadol generally has a lower risk of abuse and respiratory depression than traditional opioids [49]. Studies indicate that tramadol significantly reduces pain intensity and improves function, especially when combined with NSAIDs or other non-opioid agents [39, 50].

6. Mechanisms of action and synergy of dexketoprofen and tramadol

Dexketoprofen reduces peripheral inflammation and nociceptive signaling by inhibiting prostaglandin production [45], while tramadol modulates pain centrally through weak μ-opioid receptor agonism and serotonin-norepinephrine reuptake inhibition [51]. By addressing both peripheral and central pathways, the combination of the two drugs can deliver robust analgesia [52]. Tramadol's lower affinity for μ-opioid receptors also translates to fewer opioid-related side effects, and its synergy with dexketoprofen can lead to faster, more effective relief while limiting the need for high opioid doses [53].

6.1 Dexketoprofen's role in acute pain

The anti-inflammatory effect of dexketoprofen is particularly valuable in acute pain conditions, such as musculoskeletal injuries, acute LBP and post-surgical pain, where inflammation significantly amplifies pain intensity. Compared to some other NSAIDs, dexketoprofen often has a favorable side effect profile, making it a suitable choice for managing acute pain [54].

6.2 Tramadol's central effects on pain modulation

Due to its centrally acting analgesic properties and inhibition of serotonin and norepinephrine reuptake [55], tramadol enhances descending pain modulation pathways, improving endogenous pain control at the spinal cord and brainstem, and addressing both nociceptive and neuropathic components of acute LBP [56].

6.3 Synergy between dexketoprofen and tramadol

When dexketoprofen and tramadol are combined, they produce synergistic analgesic effects by targeting both peripheral and central mechanisms of pain [52]. This dual approach leads to faster, more robust pain relief than either drug alone [57]. Clinical data indicate that patients receiving both agents may experience a quicker onset of analgesia, greater overall pain reduction, and enhanced functional recovery in acute pain scenarios [58].

7. DANTE study insights

The DANTE (Dual Analgesic Therapy in Non-Surgical Acute Pain) study was a Phase IV, randomized, parallel-group, placebo- and active-controlled trial examining a fixed-dose combination (FDC) of dexketoprofen trometamol (25 mg) and tramadol hydrochloride (50 mg) in moderate to severe acute LBP [59]. The study included adults (18–75) with acute LBP (onset $<$7 days, numeric rating scale (NRS) $\geq$4). Exclusion criteria included peptic ulcer disease, hypersensitivity to NSAIDs or opioids, and significant comorbidities. The FDC was administered twice daily for up to 7 days. Comparison groups received either placebo or an active control (*e.g.*,

tramadol alone). Controls which included both placebo and an active comparator (single-agent therapy) strengthened the study's validity, allowing the assessment of efficacy beyond placebo effects and, in comparison, to standard care. The results of the DANTE study are summarized in Table 2.

8. Clinical implications and opioid-sparing strategies

The DANTE study significantly advanced our understanding of FDC therapies for acute pain management [59]. Specifically, the study investigated an FDC composed of an opioid and a non-opioid at a fixed ratio. Findings showed that such combinations can deliver pain relief on par with higher-dose monotherapy while reducing opioid-related side effects such as nausea, sedation and constipation. DANTE's results suggest that clinicians can incorporate FDCs early in the treatment of moderate to severe acute pain, helping control pain while curbing opioid consumption. This approach is particularly relevant given concerns about opioid overuse and its associated harms. By offering strong analgesia without excessive opioid dosing, FDCs can bolster existing pain management protocols that prioritize safety and efficacy. FDCs can simplify treatment regimens, which is crucial in fast-paced environments like emergency departments or postoperative units. The streamlined nature of an FDC—combining two analgesics into a single formulation—reduces medication errors and enhances patient adherence [60]. This benefit extends to outpatient care, where patients may find it easier to manage one combined medication rather than multiple separate drugs. Older adults often have heightened sensitivity to opioids, facing risks such as confusion, falls and respiratory depression [61]. FDCs with lower opioid content can provide adequate pain relief while minimizing these complications. Nonetheless, clinicians must monitor renal or hepatic function, which may affect drug metabolism. Those with gastrointestinal, renal or cardiovascular issues require careful selection of NSAIDs and opioids. The NSAID component in an FDC should be chosen with caution if the patient has a history of ulcers or hypertension [62]. In individuals at risk of relapse or misuse, selecting an FDC with minimal opioid content is crucial [63]. Clinicians may also consider non-pharmacological interventions or additional safeguards to prevent misuse.

8.1 Advantages of fixed-dose combinations in clinical settings

FDCs can streamline pain management by consolidating multiple medications into a single formulation [64]. This reduces the complexity of dosing schedules, helping patients adhere to their treatment more easily. Such simplification is crucial in both hospital and outpatient settings, where errors or confusion in managing multiple medications can compromise patient safety. When patients face fewer pills and simpler regimens, adherence tends to improve. The DANTE study showed that patients on FDCs were more likely to take their medication correctly and achieve satisfactory pain relief [59]. This convenience may also reduce the potential for misuse, as patients manage fewer separate prescriptions. Although the initial cost of an FDC can be higher than single-agent formulations, overall healthcare expenses may decrease through reduced opioid use, fewer side effects and fewer hospital readmissions. By minimizing complications and shortening recovery times, FDCs can provide cost savings for healthcare systems in the long run [65]. In addition to its clinical efficacy, the dexketoprofen–tramadol FDC may offer favorable cost-effectiveness compared to higher-dose opioid regimens, as previously hypothesized [17, 66]. However, no specific data or dedicated analyses are currently available exploring this aspect. Another potential advantage is that the FDC is widely available in various markets, particularly in Europe and parts of Asia, facilitating its integration into clinical practice.

TABLE 2. Results of the DANTE study exploring the FDC for acute LBP.

Outcome category	Findings
Primary and Secondary Outcomes	• Pain Intensity: Measured by the Numeric Rating Scale (NRS) • Functional Improvement: Assessed via the Roland-Morris Disability Questionnaire and Oswestry Disability Index • Adverse Events: Monitored to evaluate safety
Efficacy of the Fixed-Dose Combination	• The FDC group showed significantly greater pain reduction than placebo ($p < 0.001$), with a mean NRS decrease of 5.2 points *vs.* 2.1 points in the placebo group • Functional improvement was also notably higher in the combination group compared to placebo ($p < 0.01$) • Compared to tramadol alone, the combination therapy demonstrated a faster onset of action and better functional scores ($p < 0.05$)
Safety Profile	• Adverse events were generally mild and included gastrointestinal issues (*e.g.*, nausea, dyspepsia) and some central nervous system effects (*e.g.*, dizziness) • Overall incidence was similar to that seen with tramadol alone, with no unexpected safety concerns
Risk-Benefit Analysis	• The combination provided rapid, effective pain relief with an acceptable safety profile, supporting its use as a multimodal option for acute low back pain. Given rising concerns about opioid misuse, this combination proved to be a safer alternative to high-dose opioids

8.2 Alternative multimodal analgesic strategies in acute pain management

As previously demonstrated, this approach enhances pain relief while minimizing opioid requirements and associated risks. Below is an overview of various multimodal analgesic strategies and how dexketoprofen–tramadol compares to other combinations.

8.3 Comparing dexketoprofen and tramadol to other multimodal combinations

8.3.1 Dexketoprofen and tramadol

Dexketoprofen and tramadol complement each other by targeting peripheral and central pain mechanisms. The DANTE study found that combining these two agents offers superior analgesia versus monotherapy and reduces opioid-related side effects [59].

8.3.2 Acetaminophen and NSAIDs

This common combination tackles pain centrally (acetaminophen) and peripherally (NSAIDs), providing effective relief for moderate acute pain [67]. While generally well-tolerated, prolonged use can pose risks such as hepatotoxicity (with high-dose acetaminophen) or gastrointestinal bleeding (with NSAIDs).

8.3.3 Opioids and gabapentinoids

In severe acute pain (*e.g.*, post-surgical), combining opioids (morphine, hydromorphone) with gabapentinoids (gabapentin, pregabalin) can be beneficial [68]. Gabapentinoids reduce central sensitization, aiding in neuropathic or mixed pain. However, sedation, dizziness, and cognitive impairment can increase when these agents are used together, especially in older adults.

To provide a more comprehensive perspective, Table 3 outlines a comparison between different multimodal analgesic strategies used in the management of acute LBP. It includes both fixed-dose and loose combinations, with an evaluation of their mechanisms, benefits, limitations and potential applications.

9. Future directions in acute pain management

On the topic of multimodal analgesia, there are several ongoing studies and research. We have summarized the most important in three principal directions.

9.1 Developing new combination therapies

Researchers are exploring novel agents and biologics to enhance pain control, particularly in inflammatory and post-surgical settings [69]. Combinations of local anesthetics, corticosteroids or gabapentinoids with established analgesics are being tested to reduce opioid needs while preserving or improving outcomes [70].

9.2 Personalized pain management

Advances in pharmacogenomics enable tailoring of analgesic regimens to individual genetic profiles, potentially improving efficacy and reducing adverse effects [71–73]. Identifying polymorphisms in drug-metabolizing enzymes or opioid receptors can guide clinicians in customizing pain treatments.

9.3 Potential improvements in formulations

Emerging technologies in drug delivery and personalized medicine are poised to significantly enhance the clinical application of multimodal analgesia—particularly the dexketoprofen–tramadol combination—by optimizing efficacy, minimizing side effects, and improving patient adherence.

9.3.1 Extended-release formulations

These can offer sustained analgesia in acute pain management, potentially reducing the frequency of dosing and improving adherence by providing consistent pain relief with fewer dosing intervals and minimizing peaks and troughs in pain control [74, 75]. Future FDCs of dexketoprofen and tramadol in extended-release form may help maintain consistent therapeutic levels over time, particularly useful in outpatient settings.

TABLE 3. Comparative summary of multimodal analgesic combinations for acute LBP.

Combination Type	Example Agents	Mechanisms Targeted	Advantages	Limitations
Fixed-Dose Combination (FDC)	Dexketoprofen + Tramadol	Peripheral + Central	Simplified regimen, enhanced compliance, opioid-sparing	Limited flexibility in dosing; fixed ratios may not suit all patients
Loose Combination	Ibuprofen + Acetaminophen	Peripheral + Central	Widely used, cost-effective, well-studied	Risk of GI/hepatic toxicity with prolonged use
Opioid + Gabapentinoid	Morphine + Pregabalin	Central (opioid + α2-δ subunit)	Effective for severe or mixed pain types	Sedation, dizziness, cognitive impairment, abuse risk

GI: Gastrointestinal.

9.3.2 Transdermal patches

Transdermal patches offer a steady release of medication without gastrointestinal side effects, though skin irritation and delayed onset may occur [76]. Transdermal systems incorporating the dexketoprofen–tramadol combination could enable non-invasive, controlled drug delivery, avoiding first-pass metabolism and reducing gastrointestinal side effects. These systems may benefit patients with LBP who have difficulty tolerating oral medications. Transdermal tramadol delivery could be a significant innovation in pain management, offering sustained analgesia with improved patient compliance. Due to its favorable molecular weight and lipophilicity, tramadol is a suitable candidate for transdermal absorption. Ongoing research and advancements in permeation enhancers and patch technology will be necessary to develop this potential strategy.

9.3.3 Nanomedicine and nanoparticles

Nanomedicine and nanoparticles offer a promising strategy to deliver analgesics directly to pain sites, thereby reducing systemic exposure and enhancing therapeutic precision [77, 78]. This approach may also be applied to the dexketoprofen–tramadol combination, using natural or synthetic polymer-based carriers to enable extended-release formulations and improve efficacy while minimizing adverse effects.

9.3.4 Co-crystallization

Co-crystallization of drugs represents another cutting-edge strategy in pharmaceutical development, enabling the combination of two or more active ingredients within a single crystalline structure. This method can enhance the pharmacokinetic profiles and stability of each compound, potentially improving their solubility, bioavailability and therapeutic synergy [79]. By allowing for lower dosages of each component, co-crystallized formulations may also reduce the incidence of side effects while promoting better patient adherence through simplified dosing regimens.

9.3.5 Implantable devices

Implantable devices, including neuromodulation systems such as peripheral nerve stimulation, have recently gained popularity as adjunctive analgesic modalities in acute pain management [80]. These devices represent a valuable component of multimodal strategies, enabling continuous local or regional analgesia while reducing the need for systemic opioid use [81, 82].

Fig. 2 provides a visual summary of the pharmacological mechanisms of dexketoprofen and tramadol, their synergistic interaction in multimodal analgesia, and future directions in acute pain management.

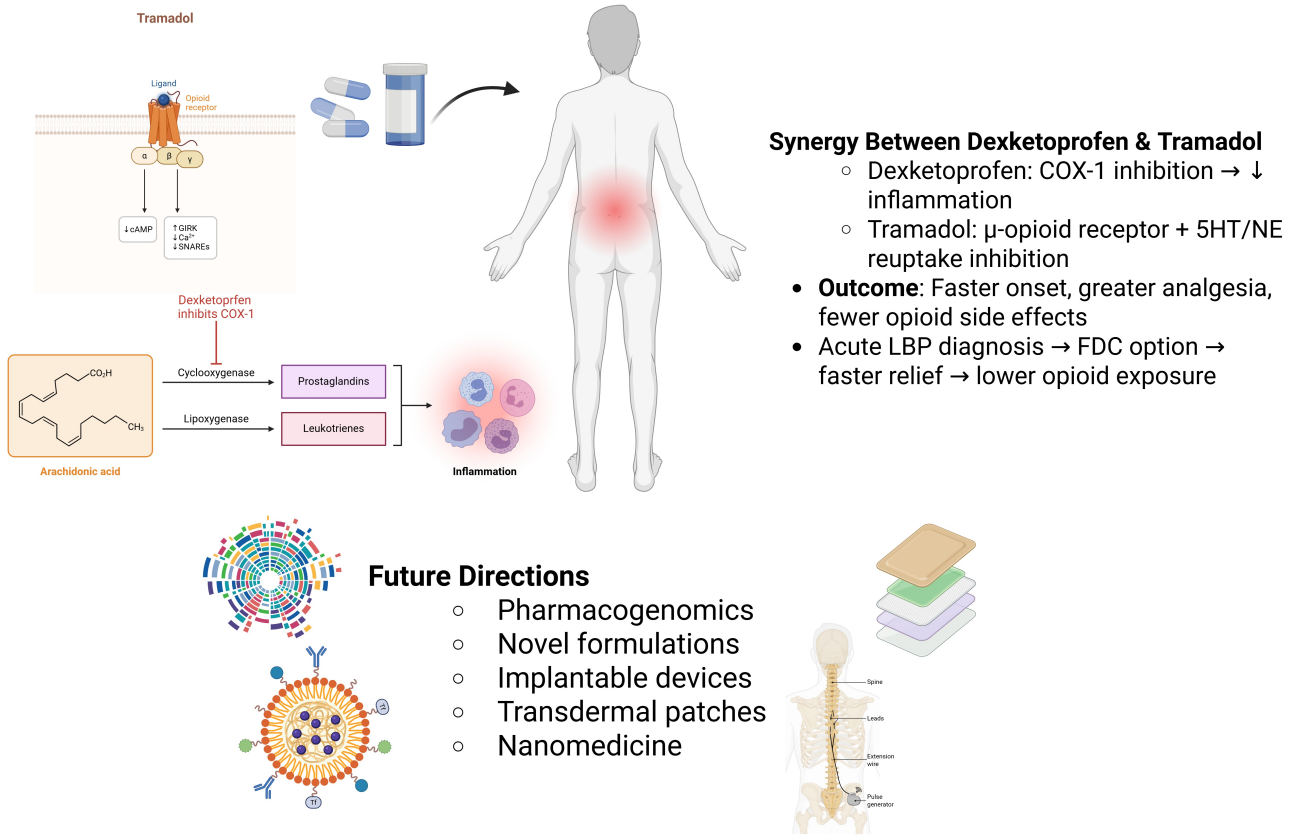

FIGURE 2. Synergistic mechanisms and future perspectives of Dexketoprofen–Tramadol combination in acute pain management. COX: cyclooxygenase; LBP: low back pain; FDC: fixed-dose combination; 5HT/NE: 5-Hydroxytryptamine (Serotonin)/Norepinephrine.

10. Limitations

Despite the encouraging findings presented in this narrative review, several limitations must be acknowledged. First, as a narrative review rather than a systematic review or meta-analysis, the study is inherently limited by potential selection bias and the absence of a standardized data synthesis protocol. The inclusion of heterogeneous studies with varying designs, patient populations, dosing regimens, and outcome measures—particularly in the context of acute low back pain—limits the generalizability and comparability of the evidence. Second, although the DANTE study provided robust clinical data supporting the efficacy and safety of the dexketoprofen–tramadol FDC, it remains a single-Phase IV trial. Broader validation through additional randomized controlled trials (RCTs) in diverse patient populations and real-world clinical settings is needed to confirm its generalizability. Third, long-term safety data, especially regarding repeated use of this FDC in recurrent acute pain episodes, are lacking. Finally, while this review highlights potential cost-effectiveness and improved adherence associated with FDC, no formal pharmacoeconomic analyses were available, and future studies should aim to quantify the economic and healthcare resource implications of such strategies.

11. Conclusions

Fixed-dose combinations, as highlighted by the DANTE study, simplify regimens, boost adherence, and may reduce overall costs. They fit into broader multimodal analgesic strategies that seek to limit opioid use and deliver robust pain relief by targeting multiple pathways. Ongoing research in drug delivery systems, pharmacogenomics, and personalized medicine holds promise for refining acute pain management, ensuring safer, more effective treatments tailored to individual patient needs.

ABBREVIATIONS

LBP, Low Back Pain; NSAID(s), Nonsteroidal Anti-Inflammatory Drug(s); COX, Cyclooxygenase; SANRA, Scale for the Assessment of Narrative Review Articles; FDC, Fixed-Dose Combination; DANTE, Dexketoprofen TrometAmol aNd Tramadol HydrochloridE; NRS, Numeric Rating Scale; SNRIs, Serotonin-Norepinephrine Reuptake Inhibitors; RCT(s), Randomized Controlled Trial(s); GI, Gastrointestinal; 5HT/NE, 5-Hydroxytryptamine (Serotonin)/Norepinephrine.

AVAILABILITY OF DATA AND MATERIALS

The data used for this publication are a common heritage, in every scientific library. In any case, they would be available to the reader, by the corresponding author on reasonable request.

AUTHOR CONTRIBUTIONS

GV and MLGL—are responsible for ideation, literature research and first draft. GF and MM—have selected the publications to be included and revised the initial draft. All the authors have reviewed and approved the final version of the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

ACKNOWLEDGMENT

We thank John Shaw and David Michael Abbott for their assistance with the English revision. We are also grateful to the Fondazione Paolo Procacci for the support in the publication process.

FUNDING

This research received no external funding.

CONFLICT OF INTEREST

The authors declare no conflict of interest. Giacomo Farì is serving as one of the Editorial Board members of this journal. We declare that Giacomo Farì had no involvement in the peer review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to GI.

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How to cite this article: Giustino Varrassi, Giacomo Farì, Marco Mercieri, Matteo Luigi Giuseppe Leoni. Acute pain management: the role of multimodal analgesia with a focus on dexketoprofen and tramadol hydrochloride fixed-dose combination in acute low back pain. Signa Vitae. 2025; 21(6): 1-10. doi: 10.22514/sv.2025.078.