International Journal of Trend in Scientific Research and Development (IJTSRD)
Volume 10 Issue 4, Jul-Aug 2026 Available Online: www.ijtsrd.com e-ISSN: 2456 – 6470

Next-Generation Drug Delivery Systems for Chronic Pain: Moving Beyond Conventional NSAID Therapy

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ABSTRACT

Chronic pain is one of the leading causes of disability worldwide and significantly affects patients' quality of life. Non-steroidal anti-inflammatory drugs (NSAIDs) remain the first-line pharmacological treatment for inflammatory and musculoskeletal pain due to their analgesic and anti-inflammatory effects. However, prolonged NSAID therapy is associated with gastrointestinal toxicity, cardiovascular complications, renal impairment, frequent dosing, and poor patient compliance. These limitations have stimulated the development of advanced drug delivery systems that provide sustained, targeted, and controlled drug release. Recent research highlights the potential of biodegradable microspheres, nanoparticles, liposomes, hydrogels, injectable depot formulations, and nanofibers to enhance therapeutic efficacy while minimising systemic adverse effects. This review summarises the limitations of conventional NSAID therapy, discusses recent advances in novel delivery platforms, and compares conventional and emerging treatment strategies for chronic pain. These innovations are expected to improve patient adherence and support personalised pain management.

KEYWORDS: *Chronic pain, NSAIDs, Microspheres, Injectable depot, Sustained release, Nanoparticles, Drug delivery, Biodegradable polymers.*

How to cite this paper: Ms. Prerana Bambale | Mr. Rajratan Thorat | Ms. Madhuri Dhure "Next-Generation Drug Delivery Systems for Chronic Pain: Moving Beyond Conventional NSAID Therapy" Published in International Journal of Trend in Scientific Research and Development (ijtsrd), ISSN: 2456-6470, Volume-10 | Issue-4, August 2026, pp.138-140, URL: www.ijtsrd.com/papers/ijtsrd141975.pdf

IJTSRD141975

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INTRODUCTION

Chronic pain persists for more than three months and affects approximately one in five adults globally. It is commonly associated with rheumatoid arthritis, osteoarthritis, lower back pain, neuropathic disorders, and inflammatory diseases. Chronic pain not only reduces physical function but also imposes substantial socioeconomic and healthcare burdens.[1,2]

NSAIDs remain the cornerstone of chronic inflammatory pain management because they inhibit cyclooxygenase (COX-1 and COX-2) enzymes, thereby reducing prostaglandin synthesis[3,4]. Despite their effectiveness, long-term administration often results in gastrointestinal ulceration, cardiovascular risks, nephrotoxicity, and reduced patient adherence due to repeated dosing. Consequently, researchers are increasingly focusing on innovative drug delivery systems capable of sustained, site-specific drug release [5].

Conventional NSAID Therapy

Conventional NSAIDs such as diclofenac, ibuprofen, naproxen, ketoprofen, celecoxib, meloxicam, and etoricoxib effectively reduce inflammation and pain through inhibition of prostaglandin synthesis.

Advantages

- Rapid onset of analgesia
- Effective anti-inflammatory action
- Widely available
- Cost-effective

Limitations

- Gastrointestinal bleeding
- Gastric ulceration
- Cardiovascular complications
- Renal toxicity
- Frequent dosing
- Poor patient compliance
- Systemic adverse effects

These drawbacks have motivated researchers to develop controlled-release formulations with improved safety profiles[6,7].

Recent Advances in Chronic Pain Therapy

Modern pharmaceutical research has shifted toward advanced drug delivery technologies that provide localised, sustained, and targeted drug release [8].

Major emerging systems include:

- Biodegradable injectable microspheres
- Polymeric nanoparticles
- Liposomes
- Solid lipid nanoparticles
- Hydrogels
- Nanoemulsions
- Polymeric micelles
- Transdermal nanovesicles
- Long-acting depot injections

These delivery systems improve drug stability, reduce dosing frequency, decrease systemic toxicity, and enhance patient compliance[9,10].

Conventional Therapy versus New Drug Delivery Systems

Parameter	Conventional NSAIDs	Advanced Drug Delivery
Drug release	Immediate	Sustained/controlled
Dosing frequency	Multiple daily doses	Weekly to monthly
Patient compliance	Moderate	High
GI toxicity	High	Reduced
Plasma fluctuation	Significant	Minimal
Drug targeting	No	Yes
Therapeutic duration	Short	Long
Clinical outcome	Symptomatic relief	Prolonged pain control

Recent Studies

Year	Major Finding
2024	Novel therapies including nanomedicine, stem cells, gene therapy, and cannabinoids are expanding chronic pain treatment options.
2025	Engineered nanocarriers showed improved targeting and prolonged analgesic activity compared with conventional NSAIDs.
2025	Sustained-release NSAID formulations manufactured by hot-melt extrusion, spray drying, and 3D printing improved release control and patient compliance.
2026	Injectable nanocarriers and hydrogels demonstrated prolonged pain relief with lower systemic toxicity in preclinical studies.

Future Perspectives

Future chronic pain therapy is expected to emphasise:

- Personalised medicine
- Long-acting injectable depots
- Biodegradable polymeric microspheres
- Targeted nanocarriers
- Stimuli-responsive drug delivery
- Combination therapies
- AI-assisted formulation development

These technologies may reduce dosing frequency from daily administration to monthly or even longer intervals while minimising adverse effects[11,12].

Conclusion

Conventional NSAIDs continue to play a vital role in chronic pain management; however, their long-term use is constrained by systemic toxicity and frequent dosing requirements. Emerging drug delivery systems, including biodegradable microspheres, nanoparticles, liposomes, hydrogels, and injectable depot formulations, offer sustained drug release, improved therapeutic efficacy, and enhanced patient compliance. Continued research and clinical translation of these technologies are expected to transform chronic pain management and support safer, more personalised therapies.

Acknowledgement

The authors sincerely acknowledge Principal, K. M. Kundnani College of Pharmacy, Mumbai, for providing the necessary academic and research support. We are grateful to the Directorate of Technical Education (DTE), Government of Maharashtra, IRC and HSNC University for their encouragement and guidance. We express our heartfelt gratitude to our respected Dr. (Mrs.) Rajani Athawale, Professor & HOD, Department of Pharmaceutics Ph.D. guide for invaluable mentorship and continuous support throughout this work.

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