INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

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Review Article

Recent Advances in Drug Delivery of NSAIDS in Cases of Inflammation: Role of Nanotechnology, Microspheres, and Individualised Medications

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ARTICLE INFO

Published: 17 Jun 2026
Keywords:
NSAIDS; inflammation, nanotechnology, microspheres-targeted drug delivery, sustained release, biodegradable polymers
DOI:
10.5281/zenodo.20728027

ABSTRACT

Inflammation is a biological process in which the body responds to tissue damage, infection, or harmful stimuli. Chronic inflammation causes many diseases, for example, rheumatoid arthritis, osteoarthritis, inflammatory bowel diseases, and musculoskeletal disorders. NSAIDs have been used for decades due to their potent pharmacological effects on pain and inflammation. However, the current regimen of conventional NSAID therapy suffers from several limitations, such as gastrointestinal side-effects, poor bioavailability, short half-life, need for frequent dosing, cardiotoxicity, and patient non-compliance. The appearance of new advances in the field of pharmacy is linked to the development of new drug delivery systems, which will help to improve the efficiency and decrease side effects of treatment. It was concluded that nanoparticles, liposomes, solid lipid nanoparticles, nanoemulsions, microspheres, hydrogels, transdermal drug delivery systems, and biodegradable depots belong to the methods that can be used in order to increase the efficiency of NSAIDs delivery. The review describes the pathophysiology of inflammation, the mechanism of action and types of NSAIDs, the problems associated with their traditional delivery, as well as modern innovations in the application of nanotechnology and microspheres for the delivery of NSAIDs in inflammation cases. Moreover, the discussion of marketed products, patient-oriented dosage forms, current trends in drug development, and prospects is also provided.

INTRODUCTION

Inflammation is an intricate process of biological defence that occurs when an organism responds to infection, injury, toxins, or immunological stimuli. Inflammation in its acute form is a beneficial phenomenon, contributing to healing[1]. Chronic inflammation can cause the development of several diseases, such as rheumatoid arthritis, osteoarthritis, inflammatory bowel disease, cardiovascular disease, and neurodegenerative disorders[2]. NSAIDS belong to one of the most prescribed medications in treating inflammation

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Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

because of their pain-relieving, fever-reducing, and anti-inflammatory effects.

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) exert their significant effects through inhibition of enzymes responsible for the synthesis of prostaglandins, known as cyclooxygenase or COX enzymes[3]. Although these medications are highly effective, chronic administration of NSAIDs leads to GI ulcers, nephrotoxicity, cardiotoxicity, hepatoxicity, and compliance problems due to the need for repetitive doses[4,5]. Usually, traditional oral administration does not enable continuous maintenance of drug levels in the bloodstream and may lead to various side effects throughout the body. In recent years, a lot of emphasis has been given to developing new ways that could address some of these limitations. Nanotechnology-based drug products, biodegradable microspheres, liposomes, hydrogels, nano-emulsions, and nanoparticles represent an incredible promise in this context and provide several advantages in terms of drug delivery, increased bioavailability and improved safety[6]. These strategies have facilitated the drug's effect to last longer owing to their sustained release properties. This paper seeks to explore the new methods of NSAID delivery, focusing particularly on nano-drugs and microsphere technology.

The physiology of inflammation lies in the activation of white blood cells, together with other substances, including cytokines, prostaglandins, leukotrienes, and reactive oxygen species. Injured tissues trigger inflammatory mediators that produce redness, swelling, pain, and dysfunction, including histamines, TNF-α, interleukins, and prostaglandins.

Different types of inflammations include:

1. Acute inflammation

2. Chronic inflammation

3. Autoimmune inflammation

4. Neuroinflammation

One of the best examples of chronic inflammation is rheumatoid arthritis. Such diseases require continuous intake of medicine, which leads to increased chances of experiencing toxic effects on patients because of taking NSAIDs.

Regarding NSAID classification, there are two types of NSAIDs:

Non-selective COX inhibitors:

I. Ibuprofen

II. Diclofenac

III. Naproxen

IV. Ketoprofen

V. Indomethacin

Selective COX inhibitors:

I. Celecoxib

II. Etoricoxib

Selective COX-2 inhibitors

I. Meloxicam

II. Nimesulide

Mechanism of action of NSAIDs:

NSAIDs produce inhibition of cyclooxygenase enzymes, which catalyse the conversion of arachidonic acid to prostaglandins. The inhibition of prostaglandin synthesis results in attenuation of:

1. Pain

2. Fever

3. Vasodilation

4. Oedema

5. Inflammation process

Limitations of traditional NSAIDs Therapy:

These include:

1. Gastric ulceration

2. Gastric bleeding

3. Renal toxicity

4. Hepatotoxicity

5. Cardiovascular hazards

6. High frequency dosage

7. Poor patient compliance

8. Non-site-specific delivery.[7]

MATERIALS AND METHODS

Recent Marketed Anti-Inflammatory Medications

Recently marketed and commonly prescribed NSAID products include:

1. Diclofenac sodium sustained-release tablets
2. Celecoxib capsules
3. Etoricoxib tablets
4. Topical diclofenac gel
5. Ketoprofen transdermal patches
6. Ibuprofen sustained-release formulations
7. Naproxen controlled-release tablets

Combination therapies with proton pump inhibitors and gastroprotective agents are increasingly utilised to minimise gastric irritation.

Nano-Based Drug Delivery Approaches

Polymeric Nanoparticles

Polymeric nanoparticles improve:

- Drug stability
- Targeted delivery
- Controlled release
- Reduced toxicity

Common polymers

a. PLGA

b. Chitosan

c. Alginate

d. PEG.

Solid Lipid Nanoparticles.

Solid lipid nanoparticles enhance Oral bioavailability, Drug penetration, Sustained release, and stability of lipophilic NSAIDs[8,9]

Liposomes

These are vesicular phospholipids capable of entrapment of both hydrophilic and lipophilic drugs. These decrease systemic toxicity and increase specificity towards inflamed tissues.

Nano Emulsions

These are effective for enhancing: Solubility, Skin Penetration and Topical Drug Delivery

NSAIDs Delivery Systems Using Microsphere Technology

Microspheres refer to spherical biodegradable drug delivery particles used for achieving controlled drug delivery and release.

Benefits

- Low dosing frequency
- Protracted drug effect
- Better patient adherence to therapy
- Better drug bioavailability
- Decreased systemic toxicity

Methods used in their preparation include:

1. Solvent Evaporation Method
2. Spray Drying Method
3. Emulsion Cross-Linking Method
4. Ionic Gelation
5. Microfluidics Technology

The readily used biodegradable polymers:

1. PLGA
2. PLA
3. Gelatin
4. Chitosan
5. Ethyl Cellulose

Microsphere systems apply to conditions such as rheumatoid arthritis and other chronic inflammatory diseases, which may necessitate long-term drug administration[10,11].

RESULTS AND DISCUSSION

Hydrogels and Depot Systems:

Hydrogels maintain localised, prolonged release and enhance retention at the site of inflammation. Injectable depot preparations ensure long-lasting action and prevent frequent dosing[12,13]. Advantages include- Enhanced compliance, Minimised systemic exposure, Enhanced therapeutic effect, Controlled drug delivery [14,15]

Strategies for Enhancing Patient Adherence

Adherence in patients may be increased by utilising sustained-release preparations, Once daily dosing, Transdermal patches, Depot injection, lowered GI toxicity, Targeted drug delivery, and combination therapy[16,17,18,19,20].

Dosage forms for chronic inflammatory conditions are becoming patient-focused

FUTURE ASPECTS

Smart nanocarriers, stimuli-responsive drug systems, targeted biological agents, and AI-based formulation design, personalised therapy, injectable biodegradable depots and hybrid nano-microspheres systems are expected to play an increasing role in anti-inflammatory therapy in the future[21,22]. Nanoparticle-based systems combined with biodegradable polymers will likely have a major impact on the treatment of chronic inflammatory diseases. [23,24]

CONCLUSION

NSAIDs remain the cornerstone in the treatment of inflammatory diseases, but are often characterised by toxic effects, poor targeting and low patient compliance. Newer drug delivery strategies, such as nanoparticles, liposomes, hydrogels and biodegradable microspheres, have demonstrated

promising effects for solving problems associated with conventional therapy. Targeted as well as sustained-release formulations would increase bioavailability, reduce peripheral side effects, and improve patient compliance. The future should aim for clinically viable, scalable, and patient-oriented systems that provide effective and safer anti-inflammatory therapy.

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HOW TO CITE: Prerana Bambale, R. Thorat, R. Athawale, Recent Advances in Drug Delivery of NSAIDS in Cases of Inflammation: Role of Nanotechnology, Microspheres, and Individualised Medications, Int. J. of Pharm. Sci., 2026, Vol 4, Issue 6, 4077-4083. https://doi.org/10.5281/zenodo.20728027