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Review Article

Nanotechnology in Rheumatoid Arthritis Therapy: Focus on Nanoemulsions

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Abstract:
Rheumatoid arthritis is an autoimmune disorder manifested by joint inflammation. Traditional treatments often have limitations, including poor bioavailability and systemic side effects. Of late nanotechnology, in particular nanoemulsions, offer an innovative solutions for enhancement of drug delivery and therapeutics. This review delves into the principles of nanoemulsions, their benefits in RA therapy, and a comparative analysis of various nanotechnology supported drug delivery, highlighting the prospectives of nanoemulsion to revolutionize RA management.
Key words: Nanoemulsion, Rheumatoid arthritis, autoimmune, bioavailability, inflammation

Introduction

Rheumatoid arthritis is an autoimmune disorder manifested by degenerative joint inflammation causing severe disability and premature death rate. With a worldwide preponderance of about 0.3%–1% RA is 3–5 times more prevailing in women than in men.[1] RA is a debilitating condition affecting millions worldwide, leading to severe pain, joint destruction, and reduced quality of life.[2] Conventional mangement with NSAIDs and antirheumatic drugs, often fall short due to issues such as poor patient compliance, limited efficacy, and adverse effects. The integration of nanotechnology into medical therapies auger well to overcome these challenges.[3]

Nanotechnology, particularly the use of nanoemulsions, has gained considerable attention for its ability to improve drug solubility, bioavailability, and targeted delivery. Nanoemulsions is a stable dispersions of oil and water stabilized by surfactants, with droplet size ranging from 20 to 200 nm. This review explores the fundamental principles of nanoemulsions, their specific benefits in RA therapy, and compares them with other nanotechnology supported drug delivery.[3,6]

CHALLENGES IN TRADITIONAL RHEUMATOID ARTHRITIS TREATMENTS

Traditional rheumatoid arthritis treatments often face limitations as poor patient adherence, short drug half-life, limited solubility and low bioavailability. These challenges can be addressed by exploring advanced drug delivery systems. Approaches like microparticles, nanoparticles, nanodispersions, nanocapsules, nanoemulsions, and nanosuspensions enhance therapeutic efficacy by ensuring targeted drug delivery at higher concentrations. Over the past 10–15 years, nanomedicine has witnessed

significant advancements and has become increasingly prominent in RA treatment strategies, as illustrated in Fig. 1.[9,10]

Principles Of Nanoemulsions

Formation and Characteristics

Nanoemulsions are thermodynamically stable, colloidal dispersion of two immiscible liquids containing an emulsifying agents. NEs can be attained through high-energy and low-energy approaches. Ultrasonication and high-pressure homogenization (HPH) are the sought after methods to formulate nanoemulsion. The high energy input in these methods causes cavitation, bubble implosion and their sussequent disruption into tiny oil droplets. Ultrasonication is suitable for laboratory-scale while for an industrial application HPH is preferred.[4,5,9,24]

- **Droplet Size**: Typically in the range of 20 to 200 nm, this enhances surface area and improves drug absorption.
- **Stability**: Nanoemulsions are thermodynamically stable and can resist phase separation over extended periods, given appropriate formulation.
- **Versatility**: They can encapsulate a wide variety of pharmaceutical actives, including hydrophilic, hydrophobic, and even macromolecular drugs.[11]

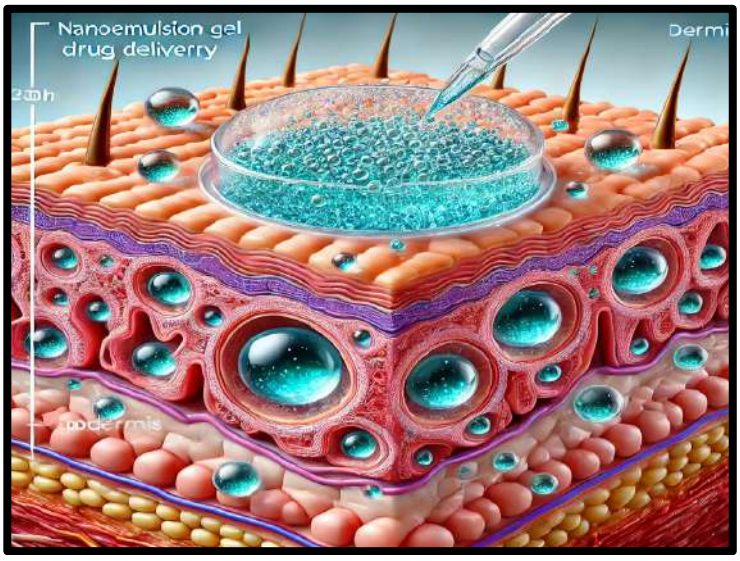

Figure 1: Nanoemulsions gel drug delivery

Nanoemulsions are way better than other dosage forms as they offer an improved rate of drug absorption, provide protection of drug from oxidation and hydrolysis, can hold both lipophilic and hydrophilic drug moieties, can control drug release, can enhance efficacy ,can serve as non-toxic and nonirritant vehicles and control control drug permeation through liquid film, besides drug formulated as nanoemulsion provide more oral bioavailability [2]

MECHANISMS OF ACTION

The mechanisms by which nanoemulsions enhance drug delivery include:

1. **Increased Bioavailability**: The small droplet size facilitates better interaction with biological membranes, leading to improved absorption and bioavailability.
2. **Controlled Release**: Nanoemulsions can be designed for sustained release of therapeutic agents, which helps maintain drug levels in the bloodstream over extended periods.
3. **Targeted Delivery**: By modifying surfactants or incorporating targeting ligands, nanoemulsions can achieve preferential accumulation in inflamed tissues, such as those affected by RA.[11,12,23]

Figure 2: Nanoemulsions targeting inflamed tissues in rheumatoid arthritis.

Cytokines like Interleukin (IL-1, IL-6, IL-8 and IL-10) are responsible for inducing inflammation in RA patients. Macrophages in synovial membrane exhibit proinflammatory properties leading to inflammation and subsequent joint damage. Nanotechnology based approches pave the way for encapsulation and delivery of variety of anti-inflammatory drugs targeting specific receptor in the effective management of rheumatoid arthitis. Table 1 i summarizes various nanoparticulate systems reported for the management of RA.[19,21]

BENEFITS OF NANOEMULSIONS IN RA THERAPY

Improved Solubility and Bioavailability

Many anti-rheumatic drugs, such as methotrexate, have poor solubility in aqueous environments, limiting their bioavailability and therapeutic effectiveness. Nanoemulsions enhance the drug solubility and subsequently improve its absorption . For instance, studies have demonstrated that entrapping methotrexate in nanoemulsions can significantly increase its bioavailability compared to conventional formulations.

Reduced Systemic Toxicity

Traditional RA treatments often lead to systemic side effects, including gastrointestinal issues and liver toxicity. By targeting the inflamed joints and minimizing systemic distribution, nanoemulsions can reduce these adverse effects. This localized delivery mechanism allows for high drug concentrations at the site of action while lowering systemic exposure, thereby enhancing the safety profile of the treatment.

Enhanced Patient Compliance

Improved bioavailability and reduced side effects contribute to higher patient compliance. Patients are much apt to adhere to treatment regimens that offer better outcomes with fewer side effects. Nanoemulsions can also enable less frequent dosing, which further enhances compliance.

Versatility in Drug Loading

Nanoemulsions are suitable to incorporate variety of therapeutic agents, such as drug actives, proteins, and nucleic acids. This allows for combination therapies, wherein different drugs can be given at the same time to targeting various pathways engaged in RA.

Possibility of Combination Therapies

The ability to formulate combination therapies using nanoemulsions presents a significant advantage in RA treatment. By co-encapsulating multiple agents, such as NSAIDs and DMARDs, it is possible to achieve synergistic effects that enhance therapeutic outcomes while minimizing side effects. [7, 8, 9.23, 25]

COMPARATIVE ANALYSIS OF NANOTECHNOLOGY-BASED DELIVERY SYSTEMS

While nanoemulsions offer several advantages, they are one of several nanotechnology-based delivery systems available for RA therapy. Here, we compare nanoemulsions with other prominent systems:

1. LIPOSOMES

Characteristics: Liposomes are spherical vesicles made of lipid bilayer and allows for encapsulation of both hydrophilic and hydrophobic drugs. They are biocompatibility and possess an ability to ameliorate the pharmacokinetics of encapsulated drugs.

Comparison: Although liposomes can improve bioavailability, they are typically larger than nanoemulsions and may require more complex manufacturing processes. Additionally, their stability can be an issue, particularly in harsh physiological environments.

2. SOLID LIPID NANOPARTICLES (SLNS)

Characteristics: SLNs are made of solid lipids and stabilized by the surfactants. They provide controlled release of drugs and have improved stability compared to liposomes.

Comparison: While SLNs can enhance drug stability and release profiles, their drug loading capacity is often limited compared to nanoemulsions. The solid lipid matrix can also restrict the range of drugs that can be incorporated.

3. POLYMERIC NANOPARTICLES

Characteristics: They are made from biodegradable polymers and can be designed for controlled release. They can encapsulate a variety of therapeutic agents, providing flexibility in formulation.

Comparison: Although polymeric nanoparticles offer advantages in terms of targeted delivery and release kinetics, they may present challenges related to biocompatibility and potential toxicity from the polymeric materials used.

4. DENDRIMERS

Characteristics: Dendrimers are extremely branched, nanoscale polymers with meticulous molecular architecture. They can be used to deliver variety of drug actives, enzymes, nucleic acid and proteins.

Comparison: Despite their highly tunable properties, dendrimers are often expensive to produce and may exhibit toxicity due to their synthetic nature, limiting their practical application in RA therapy.[13,14,15,16,17,18,20,22]

Table: 1. Comparative analysis table for various nanotechnology-based delivery systems: [13-18, 22]

Criteria	Liposomes	Polymeric Nanoparticles	Dendrimers	Solid Lipid Nanoparticles (SLNs)	Nanoemulsions
Composition	Phospholipids	Biodegradable polymers (e.g., PLGA)	Branching macromolecules	Solid lipids	Oils + surfactants + water
Size Range	50 nm - 500 nm	100 nm - 1000 nm	1 nm - 100 nm	50 nm - 1000 nm	100 nm - 200 nm
Drug Loading Capacity	Moderate	High	High	Moderate to high	Moderate
Stability	Moderate	High	High	High	Moderate
Release Profile	Controlled release	Sustained release	Controlled release	Sustained release	Rapid release
Shelf Life	Moderate	Long	Moderate	Long	Short to moderate
Toxicity	Generally low	Biocompatible	Biocompatible	Generally low	Generally low
Applications	Anticancer drugs, vaccines	Anticancer drugs, gene delivery	Gene therapy, imaging	Anticancer drugs, cosmetic	Nutraceuticals, pharmaceuticals

CONCLUSION

Nanoemulsions renders evidential advancement in the management of rheumatoid arthritis through an enhanced drug solubility, bioavailability, and attenuated systemic toxicity. The improved patient compliance and potential to carry range of therapeutic agents makes nanoemulsion a valuable tool in the management of RA. When compared to other nanotechnology-based delivery systems, nanoemulsions stand out for their simplicity, effectiveness, and versatility.

FUTURE PERSPECTIVES

Future research should focus on optimizing nanoemulsion formulations for specific RA therapies, encompassing clinical trials to establish their efficacy and safety profiles, and exploring the potential of combination therapies. Advances in personalized medicine through nanotechnology could revolutionize RA treatment paradigms, paving the way for tailored therapeutic strategies that improve patient outcomes.

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