IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

NOVEL DRUG DELIVERY SYSTEMS USED IN THE TREATMENT OF RHEUMATOID ARTHRITIS: AN OVERVIEW

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Abstract

Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by persistent joint inflammation, leading to pain, swelling, synovial hyperplasia, and progressive cartilage and bone destruction. It affects around 1% of the global population, with women being 2-3 times more susceptible than men. The development of RA involves a complex interplay of genetic predisposition, environmental factors, and preclinical triggers. Although there is currently no cure, the goal of RA treatment is to reduce disease activity and achieve remission when possible. Conventional treatment strategies primarily involve the use of anti-rheumatic drugs, which typically require high-dose, frequent, and long-term administration. However, prolonged use of these drugs is associated with serious adverse effects, leading to poor patient compliance and limiting the overall effectiveness of treatment. To address these challenges, novel drug delivery systems (NDDS) have been developed for RA therapy. NDDS are designed to improve the targeted delivery of therapeutic agents, reduce side effects, enhance bioavailability, and allow for more controlled drug release. This article reviews the potential developments in RA therapeutic regimens, with a particular focus on the role of NDDS in enhancing treatment efficacy and safety. NDDS represent a promising solution to improve clinical outcomes for RA patients by overcoming limitations of conventional therapies. Advancements in drug delivery technologies have the potential to revolutionize RA treatment, offering new hope for better management of this debilitating disease and improving the quality of life for patients.

Keywords: Rheumatoid arthritis, NSAIDs, Disease modified anti-rheumatic drugs, Glucocorticoids.

1. Introduction

Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease that primarily affects the joints [1]. It manifests as chronic systemic inflammatory symptoms due to tissue abnormalities, causing localized damage in various parts of cartilage, bone, tendons, and ligaments [2]. RA can affect any joint in the body but primarily targets the proximal interphalangeal, metacarpophalangeal, and metatarsophalangeal joints, as well as the wrists and knees, with the wrist being the most commonly affected site [3]. RA is classified as early rheumatoid arthritis when symptoms persist for less than six months, and as established rheumatoid arthritis when symptoms last for more than six months [4]. Symptoms like tenderness are seen in large joints, whereas swelling occurs in small joints [5]. Aging is one of the most significant risk factors in the development of RA [6]. The global prevalence of RA is estimated to be around 0.2 - 1%, with the

incidence in women being 2-3 times higher than in men [7]. In India, the prevalence of RA ranges from 0.28% to 0.7%, which is comparable to prevalence rates in developed nations [8]. Several drugs are used to treat RA, including glucocorticoids, DMARDs, NSAIDs, and biologics. However, their low bioavailability and high clearance rates require frequent dosing, which increases the risk of side effects like infections, and GI toxicity. The novel drug delivery system overcomes these problems to improve the patient compliance.

2. Pathogenesis

Rheumatoid arthritis (RA) is a chronic autoimmune condition marked by systemic inflammation and damage to synovial joints. Its pathogenesis arises from a complex interaction of genetic, environmental, and immune system factors. Genetic susceptibility, particularly through HLA-DR4 and HLA-DR1 alleles, predisposes individuals to immune dysregulation [9]. Environmental factors, such as smoking and certain infections, can trigger post-translational modifications like citrullination, creating neoantigens [10]. In genetically susceptible individuals, these neoantigens elicit an abnormal immune response, leading to the production of autoantibodies, including rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPAs) [11]. The process initiates in the synovium, where activated macrophages, dendritic cells, and synovial fibroblasts release pro-inflammatory cytokines, including tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-1 (IL-1) [12]. These cytokines recruit immune cells, such as T-cells and B-cells, which perpetuate inflammation [13]. T-cells activate macrophages and fibroblasts via cytokines, while B-cells produce autoantibodies that form immune complexes, triggering complement activation [14]. Persistent inflammation causes synovial hyperplasia (pannus formation) and the release of matrix metalloproteinases (MMPs), which degrade cartilage and bone [15]. Additionally, osteoclast activation mediated by receptor activator of nuclear factor kappa-B ligand (RANKL) leads to bone erosion [16]. If untreated, this inflammatory process results in progressive joint destruction, pain, and disability [17]. Insights into RA pathogenesis have driven the development of targeted therapies, such as TNF inhibitors, IL-6 blockers, and JAK inhibitors, which disrupt these immune pathways [18]. Pathogenesis of RA is shown **Fig. 1**.

2.1 Preclinical rheumatoid arthritis (RA)

Preclinical rheumatoid arthritis (RA) is an asymptomatic phase characterized by systemic autoimmunity, influenced by genetic factors (e.g., HLA-DR4), environmental triggers (e.g., smoking, infections), and the presence of autoantibodies such as ACPAs and RF. Elevated inflammatory cytokines (e.g., TNF-α, IL-6) and subclinical synovial inflammation may be detected, allowing for early intervention to halt disease progression [19].

2.2 Genetic factors

Genetic factors, especially the HLA-DR4 and HLA-DR1 alleles, play a crucial role in predisposing individuals to rheumatoid arthritis (RA). These genetic variations contribute to immune system dysregulation, heightening the risk of RA when combined with environmental triggers [20]. Additional susceptibility genes, such as PTPN22, also influence disease development [21].

2.3 Environmental factors

Environmental factors, including smoking, infections, and chemical exposures, play a significant role in the development of rheumatoid arthritis (RA). Smoking is a key risk factor, particularly in genetically predisposed individuals [22]. Additionally, periodontal disease and hormonal changes can trigger or worsen RA, further influencing disease onset and progression [23].

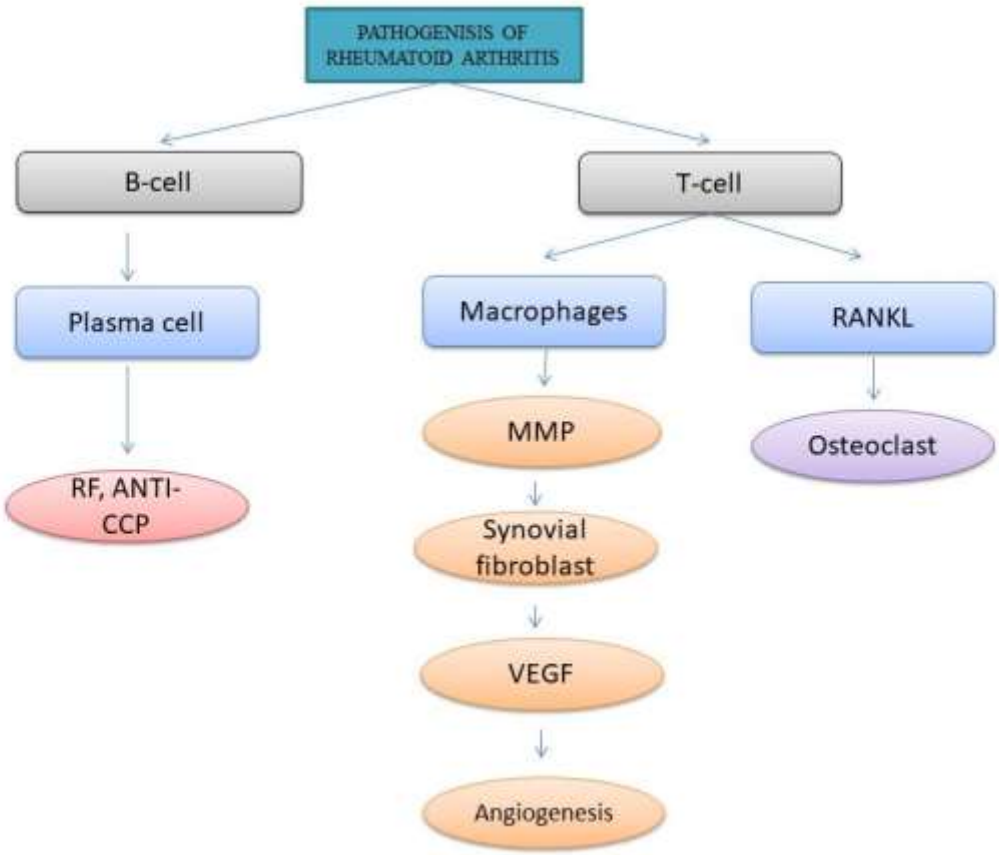

Fig.1 Pathogenesis of RA

3. Therapeutic approaches (Conventional drug delivery systems)

Currently, there is no permanent cure for rheumatoid arthritis (RA), but various therapeutic approaches can help relieve the discomfort and pain caused by inflamed joints, reduce joint damage and deformities, and ultimately enable patients to lead a healthier, more active life. RA therapeutics are generally categorized into four distinct classes based on the degree of articular function, joint damage, and the level of synovial inflammation [24]. The current standard treatments for RA patients include NSAIDs, DMARDs, glucocorticoids, and biologic medications [25].

3.1 Non-steroidal anti-inflammatory drugs (NSAIDs)

Non-steroidal anti-inflammatory drugs (NSAIDs) are the most frequently used medications for managing arthritis disorders, due to their pain-relieving and anti-inflammatory properties [26]. The NSAIDs work by inhibiting the cyclooxygenase (COX) enzyme, which is responsible for converting arachidonic acid into prostaglandins. Most of the NSAIDs are non-selective COX inhibitors, meaning they block both COX-1 and COX-2 enzymes [27]. However, concerns about the adverse effects of this class of drugs have been steadily increasing. These include acute kidney ischemia due to vasoconstriction from prostaglandin inhibition, changes in blood pressure, and heightened bleeding risk from platelet inhibition. Non-selective NSAIDs have been associated with ulcer formation, leading to severe upper gastrointestinal (GI) complications, including perforation, obstruction, and bleeding [28]. NSAIDs are associated with increased cardiovascular risks, such as myocardial infarction and strokes; however, they are commonly used in the treatment of rheumatoid arthritis (RA). Commonly used NSAIDs for treatment of RA is shown in **Fig. 2**.

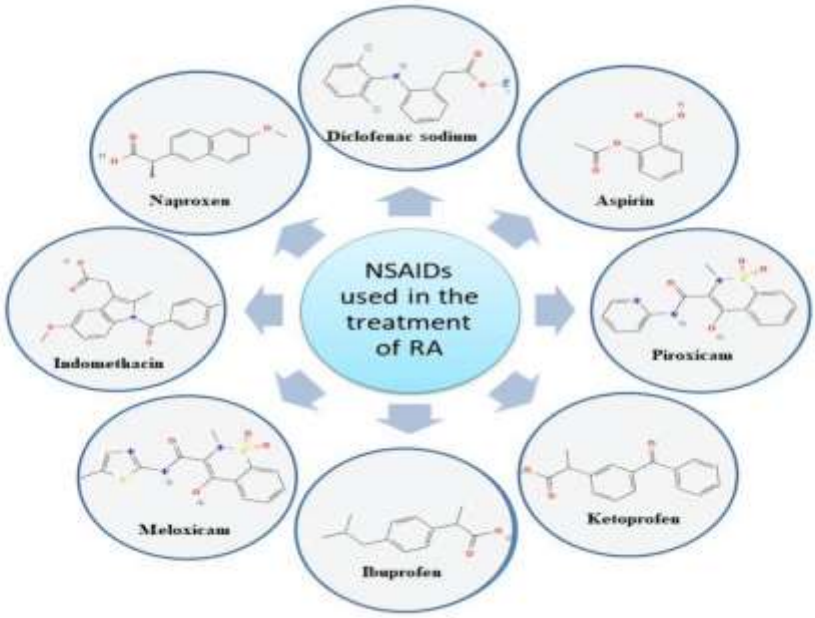

Fig .2 Commonly used NSAIDs for the treatment Rheumatoid arthritis.

3.2. Corticosteroids

Corticosteroids, especially glucocorticoids, are frequently used to treatment inflammatory disorders, including asthma, rheumatoid arthritis (RA), inflammatory bowel disease (IBD), and other autoimmune diseases [29]. The glucocorticoids act by releasing phospholipids that helps reduce joint inflammation (e.g., prednisolone, dexamethasone). Although these drugs are often prescribed in the initial stages of treatment, their frequent and prolonged use can lead to side effects such as hypertension, cardiovascular disease, obesity, and sometimes insulin resistance [30].

3.3 Disease modifying anti rheumatic drugs (DMARDs)

Disease-modifying anti-rheumatic drugs (DMARDs) are used in the treatment of rheumatoid arthritis (RA) to slow the progression of the disease and prevent joint damage [31]. These medications have a delayed onset of action, often taking weeks or months to show significant pharmacological effects. DMARDs operate through various mechanisms, and their side effects can differ widely between drugs. Some common side effects of DMARD therapy include gastrointestinal problems, liver and kidney dysfunction, stomatitis, and myelosuppression [32].

3.4 Biologics

Biologics revolutionized rheumatoid arthritis (RA) treatment by targeting immune pathways. Common classes include tumor necrosis factor (TNF) inhibitors (e.g., etanercept, adalimumab), interleukin inhibitors (e.g., tocilizumab for IL-6, anakinra for IL-1), B-cell depleters (rituximab), and T-cell modulators (abatacept). These drugs reduce inflammation, prevent joint damage, and improve quality of life [33]. Janus kinase (JAK) inhibitors (e.g., tofacitinib), though not biologics, target cytokine signaling. Treatment choice depends on disease severity and patient factors [34]. Biologics are often combined with methotrexate for enhanced efficacy.

Table 1. Conventional therapeutic agents for Rheumatoid arthritis

Drug classification	Instance	Mechanism of action	Side effects
NSAIDs	Diclofenac, Meloxicam	COX inhibitors	Gastrointestinal disorder, Kidney damage
Glucocorticoids	Prednisolone, Dexamethasone	Effect on the levels of inflammatory cytokines and the state of immunosuppression	Hypertension, Osteoporosis, Hypertension
DMARDs	Methotrexate	Inhibit the genetic material synthesis, Immunosuppression	Gastrointestinal reaction, liver and kidney damage
Biologics	Tocilizumab, Etanercept	TNF inhibition, Interleukin-6 inhibition	Gastrointestinal infection, tuberculosis

4. Various novel drug delivery systems for treatment of RA

Conventional drug delivery systems (CDDS) encounter several obstacles when treating diseases like rheumatoid arthritis (RA), including challenges such as poor solubility, low permeability, limited bioavailability, breakdown by gastrointestinal enzymes, first-pass metabolism, food interactions, high dose requirements, and potential toxicity [35]. These issues have led to the development of novel drug delivery systems (NDDS), which provide targeted, controlled, and sustained drug release, thereby improving bioavailability, minimizing toxicity, and reducing the frequency of doses [36]. A decade ago, non-steroidal anti-inflammatory drugs (NSAIDs) and analgesics were commonly used as first-line treatments for RA. However, as the disease progresses, these drugs become less effective, requiring stronger interventions like intra-articular (i-a) steroid injections to manage pain and inflammation [37]. Disease-modifying anti-rheumatic drugs (DMARDs) such as salazopyrine, chloroquine, methotrexate (MTX), and immunosuppressive agents like azathioprine were later introduced, though they are often associated with significant side effects. More recent treatments, including leflunomide and tacrolimus, target activated CD4 T-cells, which are central to RA's pathogenesis [38]. With an improved understanding of RA's inflammatory mechanisms, biologic drugs like infliximab, adalimumab, and anakinra have been developed. While these biologics are effective in managing RA, they often require frequent administration due to their systemic nature [39]. Intra-articular drug delivery has emerged as a significant breakthrough in RA treatment, enabling direct drug delivery to the affected joints with prolonged release . Novel drug delivery systems, such as liposomes, nanoparticles, and microparticles, encapsulate drugs for intra-articular injection, reducing drug clearance and extending residence time [40]. This approach enhances therapeutic effectiveness, minimizes systemic exposure, and reduces side effects, marking a major advancement in RA treatment and improving patient quality of life [41]. Different novel drug delivery systems for Rheumatoid arthritis is shown in **Fig. 3.**

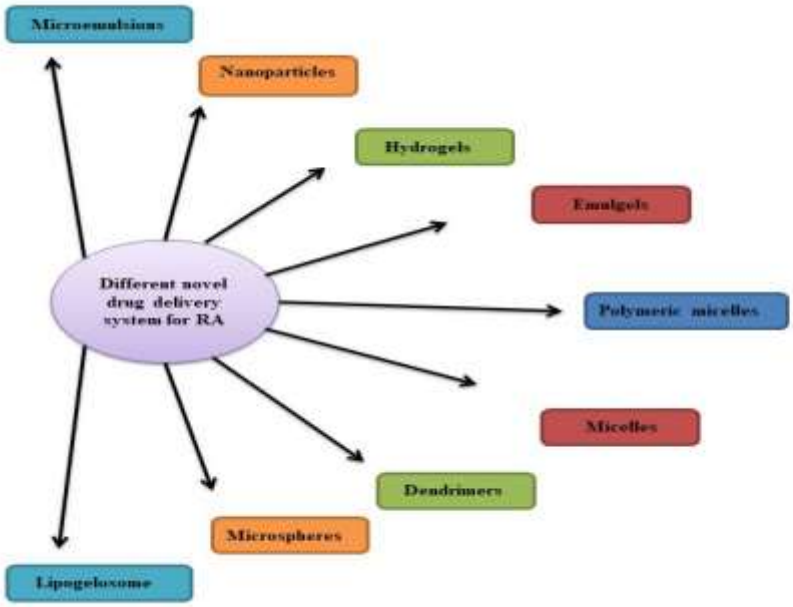

Fig. 3 Different novel drug delivery systems for Rheumatoid arthritis

4.1 Nanoparticles

Nanoparticles represent an innovative and efficient strategy for treating rheumatoid arthritis (RA) by enhancing drug delivery, targeting inflamed joints, and reducing systemic side effects. These advanced systems are designed to deliver anti-inflammatory drugs, biologics, or immunomodulators with precision and effectiveness. Liposomes, lipid-based carriers, encapsulate drugs such as methotrexate or dexamethasone, increasing bioavailability and minimizing unintended effects. Polymeric nanoparticles (e.g., PLGA or PEG) enable sustained drug release for improved outcomes. Dendrimers, with their branched structures, allow precise drug loading and delivery, while gold nanoparticles combine anti-inflammatory properties with drug-carrying capabilities [42]. Solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs) enhance the transport of hydrophobic drugs like curcumin, and magnetic nanoparticles facilitate imaging and therapy by delivering drugs under magnetic guidance. Exosome-mimicking nanoparticles are emerging as effective tools for delivering mRNA to regulate immune responses. By leveraging the enhanced permeability and retention (EPR) effect for passive targeting and surface ligands for active targeting, nanoparticles improve drug accumulation in inflamed joints. However, despite their potential demonstrated in preclinical studies, challenges such as biocompatibility, large-scale manufacturing, and regulatory approval must be overcome for their widespread use in RA treatment.

4.2 Dendrimers

Dendrimers are nanoscale, branched polymeric structures with significant potential for treating rheumatoid arthritis (RA) due to their ability to deliver therapeutic agents with precision. Their highly branched design facilitates efficient drug encapsulation or conjugation with anti-inflammatory agents like methotrexate and NSAIDs. These nanoparticles enhance drug solubility, stability, and targeted delivery while minimizing systemic side effects. Functionalization with specific ligands allows dendrimers to target inflamed joint tissues directly, boosting treatment effectiveness [43]. Moreover, they offer controlled and sustained drug release, improving overall therapeutic outcomes. Their biocompatibility and adaptable surface chemistry make them a promising tool for advancing RA treatment strategies.

4.3 Folate-coupled dendrimers

Folate-coupled dendrimers offer an effective, targeted treatment strategy for rheumatoid arthritis (RA). These highly branched polymeric nanostructures enable precise drug encapsulation and controlled release. By attaching folate molecules to their surface, dendrimers can specifically target inflamed joints, which commonly express folate receptors, leading to increased drug accumulation at the site of inflammation while minimizing systemic exposure. This folate conjugation enhances the selectivity and

efficiency of drug delivery, allowing for the direct delivery of anti-inflammatory drugs, such as methotrexate or corticosteroids, to the affected tissues. The approach reduces side effects and improves therapeutic outcomes. Additionally, dendrimers improve the solubility, stability, and bioavailability of hydrophobic drugs, and facilitate controlled, sustained drug release for prolonged therapeutic effects. Overall, folate-coupled dendrimers provide a promising, non-invasive solution for RA treatment, enhancing efficacy and patient compliance [44].

4.4 Emulgels

Emulgels are a novel topical drug delivery system that combines the properties of emulsions and gels, making them particularly effective for treating rheumatoid arthritis (RA). They offer a non-invasive method of delivering anti-inflammatory drugs like diclofenac or ketoprofen directly to inflamed joints. Emulgels improve drug solubility, skin penetration, and retention at the target site, ensuring localized action while minimizing systemic side effects. Their gel-like consistency provides enhanced stability and patient adherence compared to traditional ointments [45]. Furthermore, emulgels can accommodate both hydrophilic and lipophilic drugs, offering versatility and sustained therapeutic benefits for RA treatments.

4.5 Microemulsions

Microemulsions are stable, transparent mixtures of oil, water, and surfactants that provide an effective drug delivery system for rheumatoid arthritis (RA) treatment. They improve the solubility, bioavailability, and skin penetration of anti-inflammatory drugs like corticosteroids or NSAIDs, targeting inflamed joints directly. Microemulsions enable localized drug release, reducing systemic side effects. Their small droplet size enhances skin absorption and targeting, leading to more efficient treatment. Furthermore, microemulsions can deliver both hydrophilic and lipophilic drugs, making them a versatile and promising option for RA therapy with improved therapeutic results [46].

4.6 Micelles

Micelles are nanocarriers made from surfactant molecules that spontaneously form spherical structures with a hydrophobic core and hydrophilic outer shell. In the treatment of rheumatoid arthritis (RA), micelles enhance the solubility and bioavailability of hydrophobic anti-inflammatory drugs like corticosteroids or NSAIDs. By encapsulating these drugs, micelles improve stability and enable targeted delivery to inflamed joints, ensuring localized effects and reducing systemic side effects. Their small size and customizable surface properties make micelles ideal for penetrating biological membranes and providing sustained drug release. Consequently, micelles offer an effective, versatile, and promising approach to RA treatment [47].

4.7 Polymeric micelles

Polymeric micelles are nanocarriers formed from amphiphilic block copolymers, offering a promising strategy for rheumatoid arthritis (RA) treatment. These micelles feature a hydrophobic core and hydrophilic shell, allowing them to encapsulate hydrophobic anti-inflammatory drugs like methotrexate or corticosteroids. They enhance drug solubility, stability, and bioavailability while ensuring targeted delivery to inflamed joints. Due to their small size, polymeric micelles can efficiently penetrate biological barriers, providing localized treatment and reducing systemic side effects. Moreover, they can be designed for controlled and sustained drug release, offering prolonged therapeutic effects and enhancing patient compliance in managing RA [48].

4.8 Lipogelosomes

Lipogelosomes are an advanced drug delivery system that integrates the characteristics of liposomes and gels, making them highly promising for rheumatoid arthritis (RA) treatment. These systems feature a lipid bilayer that encapsulates active drugs, such as methotrexate or NSAIDs, within a gel matrix. The gel structure improves drug stability and retention at the site of inflammation, allowing for extended,

localized release. Lipogelosomes enhance the solubility and bioavailability of hydrophobic drugs, which are typically difficult to deliver effectively. The lipid bilayer facilitates efficient drug penetration through the skin, targeting inflamed joints more precisely. Additionally, lipogelosomes reduce systemic side effects compared to oral treatments. This combination of liposome and gel technology provides an effective, non-invasive means of delivering sustained drug release, improving therapeutic outcomes and patient compliance. Lipogelosomes present a versatile solution for RA treatment, offering controlled, localized relief [49].

4.9 Hydrogels

Hydrogels are water-based, crosslinked polymer networks that present a promising solution for treating rheumatoid arthritis (RA). Their high water content creates a biocompatible and flexible platform for drug delivery. These hydrogels can encapsulate anti-inflammatory drugs such as methotrexate, NSAIDs, or biologics, providing sustained and localized release at the site of inflammation. They enhance drug solubility, stability, and bioavailability while minimizing systemic side effects. Additionally, hydrogels help maintain moisture in affected joints, alleviating pain and stiffness. With their ability to control drug release, hydrogels offer an effective, non-invasive treatment alternative for RA [50].

4.10 Microspheres

Microspheres are small, spherical particles used in drug delivery for rheumatoid arthritis (RA) treatment. Made from biodegradable polymers like poly(lactic-co-glycolic acid) (PLGA), they can encapsulate anti-inflammatory drugs such as methotrexate, corticosteroids, or biologics. These microspheres offer several benefits, including controlled and sustained drug release, which helps maintain consistent therapeutic levels and reduces the need for frequent dosing. Their structure also protects sensitive drugs from degradation, improving stability and bioavailability. Administered via injection into inflamed joints, they enable localized drug delivery, minimizing systemic side effects. Microspheres can be engineered for targeted drug release, enhancing treatment efficacy and reducing adverse effects. Their extended drug delivery capabilities make microspheres a promising solution for RA, improving therapeutic outcomes, patient compliance, and minimizing side effects compared to conventional oral treatments [51].

4.11 Combination of hydrogels And microspheres

The combination of hydrogels and microspheres presents a promising strategy for treating rheumatoid arthritis (RA) by improving drug delivery and therapeutic outcomes. Hydrogels offer a biocompatible, flexible matrix that can encapsulate anti-inflammatory drugs, while microspheres, small spherical particles, provide controlled drug release. Together, these systems facilitate sustained, localized delivery of drugs like methotrexate or NSAIDs directly to inflamed joints. Hydrogels enhance drug solubility and stability, while microspheres ensure prolonged release and targeted delivery, reducing systemic side effects. Hydrogels also help maintain moisture in the joints, easing pain and stiffness. Microspheres protect drugs from degradation and improve drug retention and bioavailability. This combination enhances therapeutic efficacy and promotes better patient compliance by reducing the frequency of administration, making it an innovative and effective solution for RA treatment, offering sustained relief and precision [52].

4.12 Microneedle transdermal patches

Microneedle transdermal patches are an innovative drug delivery system with significant potential for treating rheumatoid arthritis (RA). These patches feature arrays of small, painless microneedles that create microchannels in the skin, enabling efficient delivery of therapeutic agents directly into the bloodstream or targeted tissue. By bypassing the digestive system and liver metabolism, microneedles enhance the bioavailability and effectiveness of drugs such as corticosteroids, methotrexate, or biologics. For RA treatment, they offer localized, sustained drug release to inflamed joints, reducing systemic side effects and improving treatment accuracy. Made from biocompatible materials, the microneedles dissolve or retract after use, ensuring minimal discomfort. This non-invasive, patient-friendly method boosts drug delivery efficiency, improving therapeutic outcomes and patient adherence. Consequently, microneedle

transdermal patches present a promising alternative to traditional RA treatments, offering greater convenience and effectiveness [53].

Table.2 Novel drug delivery systems for NSAIDs in the treatment of Rheumatoid arthritis.

Drug	Chemical class & Sub class	Drug delivery system	Components	Observations	References
Aspirin	Class: Carboxylic acid Subclass: Salicylic acid	Microspheres	Polycarbonate	High drug loading, increased particle size and drug release rate	54
Diclofenac	Class: Carboxylic acid Subclass: Acetic acid Compound	Microspheres	Bio polymer	Rapid and prolonged action	55
Diclofenac	Class: Carboxylic acid Subclass: Acetic acid Compound	Microemulsion	Isopropyl myristate, phosphate buffer	Thermodynamic stability, permition enhancement	56
Diflunisal	Class: Carboxylic acid Subclass: Salicylic acid	Dendrimer	PAMAM dendrimer	Enhanced permeation	57
Indomethacin	Class: Carboxylic acid Subclass: Acetic acid	Nanocapsules	Poly(ε-caprolactone), Capric/caprylic triglyceride, Sorbitan monostearate	Better anti-inflammatory activity	58
Ketoprofen	Class: Carboxylic acid Subclass: Propionic acid	Microspheres	Poly lactic acid, Tween 80, ethyl acetate	Increased Cmax, AUC, t1/2. [113]	59
Ibuprofen	Class: Carboxylic acid Subclass: Propionic acid	Microspheres	Ceresine, Glyceryl stearate	Stereospecific sustained release	60
Naproxen	Class: Carboxylic acid Subclass:	Nanoparticle	Poly-caprolactone	Prolonged anti-inflammatory	

	Propionic acid		nanoparticles	activity	61
Celecoxib	Class: COX-2 selective Subclass: Sulfonamide	Microspheres	Bovine serum albumin	Sustained drug release, prolonged circulation	62
Celecoxib	Class: COX-2 selective Subclass: Sulfonamide	Chitosan microspheres	Chitosan	Rapid distribution	63
Piroxicam	Class: Enolic acid Subclass: Oxicam	Oil-in-water microemulsion	Oleic acid, Labrasol, Ethanol	Improved skin permeation	64

Table.3 Novel drug delivery systems for DMARDs in the treatment of Rheumatoid arthritis.

Drug	**Chemical class & Sub class**	**Drug delivery system**	**Components**	**Observations**	**References**
Methotrexate	Class: Carboxylic acid Subclass: Pentane-dioic acid	Microspheres	Poly (1- lactic acid)	Prolonged release	65
Methotrexate	Class: Carboxylic acid Subclass: Pentane-dioic acid	Hydrogel	Poly (lactic-co-glycolic acid)	Controlled & Sustained release	66
Sulfasalazine	Class: NSAIDs Subclass: DMARDs	Hydrogel	Poly (lactic-co-glycolic acid)	Improved Bioavailability Targeted Delivery	67
Leflunomide	Class: Carboxamide	Microspheres	Poly methacrylate	Prolonged release	68
Hydroxy chloroquine	Class: Amino quinoline	Nanoparticles	Poly (lactic-co-glycolic acid)	Drug Encapsulation & Targeting	69

Table.4 Novel drug delivery systems for Corticosteroids in the treatment of Rheumatoid arthritis.

Drug	**Chemical class & Sub class**	**Drug delivery system**	**Components**	**Observations**	**References**
Prednisone	Class: Corticosteroid Subclass: Glucocorticoid	Hydrogel	Bio polymers	Controlled drug release, Reduced side effects	70
Methyl prednisone	Class: Corticosteroid Subclass: Glucocorticoid	Nanoparticles	t-Bec-glycine, cyclodextrin	Improve efficacy, Decreased dosing frequency	71
Hydrocortisone	Class: CorticosteroidSubclass: Glucocorticoid	Microspheres	Biopolymers, Tween 80	Controlled & sustained drug release, Bio degradability	72
Dexamethasone	Class: CorticosteroidSubclass: Glucocorticoid	Nanoparticles	Bio polymers	Enhanced efficacy & Sustained drug release	73

5. Conclusion

In recent years, there has been a growing interest in developing novel drug delivery systems (NDDS) for the treatment of rheumatoid arthritis (RA) due to their potential for versatile applications. These advanced systems are seen as a promising approach to improve the effectiveness of RA therapies by providing targeted, controlled, and sustained release of medications. The ability of NDDS to enhance drug bioavailability, reduce side effects, and optimize treatment regimens holds significant promise for the future of RA management. As research in this area progresses, NDDS is expected to improve patient outcomes and offer new therapeutic possibilities for those suffering from this debilitating disease.

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