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REVIEW ARTICLE

Role of Nanotechnology in the Management of Rheumatoid Arthritis

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Abstract

Rheumatoid arthritis (RA) is a debilitating autoimmune disease characterised by chronic inflammation of synovial joints, resulting in pain, stiffness and potential joint and bone damage. Left untreated, RA significantly impacts daily life and may lead to severe disability or death. Early diagnosis is critical to curbing disease progression and reducing inflammation and joint damage. Traditional drug therapies, although effective, often pose severe side effects, prompting interest in alternative and complementary approaches. Nanotechnology, particularly nanoparticles, has emerged as a transformative tool in RA management, offering enhanced drug delivery, improved diagnostic precision and reduced systemic side effects. This review explores the multifaceted role of nanotechnology in RA diagnosis and treatment, emphasising the synergistic potential of nanomedicine and natural compounds. Existing knowledge gaps and future research directions in leveraging nanotechnology for RA treatment are also discussed.

Key words: Arthritis, rheumatoid; Autoimmune diseases; Nanotechnology; Nanoparticles; Drug delivery systems; Pharmaceutical preparations; Inflammation; Joints.

Introduction

Rheumatoid arthritis (RA) is a common systemic chronic inflammatory disease which affects 1 % of the adult population globally. The term RA explains a disease spectrum. This spectrum is characterised with symmetrical occurrence and destructive nature. The disease causes significant discomfort due to joint swelling and irritation of the synovial membrane that lines the joints. Patients also suffer from inflammation of cartilage and bone. In some cases, diagnosis may involve detecting rheumatoid factor or anti-cyclic citrullinated peptide (anti-CCP) antibodies, both of which are important markers in rheumatoid arthritis. RA causes a decrease in the life quality and duration. It is an autoimmune disease with the occurrence of synovial membrane inflammation, which leads to pain and stiffness. RA can lead to the condition where the patient becomes unable to do daily routine tasks and even can cause death if left untreated. The timely diagnosis and treatment of RA is essential and beneficial. RA damages the cartilage and bone.[1, 2] As RA affects joints, it may lead to limited physical activity in the patients, leading to further systemic complications. According to research, the symptoms of RA most commonly begin between the ages of 20 and 40; however, they can also appear outside this range, including in older adults and

in children, where the condition is diagnosed as juvenile idiopathic arthritis.[3-10] The prevalence of RA is notably higher among women than men, due to a combination of genetic, hormonal and immunological factors.[3, 10]

The development of RA is influenced by a range of genetic, epigenetic and environmental factors. Environmental contributors include smoking, obesity, stress and exposure to infectious agents such as *Mycoplasma pneumoniae* and Epstein–Barr virus (EBV), which are known to activate immune responses associated with RA pathogenesis.[11-13] Additional risk factors include increasing age, female sex and family history of autoimmune diseases.[10, 14]

Advancements in RA therapy have significantly improved patient outcomes. It has been well-established that early diagnosis, along with the initiation of disease-modifying anti-rheumatic drugs (DMARDs) such as methotrexate and the use of biologic agents in appropriate cases, can improve prognosis, slow disease progression and preserve joint function.[9, 11, 14]

Chronic inflammation of the synovial joints is a hallmark of RA and plays a central role in disease progression and diagnosis.[1, 9, 10, 15] This condition leads to articular joint destruction and bone erosion, which results in severe inability. Though the leading cause and pathogenesis of RA are not known, RA has a strong genetic component, as evidenced by genome-wide association studies (GWAS) that have identified numerous susceptibility genes. Among these, the strongest association is with the HLA-DRB1 gene, particularly alleles encoding the 'shared epitope' sequence, which significantly increases the risk of developing RA. Many genes are included in genome-wide association studies. Some environmental factors also play important roles in the aetiology and pathogenesis of RA. These environmental factors include vaccine responses, emotional trauma and infections. Several infectious agents have been implicated in the development of RA, including EBV, *Parvovirus B19*, *Proteus mirabilis*, *Mycoplasma pneumoniae* and *Porphyromonas gingivalis*. In the early stages, diagnosis of RA is essential because early diagnosis reduces the progression of the disease. Reduction in the progression of disease indicates stopping the development of inflammation and continuous joint damage. Clinical identification of RA is not simple. The clinical diagnosis of RA is guided by the 2010 ACR/EULAR classification criteria, which include factors such as joint involvement, serology (rheumatoid factor and anti-CCP antibodies), acute-phase reactants (CRP and ESR) and symptom duration of at least six weeks. Efficacious and absolute repression of RA should be the initial therapeutic goal.[16-18]

However, clinical diagnosis remains challenging due to the overlapping symptoms of RA with other autoimmune and inflammatory conditions, such as systemic lupus erythematosus (SLE), psoriatic arthritis, ankylosing spondylitis and Sjögren's syndrome. Current treatment strategies primarily involve synthetic drugs, such as non-steroidal anti-inflammatory drugs (NSAIDs), disease-modifying anti-rheumatic drugs (DMARDs), which mitigate inflammation and slow disease progression. Yet, these therapies are often associated with adverse effects, high costs and limited long-term efficacy.[19, 20]

While conventional therapies have shown efficacy in managing RA, challenges remain in reducing systemic side effects and achieving long-term remission. There is a pressing need for innovative approaches to improve drug delivery, enhance therapeutic outcomes and reduce adverse effects. Nanotechnology offers significant promise in addressing these challenges, yet its potential in RA treatment is underexplored in clinical settings. Furthermore, the integration of natural products with nanomedicine for RA management is an emerging area that requires systematic investigation.

This review aims to provide an in-depth analysis of the role of nanotechnology in the diagnosis and treatment of RA. A comprehensive literature search was conducted using databases such as *PubMed, Scopus* and *Web of Science*. The search included articles published up to 2025, focusing on keywords such as "Rheumatoid Arthritis," "Nanotechnology," "Nanoparticles," "Drug Delivery Systems," "Natural Compounds," and "Rheumatoid Arthritis Diagnosis." Studies were selected based on relevance to the role of nanotechnology in RA diagnosis and treatment, as well as their focus on the integration of natural products. The application of nanoparticles, liposomes and other nanocarriers in drug delivery and diagnostics was explored. In addition, the synergistic use of natural products and nanotechnology was examined, highlighting their potential to enhance therapeutic efficacy and reduce adverse effects.

Role of nanotechnology in the treatment of rheumatoid arthritis

Nanotechnology is an interdisciplinary field that has shown remarkable promise across various domains, particularly in healthcare and biomedical research. Its unique ability to manipulate matter at the nanoscale has opened new frontiers in diagnostics, therapeutics and targeted drug delivery. By engineering materials at the molecular level, nanotechnology offers a platform to overcome the limitations of conventional treatment strategies, making it a transformative tool in modern medicine.

In the medical field, nanotechnology is being increasingly applied to enhance the efficacy and safety of therapeutic agents. Nanoparticles can improve the solubility of water-insoluble drugs, increase dissolution rates through an expanded surface area and prolong the half-life of active compounds in systemic circulation. These properties make nanocarriers highly suitable for treating a wide range of conditions, including cancer, cardiovascular diseases, asthma, infections, diabetes and various autoimmune disorders.[21] Furthermore, nanotechnology supports the development of advanced drug delivery systems that enable controlled release, targeted localisation and reduced systemic toxicity.

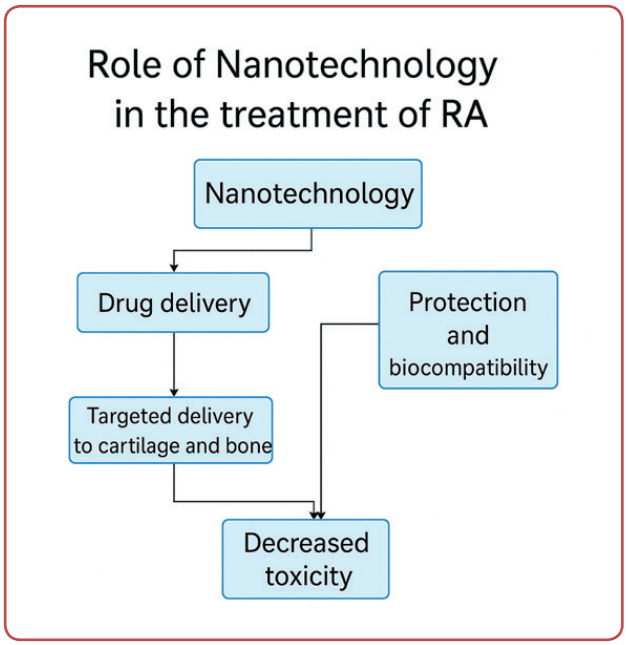

Figure 1: Role of nanotechnology in the treatment of rheumatoid arthritis

Within the context of autoimmune diseases like RA, nanotechnology plays a vital role in improving treatment outcomes. RA patients often rely on anti-inflammatory drugs, corticosteroids, DMARDs and biologics. While these treatments can alleviate symptoms, their long-term use is frequently associated with severe adverse effects such as liver damage, tuberculosis, fungal infections and heart failure.[22, 23] To address these challenges, researchers have developed nanoparticle-based drug delivery systems that allow for precise targeting of inflamed joints. These nanocarriers—engineered to transport drugs like methotrexate or dexamethasone directly to affected tissues—minimise off-target effects and improve therapeutic efficiency. The use of nanotechnology in RA therapy offers multiple advantages. Nanoparticles enhance drug bioavailability, reduce systemic side effects and enable sustained drug release, resulting in prolonged medicinal effects. Additionally, their biocompatibility and ability to interact with specific cellular targets contribute to improved joint protection and reduced inflammation. Figure 1 provides a schematic overview of how nanotechnology functions in the treatment of RA.

Nanoparticles and their role in the diagnosis and treatment of rheumatoid arthritis

Nanomaterials are beneficial for disease treatment because they are a special carrier in the drug delivery system. Nanocarriers come in various forms, including nanoparticles, liposomes, nanotubes, unique crystalline structures and superparamagnetic iron oxide particles.

Nanoparticles come in several forms, including polymer-based particles, magnetic types, liposomes, metal-based variants and polymeric micelles. Approaches to managing RA with nanomaterials can be categorised into traditional, biomimetic, or direct therapeutic use of the nanomaterials themselves.[24]

Traditional nanomaterials used in RA therapy typically include organic polymer nanocarriers, liposomes and inorganic particles, which serve as passive delivery vehicles for anti-inflammatory drugs. These nanomaterials act like anti-inflammatory drug carriers.[25] This drug is delivered to the joints for its better build-up in the joints.[26] In

this way, the outcome of the drug is increased. Some carriers of anti-inflammatory drugs are organic polymer nanocarriers, liposomes and inorganic nanomaterials. Polymer nanoparticles are being used broadly as drug carriers. These nanoparticles target certain organs and tissues. These nanoparticles have better biocompatibility and biodegradability. In this case, the drug is encased in a nanocarrier and sent to a fixed location by a targeted process. In this case, the drug is encapsulated in a nanocarrier and delivered to a specific location through a targeted process, which may involve passive targeting such as enhanced permeability and retention (EPR) effect in inflamed tissues or active targeting, where nanoparticles are functionalised with ligands (eg, antibodies or peptides) that bind to overexpressed receptors at the site of inflammation. Currently, the most familiar process is to change the exterior of nanoparticles by polyethene glycol (PEG). This surface modification enhances the physiological stability and bioavailability of the nanoparticles, allowing for prolonged circulation and improved accumulation at inflamed joint sites. Not only this, immunogenicity is also decreased by it, which makes clearance and recognition tough for the immune system. According to research, polycaprolactone–polyethylene glycol (PCL–PEG) micelles were employed as drug carriers to deliver lower doses of dexamethasone for the treatment of RA, aiming to reduce systemic exposure while maintaining therapeutic efficacy. The micelles remained in the circulatory system for a prolonged time. Then, the micelles are specifically delivered and built up in the location where the joint is inflamed. The findings indicated that delivering dexamethasone through micelles effectively reduced joint swelling, prevented bone deterioration and lowered levels of inflammation-related markers in both the bloodstream and joint tissue.

On the other hand, the negative impact of PCL-PEG micelles on parameters such as blood glucose levels, overall body mass and lymphocyte numbers was significantly lower compared to the effects seen with dexamethasone alone. Additionally, these micelles showed minimal stimulation of the complement system.[14] Another study developed alginate-based nanoparticles carrying IL-10 plasmid DNA. To enhance targeting of macrophages, the nanoparticle surface was modified with tuftsin peptides. MRI scans and tissue analysis revealed that employing nanotechnology for treatment—specifically using nanoparticles—led to a decrease in pro-inflammatory cytokine levels, particularly in joint tissues. This approach also helped to protect joints and slow the advancement of inflammation. Nanoparticles facilitated the transition of macrophages from the pro-inflammatory M1 state to the anti-inflammatory M2 type. Furthermore, in a separate study using a RA model, nanoparticles showed notable accumulation in inflamed joints, along with a significant drop in inflammatory mediator expression.[27]

Liposomes and their role in the diagnosis and treatment of rheumatoid arthritis

Liposomes are another key type of nanoparticles, characterised by their spherical shape and bilayer membrane structure. The outer layer is composed of naturally derived phospholipids, while the inner core contains an aqueous environment. Numerous studies indicate that liposomes are being explored as innovative carriers for delivering various therapeutic agents.[15] The nature of liposomes makes them capable of serving as a successful and productive system of delivery. In this system, drugs are either packed in a double-layered lipid membrane or the inner cavity. So, these liposomes are being used for the treatment of RA. Polyethylene glycol, a productive hydrophilic polymer, decreases liposome absorption and identification. This is done by the reticuloendothelial system, also known as RES. In this way, the duration of liposomes in the circulatory system is increased. For better outcome of dexamethasone in curing arthritis, liposomes are also being used as a carrier. Various studies have shown that liposomes are specifically collected in inflammatory joints. After being injected, liposomes inhibit factors that promote inflammation in the tissues of joints. They also lessen the swelling of the inflamed joints.

Metallic nanoparticles and their role in the diagnosis and treatment of rheumatoid arthritis

Metallic nanoparticles possess unique physicochemical properties such as high surface ar-

ea-to-volume ratio, surface plasmon resonance, magnetic responsiveness and ease of functionalisation, making them highly suitable for targeted drug delivery, imaging and therapeutic applications in RA and their usage increases in last few decades in biomedical applications. For the treatment of RA, nanoparticles made from metals such as iron, gold and cerium are currently in use. Research indicates that Arginine–Glycine–Aspartic acid peptides can target sites of inflammation, while the gold half-shell generates heat, which accelerates the release of drugs. This allows for both heat and therapeutic agents to be delivered directly to the inflamed joints under near-infrared light. In a collagen-induced arthritis mouse model, methotrexate-loaded nanoparticles (Au-halfshell PLGA NPs) delivered just 1/1400 of the standard MTX dose used conventionally, yet when combined with nearinfrared (NIR) irradiation, they achieved therapeutic efficacy comparable to full-dose MTX. Studies also suggest that gold nanoparticles help inhibit angiogenesis, while the hyaluronic acid-coated gold nanoparticle–tocilizumab. The hyaluronic acid-coated gold nanoparticle–tocilizumab (HA–Au NP/TCZ) complex demonstrates effectiveness in treating RA by targeting inflamed joints, where hyaluronic acid facilitates joint-specific accumulation and tocilizumab inhibits interleukin-6 receptor signalling, thereby reducing inflammation and joint damage. Additionally, HA has been observed to provide protection for joint lubrication and cartilage. Similarly, the iron half-shell enables targeted delivery of nanoparticles to inflamed joints through an external magnetic field, enhancing their persistence in the affected areas. Cerium oxide nanoparticles, when combined with albumin, present a promising new approach in the treatment of RA due to their potent antioxidant and anti-inflammatory capabilities. These nanoparticles scavenge reactive oxygen species (ROS) and modulate pro-inflammatory cytokines, helping to alleviate oxidative stress and inflammation in the synovial joints, which are key contributors to RA pathogenesis.[27]

One of the broadly used inorganic non-metallic materials for the treatment of RA is silicium. In a study, a precise model of rat arthritis was observed. This model showed that silica encourages the manufacturing of hyaluronic acid and decreases inflammation of synovial joints. It also promotes bone reconstruction. Among various hyaluronic acid (HA) delivery methods, surface functionalisation with polyethyleneimine (PEI) to carry hyaluronic acid synthase type 2 has proven more effective and easier to implement, yielding longer-lasting and more pronounced therapeutic effects.[27]

In some cases, nanomaterials coated with cell membranes are used for the treatment of RA. A biological cell delivery system decreases the immunogenicity of nanoparticles. The use of endogenous biological membranes as functional coatings prolongs the systemic circulation of nanoparticles. These membranes also mask the antigenic properties of the nanomaterials, thereby reducing immune recognition. Macrophages and neutrophils, as key innate immune cells, play a central role in mediating the body's inflammatory response. These cells increase the cellularity of the synovial membrane, leading to synovial thickening and the development of synovial hyperplasia. Ribonucleic acid and proteins are involved in the cell vesicles known as exosomes. Exosomes are used as drug carriers to enhance biocompatibility. They allow more customised treatment of inflammation.[28] Exosome-based nanoparticle drug delivery systems are being explored for the treatment of several diseases, including RA, Parkinson's disease, cancer, encephalitis and nephropathy.[29]

Non-steroidal anti-inflammatory drugs, which are also known as NSAIDS, are very effective in relieving inflammation and pain. Similarly, disease-modifying anti-rheumatic drugs, which are also known as DMARD (methotrexate, hydrochloroquinone, sulfasalazine and leflunomide), are being used as the first-line therapy. The products that are being used for the therapy or treatment of RA include non-steroidal anti-inflammatory drugs, disease-modifying anti-rheumatic drugs, biological agents and glucocorticoids. Different anti-inflammatory and disease-modifying drugs are being used for the treatment of RA, but due to the unwanted and adverse side effects of their long-term use there is a need for new therapeutic agents that are not only effective but are a safer option also. There are various herbs and plant-derived compounds available that exhibit anti-rheumatic properties and may serve as adjuncts in the treatment of RA. However, despite their natural origin, some of these products may cause adverse effects or interact with conventional medications, necessitating proper evaluation and monitoring. The exploration of natural products offers a cost-effective approach to managing RA, with several compounds demonstrating potential to relieve pain and reduce inflammation.[30]

Use of natural products by rheumatoid arthritis patients

There are several natural products that patients with RA are using to relieve symptoms and complement conventional treatment strategies. However, these natural products tend to be expensive and there is a lack of sufficient information regarding their mechanisms of action. This leads to uncertainty and scepticism among professionals and the public.

Research indicates that natural products, such as curcumin (a polyphenol derived from *Curcuma longa*), can aid in managing inflammation associated with RA by targeting several biological processes. Curcumin has been shown to reduce the activity of inflammatory mediators, including proinflammatory cytokines and chemokines, while enhancing the production of anti-inflammatory cytokines like IL-4 and IL-10. Additionally, it modulates immune cell function and maintains the balance between Th17 cells and regulatory T cells (Tregs). These therapeutic effects are largely attributed to its ability to inhibit key signalling pathways, such as NF-κB, MAPK and STAT3.[7]

Cytokines that are influenced by changes in the Th17/Treg balance include IL-1β, TGF-β and IL-6. Key transcription factors involved in this regulation process are signal transducer and activator of transcription 3, retinoic acid receptor–related orphan receptor gamma, interferon regulatory factor 4, Forkhead box P3. Overall, natural products help regulate the Th17/Treg balance by modulating these cytokines and transcription factors, which not only impacts T cell responses but also affects immune system interactions and bone health through the involvement of various signalling molecules.[31]

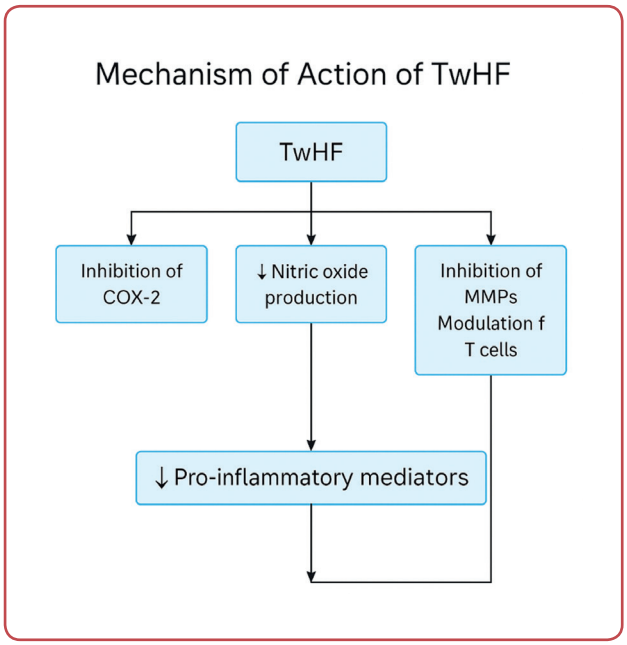

Figure 2: Mechanism of action of Tripterygium wilfordii Hook F (TwHF)

These natural products can either relieve symptoms and contribute to the treatment of RA independently, or they can be used in combination with conventional anti-arthritic drugs. For instance, studies have demonstrated that *Tripterygium wilfordii* Hook F (TwHF) used alongside methotrexate improves clinical outcomes and reduces inflammation more effectively than methotrexate alone. Similarly, compounds such as curcumin and resveratrol have shown synergistic effects when combined with standard DMARDs, enhancing therapeutic efficacy and minimising drug-induced toxicity. It is important for patients to undergo thorough assessments when using these combinations due to the potential for unexpected side effects and drug interactions.

One well-researched natural compound is TwHF, known for its therapeutic effects in RA through its ability to suppress several inflammatory factors. For instance, TwHF extract reduces the in vitro synthesis of prostaglandin E2 by inhibiting COX-2. It also lowers the expression of the inducible nitric oxide synthase gene, thus limiting nitric oxide production. In human synovial fibroblasts, TwHF promotes the activity of tissue inhibitors of metalloproteinases, which then reduce the activity of Matrix metalloproteinase-1 (interstitial collagenase) MMP1 and MMP2 Matrix metalloproteinase-2 (gelatinase A), while also decreasing the expression of MMP1 and MMP3. Additionally, TwHF reduces the levels of MMP3 and MMP13 by inhibiting their transcription. The mechanism of action of TwHF is illustrated in Figure 2.

Studies conducted by Zheng et al have shown that the transcription of inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) is regulated by nuclear factor kappa B (NF-κB) and TwHF inhibits this activation by preventing NF-κB from binding to DNA, thereby reducing the levels of nitric oxide and COX-2.[27] TwHF has also been reported to lower the production of several pro-inflammatory cytokines, including TNF-α, IL-1β, IL-6, IL-8 and IFN-γ, secreted by T cells and

macrophages.[27] Regulation of T cell populations and their differentiation is crucial in the pathogenesis of RA. Furthermore, Mittal et al highlighted that TwHF suppresses the proliferation of T cells and synovial fibroblasts, which contributes to its therapeutic efficacy in RA.[32, 33]

Studies comparing patients treated with methotrexate (MTX) alone to those receiving a combination of MTX and TwHF have shown that the combination therapy is more effective in reducing disease activity and improving clinical outcomes in RA patients.[27, 33] Additionally, multiple research findings including those by Zheng et al and Mittal et al have confirmed that TwHF is generally well-tolerated and safe for use in humans when administered within therapeutic dosage ranges.[27, 33]

Another product frequently used in the treatment of RA is triptolide. *In vitro* studies show that triptolide induces apoptosis of RA synovial fibroblasts at nanomolar concentrations (eg, ~100 nM), accompanied by suppression of STAT3 phosphorylation and JAK2/STAT3–mediated cytokine expression. Celastrol has demonstrated anti-arthritic and bone-protective effects *in vivo* at doses of 1–3 mg/kg (eg, 3 mg/kg IP in CIA mice; 1 mg/kg orally in arthritic rats). *In vitro,* it suppresses osteoclastogenesis in RAW264.7 cells at 0.03–0.3 μM, reducing expression of key transcription factors (TRAP, NFATc1, cFos). Research indicates that celastrol can reduce the severity of arthritis while suppressing the generation of inflammatory cytokines. Additionally, studies have shown that these bioactive components offer protection against bone damage, contributing to their therapeutic effect.

Patents and marketed products

As there are various causes of RA, new drugs and therapies development is important. There are different patents which are helpful in the treatment of RA. Some synthetic compounds which are used in the treatment of RA are NSAIDS, disease modifying anti RA drugs and glucocorticoids.

Non-steroidal inflammatory drugs (like ibuprofen and meloxicam, etc) are pain relievers and they lay their role by decreasing the metabolism of the arachidonic acid for the production of prostaglandins E2, thromboxane and other inflammation-causing mediators. Cyclooxygenase is inhibited by using NSAIDs. By inhibiting cyclooxygenase enzymes, NSAIDs reduce the synthesis of prostaglandins, leading to decreased hyperaemia and exudation. This mechanism contributes to the alleviation of joint pain and swelling. Non-steroidal anti-inflammatory drugs do not alter the pathogenesis of RA. Severe gastrointestinal, cardiovascular and other adverse effects mostly limit the use of non-steroidal anti-inflammatory drugs.[30, 31]

Biological modifying rheumatic drugs are being used in the treatment of RA. In current years, disease-modifying anti-inflammatory drugs are being recommended at a high rate by physicians because of their effects on the treatment of RA. Owing to the high cost of DMARDs, they are used just in case when other treatment options are not effective.[32, 33]

Marketed products for rheumatoid arthritis

Several herbal products are currently marketed for the management of RA, many of which possess anti-inflammatory, immunomodulatory and joint-protective properties. For example, "PG201" (marketed by Himalaya) contains *Angelica sinensis* (Dong Quai), *Cnidium officinale* and *Cinnamomum cassia* (cinnamon), whose active constituents such as ferulic acid, ligustilide and cinnamaldehyde help reduce inflammation by modulating the NF-κB pathway and inhibiting cyclooxygenase (COX) activity. "RumoGin 5" capsules combine *Curcuma longa* (turmeric), *Zingiber officinale* (saunth/ginger), *Boswellia serrata* (shallaki), *Camellia sinensis* (maicha) and *Piper longum* (pippali). These ingredients contain curcuminoids, gingerols and boswellic acids, which inhibit pro-inflammatory cytokines like TNF-α and IL-6 and suppress COX-2 and 5-lipoxygenase activity, helping to relieve joint pain and swelling.[34-37]

"Aamvatantak Churna" includes *Withania somnifera* (ashwagandha), *Trigonella foenum-graecum* (fenugreek), *Tinospora cordifolia* (giloy), *Boerhavia diffusa* (punarnava) and *Clerodendrum serratum* (bharangi), which act through antioxidant and immunomodulatory pathways. Withanolides

from ashwagandha and tinosporaside from giloy have been shown to inhibit pro-inflammatory mediators and support joint function. "Boswellia-curcumin" capsules, composed of *Boswellia serrata* and *Curcuma longa*, provide a synergistic effect in reducing inflammation and protecting cartilage, with standard doses often including 250 mg of boswellic acids and 500 mg of curcuminoids.[38-40]

“Joint Care B” contains *Alpinia galanga*, *Vitex negundo*, *Glycyrrhiza glabra* (licorice) and *Foeniculum vulgare* (fennel). These plants offer anti-inflammatory and analgesic effects through bioactive compounds like galangin and glycyrrhizin. “Joint Aid Plus”, another polyherbal formula, includes *Tinospora cordifolia*, *Vitex negundo*, *Zingiber officinale*, *Commiphora wightii* (guggul) and *Withania somnifera*. Guggulsterones and gingerols work synergistically to reduce inflammation and oxidative damage in joints.[41]

"Curcumin" capsules, containing ≥ 95 % curcuminoids, are widely used for their ability to inhibit inflammatory cytokines and modulate immune responses via NF-κB and MAPK signalling pathways. “Coral Calcium Complex” includes *Praval pishti* (coral calcium), *Akik pishti*, *Kombucha rasa* and *Tinospora cordifolia*, supporting bone health through mineral supplementation and immune modulation. Finally, “Bone Support” capsules, composed of *Cissus quadrangularis* (asthishrinkhala), *Laccifer lacca* (laksha), *Terminalia arjuna* and *Praval pishti*, promote bone regeneration and joint mobility, primarily through the action of flavonoids and plant sterols that reduce joint inflammation and stimulate osteoblast activity.[42-44] These herbal formulations demonstrate promising effects in managing RA. However, the concentration of active ingredients may vary by manufacturer and their use should be based on medical guidance to avoid interactions or unintended side effects.

Conclusion

RA remains a significant global health challenge, demanding innovative therapeutic strategies. Nanotechnology, with its precise drug delivery systems and diagnostic advancements, offers transformative potential in managing RA. Combined with natural products, nanomedicine could pave the way for safer, more effective treatment regimens. However, further research is essential to bridge the gap between preclinical success and clinical applications, ensuring that these advancements translate into tangible benefits for patients. By leveraging interdisciplinary approaches, we can address the unmet needs in RA management and improve patient outcomes.

Ethics

This study was a secondary analysis based on the currently existing data and did not directly involve with human participants or experimental animals. Therefore, the ethics approval was not required in this paper.

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Conflicts of interest

The authors declare that there is no conflict of interest.

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Data access

The data that support the findings of this study are available from the corresponding author upon reasonable individual request.

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