International Journal of Science and Research (IJSR)
ISSN: 2319-7064
Impact Factor 2025: 7.089

Formulation and Characterization Approaches for Herbal Extract-Based Delivery Systems in the Management of Rheumatoid Arthritis: A Review

Shruti Singh

Department of Pharmaceutics, United Institute of Pharmacy, Naini, Prayagraj, Uttar Pradesh, India

Abstract: ***Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disorder marked by persistent synovial inflammation, progressive cartilage and bone erosion, and, over time, joint deformity and functional disability. Conventional pharmacotherapy with non-steroidal anti-inflammatory drugs, corticosteroids, disease-modifying antirheumatic drugs, and biologics provides meaningful symptomatic and disease-modifying benefit, but long-term use is frequently limited by gastrointestinal, hepatic, renal, and immunosuppressive adverse effects. This has renewed interest in plant-derived extracts and phytoconstituents as adjunct or alternative anti-arthritic agents, owing to their anti-inflammatory, antioxidant, and immunomodulatory activity and generally favourable safety profile. However, most herbal extracts suffer from poor aqueous solubility, extensive first-pass metabolism, low oral bioavailability, and batch-to-batch variability, which has driven the development of novel formulation strategies-polymeric and lipidic nanoparticles, liposomes, niosomes, solid lipid nanoparticles, nanostructured lipid carriers, cubosomes, microspheres, and topical/transdermal systems-to improve their delivery to inflamed joint tissue. Robust physicochemical, solid-state, and biological characterization is central to translating these formulations from bench to a reproducible, quality-controlled product. This review consolidates the formulation strategies reported for herbal extracts in RA and provides a focused, technique-by-technique account of their characterization: phytochemical standardization, particle size/polydispersity index/zeta potential analysis, morphological evaluation by electron and atomic force microscopy, entrapment and loading efficiency determination, solid-state analysis by FTIR, DSC, XRD and TGA, in vitro release and kinetic modelling, stability assessment under ICH conditions, and in vivo evaluation in adjuvant-induced arthritis models. The challenges unique to characterizing multi-component herbal systems, and the outlook for standardized, regulatory-ready herbal nanomedicines in RA, are also discussed.***

Keywords: Rheumatoid arthritis; herbal extract; nanoparticle; formulation; characterization; phytochemical standardization; anti-arthritic activity

1. Introduction

Rheumatoid arthritis is one of the most prevalent chronic inflammatory joint disorders worldwide, affecting roughly 0.5-1% of the adult population in most regions, with a higher burden reported in women. It is driven by a complex interplay of genetic susceptibility, environmental triggers, and dysregulated innate and adaptive immunity, culminating in synovial hyperplasia, pannus formation, and progressive destruction of cartilage and juxta-articular bone. Elevated pro-inflammatory cytokines such as TNF-alpha, IL-1beta, and IL-6, together with autoantibodies including rheumatoid factor and anti-citrullinated protein antibodies, are central to disease pathogenesis and are widely used as both diagnostic markers and therapeutic targets.

Current standard-of-care agents-NSAIDs, glucocorticoids, conventional synthetic DMARDs such as methotrexate, and biologic agents targeting TNF-alpha or IL-6-can control symptoms and slow structural progression, but chronic administration is associated with gastrointestinal ulceration, hepatotoxicity, nephrotoxicity, hypertension, and increased susceptibility to infection. These limitations, combined with variable patient response and high treatment cost, particularly for biologics, have sustained interest in plant-derived alternatives that act through anti-inflammatory, antioxidant, and immunomodulatory mechanisms with comparatively favourable tolerability.

Numerous herbal extracts and isolated phytoconstituents-curcumin, boswellic acids, resveratrol, quercetin, withanolides, gingerols, and extracts from Phoenix dactylifera, Urtica dioica, Bistorta amplexicaulis, Cardiospermum halicacabum, and Vitex negundo among others-have demonstrated anti-arthritic activity in preclinical adjuvant-induced arthritis models. The clinical translation of these findings, however, is consistently constrained by poor aqueous solubility, extensive hepatic first-pass metabolism, rapid systemic clearance, and inherent variability in phytochemical composition depending on plant source, extraction method, and storage conditions. Novel drug delivery systems-particularly nanoparticulate carriers-have therefore been explored to enhance the solubility, stability, joint-tissue retention, and controlled release of these extracts, while simultaneously reducing the systemic exposure responsible for off-target toxicity.

Because a herbal nanoformulation carries the combined complexity of a multi-component natural extract and a colloidal or particulate delivery system, its characterization must be considerably more rigorous than that of a single-molecule synthetic drug product. This review brings together the formulation approaches reported for herbal extracts in RA and examines, in depth, the physicochemical, solid-state, and biological characterization techniques used to establish their identity, quality, stability, and anti-arthritic performance.

2. Rheumatoid Arthritis: Pathophysiology and Rationale for Herbal Interventions

RA pathogenesis begins with activation of innate immune cells-macrophages and dendritic cells-in a genetically susceptible individual, often following an environmental trigger such as smoking or periodontal infection with

organisms like Porphyromonas gingivalis. Citrullination of self-proteins generates neoantigens that are recognized by autoreactive T and B cells, leading to production of rheumatoid factor and anti-citrullinated protein antibodies and to sustained activation of synovial fibroblasts. The resulting synovitis is characterized by infiltration of T cells, B cells, and macrophages, angiogenesis, and hyperplastic pannus formation that progressively erodes articular cartilage and subchondral bone.

Pro-inflammatory mediators-TNF-alpha, IL-1beta, IL-6, and IL-17-drive osteoclastogenesis and matrix metalloproteinase release, both of which are central to joint destruction, while reactive oxygen species contribute to oxidative damage of synovial tissue. This mechanistic picture explains why phytoconstituents with anti-inflammatory, antioxidant, and immunomodulatory activity are mechanistically plausible anti-arthritic agents: many polyphenols and terpenoids downregulate NF-kappaB signalling, suppress cyclooxygenase and lipoxygenase pathways, scavenge free radicals, and modulate T-helper cell balance, thereby addressing several arms of RA pathophysiology simultaneously rather than a single molecular target.

The preclinical adjuvant-induced arthritis (AIA) model, most commonly produced using Freund's complete adjuvant (CFA) or collagen, remains the standard in vivo system for evaluating candidate herbal formulations. It reproduces key features of human RA-paw oedema, synovial infiltration, cartilage erosion, and elevation of inflammatory cytokines-allowing formulation performance to be assessed alongside standard anti-arthritic drugs.

3. Herbal Extracts Investigated in Rheumatoid Arthritis

A wide range of herbal extracts has been formulated and evaluated for anti-arthritic activity, either as the crude extract, a standardized fraction, or an isolated marker compound. Table 1 summarizes representative examples reported in the recent literature, spanning traditional systems of medicine and more recent green-synthesis approaches.

Table 1: Representative herbal extracts investigated for anti-arthritic activity and their formulation approaches

Plant / Extract	Key Bioactive Class	Delivery System Explored	Reported Outcome
Curcuma longa (curcumin)	Curcuminoids (polyphenol)	Polymeric NPs, SLNs, niosomes	Reduced paw oedema and cytokine levels in AIA models; improved oral bioavailability over free curcumin
Boswellia serrata	Boswellic acids (triterpenoid)	Self-emulsifying systems, NPs	5-LOX inhibition; reduced joint swelling in preclinical models
Urtica dioica (stinging nettle)	Flavonoids, phenolics	Topical herbal gel	Comparable paw-oedema inhibition to 2% indomethacin gel in carrageenan-induced models
Bistorta amplexicaulis (root)	Polyphenols; used for green synthesis	Green-synthesized CuO nanoparticles	Marked anti-arthritic activity in adjuvant-induced arthritic rats, exceeding the crude extract alone
Cardiospermum halicacabum + Vitex negundo (leaves)	Flavonoids, terpenoids	Topical herbal gel	Reduced paw volume and TNF-alpha with favourable histopathology in CFA model
Phoenix dactylifera (date seed)	Phenolics, flavonoids, polysaccharides	Chitosan nanoparticles (ionic gelation)	Box-Behnken-optimized nanoparticles showed sustained release and anti-arthritic activity in CFA-induced arthritis
Withania somnifera (ashwagandha)	Withanolides	Nanoemulsion, solid dispersion	Immunomodulatory and anti-inflammatory effects reported in preclinical arthritis studies

4. Formulation Strategies for Herbal Extracts in Rheumatoid Arthritis

Because most herbal actives are poorly water-soluble and prone to degradation in the gastrointestinal tract, the choice of delivery platform has a direct bearing on achievable joint-tissue concentrations. The principal formulation strategies reported for herbal extracts in RA are summarized below.

Polymeric nanoparticles. Biodegradable and mucoadhesive polymers such as chitosan, PLGA, and Eudragit derivatives are widely used to encapsulate herbal extracts. Chitosan nanoparticles prepared by ionic gelation with tripolyphosphate are particularly common for polyphenol-rich extracts because the process avoids organic solvents and harsh conditions that could degrade thermolabile phytoconstituents, while the cationic chitosan matrix favours mucoadhesion and sustained release. PLGA-based systems, often embedded within a hydrogel for injectable joint delivery, allow tunable, sustained release over days to weeks.

Lipid-based carriers. Solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs) improve the solubility and lymphatic uptake of lipophilic herbal actives (e.g., curcuminoids, boswellic acids) while offering better physical stability than liposomes. Liposomes and niosomes provide bilayer or non-ionic surfactant vesicles capable of co-encapsulating hydrophilic and lipophilic phytoconstituents and are frequently explored for topical or transdermal anti-arthritic gels.

Cubosomes. These self-assembled, bicontinuous cubic-phase lipid nanoparticles have emerged as a newer nanocarrier for herbal compounds in arthritis therapy, offering a large internal surface area for drug loading and the ability to improve the stability and bioavailability of encapsulated actives relative to conventional vesicular systems.

Topical and transdermal systems. Given the accessibility of affected joints, herbal gels, ointments, and microneedle- or microsponge-based transdermal systems are attractive for delivering extracts such as Urtica dioica or Cardiospermum halicacabum directly to the inflamed site, bypassing hepatic first-pass metabolism and reducing systemic exposure. Physical enhancement techniques such as sonophoresis and electroporation, along with stimuli-responsive polymers, have been investigated to further improve cutaneous penetration.

Design-of-Experiments-guided optimization. Because herbal nanoformulations typically involve several interacting process and formulation variables (polymer/extract ratio, surfactant concentration, sonication time, cross-linker concentration), response-surface methodologies such as the Box-Behnken design (BBD) or central composite design (CCD) are increasingly used to optimize particle size, entrapment efficiency, and zeta potential simultaneously, reducing the number of experimental runs while generating a validated design space.

5. Characterization of Herbal Extract-Based Delivery Systems

Characterization of a herbal extract-based delivery system must proceed at two levels: first, confirming the chemical identity, purity, and consistency of the herbal extract itself (a step not required for single synthetic molecules), and second, evaluating the physicochemical, solid-state, release, stability, and biological performance of the finished formulation. The following subsections address each of these in turn.

5.1 Phytochemical Standardization and Preformulation Studies

Phytochemical standardization is the foundation of any herbal formulation study, since batch-to-batch variability in a plant extract can confound every downstream result. Preliminary qualitative phytochemical screening (tests for alkaloids, flavonoids, tannins, saponins, glycosides, and phenolics) establishes the presence of expected chemical classes. Quantitative standardization is then performed against a validated marker compound-total phenolic content and total flavonoid content assays are common first steps, followed by chromatographic fingerprinting.

High-performance thin-layer chromatography (HPTLC) is extensively used for rapid, cost-effective standardization of herbal extracts, typically against a known reference standard such as rutin or gallic acid, generating an Rf-value fingerprint and densitometric quantification of the marker compound. High-performance liquid chromatography (HPLC) provides higher resolution and sensitivity for quantifying multiple marker compounds simultaneously and is often used to confirm extract identity before and after incorporation into a delivery system, verifying that the encapsulation process itself has not degraded the active constituents. Voucher specimen authentication (e.g., through a recognized herbarium/botanical survey authority) is a further standardization step increasingly expected by peer-reviewed journals to establish unambiguous plant identity.

5.2 Particle Size, Polydispersity Index, and Zeta Potential

Particle size and its distribution (polydispersity index, PDI) govern the biological fate of a nanoformulation-cellular uptake, joint-tissue penetration, mucoadhesion, and physical stability are all size-dependent. Dynamic light scattering (DLS), also called photon correlation spectroscopy, is the standard technique for measuring hydrodynamic diameter and PDI of nanoparticle dispersions, typically reporting particle sizes in the 100-500 nm range for herbal polymeric nanoparticles, with a PDI below 0.3-0.5 generally considered acceptable for a reasonably monodisperse system; values above this indicate a broader, potentially aggregating population.

Zeta potential, measured by laser Doppler electrophoresis (often on the same instrument platform as DLS), quantifies the net surface charge of the nanoparticles and is a key predictor of colloidal stability. Chitosan-based herbal nanoparticles typically show a positive zeta potential (often +15 to +35 mV) due to the protonated amine groups of chitosan, while anionic cross-linkers or coating polymers can shift this toward neutral or negative values. As a general rule, an absolute zeta potential value greater than about 25-30 mV indicates adequate electrostatic repulsion to resist aggregation, whereas lower values raise the risk of flocculation on storage, particularly relevant for herbal systems where phenolic constituents can also influence surface charge and stability through their own ionizable groups.

5.3 Morphological Characterization (SEM, TEM, AFM)

Morphological evaluation confirms particle shape, surface texture, and the qualitative size distribution that complements DLS data. Scanning electron microscopy (SEM) is most frequently used to visualize surface morphology and detect aggregation or porosity, and is generally performed on dried, gold- or platinum-sputter-coated samples. Transmission electron microscopy (TEM) offers higher resolution and can resolve internal structural features (such as the core-shell architecture of a lipid-polymer hybrid particle or a cubosome's internal lattice), typically requiring negative staining of the sample. Atomic force microscopy (AFM) provides three-dimensional surface topography without the need for extensive sample preparation or a vacuum environment, and is particularly useful for confirming particle size and roughness in aqueous or near-native conditions, complementing electron microscopy data.

For herbal nanoparticles specifically, morphology is often reported alongside a qualitative comment on whether particles remain discrete and spherical (a marker of successful, non-aggregating encapsulation) or show clumping and irregular shape (which can indicate incomplete cross-linking, phytoconstituent-induced flocculation, or extract-polymer incompatibility).

5.4 Entrapment Efficiency and Drug Loading

Entrapment efficiency (EE%) and drug loading capacity (DL%) quantify how effectively the herbal marker compound has been incorporated into the carrier and are central quality attributes for any encapsulated system. These are most commonly determined indirectly: the formulation is centrifuged or subjected to ultrafiltration/dialysis to separate free (unentrapped) extract from the nanoparticle pellet, and the marker compound in the supernatant is quantified by UV-visible spectrophotometry or HPLC against a validated calibration curve; entrapment efficiency is then calculated as the percentage of total marker compound not detected in the free fraction. Direct methods, involving disruption of the nanoparticles followed by extraction and quantification of the entrapped fraction, are used less often for herbal systems

because the multi-component nature of the extract can complicate the assay, but they provide a useful cross-check where a single dominant marker compound is being tracked.

Reported entrapment efficiencies for polymeric herbal nanoparticles commonly range from roughly 50% to 85%, depending on the extract-polymer ratio, cross-linker concentration, and the specific marker compound's affinity for the carrier matrix; drug (or marker-compound) loading is generally lower than EE% and is reported as a percentage of total nanoparticle mass, giving a more clinically meaningful picture of how much active material a given formulation dose actually delivers.

5.5 Solid-State Characterization (FTIR, DSC, XRD, TGA)

Solid-state characterization establishes whether the herbal marker compound retains its chemical integrity after processing and whether it exists in a different physical form (crystalline vs. amorphous, free vs. complexed) within the carrier-both of which affect stability and release behaviour.

Fourier-transform infrared (FTIR) spectroscopy is used to confirm the chemical identity of the extract's functional groups and to detect any new or shifted absorption bands that would indicate a chemical interaction (rather than simple physical entrapment) between the extract and the polymer or lipid matrix; disappearance or broadening of characteristic peaks (e.g., O-H, C=O, or aromatic C-H stretches typical of polyphenols) on encapsulation is commonly interpreted as evidence of successful entrapment or hydrogen bonding with the carrier.

Differential scanning calorimetry (DSC) evaluates the thermal behaviour of the extract, the carrier, and the final formulation, typically detecting melting or decomposition endotherms. A reduction in intensity, broadening, or disappearance of the extract's characteristic endothermic peak in the loaded formulation, relative to the physical mixture, is generally taken as evidence that the marker compound has transitioned from a crystalline to an amorphous or molecularly dispersed state within the carrier-often correlated with improved apparent solubility.

X-ray diffraction (XRD or PXRD) provides complementary confirmation of crystallinity: a loss of the sharp diffraction peaks seen in the crystalline raw extract, replaced by a diffuse pattern in the nanoparticle formulation, supports the amorphization inferred from DSC. Thermogravimetric analysis (TGA) is used less routinely but is valuable for quantifying the amount of bound water or solvent and for confirming the thermal stability window within which subsequent processing (e.g., lyophilization) or storage should be conducted.

5.6 In Vitro Release Studies and Release Kinetics

In vitro release studies characterize how the marker compound is liberated from the carrier under simulated physiological conditions and are essential for predicting in vivo performance. The dialysis bag method-in which the formulation is placed inside a dialysis membrane immersed in release medium (commonly phosphate buffer at pH 6.8 or 7.4, sometimes with a surfactant to aid solubilization of lipophilic actives)-is the most widely used approach for nanoparticulate herbal systems, with aliquots withdrawn at set intervals and quantified by UV-spectrophotometry or HPLC.

Release data are typically fitted to kinetic models-zero-order, first-order, Higuchi, and Korsmeyer-Peppas-to infer the dominant release mechanism. A Korsmeyer-Peppas release exponent (n) below 0.45 is generally interpreted as Fickian diffusion-controlled release, values between 0.45 and 0.89 as anomalous (non-Fickian) transport combining diffusion and polymer relaxation/erosion, and values above 0.89 as case-II (erosion-dominated) release; herbal polymeric nanoparticles most often show an initial burst release (attributed to surface-adsorbed extract) followed by a slower, sustained phase consistent with diffusion through the polymer matrix.

5.7 Stability Studies

Stability studies establish the shelf-life and storage conditions of the formulation and are typically conducted in accordance with ICH Q1A(R2) guidance, which specifies long-term (25 degC/60% RH or 30 degC/65% RH), intermediate (30 degC/65% RH), and accelerated (40 degC/75% RH) storage conditions with defined sampling intervals (commonly 0, 1, 3, and 6 months for accelerated studies). Formulations are re-evaluated at each interval for particle size, PDI, zeta potential, entrapment efficiency, and marker-compound content (by HPLC/HPTLC) to detect any physical instability (aggregation, sedimentation, or Ostwald ripening) or chemical degradation of the phytoconstituents, the latter being a particular concern for photolabile or oxidation-prone polyphenols.

For herbal systems, freeze-thaw cycling and photostability testing are often added to the standard ICH battery, given the known susceptibility of many polyphenolic and flavonoid marker compounds to light- and temperature-induced degradation; lyophilization with a cryoprotectant (e.g., trehalose or mannitol) is frequently adopted to extend shelf-life where liquid-state instability is observed.

5.8 In Vivo Characterization and Pharmacodynamic Evaluation

Ultimately, physicochemical characterization must be corroborated by pharmacodynamic evidence of anti-arthritic activity, most often generated in the Freund's complete adjuvant (CFA)-induced or collagen-induced arthritis rat model. Paw volume, measured by a plethysmometer at defined intervals after adjuvant injection, is the primary and most widely reported efficacy endpoint, with percentage inhibition of paw oedema relative to an arthritic control group used to benchmark the herbal formulation against a standard anti-arthritic drug.

Biochemical and haematological markers-erythrocyte sedimentation rate, C-reactive protein, rheumatoid factor, and pro-inflammatory cytokines such as TNF-alpha, IL-1beta, and IL-6 (typically quantified by ELISA)-provide mechanistic confirmation that the observed reduction in paw

swelling reflects genuine suppression of the underlying inflammatory cascade rather than a purely symptomatic effect. Radiographic and histopathological examination of the affected joint (synovial hyperplasia, cartilage erosion, pannus formation, and inflammatory cell infiltration scored against control and treated groups) remains the most direct structural evidence of anti-arthritic efficacy and is considered essential supporting data in most peer-reviewed reports.

Body-weight monitoring and organ-to-body-weight ratios for liver, spleen, and kidney are commonly included as basic safety/toxicity indicators alongside efficacy data, particularly important for herbal nanoformulations where the carrier polymer itself, and not only the extract, must be shown to be biocompatible.

5.9 Design of Experiments as an Optimization and Characterization Tool

Response-surface optimization techniques such as the Box-Behnken design occupy a distinctive position at the intersection of formulation development and characterization: the same particle size, PDI, zeta potential, and entrapment efficiency data generated to characterize a batch also serve as the response variables used to build a statistically validated model of how formulation and process variables influence product quality. ANOVA-based model validation, regression equations, and 3-D response-surface/contour plots are then used to identify the optimized formulation, which is subsequently confirmed experimentally-providing not only an efficient formulation strategy but also a documented, defensible design space that strengthens the overall characterization package presented in a research article or regulatory submission.

6. Analytical Challenges and Limitations

Characterizing herbal extract-based nanoformulations presents challenges beyond those encountered with single-molecule synthetic drugs. First, herbal extracts are inherently multi-component, so entrapment efficiency, release, and stability data generated for a single marker compound may not represent the behaviour of the extract's other bioactive constituents, some of which may contribute independently to the observed pharmacological effect. Second, natural variability in raw plant material-driven by geographic origin, harvest season, and extraction method-means that formulation and characterization results are not always directly comparable across studies unless extracts are rigorously standardized against a validated marker and, ideally, a voucher specimen.

Third, the presence of pigments, tannins, and other extract components can interfere with common analytical assays (e.g., UV-based entrapment-efficiency determinations), necessitating extract-specific method validation rather than reliance on generic protocols developed for pure synthetic drugs. Fourth, many published studies report favourable preclinical (CFA-model) anti-arthritic activity but stop short of pharmacokinetic, cytokine-panel, or long-term toxicity data, and animal studies are frequently limited to a single sex and a short observation window, all of which constrain translational confidence. Finally, regulatory pathways for herbal nanomedicines remain less well-defined than those for conventional herbal products or single-molecule nanomedicines, creating uncertainty about which characterization package (physicochemical, phytochemical, and toxicological) will be considered sufficient for clinical progression.

7. Future Perspectives

Closing these gaps will likely require several parallel efforts. Wider adoption of chromatographic multi-marker fingerprinting (rather than single-marker quantification) would better capture the true multi-component nature of herbal entrapment and release. Greater use of advanced imaging (cryo-TEM, small-angle X-ray/neutron scattering) could resolve internal nanostructure with less sample-preparation artefact than conventional electron microscopy. Incorporation of cytokine-panel and joint-imaging endpoints (micro-CT, MRI) as standard preclinical outputs, alongside pharmacokinetic and tissue-distribution studies, would strengthen the translational evidence base beyond paw-volume measurements alone.

On the formulation side, continued exploration of newer platforms-cubosomes, stimuli-responsive and joint-targeted (e.g., folate- or hyaluronic-acid-decorated) nanocarriers, and combination systems pairing a herbal extract with a low-dose synthetic DMARD-offers a plausible route to synergistic efficacy with reduced systemic drug burden. Finally, harmonized standardization protocols (agreed marker compounds, extraction methods, and voucher-authentication requirements) and clearer regulatory guidance specific to herbal nanomedicines would substantially improve the comparability and translational value of future studies in this field.

8. Conclusion

Herbal extracts remain a scientifically credible and clinically attractive avenue for managing rheumatoid arthritis, offering multi-target anti-inflammatory, antioxidant, and immunomodulatory activity with a generally favourable tolerability profile relative to conventional DMARDs and biologics. Realizing this potential depends on formulation strategies-polymeric and lipidic nanoparticles, vesicular and cubosomal systems, and topical/transdermal platforms-capable of overcoming the poor solubility and bioavailability that limit crude extracts, and on a characterization framework rigorous enough to establish the identity, quality, stability, and anti-arthritic performance of the resulting product. As reviewed here, this framework spans phytochemical standardization, particle size/zeta potential analysis, morphological and solid-state characterization, in vitro release kinetics, ICH-aligned stability testing, and in vivo evaluation in adjuvant-induced arthritis models, ideally integrated within a Design-of-Experiments-driven optimization strategy. Continued refinement of these characterization practices, alongside more comprehensive translational (pharmacokinetic, biomarker, and imaging) data, will be essential to move herbal anti-arthritic nanoformulations from promising preclinical candidates toward clinically validated, regulatory-ready therapeutics.

References

[1] Biomolecules (MDPI). Therapeutic Potential of Plant-Derived Compounds and Plant Extracts in Rheumatoid Arthritis-Comprehensive Review. 2024. Available at: https://www.mdpi.com/2076-3921/13/7/775
[2] PMC (NCBI). Therapeutic Potential of Plant-Derived Compounds and Plant Extracts in Rheumatoid Arthritis-Comprehensive Review. 2024. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11274232/
[3] PMC (NCBI). Phytochemical characterization and anti-arthritic potential of green-synthesized CuO nanoparticles derived from the Bistorta amplexicaulis root extract. 2024. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11685013/
[4] Inflammopharmacology (Springer Nature). Innovative nanocarriers in arthritis therapy: the role of herbal cubosomes. 2025. Available at: https://link.springer.com/article/10.1007/s10787-025-01714-0
[5] PMC (NCBI). Lipid Nano-System Based Topical Drug Delivery for Management of Rheumatoid Arthritis: An Overview. 2023. Available at: https://pmc.ncbi.nlm.nih.gov/articles/PMC10676558/
[6] Nanoscale (RSC Publishing). Revolutionizing rheumatoid arthritis treatment with emerging cutaneous drug delivery systems: overcoming the challenges and paving the way forward. 2024. DOI:10.1039/D4NR03611E.
[7] bioRxiv (preprint). Fabrication & Characterization of Hyaluronic Acid/Eucalyptus Hydrogels Loaded with PLGA Nanoparticles with Methotrexate as an Injectable Therapy for Rheumatoid Arthritis. 2025. Available at: https://www.biorxiv.org/content/10.1101/2025.02.18.638769
[8] ScienceDirect. Natural product extract fractions as potential arthritis treatments: A detailed analysis using in-silico, in-vivo, and in-vitro methods. 2024. Available at: https://www.sciencedirect.com/science/article/pii/S1567576924021179
[9] PMC (NCBI). Formulation Development and Characterization of pH Responsive Polymeric Nano-Pharmaceuticals for Targeted Delivery of Anti-Cancer Drug (Methotrexate). 2022. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9291017/
[10] PMC (NCBI). d-alpha-tocopheryl polyethylene glycol 1000 succinate surface scaffold polysarcosine based polymeric nanoparticles of enzalutamide: In vitro, in vivo characterizations. 2024. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10850913/
[11] PMC (NCBI). Nanocrystals of Mangiferin Using Design Expert: Preparation, Characterization, and Pharmacokinetic Evaluation. 2023. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10420877/
[12] PMC (NCBI). Synthesis, Characterization and In Vitro Evaluation of Chitosan Nanoparticles Physically Admixed with Lactose Microspheres for Pulmonary Delivery of Montelukast. 2022. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9460706/
[13] ResearchGate. Development and Characterization of Nanoparticle-Based Drug Delivery Systems. 2024. Available at: https://www.researchgate.net/publication/394673169
[14] ICH Harmonised Tripartite Guideline. Stability Testing of New Drug Substances and Products Q1A(R2). International Council for Harmonisation.