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Nano-encapsulation of herbal bioactive: A next-generation approach for anti-inflammatory therapy

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Although inflammation is a basic biological reaction to damage or infection, persistent or unchecked inflammation is the root cause of many illnesses, including as cancer, diabetes, heart disease, and arthritis. Even though there are many synthetic anti-inflammatory medications on the market, prolonged use of these medications is frequently linked to side effects and low therapeutic efficacy. By altering molecular pathways like NF-κB, COX-2, and NLRP3 inflammasome signalling, herbal bioactive like curcumin, quercetin, resveratrol, and boswellic acids have shown strong anti-inflammatory potential. However, their clinical translation is limited by their quick metabolism, low bioavailability, and poor solubility. A next-generation approach to overcoming these obstacles is nano-encapsulation, which improves the solubility, stability, and targeted delivery of herbal bioactives. The pharmacokinetic profiles and controlled release of chemicals originating from plants can be improved by using nanocarrier systems such liposomes, polymeric nanoparticles, solid lipid nanoparticles, and nanoemulsions. Additionally, ligand conjugation and surface modification allow for site-specific distribution to inflammatory regions, reducing systemic toxicity and enhancing therapeutic results. Recent developments in nano-encapsulation techniques for herbal anti-inflammatory drugs are thoroughly reviewed in this paper, which also highlights formulation techniques and mechanisms of action. Current issues with clinical translation, large-scale manufacturing, and regulatory approval are highlighted, along with the interaction between nanoparticle design and biological response. The combination of nanotechnology with phytotherapy has created a revolutionary platform for the safe, efficient, and long-term treatment of inflammatory diseases: nano-encapsulated herbal bioactive.

Keywords: Nanotechnology, Bioactive, Nano-encapsulation, Anti-inflammatory therapy, Phytomedicine, Targeted delivery herbal

INTRODUCTION

An essential physiological reaction of the immune system to viruses, damaged cells, or irritants is inflammation. Acute inflammation is a defence mechanism that works to remove the original source of cell damage, remove necrotic tissues and cells, and start the healing process. But when this reaction persists or becomes dysregulated, it turns into chronic inflammation, which is linked to the etiology of a number of illnesses, such as cancer, diabetes, heart disease, neurological conditions, and arthritis. The persistent presence of pro-inflammatory mediators, oxidative stress, and immune cell infiltration are characteristics of chronic inflammation, which results in tissue damage and the disturbance of regular physiological processes[1–4]. Traditional anti-inflammatory medications, like corticosteroids and non-steroidal anti-inflammatory medicines (NSAIDs), have been widely utilized to treat inflammatory diseases. Long-term use is frequently linked to serious side effects,

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such as cardiovascular problems, immunosuppression, renal toxicity, and gastrointestinal bleeding, despite its effectiveness. Additionally, these medications usually target both healthy and inflammatory tissues with low selectivity, which reduces their therapeutic index and increases patient non-compliance. Herbal bioactive compounds have gained popularity recently due to their strong immunomodulatory, antioxidant, and anti-inflammatory effects. Natural plant-based compounds with a good safety record and the potential for long-term use include boswellic acids, resveratrol, curcumin, and quercetin. However, inherent physicochemical limitations, such as low oral bioavailability, quick metabolism, poor water solubility, and chemical instability under physiological conditions, impede their practical applicability. Despite compelling preclinical evidence, these obstacles significantly limit their therapeutic potential[5,6]. One possible method to get beyond these restrictions and improve the clinical usability of herbal bioactives is nano-encapsulation. These chemicals' solubility, stability, bioavailability, and targeted distribution can all be enhanced by encapsulating them in nanoscale carriers as liposomes, polymeric nanoparticles, solid lipid nanoparticles, and nanomicelles. Moreover, nanoformulations can maximize therapeutic efficacy by facilitating controlled and prolonged release, lowering systemic toxicity, and promoting the accumulation of bioactive in inflammatory or diseased locations[7–11].

The goal of this review is to present a thorough analysis of the nano-encapsulation techniques used for herbal bioactive in anti-inflammatory treatment. It focuses on the therapeutic potential of chemicals produced from plants, the mechanistic insights of inflammation, and the latest developments in delivery systems based on nanotechnology. This study emphasizes the case for nano-encapsulation as a next-generation strategy for safer, more potent anti-inflammatory treatments by critically assessing recent advancements and pointing out current obstacles.

Herbal bioactive with anti-inflammatory potential

The potential of phytochemicals, which are naturally occurring bioactive substances derived from plants, to alter inflammatory pathways has been extensively researched. By inhibiting pro-inflammatory media-tors, controlling oxidative stress, and altering important signalling pathways involved in immune responses, these substances have anti-inflammatory actions. They are potential options for the treatment of chronic inflammatory diseases because of their diverse mechanisms of action[9,12,13].

Curcumin

Due to its anti-inflammatory qualities, curcumin, a bioactive polyphenolic molecule obtained from *Curcuma longa* (turmeric), is one of the phytochemicals that has been investigated the most. The two main ways it works are by blocking cyclooxygenase-2 (COX-2), an important enzyme that makes prostaglandins, and by modifying nuclear factor kappa B (NF-κB), a crucial transcription factor that controls the production of many pro-inflammatory cytokines. The production of inflammatory mediators, including interleukin-1 beta (IL-1β), tumor necrosis factor-alpha (TNF-α), and other cytokines involved in the start and spread of inflammatory responses, is effectively suppressed by curcumin by targeting these pathways. As a result, curcumin has strong potential as a treatment for a variety of inflammatory diseases by reducing both acute and chronic inflammation[14–18] (Fig. 1).

Quercetin

A polyphenolic flavonoid that is commonly found in fruits and vegetables, quercetin has strong antioxidant and anti-inflammatory properties. Enhancement of the cellular antioxidant defense system and control of cytokine production are the main mechanisms by which it reduces inflammation. Quercetin mitigates oxidative stress by upregulating antioxidant enzymes including glutathione peroxidase, catalase, and superoxide dismutase (SOD) and dramatically lowering levels of important pro-inflammatory cytokines like IL-6, TNF-α, and IL-1β. Furthermore, quercetin prevents the activation of key inflammatory signaling pathways that are essential for coordinating inflammatory responses, such as NF-κB and mitogen-activated protein kinases (MAPKs). Quercetin successfully reduces inflammatory processes through this multi-targeted modulation, demonstrating its potential as a natural treatment for long-term inflammatory conditions[4,19–21].

Resveratrol

Strong anti-inflammatory and antioxidant qualities are demonstrated by resveratrol, a naturally occurring stilbene that is mostly found in grapes, berries, and some nuts. The main mechanism by which it reduces inflammation is by controlling the signalling pathways for MAPK (mitogen-activated protein kinase) and SIRT1 (sirtuin 1). NF-κB (nuclear factor kappa B) signalling, a key

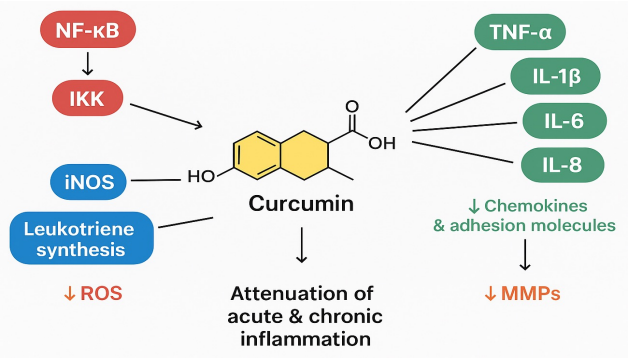

Figure 1. Mechanisms of curcumin-mediated anti-inflammatory activity

transcription factor involved in the development of many pro-inflammatory cytokines, chemokines, and adhesion molecules, is suppressed when resveratrol activates SIRT1. Resveratrol efficiently lowers the synthesis of important pro-inflammatory mediators, such as TNF-α, IL-1β, and IL-6, by blocking NF-κB activation. Resveratrol also affects cellular reactions to stress, apoptosis, and inflammatory stimuli via modulating MAPK pathways, including ERK, JNK, and p38. Beyond these signalling pathways, resveratrol exhibits potent antioxidant activity by scavenging reactive oxygen species (ROS) and boosting endogenous antioxidant defences. These actions together lessen inflammation and tissue damage brought on by oxidative stress. Resveratrol's promise as a treatment for chronic inflammatory illnesses is highlighted by its combined control of oxidative stress and inflammatory signals[19,22–24].

Boswellic acids

Boswellia serrata resin yields bioactive triterpenoids called boswellic acids, which are known to have strong anti-inflammatory effects. Inhibiting 5-lipoxygenase (5-LOX), a crucial enzyme involved in the manufacture of leukotrienes—lipid mediators that are essential in fostering inflammation—is their main mode of action. Boswellic acids are especially helpful in disorders like arthritis, asthma, and inflammatory bowel diseases because they efficiently inhibit leukotriene-mediated inflammatory reactions by reducing 5-LOX activity. The expression of pro-inflammatory cytokines and enzymes is reduced by boswellic acids, which also target leukotriene pathways and modulate other important inflammatory signaling cascades, such as the NF-κB pathway. Because of their multi-targeted regulation, boswellic acids have a broad-spectrum anti-inflammatory impact, making them a promising natural treatment for chronic inflammatory diseases[25–28].

Other notable phytochemicals

Significant anti-inflammatory effects have been shown by a number of additional bioactive substances produced from plants. The primary mechanism by which gingerols, the active ingredients in Zingiber officinale (ginger), work is by blocking the cyclooxygenase (COX) and lipoxygenase (LOX) pathways, which lowers the production of pro-inflammatory prostaglandins and leukotrienes. Green tea (Camellia sinensis) is rich in catechins, which reduce the expression of pro-inflammatory mediators and attenuate oxidative stress by modulating important signaling pathways like NF-κB and MAPK. Derived from Berberis species, berberine is an isoquinoline alkaloid that increases endogenous antioxidant defenses while decreasing the production of pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6. When combined, these phytochemicals offer a multifaceted strategy for reducing inflammation, underscoring the promise of natural substances as therapeutic agents for the treatment of chronic inflammatory diseases[29–33].

Nano-encapsulation: concepts and design strategies

The technique of adding bioactive substances to nanoscale carriers (usually 1–500 nm) in order to prevent degradation, enhance their pharmacokinetic characteristics, and boost their therapeutic efficiency is known as nano-encapsulation. Limitations that are frequently linked to herbal bioactives, such as poor solubility, low bioavailability, quick metabolism, and chemical instability, can be addressed by enclosing the active molecules in a nanosystem. Therefore, nano-encapsulation is a next-generation anti-inflammatory drug delivery method (Fig. 2). Encasing, dissolving, or adsorbing bioactive substances within a nanocarrier matrix is the basic idea of nano-encapsulation. These carriers may be polymeric (PLGA, chitosan), lipid-based (liposomes, solid lipid nanoparticles), or surfactant-based (nanomicelles, nanoemulsions). Improved surface area, more cellular absorption, and the capacity to alter release kinetics in accordance with therapeutic requirements are just a few benefits that come with the nanoscale dimension[29,34–37].

Nano-encapsulation offers multiple benefits compared to traditional formulations:

Increased stability and solubility: Hydrophobic herbal substances, such as resveratrol and curcumin, can dissolve in nanocarriers and be shielded against deterioration in physiological settings.

Controlled and sustained release: Bioactives can be progressively released via nanocarriers, lowering the frequency of doses and preserving therapeutic concentrations for longer.

Targeted tissue accumulation: By enabling targeted distribution to inflammatory tissues or particular cell types, surface modification and functionalization improve therapeutic efficacy and reduce off-target consequences.

Decreased systemic toxicity: Nano-encapsulation lowers the risk of side effects linked to high-dose conventional therapy by concentrating bioactives at the site of inflammation and minimizing systemic exposure.

Types of nanocarriers for herbal bioactive

To improve the transport, stability, and bioavailability of herbal bioactive, a number of nanocarrier systems have been created. The content, structure, and functional characteristics of these systems vary, allowing for customized anti-inflammatory treatment approaches[38–40].

Polymeric nanoparticles

A flexible platform for the regulated and prolonged administration of bioactive substances is provided by

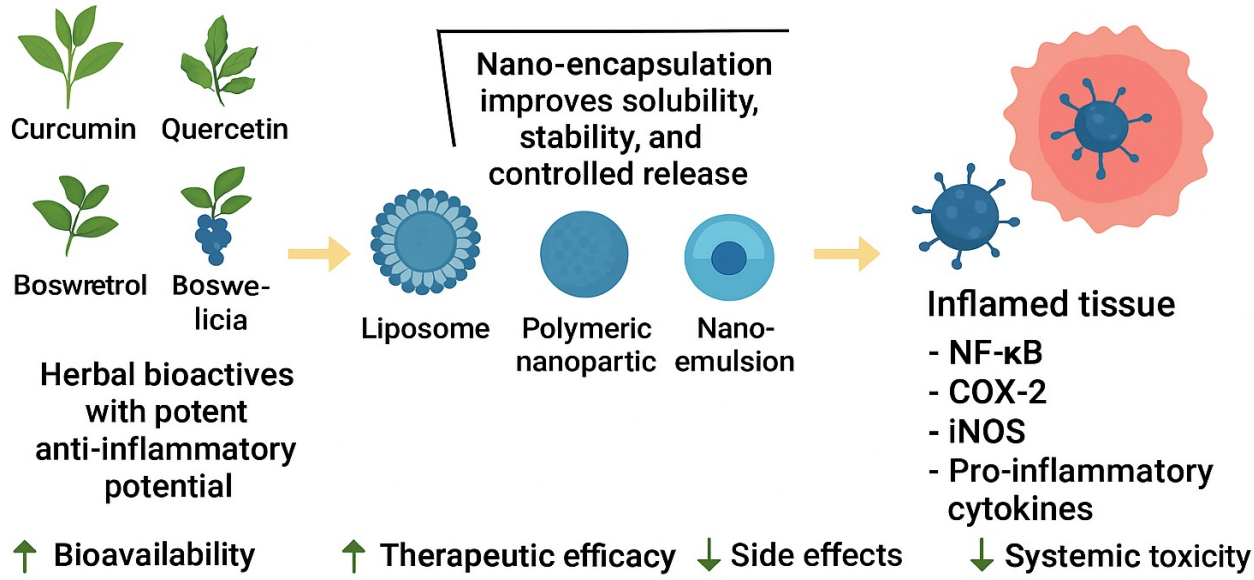

Figure 2. Nano-encapsulated herbal bioactives offer safe and effective next-generation anti-inflammatory therapy

polymeric nanoparticles, which are made of biodegradable and biocompatible polymers like chitosan, alginate, and PLGA (poly(lactic-co-glycolic acid)). In addition to their proven safety and regulatory approval for clinical usage, PLGA nanoparticles are highly prized for their programmable degradation rates, which provide exact control over drug release kinetics. Other benefits of chitosan and alginate-based nanoparticles include their mucoadhesive qualities, which improve retention at mucosal locations and make oral or topical administration easier. By encasing herbal bioactives in these polymeric carriers, nanoparticles promote cellular absorption, greatly increase oral bioavailability, and shield the compounds from harsh gastrointestinal conditions and enzyme destruction. Moreover, polymeric nanoparticles can be engineered to achieve targeted delivery, minimize systemic side effects, and maintain therapeutic concentrations over extended periods, making them highly promising for the delivery of plant-derived anti-inflammatory agents[41–43].

Liposomes and phytosomes

A flexible platform for the delivery of herbal bioactives, liposomes are vesicular nanocarriers made of phospholipid bilayers that can encapsulate both hydrophilic and lipophilic substances. Liposomes boost systemic bioavailability, shield the payload from enzymatic and chemical degradation, and increase solubility by encasing bioactive substances within these bilayers. Contrarily, phytosomes are specialized complexes in which phospholipids and phytochemicals are chemically bonded, greatly improving cellular uptake, gastrointestinal absorption, and membrane permeability. When compared to their unformulated counterparts, these delivery methods have produced better pharmacokinetic profiles, higher plasma concentrations, and enhanced therapeutic efficacy for substances including curcumin, quercetin, and silymarin. The ability of liposomes and phytosomes to enhance stability, bioavailability, and targeted delivery underscores their potential as effective carriers for plant-derived anti-inflammatory and antioxidant agents[44–47].

Solid lipid nanoparticles (SLNs) and nano-structured lipid carriers (NLCs)

Solid lipid nanoparticles (SLNs) are nanoscale carriers made of solid lipids stabilized by surfactants. They provide enhanced physicochemical stability of the encapsulated chemicals, controlled and sustained release, and excellent encapsulation efficiency. Second-generation lipid nanoparticles known as nanostructured lipid carriers (NLCs) combine liquid and solid lipids to improve drug loading capacity, stop drug expulsion during storage, and preserve stability over time. Hydrophobic herbal bioactives are especially well-suited for delivery via both SLNs and NLCs, which enhance their bioavailability and prevent degradation. These lipid-based nanoparticles are attractive candidates for the creation of successful herbal nanotherapeutics since preclinical research has shown that they not only improve the pharmacokinetic profiles of encapsulated phytochemicals but also intensify their anti-inflammatory action[48–53].

Nanoemulsions and self-nanoemulsifying drug delivery systems (SNEDDS)

Because of their small droplet size and large surface area, nanoemulsions—oil-in-water colloidal dispersions

stabilized by surfactants—allow lipophilic bioactive chemicals to dissolve and absorb more quickly. When gastrointestinal fluids come into contact with self-nanoemulsifying drug delivery systems (SNEDDS), which are isotropic combinations of oils, surfactants, and co-surfactants, they spontaneously create fine oil-in-water nanoemulsions, greatly increasing oral bioavailability. SNEDDS and nanoemulsions have both been successfully used to transport herbal bioactives, including resveratrol, curcumin, and other lipophilic phytochemicals, showing enhanced stability, solubility, and therapeutic efficacy. A promising approach to overcoming the limited oral absorption and poor water solubility that frequently limit the clinical potential of plant-derived anti-inflammatory drugs is provided by these lipid-based nanosystems[54–58].

Dendrimers and metallic nanoparticles

Dendrimers are monodisperse, highly branched, nanoscale polymers with variable surface functions and well-defined topologies that allow for targeted delivery, controlled release, and high loading capacity of medicinal drugs. To increase selectivity and efficacy, their multivalent surfaces can be conjugated with imaging agents, targeted ligands, or herbal bioactives. In addition to their use as delivery vehicles, metallic nanoparticles—such as gold and silver nanoparticles—have also been used as carriers or conjugates for chemicals originating from plants, providing inherent anti-inflammatory and antioxidant qualities. The stability, bioavailability, and general pharmacological performance of encapsulated herbal bioactives are enhanced by the fine control that dendrimers and metallic nanoparticles offer over particle size, surface chemistry, and release kinetics. These nanosystems are cutting-edge platforms that optimize the natural anti-inflammatory drugs' therapeutic potential[59,60].

Plant-derived nanocarriers

Extracellular vesicles (EVs) and biogenic nanoparticles are two examples of plant-derived nanocarriers, which are a new class of biocompatible and natural delivery systems. Nanosized vesicles called plant-derived EVs are naturally released by plants and have the ability to carry bioactive substances including proteins, nucleic acids, and phytochemicals across biological barriers while exhibiting low immunogenicity and excellent biocompatibility. These vesicles improve the stability and therapeutic potential of encapsulated drugs by providing inherent targeting capabilities and shielding them from enzymatic destruction. An environmentally benign, scalable, and biocompatible substitute for traditional synthetic nanoparticles are biogenic nanoparticles, which are made from plant extracts. These nanoparticles combine the benefits of nanoscale delivery, such as enhanced solubility, cellular absorption, and controlled release, with the natural biological activity of the plant source[61–63]. A detailed comparative analysis of nanocarrier system are mentioned in Table 1.

Mechanisms of anti-inflammatory action via nanoformulations

By altering important inflammatory mechanisms at the cellular and molecular levels, nano-encapsulation not only improves the pharmacodynamic effects of herbal bioactives but also their distribution. Numerous mechanisms that together improve anti-inflammatory efficacy are made possible by the special characteristics of nanoscale carriers, such as their small size, large surface area, and surface functionalization[6,64].

Enhanced cellular uptake and bioavailability

Using a variety of delivery methods, such as oral, topical, and intravenous, nanocarriers greatly improve the absorption and therapeutic effectiveness of herbal bioactives. Their nanoscale size allows for effective uptake and cellular internalization by endocytosis, avoiding metabolic breakdown and efflux transporters that normally restrict the availability of bioactive substances. Higher intracellular concentrations brought about by this enhanced bioavailability enable bioactives to more successfully influence important inflammatory signaling pathways like NF-κB, MAPK, and JAK-STAT. For instance, compared to free curcumin, curcumin-loaded PLGA nanoparticles have shown significantly greater intracellular accumulation in macrophages, which leads to a more noticeable suppression of pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6. The potential of nanocarrier systems to optimize the anti-inflammatory and therapeutic benefits of chemicals generated from plants is highlighted by this targeted and effective delivery[2,29,65,66].

Controlled release kinetics and sustained therapeutic action

Therapeutic concentrations are maintained at the target location for extended periods of time thanks to the controlled and sustained release of bioactive chemicals provided by nanoformulations. The frequency of administration is decreased, and variations in plasma drug levels are minimized, both of which can jeopardize the effectiveness of treatment. For example, in preclinical models, solid lipid nanoparticles (SLNs) and polymeric nanoparticles have shown prolonged release profiles for phytochemicals like resveratrol and curcumin, which results in long-term downregulation of important pro-inflammatory mediators like TNF-α and COX-2. These nanocarriers improve patient compliance, increase anti-inflammatory efficacy, and present a promising long-term management approach for chronic inflammatory disorders by continuously exposing target cells to active chemicals[1,29,65].

Table 1. Comparative analysis of nanocarrier systems for herbal bioactives

S. No.	Nanocarrier type	Herbal bioactive	Advantage	Limitation
1	Polymeric Nanoparticles	Curcumin, berberine, resveratrol	Controlled release, good stability, mucoadhesive properties, scalable	Complex fabrication, possible polymer toxicity
2	Liposome	Quercetin, silymarin, curcumin	Biocompatible, encapsulate hydrophilic & lipophilic compounds, improved bioavailability	Physical instability, high cost, leakage
3	Phytosome	Silymarin, rutin, curcumin	Superior absorption, enhanced membrane permeability	Limited drug-loading flexibility
4	SLN	Hydrophobic flavonoids, terpenoids	High stability, controlled release, good protection	Low drug loading, risk of drug expulsion
5	NLC	Curcuminoids, polyphenols	Higher loading capacity, better stability than SLNs	Limited long-term clinical data
6	Nanoemulsions & Snedd	Resveratrol, curcumin, essential oils Lipophilic polyphenols	Rapid absorption, high solubilization, easy oral use	Surfactant irritation, physical instability
7	Dendrimers	Polyphenols, alkaloids	High loading, precise targeting, surface modification	Cytotoxicity, high cost
8	Plant-Derived EVs	Proteins, nucleic acids, phytochemicals	Excellent biocompatibility, targeting ability, low immunogenicity	Low yield, isolation difficulty

Targeted delivery to macrophages and inflamed tissues

Surface modification of nanocarriers allows for targeted distribution to important mediators of chronic inflammation, such as macrophages and inflamed tissues. By functionalizing with particular ligands like mannose, folic acid, or antibodies, activated immune cells can recognize and absorb the encapsulated bioactives selectively, increasing local concentrations while reducing systemic exposure and off-target consequences. For instance, in preclinical arthritis models, quercetin-loaded liposomes functionalized with folate have shown preferential accumulation in inflammatory joints, leading to enhanced anti-inflammatory activity as compared to non-targeted formulations. Such focused approaches highlight the benefit of ligand-mediated nanocarrier design in the treatment of chronic inflammatory diseases by both increasing the therapeutic potential of herbal medicines and lowering the danger of systemic toxicity[67–69].

Synergistic effects from nanocarrier–bioactive interactions

Nanocarriers can exert complementary biological effects that enhance the therapeutic activity of encapsulated herbal bioactive. Lipid-based carriers, such as liposomes, SLNs, and NLCs, not only stabilize bioactive compounds but also facilitate interactions with cellular membranes, promoting efficient uptake and intracellular delivery. Polymeric matrices, in addition to providing controlled release, can influence cellular redox balance and mitigate oxidative stress, thereby supporting the anti-inflammatory action of the encapsulated phytochemicals. These intrinsic properties of nanocarriers often act synergistically with the bioactives they deliver, resulting in more pronounced and sustained suppression of inflammatory mediators compared to free compounds. Such dual functionality underscores the potential of nanocarrier systems to amplify the efficacy of plant-derived anti-inflammatory agents while improving their pharmacokinetic and pharmacodynamic profiles[12,63,70].

Case studies and recent advances

Nano-encapsulation has the potential to improve the medicinal effectiveness of herbal anti-inflammatory substances, according to recent studies. Preclinical research on a range of illness models offers strong support for enhanced bioavailability, focused administration, and long-lasting anti-inflammatory effects. Table 2 contains the detail of case study of nano formulation.

Safety, toxicity, and regulatory considerations

While nano-encapsulation offers numerous advantages for herbal bioactives, translating these formulations into clinical applications requires careful evaluation of safety, toxicity, pharmacokinetics, and regulatory compliance. Biocompatibility and safety are critical considerations in the design and application of nanocarriers for herbal bioactive delivery. While many carriers such as PLGA, chitosan, and lipid-based nanoparticles are generally recognized as safe, factors including surface chemistry, particle size,

Table 2. Case studies and recent advances of nano-formulation

S. No.	Nano formulation	Compound	Model	Key Observation	Reference
1	Liposomes	Curcumin	Rat model of arthritis	Reduced paw edema, decreased TNF-α and IL-6, enhanced joint tissue penetration	71, 72
2	Nanoemulsion	Quercetin	Mouse model of topical inflammation	Improved skin absorption, decreased cytokine expression, reduced oxidative stress	73, 74
3	PLGA nanoparticles	Resveratrol	Rat model of colitis	Higher oral bioavailability, sustained release, reduced inflammatory markers (COX-2, IL-1β)	75, 76
4	Solid lipid nanoparticles (SLNs)	Boswellic acids	Rat arthritis model	Improved joint accumulation, reduced leukotriene-mediated inflammation, enhanced therapeutic effect	77, 78
5	Hybrid nanocarriers	Curcumin & Quercetin	*In vitro* macrophage inflammation	Synergistic inhibition of NF-κB and MAPK pathways, enhanced cellular uptake	79, 80

shape, and administered dose can significantly influence cytotoxicity and immune responses. For example, cationic nanoparticles, due to their strong electrostatic interactions with cell membranes, may induce membrane disruption or trigger inflammatory reactions at high concentrations. Therefore, comprehensive preclinical evaluation is essential, encompassing in vitro cytotoxicity assays (e.g., cell viability, proliferation, and hemolysis) and in vivo assessments of immune responses and organ toxicity. Such thorough safety profiling ensures that nanocarriers can be administered safely and paves the way for successful clinical translation of herbal nanotherapeutics[75,76,81]Although nanocarriers substantially improve the bioavailability of herbal bioactives, they can also alter pharmacokinetics and tissue biodistribution, which may impact both efficacy and safety. Critical factors such as particle size, surface charge, hydrophobicity, and surface modifications influence circulation time, cellular uptake, organ accumulation, and clearance pathways. For instance, nanoparticles may accumulate unintentionally in the liver, spleen, or kidneys, potentially leading to organ-specific toxicity. Therefore, careful optimization of formulation parameters, along with thorough pharmacokinetic and biodistribution studies, is essential to balance enhanced therapeutic efficacy with safety. Such evaluations are critical for translating herbal nanotherapeutics from preclinical models to clinical applications while minimizing off-target effects. Translation from laboratory-scale synthesis to large-scale production remains a challenge. Maintaining reproducibility in particle size, encapsulation efficiency, stability, and release kinetics is essential for consistent therapeutic outcomes. Techniques such as microfluidics and high-pressure homogenization are being explored to address these issues, but cost, scalability, and process standardization remain significant hurdles[82,83].

Challenges and future perspectives

The development of herbal bioactives encapsulated in nanoparticles has advanced significantly, but a number of obstacles still stand in the way of their transition from preclinical to clinical use. To fully realize the therapeutic promise of nano-herbal anti-inflammatory medicines, these limitations must be filled. The majority of research on herbal bioactives that have been nanoformulated is restricted to animal models or in vitro tests. There are still few human clinical trials, despite the fact that these investigations show improved bioavailability, targeted distribution, and superior anti-inflammatory benefits. There are substantial translational problems since preclinical models and people differ in metabolism, immunological responses, and disease pathology. To confirm long-term safety, ideal dosage, and efficacy, thorough clinical research is required. Aggregation, drug leakage, and chemical degradation during storage are some of the stability issues that many nanoformulations encounter. Recent developments in machine learning (ML) and artificial intelligence (AI) present chances to speed up the design and optimization of nanocarriers. By predicting ideal polymer-lipid ratios, particle sizes, surface functionalization, and release kinetics, AI-driven models can expedite formulation development and minimize experimental trial-and-error. When creating customized anti-inflammatory nanomedicines, such computational methods can improve accuracy and efficiency. Personalized medicine, where formulations are customized to each patient's unique profile, including genetic background, disease severity, and immune condition, holds the key to the future of nano-herbal therapy. It is possible to design nanocarriers to specifically target particular cell populations or tissues, allowing for individualized treatment plans and reducing side effects. The development of customized nano-herbal treatments can be guided by the

integration of biomarkers and inflammatory profiles unique to each patient. Combination treatments, which combine traditional synthetic medications with natural substances encased in nanoparticles, have great potential. These tactics can improve treatment results, lower dosage requirements, and take advantage of synergistic effects. Co-delivering curcumin nanoparticles with low-dose NSAIDs, for example, may provide strong anti-inflammatory benefits while reducing adverse effects. New possibilities for combination therapy are made possible by hybrid and co-loaded nanocarriers, which allow for accurate co-delivery, controlled release, and tissue-specific targeting[84–86].

Conclusions

Numerous illnesses, from diabetes and arthritis to cancer and neurological diseases, are caused by chronic inflammation. Even though traditional anti-inflammatory medications are still useful, side effects, poor selectivity, and diminished potency sometimes restrict their long-term usage. Herbal bioactive substances with multi-targeted anti-inflammatory, antioxidant, and immunomodulatory qualities, such as curcumin, quercetin, resveratrol, and boswellic acids, present intriguing substitutes. However, their quick metabolism, low bioavailability, poor solubility, and chemical instability have hindered their clinical translation. One revolutionary method to get over these restrictions is nano-encapsulation. Researchers have increased solubility, stability, targeted tissue distribution, controlled release, and therapeutic efficiency by integrating herbal bioactives into polymeric nanoparticles, liposomes, solid lipid nanoparticles, nanoemulsions, dendrimers, and plant-derived nanocarriers. Preclinical research shows that, in comparison to free bioactives, nanoformulated herbal substances had better cellular absorption, longer-lasting anti-inflammatory effects, and synergistic interactions with nanocarriers. Notwithstanding these developments, a number of obstacles still need to be overcome, such as guaranteeing biocompatibility, enhancing pharmacokinetics, increasing production volume, developing standardized assessment techniques, and negotiating regulatory frameworks. Future directions include the creation of customized nano-herbal treatments, the integration of AI and machine learning for optimal nanocarrier design, and the investigation of combination tactics with synthetic medications to optimize therapeutic results. In conclusion, bridging the gap between preclinical promise and clinical application, nano-encapsulation provides a next-generation method for delivering herbal bioactives. Nano-herbal formulations have the potential to become safe, precise, and effective anti-inflammatory treatments that meet unmet medical needs in chronic inflammatory illnesses with more interdisciplinary research and strong clinical validation.

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