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Review Article

# Curcumin-Loaded Nanoemulsions: Advances in Formulation Strategies and Anti-Inflammatory Therapeutic Applications

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Abstract

Curcumin, the principal bioactive compound of *Curcuma longa*, has drawn significant attention for its potent anti-inflammatory properties. However, its clinical translation remains limited due to poor solubility in aqueous environments, rapid degradation, and extremely low oral bioavailability. In recent years, nanoemulsion-based delivery systems have emerged as a promising strategy to overcome these barriers. By encapsulating curcumin within nanoscale oil-in-water emulsions, researchers have achieved enhanced solubility, improved physicochemical stability, and more efficient absorption across biological membranes. Preclinical studies demonstrate that curcumin-loaded nanoemulsions exhibit superior anti-inflammatory activity compared to free curcumin, as evidenced by greater suppression of pro-inflammatory cytokines, reduced oxidative stress, and more effective modulation of key signalling pathways in both in vitro and in vivo models. These advances highlight nanoemulsions not only as carriers that protect curcumin from degradation but also as facilitators of targeted and sustained therapeutic action. Future directions should prioritise large-scale clinical evaluations, standardised formulation protocols, and clear regulatory frameworks to ensure safety, reproducibility, and patient accessibility. Overall, curcumin-loaded nanoemulsions represent a compelling avenue for harnessing the therapeutic potential of curcumin, particularly for managing inflammation-driven disorders.

**Keywords:** Curcumin, Nanoemulsion, Drug delivery, Anti-inflammatory therapy, Bioavailability, Clinical translation

## Introduction

Inflammation is a fundamental biological response that plays a dual role in maintaining human health. On one hand, it serves as a protective mechanism that eliminates harmful stimuli and initiates tissue repair. On the other hand, when inflammation becomes chronic or dysregulated, it underlies the pathogenesis of numerous debilitating diseases. Global epidemiological data consistently underscore the massive burden posed by inflammation-related disorders. Conditions such as rheumatoid arthritis, inflammatory bowel disease (IBD), cardiovascular disease, diabetes, and neurodegenerative disorders like Alzheimer's disease are strongly linked to chronic inflammation.[1,2] The World Health Organisation identifies non-communicable diseases, many of which are driven by persistent inflammatory processes, as the leading cause of mortality worldwide, accounting for more than 70% of deaths annually. Beyond the human toll, these conditions impose enormous economic costs on healthcare systems and society through loss of productivity, long-term treatment needs, and reduced quality of life.[3]

Within this context, there is an urgent need for therapeutic strategies that can safely and effectively modulate inflammatory pathways. While conventional anti-inflammatory drugs, including corticosteroids and nonsteroidal anti-inflammatory drugs (NSAIDs), are widely prescribed, their long-term use is limited by adverse effects such as gastrointestinal toxicity, cardiovascular risks, and immune suppression. This therapeutic gap has spurred interest in natural bioactive compounds with anti-inflammatory potential, particularly polyphenols derived from medicinal plants. Among these, curcumin, the yellow pigment isolated from the rhizome of *Curcuma longa* (turmeric), has emerged as one of the most extensively studied candidates.[4]

## Curcumin as a Natural Polyphenol with Therapeutic Promise

Curcumin is a diferuloylmethane polyphenol with a long history of use in traditional medicine across South Asia, especially in Ayurveda and Chinese medicine. Over the past three decades, extensive preclinical research has illuminated its broad spectrum of pharmacological

properties, including antioxidant, anticancer, antimicrobial, and, notably, anti-inflammatory effects.[5] Mechanistically, curcumin modulates key molecular targets implicated in inflammation, including nuclear factor kappa B (NF-κB), cyclooxygenase-2 (COX-2), inducible nitric oxide synthase (iNOS), and pro-inflammatory cytokines such as tumour necrosis factor-alpha (TNF-α), interleukin-1β, and interleukin-6. Through these pleiotropic actions, curcumin has demonstrated efficacy in reducing tissue damage, attenuating oxidative stress, and suppressing inflammatory cascades across a variety of disease models.[6]

In clinical studies, curcumin supplementation has been associated with symptomatic improvement in patients with arthritis, reduced relapse rates in ulcerative colitis, and beneficial effects in metabolic syndrome and depression. Importantly, curcumin's favourable safety profile, even at relatively high oral doses, positions it as an attractive alternative or adjunct to conventional therapies. Despite these promising attributes, the clinical success of curcumin has been hampered by critical pharmacokinetic limitations.[7]

## Limitations of Conventional Curcumin Formulations

The therapeutic potential of curcumin is limited by its unfavourable physicochemical and pharmacokinetic properties. Being highly hydrophobic, it shows minimal solubility in aqueous environments, restricting dissolution in gastrointestinal fluids. It is also chemically unstable at physiological pH, undergoing rapid hydrolytic and oxidative degradation. Furthermore, after absorption, curcumin experiences extensive first-pass metabolism in the liver and intestinal mucosa, leading to the formation of glucuronide and sulphate conjugates that are rapidly eliminated. Consequently, its systemic bioavailability after oral administration remains extremely low, with plasma levels of free curcumin often undetectable or short-lived, even at high doses.[8]

Conventional formulations such as curcumin capsules or powders do not effectively overcome its poor solubility and bioavailability. Approaches like co-administration with bioenhancers such as Piperine from black pepper can improve absorption but raise safety concerns due to non-selective inhibition of drug-metabolising enzymes. Likewise, complexation with phospholipids or cyclodextrins offers only modest improvements, failing to fully address issues of solubility, stability, and targeted delivery. These limitations highlight the need for more sophisticated delivery systems capable of overcoming the intrinsic barriers that restrict curcumin's therapeutic potential.[9]

## Nanotechnology as a Solution for Curcumin Delivery

Advances in nanotechnology have created new opportunities to improve the pharmacokinetic and therapeutic performance of poorly soluble bioactive compounds. Nanocarriers, with their submicron dimensions and customisable physicochemical properties, can protect encapsulated drugs from degradation, enhance solubility and absorption, and enable controlled or targeted delivery. Various nanocarrier systems have been explored for curcumin, including polymeric nanoparticles, liposomes, micelles, solid lipid nanoparticles, and dendrimers. Among these, nanoemulsions have gained particular attention for curcumin delivery because of their distinctive advantages in enhancing stability, solubility, and bioavailability.[10]

Nanoemulsions are kinetically stable colloidal dispersions of oil and water stabilised by surfactants, with droplet sizes typically in the range of 20-200 nm. Their small droplet size not only increases the surface area for dissolution but also enhances intestinal absorption through passive diffusion or endocytosis. Furthermore, nanoemulsions can be designed to improve curcumin's chemical stability by protecting it from environmental degradation, while their fluid nature allows for scalability and versatility in formulation. Importantly, nanoemulsions are often composed of food-grade lipids and surfactants, which makes them particularly attractive for nutraceutical and pharmaceutical applications.[11]

## Curcumin-Loaded Nanoemulsions: Anti-Inflammatory Potential

Recent preclinical investigations have demonstrated that curcumin-loaded nanoemulsions exert superior anti-inflammatory effects compared to unformulated curcumin. In animal models of arthritis, nanoemulsions have led to more pronounced reductions in paw oedema, histological inflammation, and cytokine expression. In models of colitis, they have improved mucosal healing and reduced markers of oxidative stress. These findings highlight how the improved solubility, absorption, and tissue distribution of nanoemulsion-encapsulated curcumin translate directly into enhanced therapeutic efficacy. Beyond systemic delivery, topical and transdermal curcumin nanoemulsions have also shown promise in reducing localised inflammation, underscoring their versatility.[12]

In vitro studies complement these findings, showing that nanoemulsion formulations increase cellular uptake of curcumin, leading to stronger inhibition of NF-κB activation and downstream inflammatory gene expression. Together, these observations support the rationale for continued exploration of nanoemulsions as a platform for curcumin delivery in inflammatory diseases.[13]

## Objective of this Review

Despite extensive research, studies on curcumin nanoemulsions remain fragmented, with diverse formulation methods and inconsistent outcomes. A critical synthesis of existing advances is therefore essential to guide future research and development. This review aims to provide a comprehensive and analytical overview of curcumin-loaded nanoemulsions, focusing on formulation strategies, physicochemical and biological evaluations, and their therapeutic potential in inflammatory disease models. By integrating findings from recent literature, we seek to clarify the current

understanding of the field, identify major challenges, and outline prospects for clinical translation.

Ultimately, this review endeavours to bridge the gap between promising experimental outcomes and real-world therapeutic application, underscoring the potential of nanoemulsions as an efficient and practical delivery platform to fully harness curcumin's anti-inflammatory efficacy.

## Curcumin: Pharmacological Basis for Anti-Inflammatory Activity

Curcumin, the primary curcuminoid derived from the rhizome of *Curcuma longa*, is one of the most extensively studied natural polyphenols in modern pharmacology. Its promise as an anti-inflammatory agent stems from its unique chemical structure and broad modulation of molecular pathways implicated in inflammation. This section discusses the chemical and physicochemical properties that define curcumin, its mechanisms of anti-inflammatory activity, the barriers that limit its bioavailability, and how its activity compares with that of synthetic anti-inflammatory agents.

## Chemical Structure and Physicochemical Properties:

Curcumin is chemically described as diferuloylmethane, belonging to the diarylheptanoid class of natural products. Structurally, it is composed of two aromatic ring systems bearing o-methoxy phenolic groups linked by a seven-carbon chain containing an α,β-unsaturated β-diketone moiety. This conjugated structure is largely responsible for curcumin's distinctive yellow colour and its antioxidant capacity, as the phenolic hydroxyl groups and conjugated double bonds readily participate in electron transfer and free radical scavenging.[14]

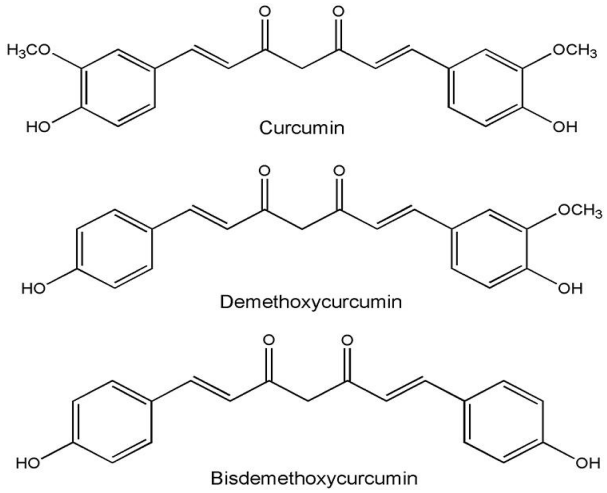


**Figure 1.** Chemical structure of curcuminoids (including Curcumin, Desmethoxycurcumin, bisdemethoxycurcumin).[4]

From a physicochemical standpoint, curcumin exhibits a high degree of hydrophobicity, with an aqueous solubility of less than 0.1 mg/mL under physiological conditions. It is soluble in organic solvents such as ethanol, dimethyl sulfoxide, and acetone, but its limited water solubility severely hampers its dissolution in gastrointestinal fluids. Furthermore, curcumin is chemically unstable, undergoing rapid hydrolytic degradation at neutral to alkaline pH, producing ferulic acid, vanillin, and other metabolites with diminished bioactivity. These properties, while central to its biological interactions, create significant hurdles for therapeutic application, necessitating novel delivery approaches such as nanoemulsions. [15]

## Mechanisms of Anti-Inflammatory Action:

Curcumin's anti-inflammatory activity is pleiotropic, targeting multiple signalling cascades that orchestrate the inflammatory response. Rather than acting through a single receptor or enzyme, curcumin exerts broad-spectrum modulation of transcription factors, enzymes, and cytokines.

### 1) Inhibition of the NF-κB Pathway

One of the most well-established mechanisms involves inhibition of nuclear factor kappa B (NF-κB), a transcription factor that regulates genes responsible for cytokine production, adhesion molecules, and inflammatory mediators. In unstimulated cells, NF-κB remains sequestered in the cytoplasm bound to inhibitor proteins (IκBs). Pro-inflammatory stimuli such as lipopolysaccharides (LPS) or cytokines trigger the phosphorylation and degradation of IκBs, releasing NF-κB to translocate into the nucleus. Curcumin interferes with this process by inhibiting IκB kinase (IKK) activity, thereby preventing IκB degradation and nuclear translocation of NF-κB. This leads to reduced expression of TNF-α, interleukin-1β (IL-1β), and other downstream mediators central to chronic inflammation.[16,17]

### 2) Downregulation of COX-2 and LOX Enzymes

Curcumin also exerts inhibitory effects on cyclooxygenase-2 (COX-2) and lipoxygenase (LOX), two key enzymes responsible for the synthesis of prostaglandins and leukotrienes from arachidonic acid. By suppressing COX-2 expression and directly inhibiting LOX activity, curcumin reduces the generation of eicosanoids that sustain inflammatory signalling and pain perception. This dual targeting of both enzymatic pathways is particularly valuable, as it offers broader anti-inflammatory coverage compared to conventional NSAIDs, which mainly target COX isoforms.[18]

### 3) Modulation of Pro- and Anti-Inflammatory Cytokines

Cytokine imbalance lies at the heart of many inflammatory disorders. Curcumin has been shown to downregulate the production of pro-inflammatory cytokines such as TNF-α, IL-6, and IL-8, while promoting anti-inflammatory cytokines like IL-10. This rebalancing of the cytokine milieu attenuates immune cell recruitment and tissue injury, particularly in diseases like rheumatoid arthritis and inflammatory bowel disease.[19]

### 4) Suppression of MAPK and JAK/STAT Pathways

Mitogen-activated protein kinases (MAPKs) and Janus kinase/signal transducer and activator of transcription (JAK/STAT) pathways are critical for signal transduction in immune cells. Curcumin interferes with phosphorylation events in these pathways, resulting in

decreased transcription of genes involved in inflammation and cell proliferation.[20]

**5) Antioxidant and Redox Modulation**

In addition to direct signalling effects, curcumin enhances cellular antioxidant defences by activating nuclear factor erythroid 2-related factor 2 (Nrf2). This transcription factor regulates the expression of antioxidant enzymes such as superoxide dismutase and catalase. By countering oxidative stress, curcumin indirectly reduces inflammation, as reactive oxygen species (ROS) are potent activators of NF-κB and other pro-inflammatory pathways.[21]

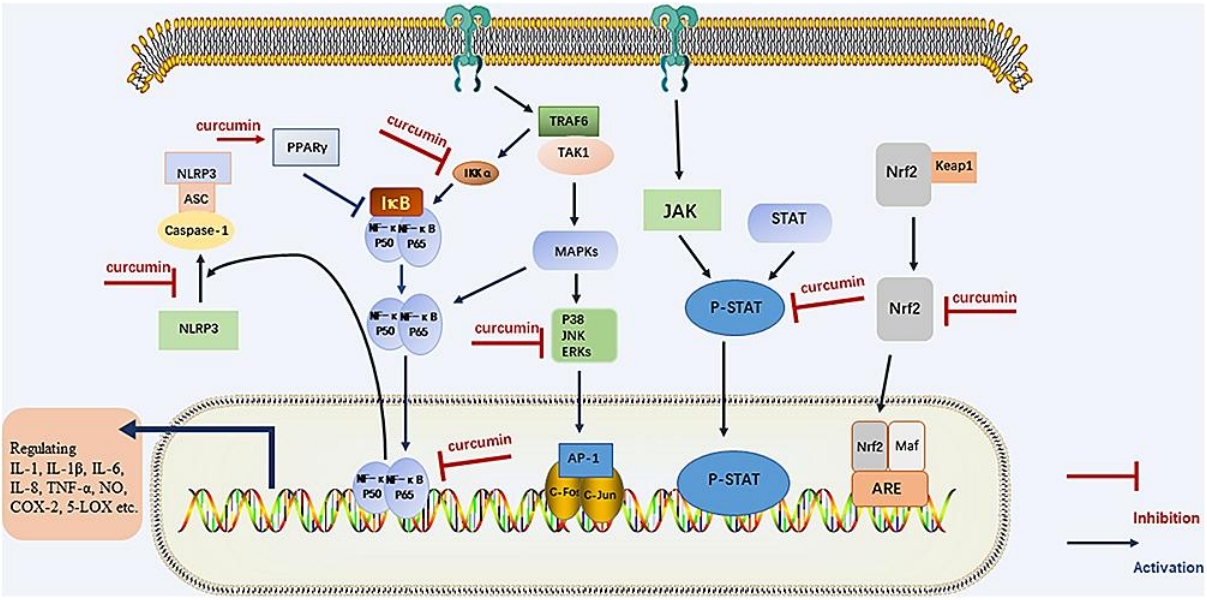


**Figure 2:** Mechanisms of Anti-Inflammatory Action of Curcumin.[4]

Collectively, these mechanisms underscore curcumin's role as a multitarget anti-inflammatory agent, capable of addressing the complexity of chronic inflammatory diseases more holistically than many single-target drugs.

## Bioavailability Barriers:

Despite its broad pharmacological activity, curcumin's clinical application has been significantly hindered by pharmacokinetic limitations. Oral administration leads to very low plasma and tissue concentrations due to:

1) **Poor aqueous solubility** – limits dissolution in the gastrointestinal tract.
2) **Chemical instability** – rapid degradation under physiological conditions reduces the intact compound available for absorption.
3) **Extensive metabolism** – curcumin undergoes rapid conjugation in the liver and intestinal mucosa, forming glucuronide and sulphate metabolites with reduced biological activity.
4) **Poor systemic distribution** – even when absorbed, curcumin's hydrophobicity restricts its biodistribution, and rapid systemic clearance limits therapeutic exposure.

As a result, even high oral doses (up to 8–12 g/day in some trials) yield minimal systemic bioavailability, highlighting the urgent need for advanced delivery systems such as nanoemulsions, nanoparticles, or liposomes to overcome these barriers.[22]

## Nanoemulsion Technology Overview

**Definition and Types of Nanoemulsions:**

Nanoemulsions are thermodynamically unstable yet kinetically stable colloidal dispersions of two immiscible liquids, commonly oil and water, stabilised by surfactants and co-surfactants, with droplet sizes typically in the range of 20–200 nm. Their small droplet size confers unique physicochemical properties, such as transparency or translucency, high surface area, and enhanced solubilisation of lipophilic compounds.[23]

Depending on the relative proportions of oil and water phases, nanoemulsions can be classified into three primary types:

**1) Oil-in-Water (O/W) Nanoemulsions**

In this system, oil droplets are dispersed within a continuous aqueous phase. O/W nanoemulsions are particularly suitable for oral, intravenous, and topical delivery of hydrophobic drugs such as curcumin because the aqueous phase allows for compatibility with biological environments.

**2) Water-in-Oil (W/O) Nanoemulsions**

Here, water droplets are dispersed in a continuous oil phase. These systems are less commonly used in oral or systemic delivery but can be valuable for transdermal or cosmetic applications where sustained release in a lipophilic medium is beneficial.

### 3) Bi-Continuous Nanoemulsions

These exhibit a bicontinuous structure where both oil and water phases form interpenetrating domains. They are less common than O/W or W/O types but may offer unique drug delivery advantages due to their ability to solubilise both hydrophilic and lipophilic molecules simultaneously.[24]

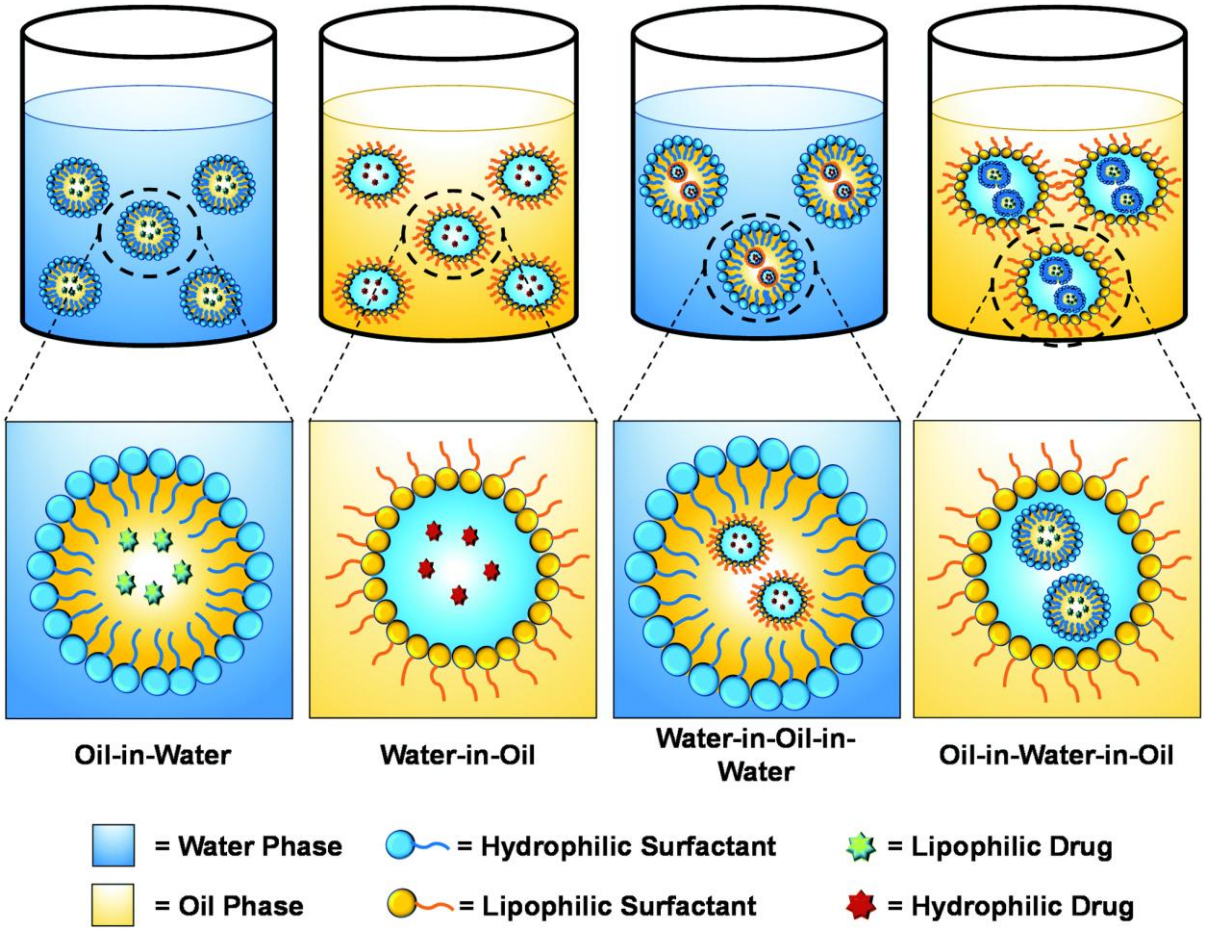


**Figure 3.** Three primary types of Nanoemulsions based on their dispersed and continuous phases: oil-in-water (O/W), water-in-oil (W/O), and bi-continuous Nanoemulsions.[25]

## Composition of Nanoemulsions:

The successful design of nanoemulsions depends on careful selection of their components:

- **Oils:** Oils serve as the hydrophobic phase that solubilises poorly water-soluble drugs like curcumin. Commonly used oils include medium-chain triglycerides (MCTs), long-chain triglycerides (LCTs), and natural oils (e.g., soybean oil, sesame oil, or fish oil). The choice of oil significantly influences solubilization capacity, stability, and drug release profile.
- **Surfactants:** Surfactants reduce the interfacial tension between oil and water, stabilising nano-sized droplets. Non-ionic surfactants (e.g., Tween 20, Tween 80, and poloxamers) are widely preferred due to their low toxicity and biocompatibility. The hydrophilic–lipophilic balance (HLB) of the surfactant determines whether an O/W or W/O nanoemulsion is formed.
- **Co-Surfactants:** Short-chain alcohols (e.g., ethanol, propylene glycol) or glycols are often used as co-surfactants to further reduce interfacial tension and improve fluidity of the interfacial film, enabling the formation of stable nano-sized droplets.
- **Aqueous Phase:** The continuous phase, usually water or buffer, forms the bulk medium in O/W systems. It may also contain stabilisers, pH adjusters, or cryoprotectants depending on the intended route of administration.

The interplay of these components determines the droplet size, stability, and drug-loading efficiency of the final nanoemulsion.[26]

## Preparation Techniques:

Nanoemulsions can be prepared using high-energy methods or low-energy methods, each offering distinct advantages depending on the desired formulation characteristics and scalability.

**High-Energy Methods**

**1) High-Pressure Homogenisation (HPH):**

In this widely used technique, coarse emulsions are passed through a narrow gap at very high pressure (500–2000 bar). The intense shear forces, turbulence, and cavitation reduce droplet sizes to the nanometre range. HPH is scalable and reproducible, making it suitable for industrial production of curcumin nanoemulsions.

**2) Ultrasonication:**

This method uses ultrasonic waves to generate cavitation bubbles in the liquid, which collapse and produce intense shear forces that break down droplets. Ultrasonication is particularly useful for small-scale preparation and allows fine control over droplet size, though scalability can be a limitation.[26]

**Low-Energy Methods**

**1) Phase Inversion Temperature (PIT):**

PIT relies on the temperature-dependent solubility of non-ionic surfactants. At specific temperatures, the surfactant's affinity shifts between hydrophilic and lipophilic phases, leading to the spontaneous formation of nano-sized droplets. Cooling or heating the system away from the PIT locks the droplets in place.

**2) Spontaneous Emulsification:**

This involves mixing oil, surfactant, and co-surfactant with water under controlled conditions. Interfacial turbulence and diffusion gradients cause the spontaneous formation of small droplets without requiring external energy. While simple, this method may be less efficient for large-scale applications.

The choice of method depends on factors such as the desired droplet size, scalability, cost, and thermosensitivity of the bioactive compound.[26]

**Factors Affecting Stability:**

Stability is a critical concern for nanoemulsions, as their high surface energy makes them prone to destabilisation. Several factors play key roles:

- **Droplet Size:** Smaller droplets (<100 nm) improve physical stability by minimising gravitational separation phenomena like creaming or sedimentation. They also enhance transparency and bioavailability.
- **Zeta Potential:** The surface charge of droplets, expressed as zeta potential, influences electrostatic repulsion between particles. High absolute zeta potential values (>±30 mV) reduce aggregation and coalescence.
- **Surfactant Choice and Concentration:** The type and amount of surfactant determine interfacial film strength. Insufficient surfactant leads to droplet coalescence, whereas excessive surfactant may cause toxicity or destabilise the system by forming micelles.
- **Environmental Conditions:** Factors such as pH, ionic strength, and temperature can destabilise nanoemulsions by promoting phase separation or altering surfactant properties. Careful optimisation is therefore essential.[27]

## Advantages over Other Nanocarriers:

Several nanocarrier systems have been developed to enhance the delivery of hydrophobic drugs, but nanoemulsions offer unique advantages:

- **Versatility in Composition:** Nanoemulsions can incorporate a wide range of oils and surfactants, allowing flexibility in tailoring solubility and release profiles.
- **Ease of Scale-Up:** Compared to polymeric nanoparticles or liposomes, nanoemulsions can often be produced on a large scale using standard homogenisation equipment, making them more industrially feasible.
- **High Solubilisation Capacity:** Due to their oil phase, nanoemulsions are particularly effective at solubilising highly lipophilic compounds like curcumin, often surpassing the loading capacity of solid lipid nanoparticles or micelles.
- **Biocompatibility:** Formulated with food-grade lipids and surfactants, nanoemulsions are generally considered safe and suitable for oral, topical, and parenteral routes of administration.
- **Enhanced Absorption:** The small droplet size and large surface area facilitate improved drug absorption through the gastrointestinal tract or skin. Nanoemulsions also enhance lymphatic transport, bypassing first-pass metabolism and further improving systemic bioavailability.

In contrast, liposomes can carry both water- and fat-loving drugs but often face stability problems such as fusion and leakage. Polymeric nanoparticles allow controlled release but are harder to make and may cause toxicity. Solid lipid nanoparticles are more stable but hold less drug and can change form during storage. In comparison, nanoemulsions are easier to prepare, more stable, and can load more drug efficiently, making them a better option for curcumin delivery.[28]

## Formulation Strategies of Curcumin-Loaded Nanoemulsions

Formulating curcumin-loaded nanoemulsions requires a careful approach to overcome its poor solubility, instability, and low bioavailability while maintaining safety and scalability. The choice of suitable oils, surfactants, and co-surfactants, along with optimisation of formulation parameters, is essential for achieving effective delivery. This section discusses strategies to improve solubility, the roles of key excipients, the use of design of experiments (DoE) for systematic optimisation, and important evaluation factors such as encapsulation efficiency and stability, supported by examples of successful formulations.[29]

## Solubility Enhancement Approaches:

The first step in formulating curcumin nanoemulsions is improving its solubility within the oil phase. Unlike water-soluble drugs, curcumin requires hydrophobic carriers capable of dissolving it at sufficiently high concentrations. Several approaches have been employed:

1) **Oil Selection:** Medium-chain triglycerides (MCTs), long-chain triglycerides (LCTs), and essential oils such as clove, eucalyptus, and black seed oil have been tested for curcumin solubilisation. MCTs, in particular, are favoured for their superior solubilising capacity and ability to stimulate lymphatic transport, bypassing hepatic first-pass metabolism.
2) **Use of Mixed Oils:** Combining triglycerides with essential oils not only enhances solubility but also provides synergistic pharmacological benefits, such as anti-inflammatory or antioxidant effects inherent to the oils themselves.
3) **Pre-Solubilisation with Co-Solvents:** Solvents like ethanol, propylene glycol, and polyethylene glycol (PEG) can temporarily improve curcumin's solubility during formulation, though their concentration must be controlled to prevent toxicity.
4) **Solidification of Liquid Phases:** In some formulations, curcumin is first dissolved in the oil phase and subsequently incorporated into nanoemulsions, ensuring high drug loading.

By carefully optimising these approaches, researchers have achieved solubility improvements of several hundred-fold compared to curcumin's native solubility in water.[30]

## Role of Excipients:

The excipients in nanoemulsion formulations are not merely passive carriers; they profoundly influence solubility, stability, droplet size, and therapeutic performance.

### Oils

- **Medium-Chain Triglycerides (MCTs):** Widely used due to their excellent solubilization capacity, biocompatibility, and ability to stimulate chylomicron-mediated lymphatic absorption.
- **Long-Chain Triglycerides (LCTs):** Provide sustained release but may limit drug solubility compared to MCTs.
- **Essential Oils:** Oils such as peppermint, clove, and black cumin not only dissolve curcumin effectively but also impart intrinsic biological activities, including antimicrobial and anti-inflammatory effects, which can synergise with curcumin's activity.[31]

### Surfactants

- **Polysorbates (Tween 20, Tween 80):** Non-ionic surfactants commonly used for their safety and ability to produce stable O/W emulsions. Tween 80, with an HLB value around 15, is particularly effective for curcumin solubilisation.
- **Sorbitan esters (Span 20, Span 80):** Often used in combination with Tweens to achieve the right hydrophilic–lipophilic balance and stabilise droplets.
- **Poloxamers:** Amphiphilic block copolymers that can improve stability and protect against enzymatic degradation.[32]

### Co-Surfactants/Solvents

- **Ethanol:** Reduces interfacial tension and improves miscibility, though excessive amounts may destabilise the emulsion.
- **Propylene Glycol and PEG:** Provide both co-solvent and stabilising effects, enhancing solubilization and reducing droplet size.[33]

**Table 1:** Role of Excipients in Curcumin Nanoemulsions

| Component | Example | Function in Nanoemulsion | References |
|---|---|---|---|
| **Oils** | Medium Chain Triglycerides (MCT), Sesame oil, Soybean oil | Solubilise curcumin and improve absorption. | [26], [31], [33] |
| **Surfactants** | Tween 80, Span 20, Poloxamer 188 | Reduce interfacial tension, stabilise droplets | [26], [31] |
| **Co-surfactants** | Ethanol, Propylene glycol, PEG 400 | Improve the flexibility of the interfacial film and enhance stability. | [31], [32] |
| **Aqueous phase** | Distilled water, phosphate buffer | Continuous phase for dispersion | [32] |
| **Essential oils** | Clove oil, Eucalyptus oil, Thyme oil | Provide solubilization and additional anti-inflammatory effects. | [31], [33] |
| **Antioxidants/Stabilisers** | Tocopherol, Ascorbic acid | Prevent oxidation and degradation of curcumin. | [33] |

The combination of surfactant and co-surfactant, often referred to as the "Smix", determines whether a stable nanoemulsion system can form. The optimal Smix ratio is typically identified through phase diagrams and experimental screening.

## Encapsulation Efficiency, Drug Loading, and Stability Aspects:

The performance of curcumin nanoemulsions is often assessed through three critical parameters:

1) **Encapsulation Efficiency (EE):** Represents the percentage of curcumin successfully entrapped in the oil phase relative to the total amount used. High EE values (>90%) are typically achievable due to curcumin's lipophilic nature, though stability issues such as precipitation may arise if the solubility limit is exceeded.
2) **Drug Loading (DL):** Expressed as the ratio of drug to total formulation weight, DL indicates the formulation's capacity to deliver therapeutic doses. Higher drug loading is desirable for clinical translation to reduce dosing volume.
3) **Stability:** Physical stability is monitored by droplet size distribution, zeta potential, and resistance to phase separation. Chemical stability involves protecting curcumin against degradation from light, oxygen, or hydrolysis. Nanoemulsions stabilised with antioxidants or stored under controlled conditions can significantly extend curcumin's shelf life compared to free curcumin powder.[34]

## Evaluation Parameters of Curcumin Nanoemulsions

The successful development of curcumin-loaded nanoemulsions depends on both smart formulation design and thorough evaluation across physicochemical, biological, and pharmacokinetic aspects. This ensures that the system is stable, safe, and therapeutically effective. This section outlines the key parameters and methods used to assess curcumin nanoemulsions, including particle characterisation, stability testing, and in vivo evaluation of anti-inflammatory activity.

### Physicochemical Evaluation:

### Particle Size and Polydispersity Index (PDI)

Particle size is a fundamental determinant of nanoemulsion performance, influencing solubility enhancement, stability, and bioavailability. Nanoemulsions typically fall within the 20–200 nm range, with smaller droplets offering increased surface area for drug dissolution and absorption.

**Dynamic Light Scattering (DLS):** The most widely used technique for particle size determination. DLS also provides the PDI, which reflects the uniformity of particle distribution. A PDI value below 0.3 is generally considered acceptable for pharmaceutical NEs, indicating narrow size distribution and minimal aggregation.

**Impact on Performance:** Smaller droplets facilitate lymphatic uptake and improve oral bioavailability, while highly uniform systems (low PDI) demonstrate better thermodynamic stability.[35]

### Zeta Potential

Zeta potential measures the electrical potential at the droplet surface, reflecting the repulsive forces between particles.

**Threshold Values:** Zeta potentials beyond ±30 mV typically indicate strong electrostatic repulsion, reducing the likelihood of aggregation.

**Relevance:** For curcumin NEs, high zeta potential values correlate with prolonged stability, particularly under physiological ionic conditions. Incorporation of charged surfactants or stabilisers can be used to tune this parameter.[36]

### Morphological Analysis (TEM/SEM)

Transmission Electron Microscopy (TEM) and Scanning Electron Microscopy (SEM) provide direct visualisation of nanoemulsion droplets.

**TEM:** Offers high-resolution imaging of droplet size and shape, confirming the spherical nature of most curcumin NEs.

**Cryo-TEM:** Enables imaging in near-native states, avoiding artefacts introduced by drying.

**SEM:** Provides complementary data but is less commonly used due to limited resolution at the nanoscale.

Together, these imaging techniques validate particle size data from DLS and reveal microstructural details critical for mechanistic understanding.[37]

### Thermodynamic Stability:

Nanoemulsions are kinetically stable but may undergo destabilisation due to Ostwald ripening, coalescence, or phase separation. Hence, rigorous stability testing is essential.

### Centrifugation Test

Nanoemulsions are subjected to centrifugation (typically at 3000–5000 rpm for 30–60 min). The absence of phase separation or precipitation indicates physical stability under mechanical stress.

### Heating–Cooling Cycles

Formulations are cycled between 4°C and 40°C for several days. Stable formulations retain clarity, droplet size, and homogeneity. This test mimics storage and transportation conditions.

### Freeze–Thaw Tests

Repeated cycles between −20°C and +25°C assess the robustness of nanoemulsions under extreme storage conditions. Successful formulations remain free from creaming, cracking, or curcumin precipitation.

Thermodynamic stability evaluations serve as predictive indicators of shelf life and robustness, particularly important for large-scale manufacturing and clinical deployment.[38]

**In Vitro Anti-Inflammatory Models:**

To establish biological relevance, curcumin nanoemulsions are routinely evaluated in vitro using assays that model inflammatory processes.

**Protein Denaturation Assay**

Protein denaturation is a hallmark of inflammatory responses. Curcumin NEs are assessed for their ability to inhibit heat- or chemical-induced protein denaturation (e.g., bovine serum albumin). Superior inhibition compared to free curcumin reflects enhanced stabilisation and bioactivity.

**Membrane Stabilisation Assay**

Erythrocytes are used as surrogate models for lysosomal membranes. Curcumin NEs prevent haemolysis induced by hypotonic or chemical stress, indicating potential to stabilise cellular membranes under inflammatory conditions.

**In Vivo Anti-Inflammatory Studies:**

Animal models provide the next tier of evidence, demonstrating pharmacological efficacy under complex biological conditions.

**Carrageenan-Induced Paw Oedema**

This classic acute inflammation model measures oedema formation following carrageenan injection in rodents. Oral or parenteral administration of curcumin NEs results in significant inhibition of paw swelling, typically surpassing that of free curcumin.

**Arthritis Models**

Curcumin NEs have been tested in collagen-induced or adjuvant-induced arthritis models. Outcomes include reduced paw swelling, joint destruction, and inflammatory cytokine levels (TNF-α, IL-6, IL-1β). These models closely mimic human rheumatoid arthritis, providing translational relevance.

Together, these in vivo studies establish the superiority of curcumin nanoemulsions in mitigating both acute and chronic inflammatory responses.[39]

**Pharmacokinetic Studies:**

Pharmacokinetic profiling provides critical insights into how nanoemulsions modify curcumin's absorption, distribution, metabolism, and excretion (ADME).

**Absorption**

Compared to free curcumin, nanoemulsions markedly enhance oral absorption due to improved solubilisation, protection from gastrointestinal degradation, and lymphatic transport. Pharmacokinetic studies consistently report higher Cmax (peak plasma concentration) and AUC (area under the curve) for curcumin NEs.

**Distribution**

Nanoemulsions facilitate broader tissue distribution, particularly in the liver, spleen, and inflamed tissues. PEGylated NEs further prolong circulation and enhance passive targeting of inflamed or tumour tissues via the enhanced permeability and retention (EPR) effect.

**Metabolism**

Curcumin undergoes extensive first-pass metabolism to glucuronides and sulphates, limiting bioactive concentrations. By promoting lymphatic transport and protecting curcumin in micellar droplets, nanoemulsions significantly reduce premature metabolism.

**Excretion**

Curcumin NEs exhibit prolonged half-life and reduced renal clearance, ensuring sustained systemic exposure.[40]

**Table 2:** Evaluation Parameters & Techniques.

| Parameter | Purpose | Analytical Method/Technique | References |
|---|---|---|---|
| **Particle size and PDI** | Assess droplet size and distribution. | Dynamic Light Scattering (DLS) | [23], [36], [40] |
| **Zeta potential** | Determine surface charge and predict stability. | Electrophoretic light scattering | [36], [38] |
| **Morphology** | Confirm droplet shape and structure. | TEM, SEM, Cryo-TEM imaging | [37], [40] |
| **Thermodynamic stability** | Evaluate resistance to phase separation. | Centrifugation, heating–cooling, freeze–thaw tests | [23], [38] |
| **In vitro release** | Assess drug diffusion and release profile. | Dialysis bag, Franz diffusion cell | [23], [40] |
| **In vitro anti-inflammatory activity** | Measure biological efficacy. | Protein denaturation, membrane stabilisation, and NO inhibition assays | [39], [40] |
| **In vivo anti-inflammatory studies** | Evaluate pharmacological activity. | Carrageenan paw oedema, cotton pellet granuloma, and arthritis models | [39] |
| **Pharmacokinetic evaluation** | Assess absorption and bioavailability. | HPLC or LC-MS/MS analysis | [23], [40] |

## Anti-Inflammatory Applications of Curcumin-Loaded Nanoemulsions

Curcumin-loaded nanoemulsions have demonstrated remarkable therapeutic potential across a wide range of inflammation-related disorders due to their ability to enhance curcumin's solubility, stability, and bioavailability. The nanoscale droplet size and large surface area enable more efficient cellular uptake and interaction with inflammatory mediators, making nanoemulsions a superior delivery platform for curcumin compared to conventional formulations.

### Systemic and Acute Inflammation

In models of acute inflammation, curcumin nanoemulsions exhibit significant suppression of inflammatory responses, such as reduced paw oedema, lowered tissue infiltration by immune cells, and decreased expression of pro-inflammatory cytokines. These effects are primarily attributed to inhibition of key signalling pathways, including NF-κB and COX-2, which regulate the synthesis of cytokines like TNF-α, IL-1β, and IL-6. The rapid absorption and sustained release properties of nanoemulsions ensure prolonged anti-inflammatory action at lower doses.[41]

### Chronic Inflammatory and Arthritic Conditions

Chronic inflammatory disorders such as rheumatoid arthritis and osteoarthritis benefit greatly from nanoemulsion-based curcumin therapy. In preclinical studies, curcumin nanoemulsions effectively attenuate joint inflammation, cartilage degradation, and oxidative stress, leading to improved joint function. Enhanced systemic bioavailability allows for consistent modulation of inflammatory biomarkers and improved antioxidant defence mechanisms, offering a safer and more effective alternative to nonsteroidal anti-inflammatory drugs.[42]

### Gastrointestinal Inflammation

Orally administered curcumin nanoemulsions have shown substantial efficacy in models of inflammatory bowel disease and colitis. The formulation protects curcumin from degradation in the gastrointestinal tract, enabling greater mucosal absorption and localised anti-inflammatory activity. Treated subjects exhibit reduced ulceration, lower myeloperoxidase activity, and improved epithelial integrity, suggesting potential use in managing intestinal inflammation and oxidative injury.[43]

### Neuroinflammatory Disorders

Curcumin's ability to cross the blood–brain barrier is significantly enhanced when formulated as a nanoemulsion. This allows for targeted modulation of neuroinflammatory processes implicated in disorders such as Alzheimer's disease and Parkinson's disease. Curcumin nanoemulsions help reduce microglial activation, oxidative stress, and neuronal damage, leading to improved cognitive and neuroprotective outcomes.[44]

### Topical and Transdermal Applications

Topically applied curcumin nanoemulsion gels demonstrate strong anti-inflammatory and wound-healing activity. The small droplet size promotes deeper skin penetration, sustained local release, and enhanced retention at inflamed sites. Such formulations accelerate tissue regeneration, reduce erythema, and improve healing outcomes, making them attractive for dermatological and post-surgical applications.[45]

### Combination and Synergistic Therapies

Combining curcumin nanoemulsions with other natural bioactives, such as piperine, resveratrol, or essential oils, yields synergistic effects. These combinations amplify anti-inflammatory and antioxidant actions by simultaneously targeting multiple signalling pathways. Moreover, essential oils used as the oil phase often contribute additional antimicrobial and healing benefits.[46]

## Limitations of current data

Despite strong preclinical evidence, translation to clinical application is still constrained by several factors.

### Limited Clinical Trials

Only a handful of clinical studies have tested curcumin nanoemulsions in humans. While early-phase trials suggest enhanced bioavailability and good tolerability, large-scale randomised controlled trials (RCTs) assessing efficacy in arthritis, IBD, or neurodegenerative diseases are lacking. This evidentiary gap impedes clinical validation.

### Variability in Formulation Designs

Diversity in oils, surfactants, preparation techniques, and evaluation methods complicates direct comparison between studies. Lack of standardised protocols results in heterogeneous findings and slows regulatory approval.

### Scale-Up Challenges

Nanoemulsion production often relies on high-pressure homogenisation or ultrasonication, which may not be economically or technically feasible for mass manufacturing. Ensuring consistent droplet size, stability, and reproducibility during scale-up remains a critical barrier.

### Incomplete Safety Profiles

While acute toxicity is well studied, data on chronic administration, reproductive safety, and immunotoxicity are insufficient. This limits confidence in their suitability for long-term management of chronic inflammatory diseases.

## Future Perspectives

The therapeutic utility of curcumin-loaded nanoemulsions has been well demonstrated in preclinical settings. Still, their broader impact lies in how the technology can evolve to meet the needs of modern medicine. Several emerging directions point toward an exciting future for these systems.

### Personalised Medicine and Targeted Delivery

The paradigm shift toward personalised medicine demands drug delivery systems that account for patient-specific variability in genetics, metabolism, and disease

pathology. Nanoemulsions can be tailored by adjusting the oil composition, surfactant ratios, and droplet size to meet the unique pharmacokinetic profiles of individual patients. Advances in surface engineering, such as ligand-functionalised Nanoemulsions that target overexpressed receptors on inflamed or cancerous tissues may further enhance site-specific curcumin delivery, maximising therapeutic outcomes while minimising systemic side effects.[47,48]

### Smart Nanoemulsions

The next generation of curcumin formulations may integrate stimuli-responsive features. For example, pH-sensitive nanoemulsions could release curcumin selectively in the acidic microenvironment of tumours or inflamed tissues. At the same time, enzyme-responsive systems could exploit disease-specific biomarkers for controlled drug release. Hybrid carriers that combine the oil-based solubilization advantages of nanoemulsions with polymeric or lipidic shells may also improve stability and enable multidimensional responsiveness.[49]

### Combination Therapies

Given the multifactorial nature of inflammation-related diseases, curcumin nanoemulsions could be leveraged in combination therapies. Co-loading with synergistic bioactives such as resveratrol, quercetin, or omega-3 fatty acids may provide multi-pronged action against oxidative stress, cytokine overproduction, and immune dysregulation. Additionally, combining curcumin with conventional anti-inflammatory drugs (e.g., NSAIDs) in nanoemulsion platforms could reduce required doses and attenuate adverse effects.[50]

### Integration with Artificial Intelligence and Machine Learning

Formulation optimisation has traditionally relied on trial-and-error or design of experiments. Incorporating artificial intelligence (AI) and machine learning (ML) could revolutionise this process by predicting optimal component ratios, stability outcomes, and in vivo performance from large datasets. AI-driven predictive models may accelerate formulation development, minimise experimental costs, and improve the translational success of curcumin nanoemulsions. [51,52]

### Outlook for Pharmaceutical Industry Applications

From a translational perspective, curcumin nanoemulsions align well with current industry trends prioritising natural compounds and advanced delivery systems. Scalable technologies such as high-pressure homogenisation and microfluidisation already exist, facilitating potential commercialisation. Beyond pharmaceuticals, opportunities extend to nutraceuticals, functional foods, and cosmeceuticals. However, addressing regulatory challenges, ensuring reproducibility at an industrial scale, and generating robust clinical data will be critical steps for widespread acceptance.[31,53]

## Conclusion

Curcumin, a natural polyphenol with potent anti-inflammatory activity, faces limitations in clinical use due to poor solubility, instability, and rapid metabolism. Nanoemulsion-based delivery systems offer a promising solution, enhancing solubility, bioavailability, and targeted action. Preclinical studies show that nanoemulsions outperform free curcumin in reducing inflammation across various disease models, and synergistic formulations further broaden their therapeutic scope.

However, challenges remain, including limited clinical data, insufficient long-term safety evidence, and the need for scalable, standardised production. Future research should focus on detailed pharmacokinetic and clinical assessments, integration of smart delivery technologies, and regulatory harmonisation.

Overall, curcumin-loaded nanoemulsions represent a major advancement in drug delivery, paving the way for natural compounds to achieve true therapeutic impact in modern medicine through sustained innovation and translational research.

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## References:

1. Soares CLR, Wilairatana P, Silva LR, et al. Biochemical aspects of the inflammatory process: A narrative review. Biomedicine & Pharmacotherapy 2023;168:115764; https://doi.org/10.1016/j.biopha.2023.115764 PMid:37897973

2. Pache M, Kedar H, Kond S, et al. Pharmacological Management of Neurodegenerative Disorders: Current and Future Approaches. Int J Sci R Tech 2025;2(3):405-520;

3. Shukla V, Arora R. The Economic Cost of Rising Non-communicable Diseases in India: A Systematic Literature Review of Methods and Estimates. Appl Health Econ Health Policy 2023;21(5):719-730; https://doi.org/10.1007/s40258-023-00822-8 PMid:37505413

4. Peng Y, Ao M, Dong B, et al. Anti-Inflammatory Effects of Curcumin in the Inflammatory Diseases: Status, Limitations and Countermeasures. DDDT 2021;Volume 15:4503-4525; https://doi.org/10.2147/DDDT.S327378 PMid:34754179 PMCid:PMC8572027

5. Fu Y-S, Chen T-H, Weng L, et al. Pharmacological properties and underlying mechanisms of curcumin and prospects in medicinal

potential. Biomedicine & Pharmacotherapy 2021;141:111888; https://doi.org/10.1016/j.biopha.2021.111888 PMid:34237598

6. Elzoheiry A, Ayad E, Omar N, et al. Anti-liver fibrosis activity of curcumin/chitosan-coated green silver nanoparticles. Sci Rep 2022;12(1):18403; https://doi.org/10.1038/s41598-022-23276-9 PMid:36319750 PMCid:PMC9626641

7. Panknin TM, Howe CL, Hauer M, et al. Curcumin Supplementation and Human Disease: A Scoping Review of Clinical Trials. IJMS 2023;24(5):4476; https://doi.org/10.3390/ijms24054476 PMid:36901908 PMCid:PMC10003109

8. Sohn S-I, Priya A, Balasubramaniam B, et al. Biomedical Applications and Bioavailability of Curcumin-An Updated Overview. Pharmaceutics 2021;13(12):2102; https://doi.org/10.3390/pharmaceutics13122102 PMid:34959384 PMCid:PMC8703330

9. Pan-On S, Dilokthornsakul P, Tiyaboonchai W. Trends in advanced oral drug delivery systems for curcumin: A systematic review. Journal of Controlled Release 2022;348:335-345; https://doi.org/10.1016/j.jconrel.2022.05.048 PMid:35654170

10. Parvaneh S, Pourmadadi M, Abdouss M, et al. Carboxymethyl cellulose/starch/reduced graphene oxide composite as a pH-sensitive nanocarrier for curcumin drug delivery. International Journal of Biological Macromolecules 2023;241:124566; https://doi.org/10.1016/j.ijbiomac.2023.124566 PMid:37100314

11. D'Acierno F, Michal CA, MacLachlan MJ. Thermal Stability of Cellulose Nanomaterials. Chem Rev 2023;123(11):7295-7325; https://doi.org/10.1021/acs.chemrev.2c00816 PMid:37132652

12. Singh PA, Awasthi R, Pandey RP, et al. Curcumin-loaded nanoemulsion for acute lung injury treatment via nebulization: Formulation, optimization and in vivo studies: Original scientific article. ADMET DMPK 2025;2661; https://doi.org/10.5599/admet.2661 PMid:40314003 PMCid:PMC12043102

13. Marwa A, Iskandarsyah, Jufri M. Nanoemulsion curcumin injection showed significant anti-inflammatory activities on carrageenan-induced paw edema in Sprague-Dawley rats. Heliyon 2023;9(4):e15457; https://doi.org/10.1016/j.heliyon.2023.e15457 PMid:37151685 PMCid:PMC10161698

14. Jakubczyk K, Drużga A, Katarzyna J, et al. Antioxidant Potential of Curcumin-A Meta-Analysis of Randomized Clinical Trials. Antioxidants 2020;9(11):1092; https://doi.org/10.3390/antiox9111092 PMid:33172016 PMCid:PMC7694612

15. Zhai SS, Ruan D, Zhu YW, et al. Protective effect of curcumin on ochratoxin A-induced liver oxidative injury in duck is mediated by modulating lipid metabolism and the intestinal microbiota. Poultry Science 2020;99(2):1124-1134; https://doi.org/10.1016/j.psj.2019.10.041 PMid:32036964 PMCid:PMC7587726

16. Zhu H, Wang X, Wang X, et al. Curcumin attenuates inflammation and cell apoptosis through regulating NF-κB and JAK2/STAT3 signaling pathway against acute kidney injury. Cell Cycle 2020;19(15):1941-1951; https://doi.org/10.1080/15384101.2020.1784599 PMid:32615888 PMCid:PMC7469468

17. Pache MM, Pangavhane RR. Immunotherapy in Autoimmune Diseases: Current Advances and Future Directions. Asian Journal of Pharmaceutical Research 2025;15(02):183-191; https://doi.org/10.52711/2231-5691.2025.00030

18. Rudrapal M, Eltayeb WA, Rakshit G, et al. Dual synergistic inhibition of COX and LOX by potential chemicals from Indian daily spices investigated through detailed computational studies. Sci Rep 2023;13(1):8656; https://doi.org/10.1038/s41598-023-35161-0 PMid:37244921 PMCid:PMC10224994

19. Mollazadeh H, Cicero AFG, Blesso CN, et al. Immune modulation by curcumin: The role of interleukin-10. Critical Reviews in Food Science and Nutrition 2019;59(1):89-101; https://doi.org/10.1080/10408398.2017.1358139 PMid:28799796

20. Kahkhaie KR, Mirhosseini A, Aliabadi A, et al. Curcumin: a modulator of inflammatory signaling pathways in the immune system. Inflammopharmacol 2019;27(5):885-900; https://doi.org/10.1007/s10787-019-00607-3 PMid:31140036

21. Yang S, Huang X-L, Chen J, et al. Curcumin protects BEAS-2B cells from PM2.5 -induced oxidative stress and inflammation by activating NRF2/antioxidant response element pathways. Int J Mol Med 2021;47(4):45; https://doi.org/10.3892/ijmm.2021.4878 PMid:33655321 PMCid:PMC7895536

22. Jamwal R. Bioavailable curcumin formulations: A review of pharmacokinetic studies in healthy volunteers. Journal of Integrative Medicine 2018;16(6):367-374; https://doi.org/10.1016/j.joim.2018.07.001 PMid:30006023

23. Mushtaq A, Mohd Wani S, Malik AR, et al. Recent insights into Nanoemulsions: Their preparation, properties and applications. Food Chemistry: X 2023;18:100684; https://doi.org/10.1016/j.fochx.2023.100684 PMid:37131847 PMCid:PMC10149285

24. Wilson RJ, Li Y, Yang G, et al. Nanoemulsions for drug delivery. Particuology 2022;64:85-97; https://doi.org/10.1016/j.partic.2021.05.009

25. Garcia CR, Malik MH, Biswas S, et al. Nanoemulsion delivery systems for enhanced efficacy of antimicrobials and essential oils. Biomater Sci 2022;10(3):633-653; https://doi.org/10.1039/D1BM01537K PMid:34994371

26. Dasgupta N, Ranjan S, Gandhi M. Nanoemulsion ingredients and components. Environ Chem Lett 2019;17(2):917-928; https://doi.org/10.1007/s10311-018-00849-7

27. Al-Sakkaf MK, Onaizi SA. Crude oil/water nanoemulsions stabilized by rhamnolipid biosurfactant: Effects of acidity/basicity and salinity on emulsion characteristics, stability, and demulsification. Fuel 2023;344:128052; https://doi.org/10.1016/j.fuel.2023.128052

28. Ozogul Y, Karsli GT, Durmuş M, et al. Recent developments in industrial applications of nanoemulsions. Advances in Colloid and Interface Science 2022;304:102685; https://doi.org/10.1016/j.cis.2022.102685 PMid:35504214

29. Guerrero S, Inostroza-Riquelme M, Contreras-Orellana P, et al. Curcumin-loaded nanoemulsion: a new safe and effective formulation to prevent tumor reincidence and metastasis. Nanoscale 2018;10(47):22612-22622; https://doi.org/10.1039/C8NR06173D PMid:30484463

30. Kang S, Kim M, Kim H, et al. Enhancement of Solubility, Stability, Cellular Uptake, and Bioactivity of Curcumin by Polyvinyl Alcohol. IJMS 2024;25(11):6278; https://doi.org/10.3390/ijms25116278 PMid:38892468 PMCid:PMC11172464

31. Jiang T, Liao W, Charcosset C. Recent advances in encapsulation of curcumin in nanoemulsions: A review of encapsulation technologies, bioaccessibility and applications. Food Research International 2020;132:109035; https://doi.org/10.1016/j.foodres.2020.109035 PMid:32331634

32. Guo Q, Bayram I, Zhang W, et al. Fabrication and characterization of curcumin-loaded pea protein isolate-surfactant complexes at neutral pH. Food Hydrocolloids 2021;111:106214; https://doi.org/10.1016/j.foodhyd.2020.106214

33. Lv R, Zhang X, Xing R, et al. Comprehensive understanding on solubility and solvation performance of curcumin (form I) in aqueous co-solvent blends. The Journal of Chemical Thermodynamics 2022;167:106718; https://doi.org/10.1016/j.jct.2021.106718

34. Palla CA, Aguilera-Garrido A, Carrín ME, et al. Preparation of highly stable oleogel-based nanoemulsions for encapsulation and controlled release of curcumin. Food Chemistry 2022;378:132132; https://doi.org/10.1016/j.foodchem.2022.132132 PMid:35045370

35. Ashagrie YN, Tadesse MG, Bachheti RK, et al. Formulation and characterization of Caesalpinia decapetala seed oil nanoemulsion:

physicochemical properties, stability, and antibacterial activity. Sci Rep 2025;15(1):14598; https://doi.org/10.1038/s41598-025-87732-y PMid:40287524 PMCid:PMC12033336

36. Sharifi F, Jahangiri M, Nazir I, et al. Zeta potential changing nanoemulsions based on a simple zwitterion. Journal of Colloid and Interface Science 2021;585:126-137; https://doi.org/10.1016/j.jcis.2020.11.054 PMid:33279695

37. Sun Z, Shi J, Wang J, et al. A deep learning-based framework for automatic analysis of the nanoparticle morphology in SEM/TEM images. Nanoscale 2022;14(30):10761-10772; https://doi.org/10.1039/D2NR01029A PMid:35790114

38. Marhamati M, Ranjbar G, Rezaie M. Effects of emulsifiers on the physicochemical stability of Oil-in-water Nanoemulsions: A critical review. Journal of Molecular Liquids 2021;340:117218; https://doi.org/10.1016/j.molliq.2021.117218

39. Bernardette Martínez-Rizo A, Fosado-Rodríguez R, César Torres-Romero J, et al. Models in vivo and in vitro for the study of acute and chronic inflammatory activity: A comprehensive review. International Immunopharmacology 2024;135:112292; https://doi.org/10.1016/j.intimp.2024.112292 PMid:38788446

40. Borrin TR, Georges EL, Moraes ICF, et al. Curcumin-loaded nanoemulsions produced by the emulsion inversion point (EIP) method: An evaluation of process parameters and physico-chemical stability. Journal of Food Engineering 2016;169:1-9; https://doi.org/10.1016/j.jfoodeng.2015.08.012

41. Vichare R, Kulahci Y, McCallin R, et al. Theranostic nanoemulsions suppress macrophage-mediated acute inflammation in rats. J Nanobiotechnol 2025;23(1):80; https://doi.org/10.1186/s12951-025-03164-w PMid:39905487 PMCid:PMC11792706

42. Laurindo LF, De Carvalho GM, De Oliveira Zanuso B, et al. Curcumin-Based Nanomedicines in the Treatment of Inflammatory and Immunomodulated Diseases: An Evidence-Based Comprehensive Review. Pharmaceutics 2023;15(1):229; https://doi.org/10.3390/pharmaceutics15010229 PMid:36678859 PMCid:PMC9861982

43. Lei F, Zeng F, Yu X, et al. Oral hydrogel nanoemulsion co-delivery system treats inflammatory bowel disease via anti-inflammatory and promoting intestinal mucosa repair. J Nanobiotechnol 2023;21(1):275; https://doi.org/10.1186/s12951-023-02045-4 PMid:37596598 PMCid:PMC10436423

44. Wang Y, Luo J, Li S-Y. Nano-Curcumin Simultaneously Protects the Blood-Brain Barrier and Reduces M1 Microglial Activation During Cerebral Ischemia-Reperfusion Injury. ACS Appl Mater Interfaces 2019;11(4):3763-3770; https://doi.org/10.1021/acsami.8b20594 PMid:30618231

45. Bagheri AM, Ranjbar M, Karami-Mohajeri S, et al. Curcumin Nanoemulgel: Characterization, Optimization, and Evaluation of Photoprotective Efficacy, Anti-Inflammatory Properties, and Antibacterial Activity. J Clust Sci 2024;35(7):2253-2272; https://doi.org/10.1007/s10876-024-02651-8

46. Ghobadi N, Asoodeh A. Co-administration of curcumin with other phytochemicals improves anticancer activity by regulating multiple molecular targets. Phytotherapy Research 2023;37(4):1688-1702; https://doi.org/10.1002/ptr.7794 PMid:36883534

47. Huang M, Zhai B-T, Fan Y, et al. Targeted Drug Delivery Systems for Curcumin in Breast Cancer Therapy. IJN 2023;Volume 18:4275-4311; https://doi.org/10.2147/IJN.S410688 PMid:37534056 PMCid:PMC10392909

48. Pache M, Bachhav G, Bhamare A, et al. Mapping Drug Responses Through Multi-Omics: A New Era of Bioinformatics in Precision Medicine. Int J Sci R Tech 2025;02(08):319-335;

49. Hake G, Mhaske A, Shukla R, et al. Copper-Induced Neurodegenerative Disorders and Therapeutic Potential of Curcumin-Loaded Nanoemulsion. Toxics 2025;13(2):108; https://doi.org/10.3390/toxics13020108 PMid:39997923 PMCid:PMC11862003

50. Bolat ZB, Islek Z, Demir BN, et al. Curcumin- and Piperine-Loaded Emulsomes as Combinational Treatment Approach Enhance the Anticancer Activity of Curcumin on HCT116 Colorectal Cancer Model. Front Bioeng Biotechnol 2020;8:50; https://doi.org/10.3389/fbioe.2020.00050 PMid:32117930 PMCid:PMC7026030

51. Hoseini B, Jaafari MR, Golabpour A, et al. Optimizing nanoliposomal formulations: Assessing factors affecting entrapment efficiency of curcumin-loaded liposomes using machine learning. International Journal of Pharmaceutics 2023;646:123414; https://doi.org/10.1016/j.ijpharm.2023.123414 PMid:37714314

52. Pache MM, Pangavhane RR, Jagtap MN, et al. The AI-Driven Future of Drug Discovery: Innovations, Applications, and Challenges. Asian J Res Pharm Sci 2025;15(1):61-67; https://doi.org/10.52711/2231-5659.2025.00009

53. Sharifi S, Fathi N, Memar MY, et al. Anti-microbial activity of curcumin nanoformulations: New trends and future perspectives. Phytotherapy Research 2020;34(8):1926-1946; https://doi.org/10.1002/ptr.6658 PMid:32166813