A COMPREHENSIVE REVIEW OF CURCUMIN: THERAPEUTIC POTENTIAL AND DRUG DELIVERY APPROACH

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Abstract

Curcumin, a strong natural substance derived from Curcuma longa, has received a lot of interest due to its remarkable therapeutic potential in the treatment of cancer, cardiovascular illnesses, and neurological disorders. However, its clinical applicability has been limited due to issues such as low bioavailability, instability, and rapid metabolism. Nanotechnology has the potential to overcome these constraints by increasing curcumin's solubility, stability, and bioavailability. This review looks at current advancements in nanocarrier-based curcumin delivery systems such as nanoparticles, liposomes, niosomes, nanoemulsions, films, and transdermal patches. Several nanoparticle-based formulations, including silica nanoparticles, liposomes, and hydrogels, have showed improved drug stability, targeted distribution, and controlled release, making curcumin more effective in treating complicated disorders. Liposomes, for example, have been tailored to target cancer cells, whereas niosomes show promise for crossing the blood-brain barrier in neurological applications. Furthermore, curcumin-loaded nanofibers and composite films offer long-term release and therapeutic effects in wound healing and cancer treatment. Nanoemulsions and emulsions increase the solubility of curcumin, while polymeric micelles and hydrogels allow for controlled drug release for targeted cancer therapy. In addition, curcumin-based transdermal patches hold great promise for localized drug delivery. Combining these advanced delivery systems with curcumin's therapeutic properties holds great promise for improving its clinical efficacy, enabling more effective treatment strategies for various diseases. Despite significant progress, further research is needed to optimize these formulations and address challenges such as expanding clinical use and improving patient adherence to treatment.

Keywords:

Curcumin, Nanocarriers, Nanoparticles, Liposomes, Niosomes, Nanoemulsions, Nanofibers, Drug Delivery Systems, Bioavailability, Controlled Release, Cancer, Neurological Disorders, Transdermal Patches.

1 Introduction

1.1 Origin and Background of Curcumin

For quite a while, customary clinical frameworks like Ayurveda and Chinese medication have utilized curcumin, the imperatively dynamic fixing in turmeric (Curcuma longa). Frequently alluded to as the "splendid zing," turmeric has been utilized for its antimicrobial, quieting, and malignant growth preventive characteristics. It is encouraged in Ayurveda to screen illnesses, for example, respiratory issues, stomach-related issues, and joint agony (1, 2). Turmeric has likewise been utilized in Chinese medication to advance injury mending and blood stream (3).

Fig: 1 Curcuma longa plant

Curcumin has acquired consideration in present day medication because of its possible remedial purposes in constant circumstances like malignant growth, diabetes, coronary illness, and neurological problems (4,5). The ability of Curucmin in flagging pathways including with the atomic component kappa B, making it a promising component for remedial intervention (6). Still the low bioavailability of curcumin is still a significant barrier of its clinical sucess.

1.2 Chemical and Biological Characteristics

1.2.1 Chemical Structure of Curcumin

Curcumin is a polyphenolic compound with the subatomic condition C21H20O6 and a subatomic load of 368.38 g/mol. It basically comprises of two sweet-smelling rings associated by a seven-carbon chain containing keto and enol gatherings, which are added to its real tautomeric bonds (7). This construction is liable for its cell upgrade and its capacity to rummage free extremists.

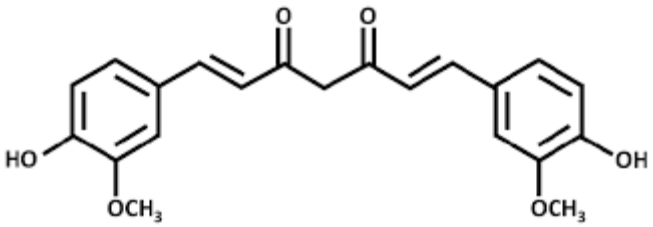

Fig : 2 Chemical structure of Curcumin

1.2.2 Drug Profile

Curcumin has various different type of pharmacokinetic properties, some properties include its dissolvability in fluids that is very low (< 0.01 g/mol) and its faster metabolic turnover, due to this its basal bioavailability is restricted. Irrespective of these challenges, the security profile is outstanding, with no harmfulness that shows up on dosages up to 12 g/day in people (8).

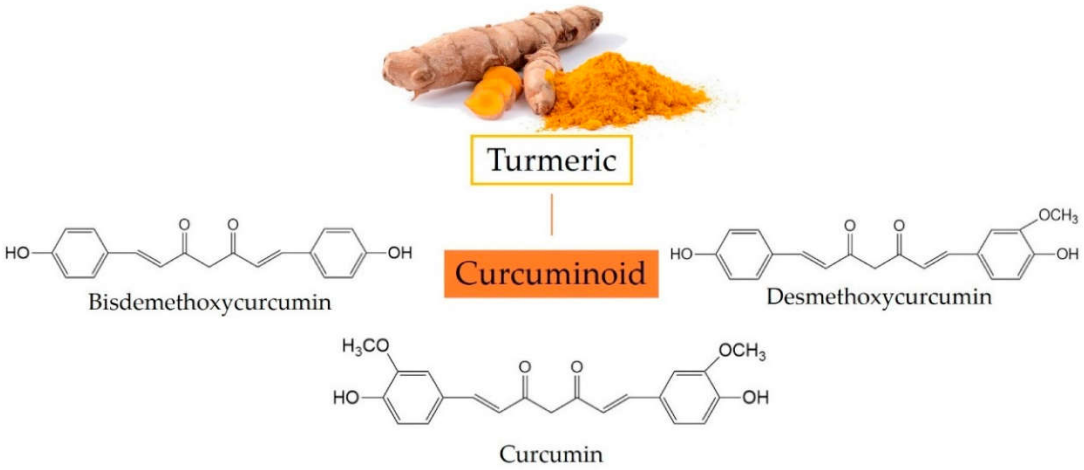

Fig: 3 Three major curcuminoids in turmeric and their chemical structures.

1.2.1 Physicochemical Properties

Curcumin is hydrophobic, with a logP worth of 3.29, showing lipophilicity. It is steady at acidic and impartial pH, yet goes through changes under solvent circumstances (9). These properties are fundamental in the plan of medication conveyance frameworks to work on their security and dissolvability.

1.2.2 Biological Activities

Curcumin proposes different regular exercises, including quieting, cell fortifying, antimicrobial, and anticancer impacts. It influences sub-atomic targets like cyclooxygenase-2 (COX-2),

interleukin-6 (IL-6), and cancer rot factor alpha (TNF-α), demonstrating its advantageous potential (10, 11).

1.3 Therapeutic Potential of Curcumin

Curcumin has shown beneficial outcomes specifically regions like malignant growth, cardiovascular sicknesses, diabetes, and neurological issues. Its anticancer properties are connected to its capacity to prompt apoptosis, cause cell cycle capture, and repress angiogenesis in impacted cells (12, 13). Also, curcumin has been read up for its neuroprotective impacts in patients with Alzheimer's and Parkinson's by diminishing oxidative pressure and amyloid plaque development (14, 15).

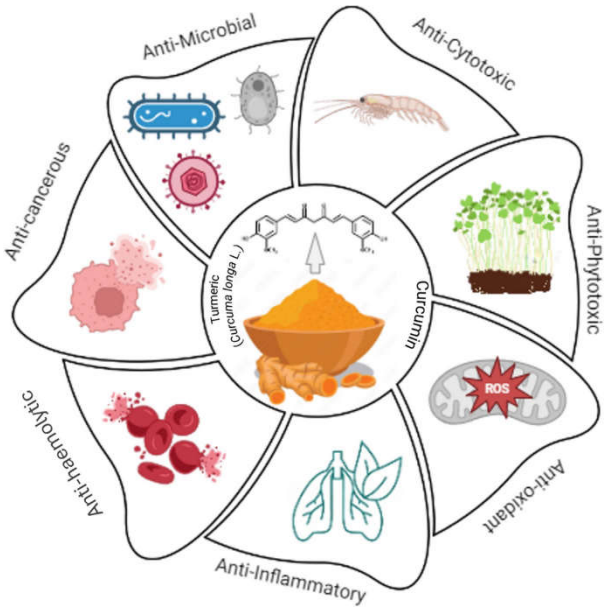

Fig 4: Therapeutic benefits of curcumin

Regardless of its certified advantages, curcumin faces difficulties in clinical use, fundamentally because of its low bioavailability. Issues like unfortunate solvency, quick digestion, and restricted fundamental dispersion upset its adequacy. Methodologies, for example, nanoparticles, liposomes, and micelles have been created to address these difficulties (16, 17).

2 Drug Delivery Challenges and Solutions for Curcumin

2.1 Bioavailability Issues

Curcumin exhibits promising therapeutic potential; however, its clinical applications are severely hindered by bioavailability issues. The primary challenges include poor aqueous solubility, rapid metabolism, and low systemic absorption (12, 18). Curcumin's hydrophobic nature limits its solubility in physiological fluids, leading to inadequate absorption in the gastrointestinal tract. Furthermore, once absorbed, it undergoes rapid metabolism in the liver and intestinal mucosa, forming inactive metabolites such as glucuronides and sulfates (19, 20). These factors significantly reduce its plasma concentration and therapeutic efficacy.

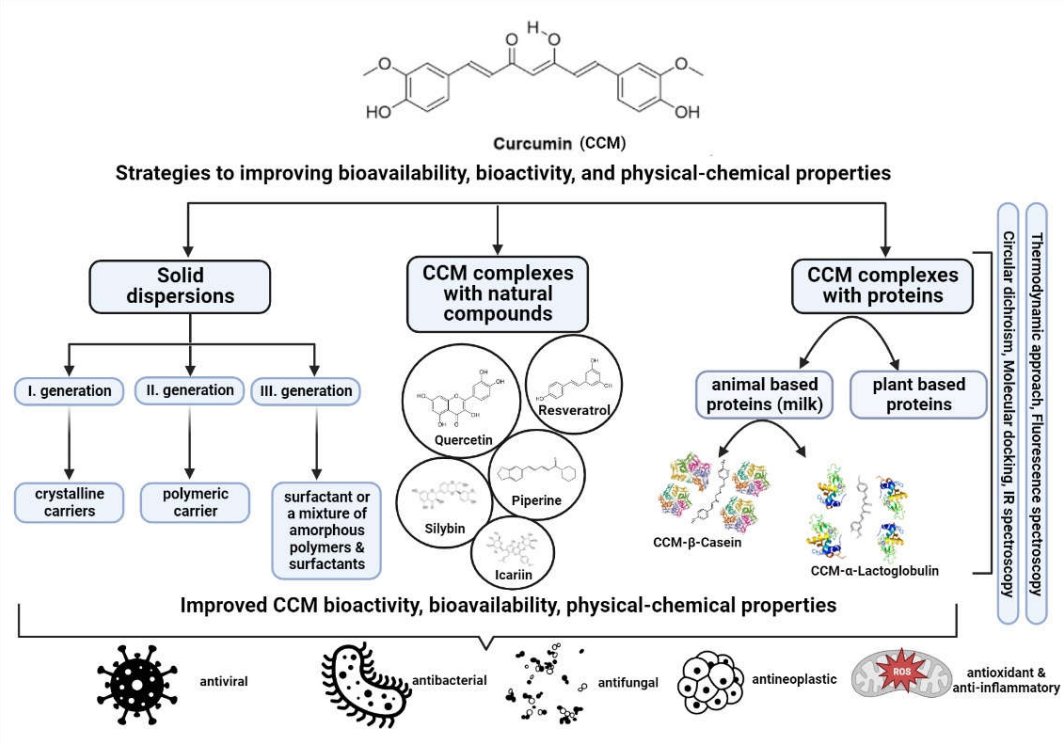

Fig: 5 Strategies to Enhance Curcumin Bioavailability and Stability

To address these challenges, several strategies have been developed:

- **Use of Adjuvants:** Compounds like piperine, a bioenhancer, inhibit the metabolism of curcumin and improve its bioavailability by up to 2000% (21).
- **Lipid-Based Systems:** Liposomes and solid lipid nanoparticles enhance solubility and stability by encapsulating curcumin in a lipid matrix (22).
- **Polymeric Nanoparticles:** These systems provide controlled release and target-specific delivery, improving circulation time and bioavailability (23).

- **Micelles and Cyclodextrins:** Surfactant-based micelles and cyclodextrin inclusion complexes enhance water solubility and protect curcumin from degradation (24, 25).

2.2 Need for Improved Delivery Systems

The limitations of curcumin's bioavailability underscore the urgent need for advanced drug delivery systems to enhance its therapeutic efficacy. These systems not only address solubility and stability concerns but also enable targeted and controlled release, minimizing off-target effects (16).

2.3 Advanced Delivery Systems for Curcumin

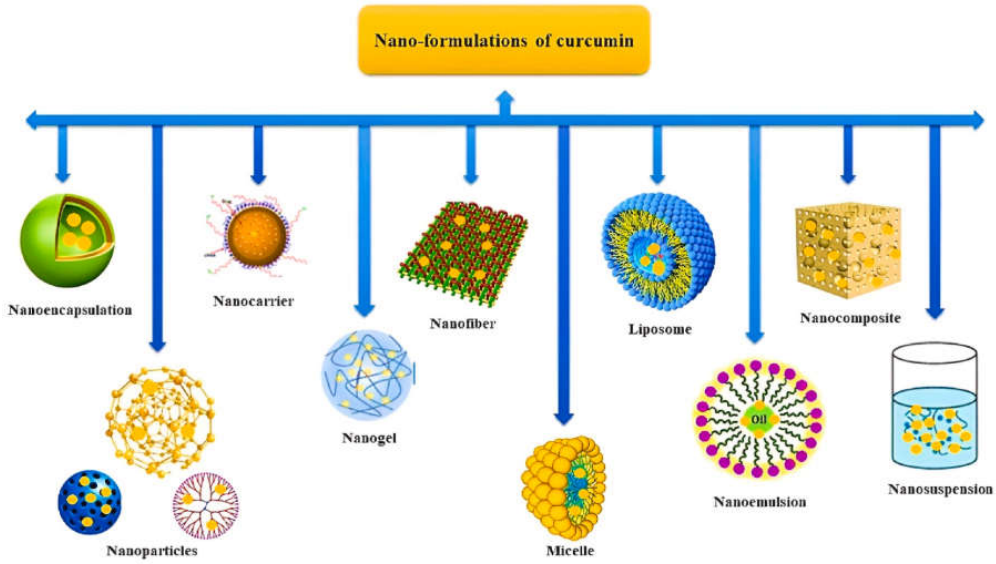

Fig : 6 Nano-formulation of Curcumin

1. **Nanoparticles:** Polymeric and lipid nanoparticles increase curcumin's stability and allow sustained release. For instance, polymeric nanoparticles like PLGA (poly-lactic-co-glycolic acid) improve drug residence time and intracellular uptake (26).

2. **Liposome:** By encasing curcumin in a phospholipid bi-layer, liposomes postpone its half-existence and guard it from enzymatic breakdown (27).

3. **Hydrogels:** Curcumin's energy below physiological instances is progressed with the aid of using biocompatible hydrogels, which proposition managed discharge (28).

4. **SNEDDS:** These frameworks altogether paintings at the dissolvability and retention of curcumin with the aid of using speaking with gastrointestinal drinks to form exceptional oil-in-water emulsions (29).

5. **Nanofibers:** Curcumin is privately conveyed with the aid of using electrospun nano-fibers for malignant boom and wound mending applications (30).

2.3 Challenges and Solutions for Curcumin Bioavailability

Table: 1 Summary of Delivery Systems and Their Applications

Delivery System	Advantages	Applications
Nanoparticles	Improved stability, controlled release, better bioa-vailability	Cancer therapy, wound healing
Liposomes	Targeted delivery, solubility enhancement	Neurological and cancer treatments
Hydrogels	Biocompatible, sustained release	Skin disorders, localized treatment
Transdermal Patches	Sustained drug release, targeted treatment	Pain management, chronic inflammation
Nano-emulsions	Increased solubility, long-term stability	Oral drug delivery
Nanofibers	High encapsulation, sustained release	Chronic diseases, wound healing

3 Formulation Strategies for Curcumin

3.1 Nanoparticles

Nanoparticles are one of the most encouraging conveyance frameworks for curcumin because of their capacity to upgrade dissolvability, security, and bioavailability. There are two principal kinds of na-noparticles utilized for curcumin conveyance: polymeric nanoparticles and lipid-based nanoparticles.

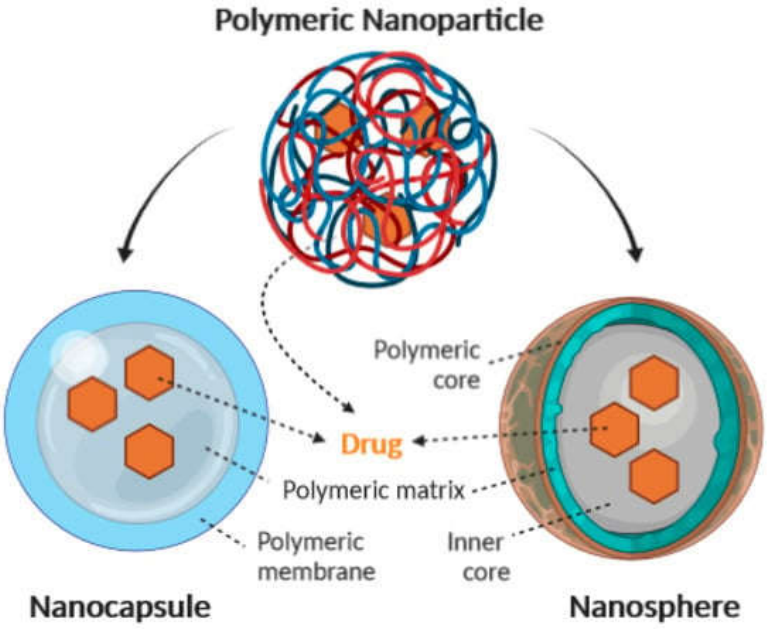

Fig: 7 Schematic representation of the structure of nanocapsules and nanospheres

- **Polymeric Nanoparticles:** These nanoparticles are produced using biodegradable and biocompatible polymers like PLGA (poly-lactic-co-glycolic corrosive) and PVA (polyvinyl liquor), which give controlled arrival of curcumin, expanding its therapeutic viability (31). Methods, for example, dissolvable dissipation, emulsion polymerization, and supercritical liquid handling are utilized for embodying curcumin in polymeric frameworks (32).
- **Lipid-Based Nanoparticles:** Lipid-based frameworks, for example, nanostructured lipid vehicle riers (NLC) and strong lipid nanoparticles (SLN), have acquired ubiquity because of their improved security and controlled drug discharge (33). These frameworks improve curcu-min's solvency and forestall its debasement by giving a defensive lipid environ-ment (34).
- **Applications:** Polymeric and lipid nanoparticles have been used in different therapeutic regions, including malignant growth treatment, neuroprotection, and wound mending (35, 36).
- **Benefits:** Nanoparticles further develop solvency, bioavailability, and give designated conveyance, limiting secondary effects. They can likewise be designed to deliver curcumin in a controlled way (37).

Table : 2 Herbal formulation of application

Formulation	Technique Involved	Polymer Used	Application	Attributes	References
Curcumin–laponite nanoparticles	Neutron reflectometry, atomic force microscopy, quartz crystal microbalance with dissipation, infrared spectroscopy	Laponite (synthetic nanoclay)	Targeted delivery for cardiovascular, neurological, and oncological diseases	Enhanced stability, controlled release across membranes, improved bioavailability, dual charge, large surface area	Pawar et al. 2024 [38]
Curcumin-loaded superparamagnetic silica nanoparticles	Encapsulation within magnetic nanoparticles, controlled release over 36 hours	Superparamagnetic silica nanoparticles	Improved solubility and sustained release of curcumin for therapeutic applications	Enhanced aqueous solubility, controlled release (36 hours), stability under physiological pH, potential for TDDS	Prabakaran et al. 2024 [39]
Folate Conjugated Nanoparticles	Folic acid (Fa) conjugated to silica and gold nanoparticles, SEM, AFM, FTIR	Polyvinyl pyrrolidone (PVP)	Targeted cancer drug delivery (breast cancer and melanoma), diagnostics, theranostics	Targeted delivery to folate receptor-overexpressing cancer cells, high catalytic activity, no biological hazards, effective in vivo treatment	Telli et al. 2024 [40]

Carrier-free Curcumin and Piperine nanoparticles	High-gravity technology for controlled nucleation and crystal growth	Curcumin, Piperine	Oral bioavailability enhancement	Uniform particle size (130 nm), co-amorphous drug nanoparticles, improved dissolution, enhanced bioavailability	Ning et al. 2024 [41]
Curcumin- and piperine-loaded niosomal nanoparticles	Thin film hydration method	Non-ionic surfactants and cholesterol	Mitigation of paraquat-induced acute pulmonary toxicity	High encapsulation efficiency (>85%), particle size (264–286 nm), good stability, reduced oxidative stress	Aram et al. 2024 [42]
Chitosan-Lipoic Acid Nanoparticles	MTT assay, cell cytotoxicity, caspase-3 assay, mitochondrial membrane potential, drug release kinetics	Chitosan, Lipoic acid	Breast cancer treatment, enhanced drug delivery	Particle size: 249 nm, 18.22% drug loading, increased drug release in GSH conditions, tumor inhibitory activity	Rezaei et al. 2021 [43]
Curcumin-loaded Poly (lactic-co-glycolic acid) Nanoparticles	Wound closure analysis, real-time PCR, western blot analysis	Poly (lactic-co-glycolic acid)	Deep tissue injury wound healing	Improved wound contraction, modulation of JAK2/STAT3 pathway, suppression of pro-inflammatory markers	Zhang et al. 2021 [44]
Curcumin-loaded magnetic iron oxide nanoparticles	TEM, UV spectroscopy	Magnetic iron oxide (MNPs)	Cancer therapy	Cytotoxic effect on MCF-7 cells, evaluated for characterization and activity	Mohamed et al. 2019 [45]
Curcumin-Encapsulated Casein Nanoparticles	Casein nanoparticles used as nanocarriers	Casein	Cancer therapy, enhanced drug bioavailability	Good water dispersibility, higher curcumin release in acidic environments, enhanced toxicity towards cancer cells	Dutta et al. 2020 [46]
Curcumin-loaded Zinc Oxide Nanoparticles	UV-Visible absorption spectroscopy, XRD, FTIR, SEM, TEM	Ethylene-vinyl alcohol copolymer (EVOH)	Drug delivery system for curcumin	Crystalline hexagonal wurtzite phase, curcumin release after 6 hours, potential for anticancer, antimicrobial, anti-inflammatory activities	Souza et al. 2019 [47]
Folic acid-mediated β-cyclodextrin functionalized Fe3O4 nanoparticles	Drug release studies, cytotoxicity assays	Folic acid, β-cyclodextrin derivatives	Targeted cancer therapy, controlled curcumin release	High biocompatibility, selective targeting, optimal release at pH=5.0	Shengmei et al. 2018 [48]
Curcumin-loaded Chitosan Phosphate Nanoparticles	DLS, TEM, cytocompatibility studies	Chitosan phosphate	Chemotherapeutic agent, antimicrobial applications	Sustained release, higher curcumin release at acidic pH, effective against bacteria and fungi	Deka et al. 2016 [49]

Study of the data: This data gives an in depth define of various nanoparticle info meant to improve the conveyance and restorative viability of curcumin.These formu-lations use diverse methods, for example, neutron reflectometry, nuclear electricity mi-croscopy, flimsy movie

hydration, and excessive-gravity innovation to create nanoparticles with unique properties, inclusive of upgraded solvency, managed discharge, and im-proven bioavailability.Polymers applied in those plans fluctuate, with substances like chitosan, poly (lactic-co-glycolic corrosive), and silica nanoparticles being ordinary decisions.Applications variety exclusive restorative regions, inclusive of malignant boom treatment, neurological sicknesses, and twisted mending, with distinct conveyance frameworks regularly lev-eraging receptor-express atoms like folic corrosive for progressed particularity.Key at-recognitions of those info include excessive exemplification effectiveness, supported drug discharge, and cytotoxic effects for ailment cells, for sure plans likewise evil presence strating antimicrobial and mitigating exercises.This combination manner to cope with curcumin-primarily based totally nanoparticle plans capabilities their promising capability in conquering curcumin's intrinsic bioavailability demanding situations and offers a founda-tion to extra research in drug and useful applications.

3.2 Liposomes

Liposomes are round vesicles fabricated from lipid bilayers which can be often used to supply curcumin due to the fact they are able to encapsulate each lipophilic and hydrophilic medication. They are ideal for drug transport structures due to the fact they're non-poisonous and biocompatible (50).

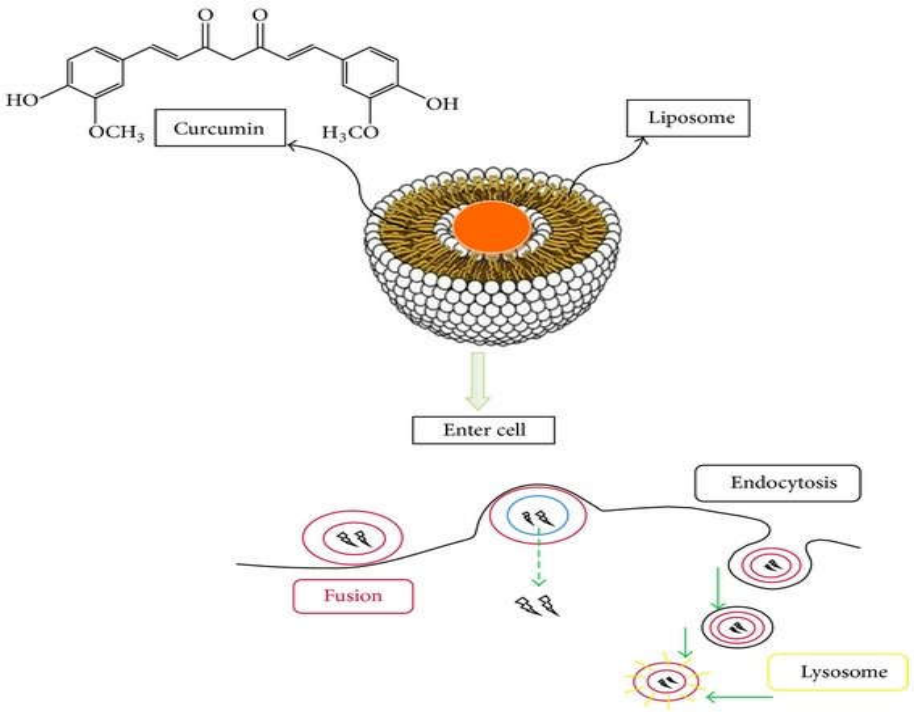

Fig: 8 Curcumin Loaded Nanoparticles

- **Structure and Function:** Curcumin may be housed withinside the aqueous middle of liposomes, and the lipid bilayer will increase curcumin's balance with the aid of using halting its breakdown in organic settings (51)**.**
- **Strategies for Curcumin Encapsulation:** Techniques like solvent injection, thin-movie hydration, and reverse-section evaporation may be used to encapsulate curcumin in liposomes (52).The balance and bioavailability of curcumin are stronger with the aid of using those tactics.
- **Advantages:** Liposomes enhance curcumin's healing capacity with the aid of using providing safety in opposition to enzymatic degradation, multiplied drug solubility, and focused transport to unique tissues (53).
- **Uses:** Liposomal formulations had been implemented to the remedy of irritation and cancer (54).
- **Studies:** This section presents nanoparticle-based formulations of curcumin designed for enhanced therapeutic efficacy, particularly in targeted drug delivery and combination therapies. One notable formulation is the curcumin-loaded thermosensitive magneto liposomes, created through a thin film hydration method. This formulation incorporates L-alpha phosphatidylcholine, Pluronic block copolymer (P123), and Fe3O4 nanoparticles, achieving an encapsulation efficiency of 81±3% for curcumin and 65±5% for Fe3O4 nanoparticles. The formulation exhibits thermosensitive drug release, with higher release rates at 43°C, making it suitable for combined chemotherapy and hyperthermia treatments. Another formulation, EGF-conjugated liposomes containing curcumin, targets pancreatic cancer cells. The conjugation with epidermal growth factor (EGF) enhances cellular uptake through EGFR-mediated mechanisms, resulting in higher cytotoxicity and improved anti-tumor activity. These formulations illustrate the potential of nanoparticle-based curcumin delivery systems in improving drug bioavailability, achieving targeted delivery, and facilitating synergistic therapies for cancer treatment.

3.3 Niosomes

Niosomes are non-ionic surfactant-based vesicular systems that offer several advantages over liposomes, particularly in terms of stability and cost-effectiveness.

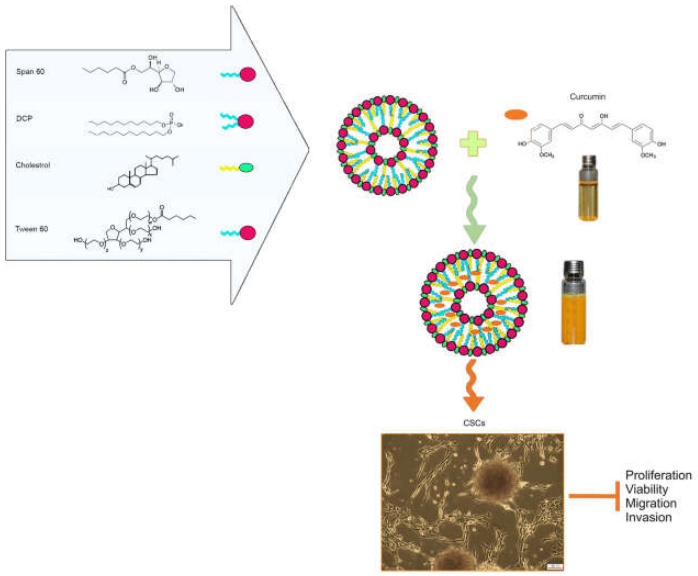

Fig: 9 Curcumin Loaded Niosome for Improved Anti-tumor Activity

- **Comparison with Liposomes:** Unlike liposomes, niosomes are formed using non-ionic surfactants, which makes them more stable and less expensive to manufacture (57).
- **Advantages:** Niosomes offer better stability and extended shelf life, which makes them more suitable for large-scale production. They are also less toxic and can be used for both hydrophilic and hydrophobic drug delivery (58).
- **Examples of Studies:** Curcumin-loaded niosomes have been studied for their ability to deliver curcumin to cancerous tissues with enhanced cellular uptake and sustained release (59).

3.4 Nanofibers

Nanofibers are a unique drug delivery system that has been explored for the controlled release of curcumin, particularly for its sustained release and stability properties.

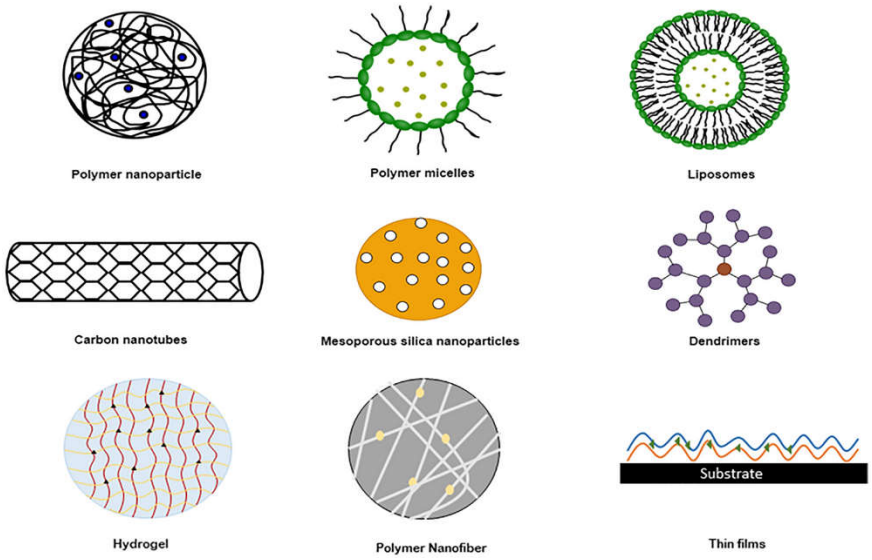

Fig: 10Curcumin Loaded Nanofibres

- **Fabrication Techniques:** Electrospinning is one of the most widely used techniques for fabricating nanofibers. It involves the application of an electric field to a polymer solution, leading to the formation of fine fibers that can encapsulate curcumin (62). Other methods include phase separation and melt electrospinning (63).
- **Benefits for Sustained Release:** Nanofibers provide a high surface area, which promotes the sustained release of curcumin over time. This results in prolonged therapeutic effects, particularly in treating chronic diseases like cancer and inflammation (64).
- **Examples:** Curcumin-loaded nanofibers have demonstrated improved stability and enhanced bioavailability compared to free curcumin.
- **Emulsion & Nanoemulsion**

Emulsion and nanoemulsion systems are colloidal dispersions of oil in water or water in oil, offering an effective strategy for improving the solubility and bioavailability of curcumin.

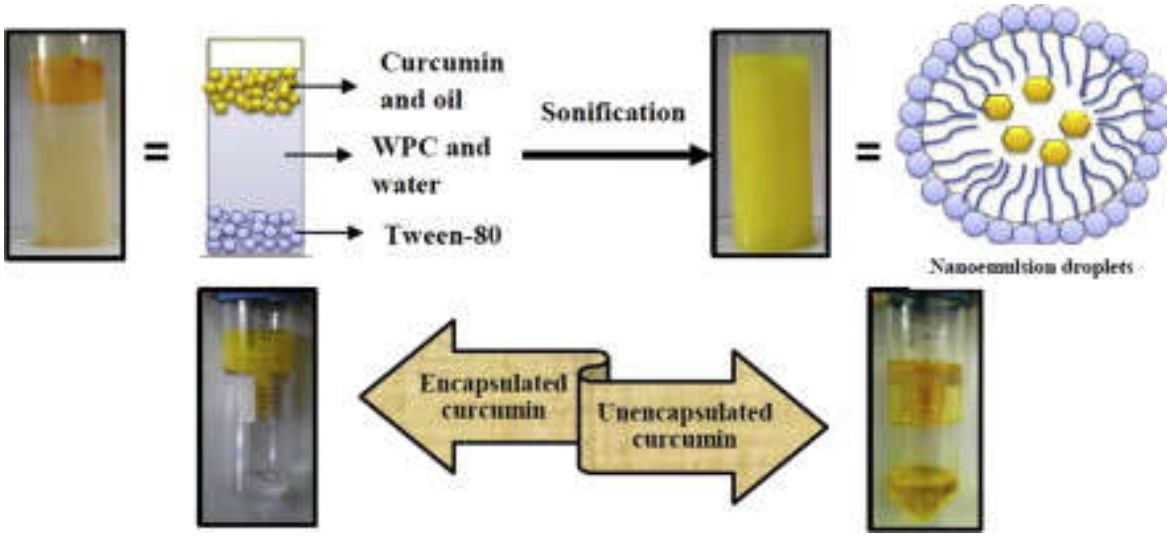

Fig: 11 : Curcumin loaded Nano-emulsion

- **Mechanism and Formulation Strategies:** Emulsions and nanoemulsions typically consist of an oily phase (containing curcumin), a surfactant, and an aqueous phase. Nanoemulsions have smaller droplet sizes (below 200 nm), which enhances the solubility and absorption of curcumin (68). The formulation process includes methods like high-pressure homogenization, microfluidization, and solvent diffusion (69).

3.5 Films & Composite Films

Films and composite films are used for controlled and sustained release of curcumin, especially in topical and transdermal drug delivery applications.

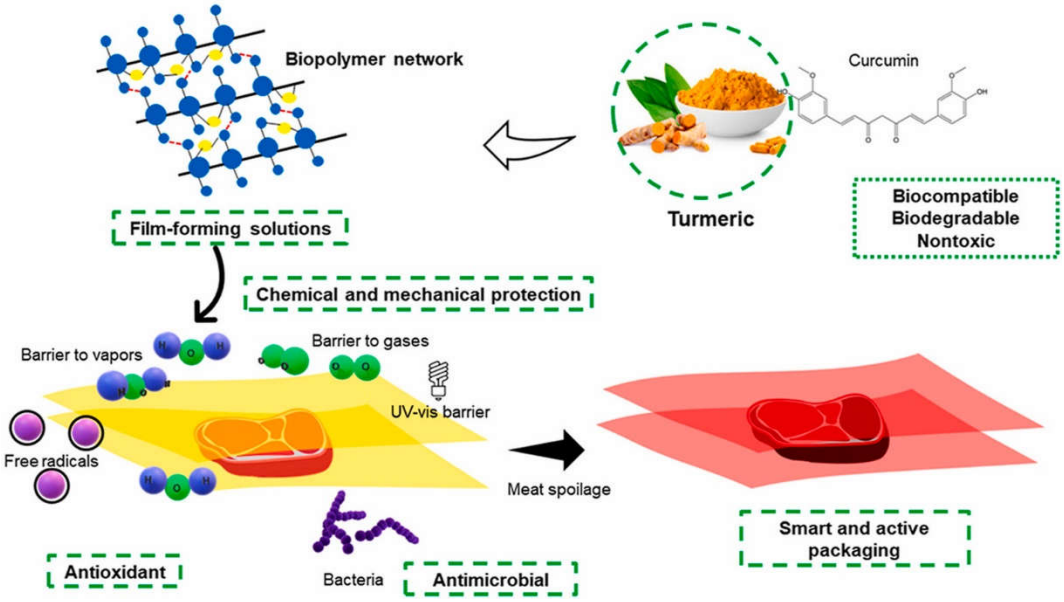

Fig: 12 Curcumin Loaded Film

- **Types of Films for Curcumin Delivery:** Polymeric films, hydrogel films, and composite films (films made from different materials) are commonly used. These films can be prepared by techniques like casting, solvent evaporation, and hot-melt extrusion (73)

3.6 Micelles

Micellar formulations have been extensively studied as a means to improve the solubility and bioavailability of curcumin, especially in oral and systemic delivery applications.

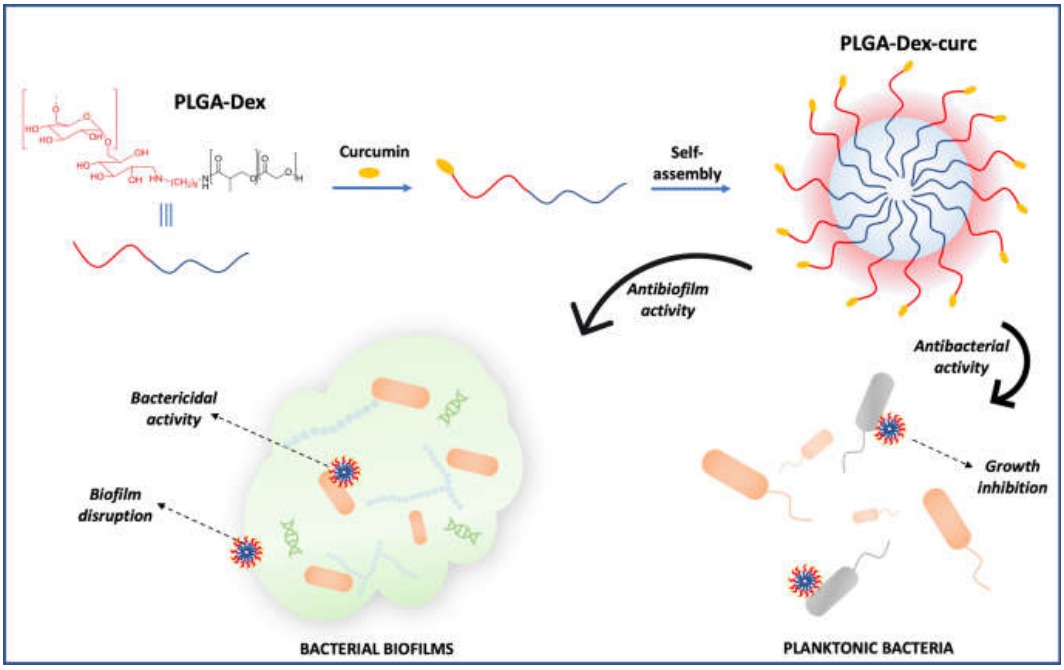

Fig: 13 Curcumin Loaded Polymeric Micelles

- **Micellar Formulations for Enhancing Curcumin Solubility:** Micelles are formed by surfactants that self-assemble in aqueous environments, encapsulating hydrophobic drugs like curcumin in their core. This increases curcumin's solubility in water and enhances its absorption (87).

3.7 Gels, Hydrogels, and Nanogels

Gels, hydrogels, and nanogels have become popular in curcumin delivery, particularly for localized treatment, as they can provide sustained release, enhance solubility, and improve therapeutic effects.

- **Differences and Applications for Curcumin Delivery:** Gels and hydrogels are colloidal systems that can be used for topical and transdermal curcumin delivery. Nanogels, due to their nanoscale size, offer enhanced drug loading capacity and stability

(92). Hydrogels are typically water-swollen polymers, whereas nanogels are cross-linked nanostructures.

- **Sustained Release and Localized Application Advantages:** These systems can provide controlled drug release over extended periods, making them ideal for chronic treatments or for localized application to the skin (93). For example, curcumin-loaded hydrogels have been used for wound healing and skin disorders.

Formulation	Technique Involved	Polymer Used	Application	Attributes	References
Bovine Serum Albumin (BSA)-Oxidized Gellan (OxG) Hydrogel Films with Curcumin-β-Cyclodextrin (β-CD–Curc) Complex	Cross-linking, FT-IR, NMR, SEM, swelling degree, skin permeability study	Bovine serum albumin (BSA), oxidized gellan (OxG), β-cyclodextrin (β-CD), curcumin (Curc)	Biomedical applications, drug delivery system for curcumin	Non-toxic, biodegradable, biocompatible; enhanced curcumin solubility and bioavailability; controlled release at pH = 5.5, better film adhesion, and improved antioxidant activity.	Marcel Popa et al. 2024 [94]
Curcumin-loaded gum arabic aldehyde-gelatin (GA Ald-Gel) nanogels	Dynamic Light Scattering (DLS), NMR Spectroscopy, Scanning Electron Microscopy (SEM), MTT assay, Confocal Laser Scanning Microscopy (CLSM), In vitro drug release studies	Gum arabic aldehyde (GA Ald), Gelatin	Cancer therapy, curcumin delivery to MCF-7 cells	Hydrodynamic diameter: 452 ± 8 nm Zeta potential: −27 mV Encapsulation efficiency: 65 ± 3% In vitro toxicity observed in MCF-7 cells Cellular uptake confirmed by CLSM Potential for controlled drug release Hemocompatibility and cytocompatibility	Rachel James Nirmala et al. 2016 [95]

- **Studies:** This study explores the development of advanced curcumin-loaded nanogel systems for targeted cancer therapy, focusing on two different formulations: bovine serum albumin (BSA)-oxidized gellan (OxG) hydrogel films with curcumin-β-cyclodextrin (β-CD–Curc) complex and gum arabic aldehyde-gelatin (GA Ald-Gel) nanogels. These formulations aim to enhance curcumin solubility, bioavailability, and targeted drug delivery. The BSA-OxG hydrogel films were characterized as non-toxic, biodegradable, and biocompatible, with the ability to control curcumin release at acidic pH, making them suitable for biomedical applications. Furthermore, the gum arabic aldehyde-gelatin nanogels exhibited promising characteristics, including hydrodynamic diameters of 452 nm, a zeta potential of −27 mV, and a 65% encapsulation efficiency. In vitro studies confirmed their toxicity in MCF-7 cancer cells, cellular uptake,

and the potential for controlled drug release. Additionally, both formulations demonstrated cytocompatibility and hemocompatibility, indicating their safety for clinical applications. These results suggest that curcumin-loaded nanogel systems are highly effective for cancer treatment and may be developed further for clinical use in controlled drug delivery systems with minimized side effects.

3.8 Microspheres

Microspheres are spherical particles that are used for controlled and sustained release of curcumin, allowing for targeted delivery and minimizing side effects.

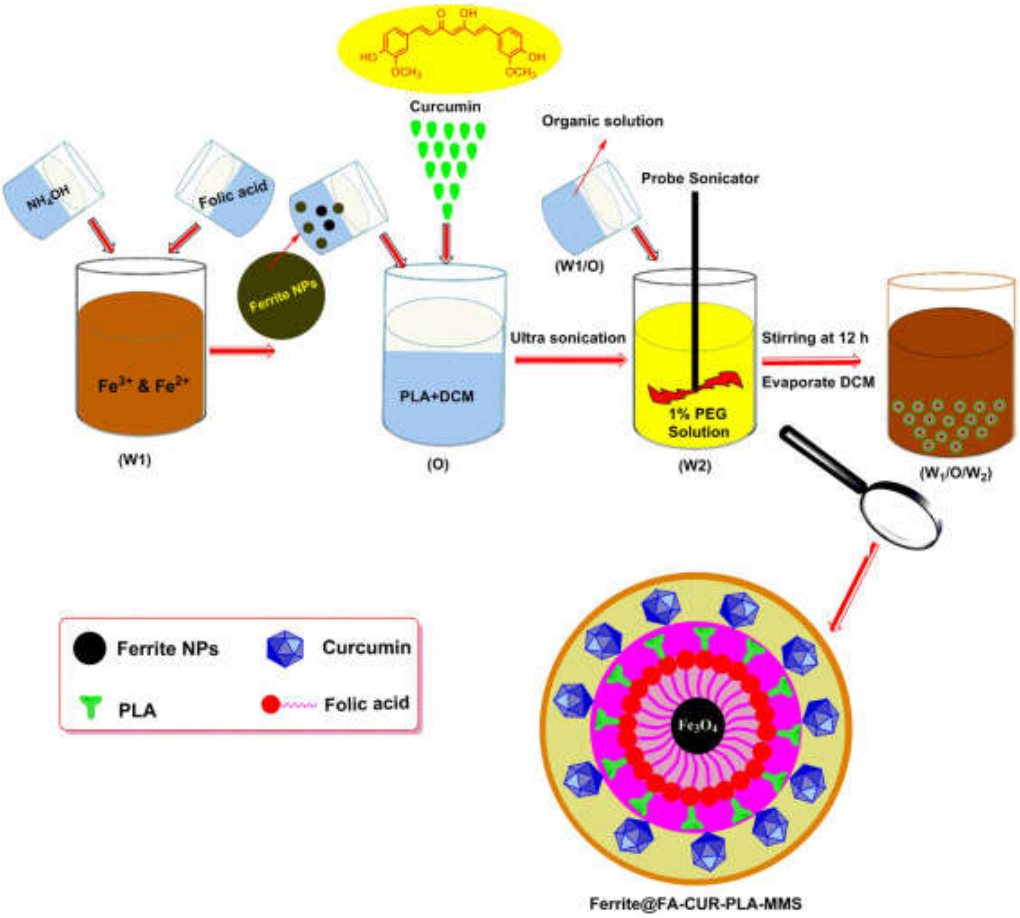

Fig: 14 Curcumin Loaded Microsphere

- **Use in Controlled Release Formulations:** Curcumin-loaded microspheres are primarily used for controlled release. They can be formulated using different materials like polymers, lipids, and proteins, which can encapsulate curcumin and release it slowly over time (96).
- **Techniques for Curcumin Encapsulation:** The encapsulation of curcumin in microspheres involves techniques such as solvent evaporation, coacervation, and emulsion-based processes (97).

4 Clinical Applications and Future Prospects

4.1 Clinical Trials and Real-World Applications

The clinical application of curcumin has garnered significant attention in recent years, primarily due to its proven therapeutic potential and the growing interest in natural product-based treatments.

- **Review of Human Clinical Trials Involving Curcumin Formulations:** Numerous clinical trials have explored curcumin's efficacy in treating various diseases, such as cancer, inflammation, and neurodegenerative disorders. Studies have demonstrated curcumin's ability to improve outcomes in conditions like arthritis, colorectal cancer, and Alzheimer's disease (99).

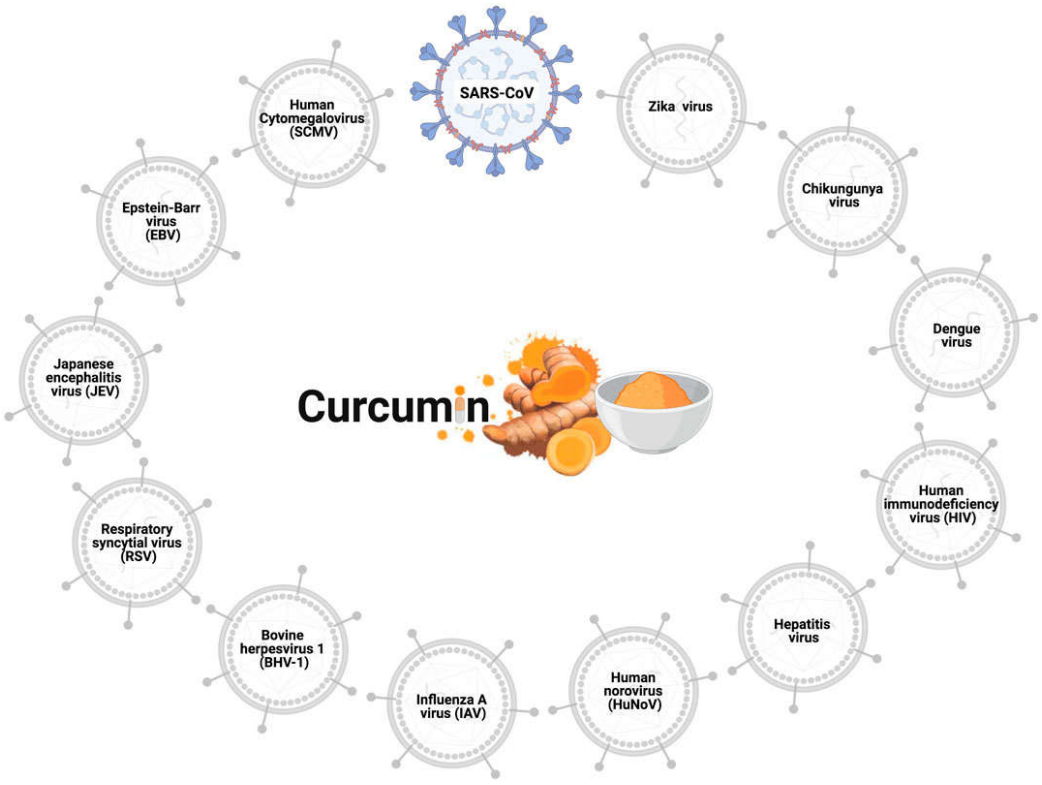

fig: 15 Curcumin Clinical and Future Prospects

- **Translational Research and the Journey from Preclinical to Clinical Settings:** While curcumin has shown promising results in preclinical studies, its translation into clinical settings has faced challenges due to bioavailability issues. Despite this, recent innovations in drug delivery systems, such as nanoparticles and liposomal formulations, have significantly improved its clinical potential (100). The journey from preclinical

animal models to clinical trials has been ongoing, with several studies focusing on overcoming bioavailability limitations by optimizing formulations.

- **Real-World Applications:** Curcumin has found its place in complementary medicine, particularly in the management of chronic inflammation, arthritis, and gastrointestinal disorders. Clinical applications also include topical formulations for wound healing and skin disorders, where curcumin's anti-inflammatory and antioxidant properties play a significant role in accelerating recovery (101).

4.2 Future Directions in Curcumin Delivery Systems

The future of curcumin delivery is promising, with ongoing advancements in nanotechnology and polymer science offering novel solutions for addressing its bioavailability challenges.

- **Innovations in Nanotechnology and Polymer Science for Curcumin Delivery**: The incorporation of curcumin into nano-sized carriers, such as nanoparticles, liposomes, and nanogels, has shown immense potential in overcoming its solubility and stability issues. Researchers are exploring polymeric nanoparticles, dendrimers, and lipid-based nanocarriers for efficient curcumin encapsulation and controlled release (102). These advanced systems can enhance the pharmacokinetics of curcumin, ensuring targeted delivery to specific tissues, thus improving therapeutic outcomes.
- **Potential for Combining Curcumin with Other Therapeutics**: Another promising direction involves combining curcumin with other therapeutic agents, such as chemotherapeutic drugs, antioxidants, or immunomodulatory agents. This combination approach could offer synergistic effects, improving the treatment of complex diseases like cancer, diabetes, and neurodegenerative disorders (103). For example, curcumin has shown potential in combination with paclitaxel in breast cancer treatment, enhancing its anticancer effects while reducing the side effects of conventional therapies (104).
- **New Areas of Research and Potential Applications**: Future research will likely focus on new areas of drug delivery, such as inhalable curcumin formulations for lung diseases and curcumin-based scaffolds for tissue engineering. Additionally, personalized medicine could play a role in curcumin therapy, tailoring its use based on genetic and biological profiles of patients to enhance treatment outcomes. Advances in smart drug delivery systems that respond to environmental stimuli (such as pH or temperature) offer exciting prospects for curcumin-based treatments (105).

5 Conclusion

The advancement of curcumin delivery through nanocarriers has shown immense promise in overcoming its inherent limitations, such as poor bioavailability and instability, thereby enhancing its therapeutic potential. A wide array of innovative nanoparticle-based systems has been explored, each contributing to better solubility, stability, and targeted release of curcumin, making it more suitable for clinical applications, particularly in cancer, neurological, and cardiovascular treatments.

1. **Nanoparticles**: Various nanoparticles, including loponite, carboxymethyl cellulose-based hydrogels, and superparamagnetic silica nanoparticles, have been successfully designed for curcumin delivery. These formulations not only improve drug stability and bioavailability but also enable targeted delivery, especially to cancer cells, demonstrating substantial in vivo efficacy. Thermoresponsive systems like poly(N-isopropylacrylamide)-modified halloysite also offer controlled drug release, opening new possibilities for temperature-sensitive clinical applications.

2. **Liposomes and Niosomes**: Liposomes, such as thermosensitive magneto liposomes and EGF-conjugated variants, show promising controlled release properties, particularly in the treatment of pancreatic cancer. Additionally, niosomes, including curcumin-loaded chitosan formulations, provide an effective means of overcoming the blood-brain barrier (BBB), presenting a significant advantage in neurological treatments by improving curcumin's bioavailability and stability.

3. **Nanofibers**: Curcumin-loaded nanofibers, composed of cellulose, gelatin, and ethylcellulose, exhibit high encapsulation efficiency, sustained release profiles, and anti-inflammatory properties. These nanofibers demonstrate therapeutic potential in cancer treatment, wound healing, and other biomedical applications, showcasing the versatility of nanofiber-based drug delivery systems.

4. **Emulsions and Nanoemulsions**: The development of Pickering emulsions and nanoemulsions has significantly enhanced curcumin’s solubility and stability. Nanoemulsions prepared through simple techniques, such as wet ball milling, offer high

encapsulation efficiency and long-term stability, making them ideal for oral drug delivery applications and increasing bioavailability.

5. **Films and Composite Films**: Curcumin-loaded composite films, like TiO2/curcumin/hydroxypropyl-cyclodextrin and curcumin-zein-EGCG-carrageenan films, provide controlled release and possess strong antibacterial properties. These films hold potential for both therapeutic and food packaging applications, underscoring their versatility in various industries.

6. **Transdermal Patches**: Curcumin-based transdermal patches, such as solid lipid nanoparticles and curcuminoid-silanol formulations, offer enhanced drug loading, flexibility, and targeted drug delivery. While further optimization is needed, these patches show considerable promise for pain management and other therapeutic applications.

7. **Micelles and Hydrogels**: Polymeric micelles and nanogels have proven effective in enhancing the solubility, stability, and bioavailability of curcumin. These systems, often conjugated with targeting agents like folic acid, demonstrate controlled and sustained release profiles, with particular promise for targeted cancer therapies.

In conclusion, the development of advanced delivery systems for curcumin has significantly improved its pharmacological profile, overcoming traditional limitations and enabling a more effective therapeutic approach. By improving solubility, bioavailability, and targeted delivery, these formulations offer a transformative potential for curcumin in the treatment of various diseases, particularly cancer. Future research focused on optimizing these delivery systems and exploring novel formulations will be crucial for the widespread clinical application of curcumin, particularly in challenging therapeutic areas.

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