INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

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Review Paper

Role of Liquid Nanoparticles in Modern Drug Delivery Approaches

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ARTICLE INFO

Published: 16 June 2026
Keywords:
Liquid Nanoparticles, Modern Drug Delivery, effective treatment for cancer
DOI:
10.5281/zenodo.20715530

ABSTRACT

Crystalline nanoparticles are suitable to show the effective treatment for cancer. Cancer, which is defined as abnormal cell growth and proliferation, is the leading cause of death worldwide. It is an incurable illness where a person's surroundings interact with their DNA to produce numerous changes. Although there are numerous cancer treatment choices, innovative drug delivery systems, or NDDS, are a more recent type of medication. Cancer is treated with NDDS, which mostly comprises of liposomes, niosomes, transferosomes, phytosomes, microspheres, nanoparticles, and liquid crystal nanoparticles. Because of their distinctive structural features, lyotropic nonlamellar liquid crystalline nanoparticles (LCNs) are believed to be effective drug delivery vehicles. Because of their highly ordered and thermodynamically stable internal nanostructure, LCNs can be used to construct a matrix for extended drug release. Because LCNPs are targeted specific, harmless to normal cells, enhanced drug solubility and bioavailability, improved drug stability, and tumor-specificity, they are now being investigated for application in a variety of cancers, including lung, prostate, and breast cancer. The current study primarily addresses LNCs, including their categories, benefits and drawbacks, mode of action, structure, use, and prospects for the future. Additionally, we have included a synopsis of how LCNPs are used in cancer therapies. LNCs have the potential to be a viable method for the focused therapy of cancer and a capable substitute for the way that cancer is now treated

INTRODUCTION

As evidenced by their ease of efflux, liquid crystals are a unique phase of condensed structures that exist in a state halfway between that of an isotropic liquid and a crystalline solid. Mesophases, which can be cubic or hexagonal in LCs, are states of matter that lie between solids and liquids. The two major categories of LCs are lyotropic liquid crystals (LLCs) and thermotropic liquid crystals (TLCs). [1,2] Materials with

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Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

characteristics halfway between those of solid crystals and normal liquids are known as liquid crystals. They are able to remain fluid while self-assembling into organised structures. Important characteristics related to medication delivery include:the capacity to encapsulate substances that are both lipophilic and hydrophilic. Amphiphilicity and biocompatibility.structural adaptability (lyotropic, cholesteric, smectic, and nematic phases).Possibility of a controlled and prolonged medication release[3,4] Because of their durable and advantageous characteristics, LCs can chaperon physiologically active principles that are often inactive due to degradation processes or unfavourable interactions with lipid membranes at the active site. LCs efficiently maximise contact duration at the site and encourage a drug's interaction with a particular target site that was previously inaccessible. By facilitating entrance into the cell and enhancing interactions between the active molecules and cell membranes, LC components support pharmacological activity.[5,6]

Basic Liquid Crystals

Liquid Crystal Types

Nematic: Although molecules lack spatial order, they align along a common axis, known as the "director." They are helpful in medication delivery systems because they are flexible and sensitive to outside stimuli.

Smectic: Within each layer, molecules are grouped in layers according to positional order. The regulated diffusion of encapsulated chemicals is made possible by this multilayer structure.

Cholesteric (Chiral Nematic): Because of chirality, molecules arrange themselves in a helical pattern. These structures are being investigated for applications in controlled release and biosensing because of their ability to selectively reflect light.[7]

MATERIALS AND METHODS:

A number of cutting-edge techniques and approaches are used in the synthesis of biologically active liquid crystal compounds, with an emphasis on the creation of novel materials with special qualities that use a variety of techniques, each specifically designed to produce particular kinds of liquid crystalline compounds. lists the most popular techniques. These techniques support the increasing focus on sustainability in chemical synthesis and make it easier to create new liquid crystalline molecules. Each technique makes a distinct contribution to the variety of physiologically active liquid crystals, opening the door for their use in industries including nanotechnology, materials research, and pharmaceuticals.[9,10]

Composition of lyotropic liquid crystalline gelling system

For distinct structures to emerge at different concentrations, this dual nature is essential. The surfactants first stabilized the solution by forming spherical aggregates and micelles at low concentrations. Different mesophases, including cubic, hexagonal, and lamellar phases, are formed as a result of these micelles changing into more complicated structures, such as cylindrical or plate-like aggregates, as the concentration rises. The concentration of surfactants, temperature, and the particular molecular structure of the surfactants used all have a major impact on the creation of these phases.[8]

Liquid crystals play a key role in herbal nanotechnology by forming advanced nanostructures that enhance herbal drug delivery. They offer biocompatibility and controlled release for plant-based actives like resveratrol. [1][7]

Key Advantages

Liquid crystals improve bioavailability of poorly soluble herbal compounds through stable nano-

carriers like cubosomes and hexosomes. They enable encapsulation of both hydrophilic and hydrophobic phytoconstituents, mimicking skin's stratum corneum for better topical penetration. Their responsiveness to stimuli allows targeted release in cancer therapy or inflammation sites. [11][12][13]

Applications

1. Enhancement of Solubility of Herbal Bioactive

Liquid crystal (LC) systems significantly improve the solubility of poorly water-soluble phytoconstituents such as curcumin, quercetin, resveratrol, berberine, and silymarin. The ordered internal structure of lyotropic liquid crystals enables efficient incorporation of hydrophobic herbal compounds within lipid domains, thereby increasing dissolution and dispersion in biological fluids. This results in improved oral absorption and enhanced therapeutic efficacy. Cubic and hexagonal mesophases are especially useful for solubilizing lipophilic herbal drugs because of their large internal surface area and amphiphilic nature.[14,15,16]

2. Improvement of Bioavailability

Many herbal drugs suffer from poor bioavailability due to low aqueous solubility, rapid metabolism, and poor permeability. Liquid crystalline nanocarriers enhance bioavailability by improving membrane penetration, prolonging gastrointestinal residence time, and protecting phytoconstituents from enzymatic degradation. LC nanoparticles facilitate efficient transport of herbal actives across biological membranes because of their bio adhesive and nanosized characteristics.[17,18,19]

3. Controlled and Sustained Drug Release

Liquid crystal nanostructures provide controlled and sustained release of herbal drugs due to their highly organized internal architecture. The diffusion of phytochemicals through cubic or hexagonal mesophases occurs gradually, thereby maintaining therapeutic drug concentrations for prolonged periods. This minimizes frequent dosing and improves patient compliance. Sustained release behavior has been demonstrated for several herbal compounds encapsulated within LC matrices.[20,21]

4. Targeted Delivery of Herbal Therapeutics

Liquid crystal nanoparticles can be engineered for site-specific delivery of herbal medicines. Surface modification of LC systems with ligands, polymers, or antibodies allows targeted delivery to tumors, inflamed tissues, or infected cells. This targeted approach increases therapeutic efficiency while reducing systemic toxicity. Herbal anticancer agents such as curcumin and paclitaxel analogues have shown enhanced cellular uptake and selective accumulation using LC-based nanocarriers.[22,23]

5. Protection of Phytoconstituents from Degradation

Many phytochemicals are chemically unstable and undergo oxidation, hydrolysis, or photodegradation during storage and administration. Liquid crystal systems protect encapsulated herbal constituents from environmental degradation by forming a stable nanostructured barrier around the active compounds. This increases shelf life and preserves pharmacological activity.[24,25]

6. Enhancement of Skin Permeation in Topical Herbal Formulations

Liquid crystalline systems are extensively used in topical and transdermal herbal formulations because they enhance skin penetration and retention of phytochemicals. Their structural similarity to biological membranes improves interaction with stratum corneum lipids, thereby facilitating deeper penetration of herbal actives. LC gels and creams containing aloe vera, curcumin, tea tree oil, and essential oils exhibit improved dermal delivery and prolonged local action .[26,27,28]

7. Application in Herbal Anticancer Therapy

Liquid crystal nanoparticles improve the therapeutic efficacy of herbal anticancer agents by increasing solubility, stability, tumor targeting, and cellular uptake. Herbal compounds such as curcumin, genistein, and resveratrol exhibit enhanced cytotoxic activity against cancer cells when delivered through LC nanocarriers. Controlled release from LC systems also helps maintain sustained anticancer activity while minimizing adverse effects. [29,30,31]

Synthesis methods for liquid crystal nanoparticles in herbal nanotechnology:

Synthesis methods for liquid crystal nanoparticles (LCNPs) in herbal nanotechnology primarily involve creating stable lyotropic structures like cubosomes or hexosomes that encapsulate herbal actives such as curcumin or resveratrol. These methods leverage amphiphilic lipids (e.g., monoglycerides) and herbal extracts to form self-assembled nano-carriers with controlled release properties.[32,33]

1) Bottom-Up Techniques

Bottom-up approaches start from molecular solutions to build nanostructures via self-assembly.

1.1 High-energy dispersion:

Heat lipid precursors (e.g., glyceryl monooleate) above transition temperature (~40°C), disperse in aqueous herbal extract with stabilizers (e.g., Poloxamer), then cool to form cubic phases; sonication or homogenization fragments into nanoparticles (~100-300 nm). Ideal for hydrophobic herbals like zedoary turmeric oil.[34,35]

1.2 Precipitation methods:

Dissolve herbal actives in organic solvents, add anti-solvents with surfactants to induce supersaturation and nucleation; supercritical CO2 aids eco-friendly evaporation for uniform LCNPs. Suited for poorly soluble phytoconstituents.[36,37]

1.3 Template-directed assembly:

Lyotropic liquid crystals act as templates for herbal nano-precipitation, evaporating solvents to yield porous nanoparticles.[38]

2) Top-Down Techniques

These mechanically reduce bulk liquid crystalline phases into nanoparticles.

2.1 High-pressure homogenization:

Form bulk cubic gel from lipids and herbal solutions, then pass through narrow gaps (e.g., 100-1500 bar, multiple cycles) to shear into stable LCNPs; used for oral resveratrol formulations.[39][40]

2.2Wet media milling:

Grind pre-formed liquid crystal dispersions with herbal beads/media, stabilizing with polymers; achieves sub-200 nm sizes for topical delivery.[41]

3) Hybrid and Advanced Methods

Combinative strategies enhance uniformity and scalability.

3.1 NanoEdge™/H69:

Precipitation followed by immediate homogenization (bottom-up + top-down) for imperfect crystals refined into monodisperse herbal LCNPs.[42]

3.2 Cubosome fragmentation:

Microfluidization or ultrasonication of isotropic precursors with herbal phytosomes; low-energy variants use phase inversion for sensitive plant volatiles.[43][44]

Key Considerations

Select methods based on herbal solubility—bottom-up for lab-scale, top-down for production. Challenges include surfactant optimization to prevent aggregation and ensure biocompatibility for herbal therapies.[45][46]

Advantages of Liquid Crystal Nanoparticles (LCNs) in Drug Delivery Systems:

1. **Controlled and Sustained Release**: LCNs provide a matrix that can control the release rate of drugs, allowing for sustained therapeutic effects over extended periods. This reduces the need for frequent dosing and maintains steady drug levels in the body.
2. **Enhanced Drug Solubility and Bioavailability**: LCNs can solubilize poorly water-soluble drugs, improving their bioavailability. This is crucial for drugs that have limited absorption due to their low solubility in bodily fluids.
3. **Improved Stability:** LCNs protect sensitive drugs from degradation due to environmental factors such as light, heat, and enzymatic activity. This enhances the shelf life and effectiveness of the drugs.
4. **Targeted Drug Delivery**: LCNs can be engineered to target specific tissues or cells, ensuring that the drug is delivered directly to the desired site of action. This minimizes side effects and maximizes therapeutic efficacy.
5. **Biocompatibility and Safety:** LCNs are often composed of biocompatible and non-toxic materials, making them safe for use in the human body. They can be designed to degrade into non-toxic byproducts.
6. **Versatility in Drug Encapsulation:** LCNs can encapsulate a wide range of drugs, including hydrophobic and hydrophilic compounds, small molecules, and macromolecules such as proteins and nucleic acids. [50]

Disadvantages of Liquid Crystal Nanoparticles (LCNs) in Drug Delivery Systems:

High Production Costs: Development and scale-up costs are increased since manufacturing calls for specialized, high-energy equipment (such high-pressure homogenizers).

Physical and Chemical Instability: It is technically difficult to preserve the particles' nanostructure over extended shelf times due to their tendency to combine or enlarge.

Excipient Toxicity Concerns: If the stabilizers and solvents employed to create the liquid crystal phases are still present as residual impurities, they may be inherently hazardous or result in unfavorable responses.

Drug Loading Limitations: They often show very low drug-loading efficiency due to their unique structural geometry (such as constricted water channels), necessitating greater doses of the carrier matrix

FUTURE PROSPECTIVES

Although LC is essential for clinical medicinal usage, there are several issues with storage conditions, such as temperature, pH, and initial burst release rate. Since the typical storage temperature for LC is 4 °C, storing LC, particularly at low temperatures, causes shape-transition. After a year of storage, an emulsion form of lyotropic liquid crystals shows no appreciable alterations , but after eighteen months, the structure begins to break down.

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HOW TO CITE: Nilam Ughade, Vidhi Jain, Pranal Pujari, Sharda Kulkarni, Sarang Kulkarni, Role of Liquid Nanoparticles In Modern Drug Delivery Approaches, Int. J. of Pharm. Sci., 2026, Vol 4, Issue 6, 3864-3871, https://doi.org/10.5281/zenodo.20715530