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# Thermotropic liquid crystals for precision drug delivery and diagnostics: Molecular design, characterization, and clinical translation

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**ABSTRACT**

Thermoresponsive drug delivery systems offer precise, on-demand, and site-specific release of therapeutic agents in response to temperature changes, thereby enhancing drug stability, minimizing side effects, and improving patient compliance. Among these, thermotropic liquid crystals (TLCs) represent a unique class of temperature-dependent mesophases with tunable properties, extended-release profiles, and targeted delivery capabilities. This review provides an in-depth examination of thermoresponsive mesophases, with a particular focus on TLCs, exploring their fundamental chemistry, structural characteristics, and adaptability in pharmaceutical sciences. A comprehensive literature survey was conducted using Scopus, PubMed, and Web of Science to analyze recent advancements in TLC-based drug delivery, biomedical applications, and associated challenges. The review discusses the mechanisms by which TLC mesophases enable thermoresponsive and sustained drug administration, as well as their integration into biosensors and diagnostic platforms, highlighting their broader biomedical potential. Key formulation strategies are outlined, alongside major obstacles such as toxicity, formulation complexity, stability, scalability, and regulatory considerations that must be addressed for clinical translation. The article also showcases recent developments and future directions in this rapidly evolving field, emphasizing the need for biocompatible and scalable TLC systems. By addressing a significant gap in the application of thermotropic mesophases specifically for drug delivery, this review underscores the promise of TLCs as intelligent drug carriers and multifunctional biomedical materials, while also identifying critical areas for future research and development.

## INTRODUCTION

Advanced drug delivery systems (DDS) play a pivotal role in biomedicine by addressing the limitations of traditional therapeutic approaches. These systems augment therapeutic efficacy by facilitating accurate, targeted drug delivery to specific locations, increasing drug concentration at the target, and minimizing off-target effects. Additionally, they help distribute drugs in a regulated or sustained manner and work with diagnostic technologies to customize treatments for patients' unique profiles [1,2]. Liquid crystals (LCs) hold significant potential in biomedicine as versatile materials with unique physicochemical properties that enable precise drug delivery, advanced biosensing, and innovative tissue engineering solutions.

LC is a distinct phase between crystalline solid and isotropic liquid, possessing attributes of both solids and liquids (Fig. 1). LC or mesophase exhibits similar mechanical characteristics to liquids, such as fluidity, inability to withstand shear, and formation of droplets. Likewise, they show anisotropy

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in their optical, electrical, and magnetic characteristics, which makes them comparable to crystals [3–7]. That is, the LCs possess physical properties such as birefringence, anisotropy, dielectric anisotropy, elastic constants, and viscosity due to their orientational order and response to external stimuli such as electric and magnetic fields.

**Shift from lyotropic to thermotropic**

LCs are classified into thermotropic and lyotropic based on their response to heat and concentration (Fig. 2). Lyotropic LC (LLC) mesophase formation is concentration-dependent, whereas thermotropic LC (TLC) mesophase formation is temperature (T)-dependent. Surfactants self-assemble in a concentration-dependent manner to form the LLC phase [6–11]. Based on the molecule's shape, micelles can be spherical, rod-like, or disc-like. When these micelles are concentrated further, they can form well-organized structures and process inverse nanomaterials such as hexagonal, cubic (non-lamellar), or lamellar phases [10].

TLCs result from partially stiff anisotropic molecules interacting and changing the order with temperature [12]. The components of TLC materials are the central core, known as the mesogen, the side chains, and the linking groups. The side chain portions are usually flexible, providing mobility, while the rigid body is the central component that gives the molecule its shape and anisotropy [11,15]. Common geometric properties are typically possessed by these TLCs, even though the compounds could belong to a range of chemical classes, including cholesteric esters, anilines, azo compounds, and azoxy compounds [16]. These systems have also been obtained with thermoresponsive hydrogels, which show distinct swelling behaviors at temperatures below and above phase transitions [17].

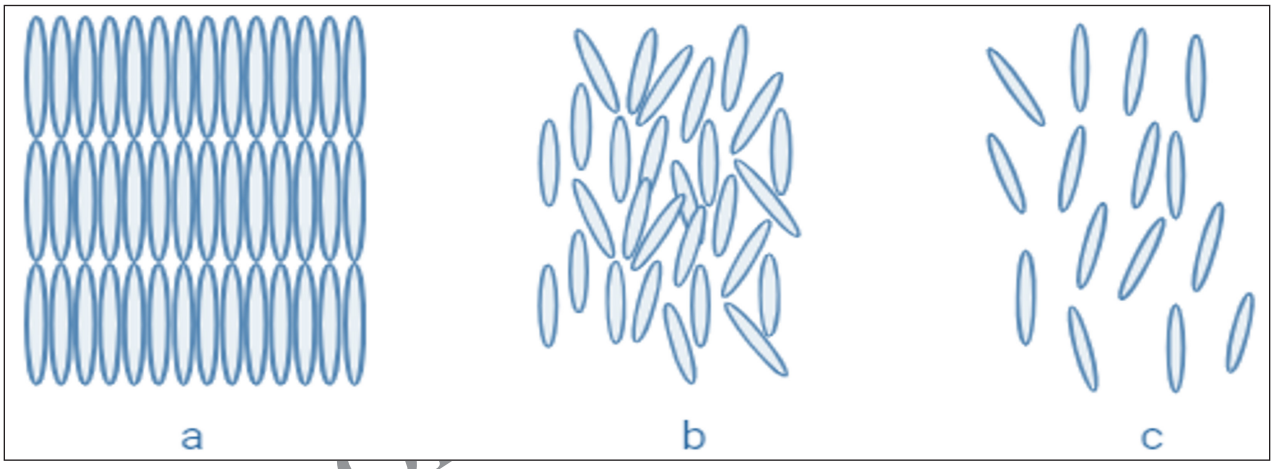


**Figure 1.** Schematic representation of (a) crystal, (b) liquid crystal, and (c) liquid.

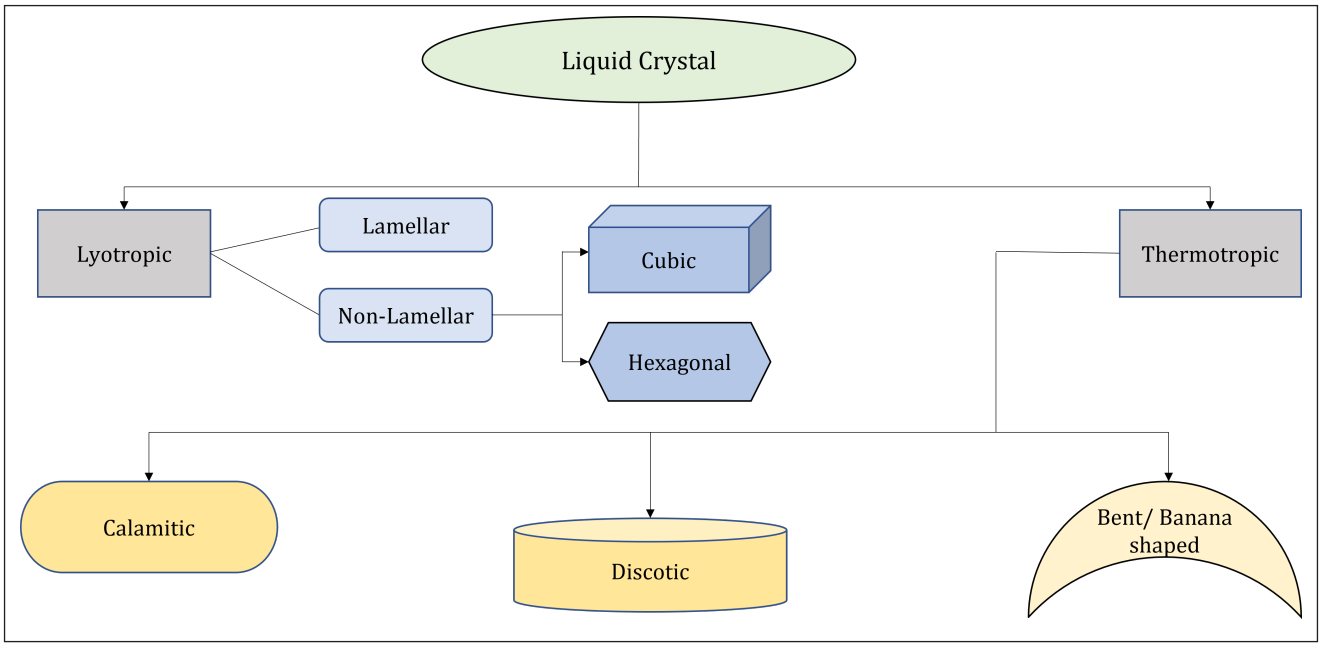


**Figure 2.** Classification of liquid crystals.

**Publication trends of thermotropics**

The publication trend in the field of TLC for drug delivery was studied on the Scopus database on May 06, 2025. Only 39 articles were found by a focused Scopus search using relevant keywords like ("thermotropic" OR "temperature-sensitive" OR "thermoresponsive" OR "thermally responsive") AND ("liquid crystal" OR "liquid crystals" OR "LC" OR "mesophase") AND ("drug delivery" OR "drug transport" OR "pharmaceutical delivery" OR "medication delivery") AND ("nanocarrier" OR "carrier" OR "vehicle" OR "system") AND ("release" OR "administration" OR "formulation" OR "dosage") suggesting that there is still a lack of research in this particular area. Interest has been steadily growing since the early 2000s, with notable peaks in recent years, particularly after 2018, according to the publication trend Figure 3. The increasing popularity of TLCs as potential delivery systems for site-specific and temperature-triggered delivery of drugs is reflected in this upward trend. Nonetheless, the small number of publications highlights a substantial research gap and the need for more investigation in this developing field.

Much literature has reported and appreciated LLCs for their capabilities in DDSs owing to their versatile self-assembled structures and biocompatibility [4,5,18–20]. Table 3 summarizes the key features of TLCs, polymeric nanoparticles, and liposomes in terms of drug release kinetics, stability, and their clinical potential over conventional dosage forms. However, scant attention has been drawn to the potential use of TLCs. The improved stability and simplicity of formulation provided by thermotropic systems are the main reasons behind the switch from lyotropic to TLCs in DDS. Thermotropic systems can preserve their mesophase structure without the use of water or other solvents, in contrast to LLCs, which need solvent concentrations to form. TLCs are more transformative and practical for clinical use because of their solvent-free nature, unlike LLC, which makes formulation and storage easier. Furthermore, TLCs react to temperature variations, enabling accurate temperature-triggered drug release that enhances patient compliance and supports targeted therapies. Their unique phase transitions and response to external factors make them even more interesting from the viewpoint of drug delivery design. This positive outlook is thus far absent within the context of DDSs, which this review seeks to remedy by addressing the role of TLCs in DDSs. The purpose of this review is to deliver an in-depth examination of thermoresponsive mesophases, emphasizing their fundamental chemistry, structural characteristics, and potential uses in biomedicine, to investigate their significance in drug delivery and various therapeutic contexts, outline formulation approaches, consider major obstacles like stability and scalability, and showcase the latest developments and future prospects within this rapidly advancing area.

## TYPES AND STRUCTURAL DIVERSITY IN TLCS

A molecule to be a TLC should contain a structure with an elastic outer moiety and a central rigid core, which is often aromatic. In accordance with the shape of the constituting molecules, the TLCs are further classified as calamitic LCs, discotic LCs, bent or banana-shaped LCs, as depicted in Table 4.

**Calamitic LCs**

The molecules possessing rod-like molecular shapes belong to this category (Fig. 4). These materials typically have a molecular length greater than their respective molecular breadths. The general rigid cores used are phenyl, biphenyl, cyclohexyl, cyclooctyl, oxadiazole, oxathiadiazole, and diazine. The linking groups are functional groups such as ester, imine, amide, stilbene, and alkyne. The molecule should possess



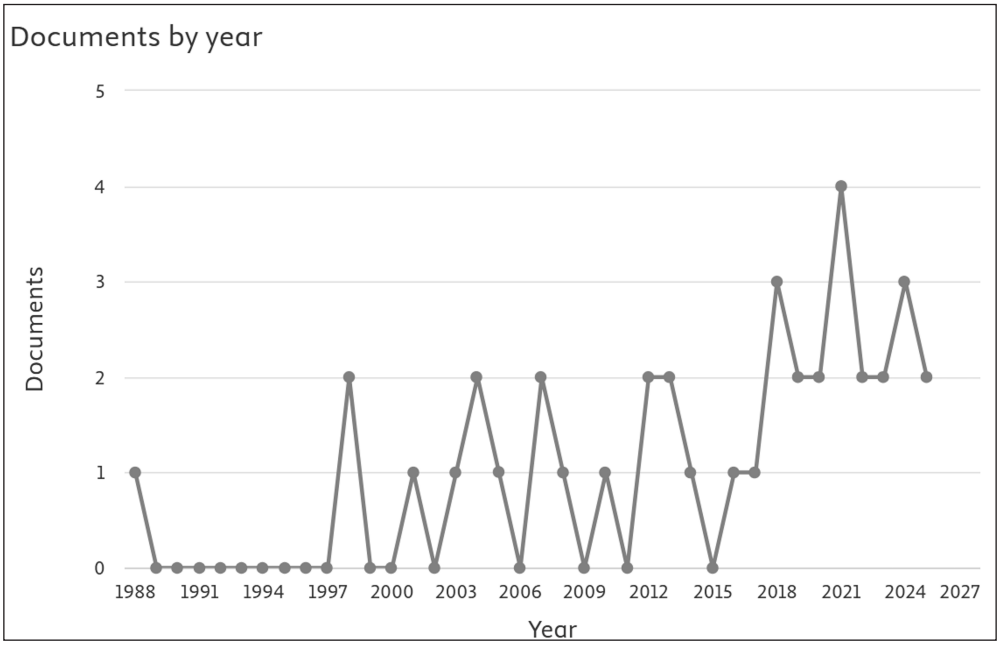


**Figure 3.** Publication trend in TLC.

**Table 1.** Characterization techniques of liquid crystals.

| Sl. No. | Property | Characterization method |
|---|---|---|
| 1 | Birefringence, molecular alignment, optical anisotropy | XRD, NMR, Microscopy |
| 2 | Rheology, viscosity | Viscosity measurement, Rheometry, FWM |
| 3 | Phase transition | POM, DSC, GISAXS |
| 4 | Energy, enthalpy, and entropy | DSC, calorimetry |
| 5 | 3-D configuration | SAXD |
| 6 | Thin nanostructures | GIXD |
| 7 | Shape and structure of mesophase | POM, TEM, SEM |
| 8 | Interaction of LC with colloids | Raman spectroscopy |
| 9 | Infrared imaging | IRT |

**Table 2.** TLC applications

| Sl. No. | Materials | Approach | Findings/applications | Author and year |
|---|---|---|---|---|
| 1. | Hydroxyurea (drug), K15, K21 | Embedding TLC in poly-HEMA membrane | LC as ″on-and-off” switches in drug delivery | Dinarvand *et al.* [74] |
| 2. | TLC arrays | Sensing device | Temperature mapping | Miskovic *et al.* [58] |
| 3. | LCE | 3D Scaffolds | Tissue engineering | Leixin *et al.* [95] |
| 4. | AmB (drug), CPC ester | Incorporation of AmB into CPC LC through the evaporation process | AmB-loaded LC for drug delivery | Chuealee *et al.* [75] |
| 5. | IDM (drug), CCC | Incorporation of IDM into CCC | Topical delivery | Aeinlang *et al.* [69] |
| 6. | IDM (drug), LA, CCC | Incorporation of IDM into CCC, LA combination | Transdermal delivery<br>Addition of LA reduced transition temperature close to body temperature | Aeinlanga *et al.* [76] |
| 7. | AmB (drug), CCC | AmB incorporated into CCC using hot melt | Drug delivery aspect | Chuealee *et al.* [77] |
| 8. | Salbutamol sulfate (drug), COC | Drug-COC mixture embedded in cellulose nitrate membrane | ″On-and-off” response to change in temperature | Lin *et al.* [80] |
| 9. | Rifampicin (drug), PEG-400, CCC | Incorporation of drug into PEG-400 and CCC | Increased solubility of the drug | Katkam *et al.* 2012 |
| 10. | CLC/PMMA | *In-situ* suspension polymerization | Thermoresponsive drug delivery | Ju *et al.* 2002 |
| 11. | COC, CN | Mixture of COC and CN incorporated into a cellulose membrane | Rate and time-controlled drug release in body temperature | Lin *et al.* [83] |
| 12. | Mesalazine, Paracetamol (drugs), CCE, COC | Drug mixed with blends of CCE/COC | Controlled drug delivery | Bhageri *et al.* [84] |
| 13. | Indomethacin (drug), PP, MTTS | Sandwich and soaking method | Thermotropic liquid crystal drug delivery | Nozawa *et al.* [72] |
| 14. | Methimazole, Paracetamol (drugs), K21 | LC embedded into cellulose nitrate and cellulose acetate membranes | Temperature-sensitive drug delivery | Dinarvand *et al.* [17] |
| 15. | Salbutamol sulfate (drug), Eudragit RL, COC | Drug incorporated into COC with Eudragit RL | Drug delivery using TLC at body temperature | Cetin *et al.* [42] |



at least one flexible end chain or substituent to exhibit the mesophases. PEGylated calamitics had been used to develop thermoresponsive DDS with the principle of phase-transition [15,21–23].

**Discotic LCs**

The molecules consist of flat, disc-like rigid cores (Fig. 5) surrounded by flexible chains (alkyl, alkyloxy, or alkenoyloxy). Examples of discotic LCs include porphyrin, triphenylene, and phthalocyanine. The diameter of these molecules is much larger than the thickness of their disc. This leads to anisotropy in the molecule. These materials find use in organic semiconductors and optoelectronic devices and frequently show strong electrical conductivity along the stacking direction [21–23].

**Bent-core or banana-shaped LCs**

Bent-core LCs resemble bent bananas as opposed to conventional rod-shaped molecules (Fig. 6). The mesogenic groups are primarily calamitic molecules that consist of two or more aromatic rings linked together by varying linking

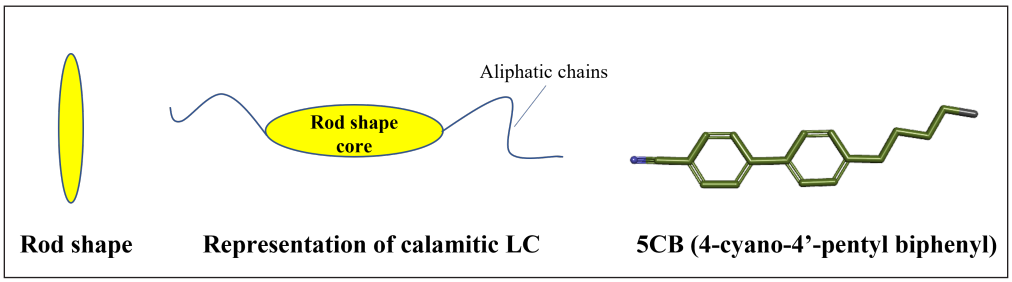


**Figure 4.** Calamitic liquid crystal.

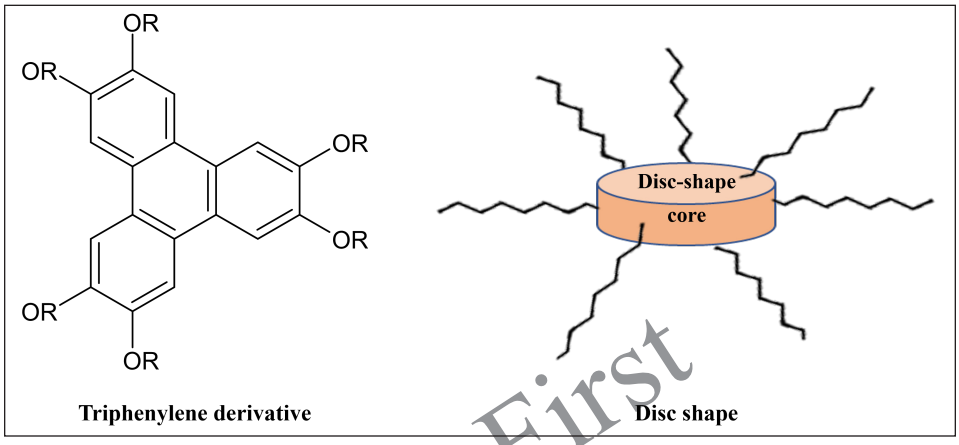


**Figure 5.** Discotic liquid crystal.



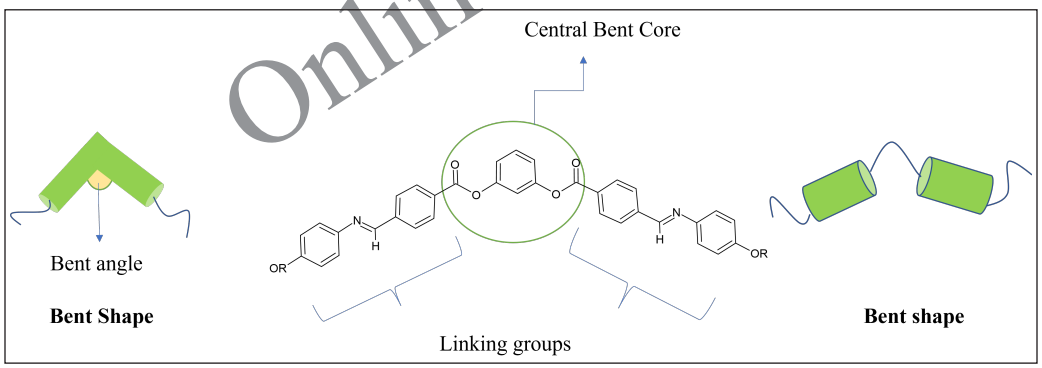


**Figure 6.** Bent-core liquid crystal.

groups (X, Y, Z) in between and have a terminal chain at the para position on one of the aromatic rings to this linking group. These materials are interesting for fundamental study and possible applications in soft matter physics and photonics since they create liquid crystalline phases with intricate structures and unique features [6].

## PHASE MORPHOLOGY IN TLCS

The phases of TLC are the arrangements of the molecules in a liquid crystalline state. In this state, the molecular axes tend to orient in one direction, called the director. The extent of the orientational order of a liquid crystalline phase is quantitatively characterized by the scalar order parameter "S," which ranges between 0 and 1. The order parameter can be calculated from the following equation:

$$S = 1/2\ (3\cos^2\theta - 1)$$

where θ (theta) represents the angle from the long axis of each molecule to the director. The brackets in the equation signify an average positive value taken over all the molecules in the sample [16].

A perfectly oriented system depicts the orientational order with S = 1. An isotropic liquid state is characterized by S = 0, as there is no orientation order. This will contrast with the liquid crystalline state, where the order parameter is usually in the range of 0.3–0.9; that is, it has a definite value at some

temperature due to the kinetic molecular motion. Thus, the mesomorphic materials (i.e., LCs) are found to possess physical properties such as birefringence anisotropy (*n*), viscosity, dielectric anisotropy (ε), and elastic constants (splay, twist, bend) due to their orientational order. They also respond to external stimuli such as magnetic and electric fields [16].

Morphological phases in TLCs include nematic, smectic, cholesteric, and columnar.

### Nematic LC

These are the most prevalent LCs, with molecules free to travel parallel to a given direction yet oriented along that direction (Fig. 7). These elongated molecules have randomly oriented centers of mass and directed long axes. Although they show long-range orientational order, they lack long-range positional order [25–28]. LC displays and other display technologies frequently use nematic LCs [4,12–15].

### Smectic LC

The molecules are layered and have long-range positional order in each layer and can travel freely within each layer. Depending on the molecular arrangement inside the layers, there are various subtypes of smectic phases, and the most common phases among them are smectic A (SmA) and smectic C (SmC). The smectic A phase, the least organized smectic phase, is characterized by layers of molecules with long molecular axes perpendicular to the layer planes and the director *n* (Fig. 7). The direction of the SmC phase is slanted at an angle rather than perpendicular to the layer plane, which distinguishes it from the SmA phase [24,29–33].

### Cholesteric LC

The molecules are arranged helically in these LCs because of their twisted shape (Fig. 7), and hence, LCs in their cholesteric phase exhibit a macroscopic helical form. This phase is also known as the chiral nematic phase. In cholesteric LCs (CLCs), rod-shaped molecules spontaneously rotate their spatial orientation along the direction of the helical axis at a constant angle [34,35]. Temperature indicators such as thermometers, reflecting displays, and other optical applications can benefit from the selective reflection of specific wavelengths of light by CLCs [35–38].

### Columnar LC

Columnar phases have long-range order inside and between the columns as the molecules are arranged into columns or stacks (Fig. 7). Two variants are rectangular and hexagonal columnar LCs. The chemistry of columnar LCs is largely defined by the structure of their mesogens, which usually consist of a rigid aromatic core flanked by flexible alkyl or alkoxy side chains. The aromatic center facilitates strong π–π stacking interactions, encouraging the molecules to align into columns, while the flexible side chains enhance solubility and help determine the distance between columns. This combination of rigid and flexible molecular parts allows for the formation of different columnar arrangements, such as hexagonal or rectangular phases, and gives the material its unique blend of fluidity and ordered structure. There are potential uses for columnar LCs in organic electronics and materials research since they combine the characteristics of crystalline solids and liquids [39,40].

## SYNTHESIS OF TLC

### Organic synthesis

Most frequently, organic chemistry techniques are used to synthesize TLC. The desired LC compound is synthesized by reacting with suitable precursors under predetermined conditions. The selection of precursors and reaction parameters dictates the final characteristics of the LC [13].

### Solvent casting

The LC material is dissolved in an appropriate solvent. As represented in Figure 8, the solvent progressively evaporates after the solution is placed onto a substrate, and a thin coating/film of the LC material is left behind. For optical and display applications, solvent casting is a standard method for LC films. For example, using this technique, the Eudragit RL membrane was made by dissolving Eudragit RL in acetone, and then propylene (PP) glycol was added [41]. Film shape can be uniquely controlled by the liquid crystalline phase seen in some conjugated polymers. Films on a templating layer can be processed and annealed above the liquid crystalline melting temperature of the polymer to create films with chains aligned in a single direction [42].

### Top-down method

To align or orient the molecules in a liquid crystalline phase, the top-down approach usually involves surface alignment, mechanical shearing, and other processes. Additionally, with techniques like lithography or nanoimprint lithography, surfaces may be designed with characteristics that regulate the arrangement of LC molecules. These top-down techniques aid in creating complex LC structures with finely regulated molecular alignment and orientation [43]. The top-down technique is ideal for commercial applications due to its ability to facilitate large-scale processing and rapid manipulation.

### Melt mixing

In this method, the individual components of the LC mixture are first combined and then heated above their melting points to form a homogeneous molten blend (Fig. 9). This elevated temperature ensures thorough mixing at the molecular level, which is essential for achieving uniformity in the final product. After the constituents are fully melted and mixed, the blend is gradually cooled at a controlled rate. This slow cooling process is crucial, as it allows the molecules to self-assemble into the desired liquid crystalline phase, such as nematic or smectic structures, by promoting the correct alignment and ordering of mesogens. Several parameters influence the efficiency and outcome of melt mixing, including the rotational speed of mixing, the temperature at which the mixing occurs, and the duration of both the heating and cooling

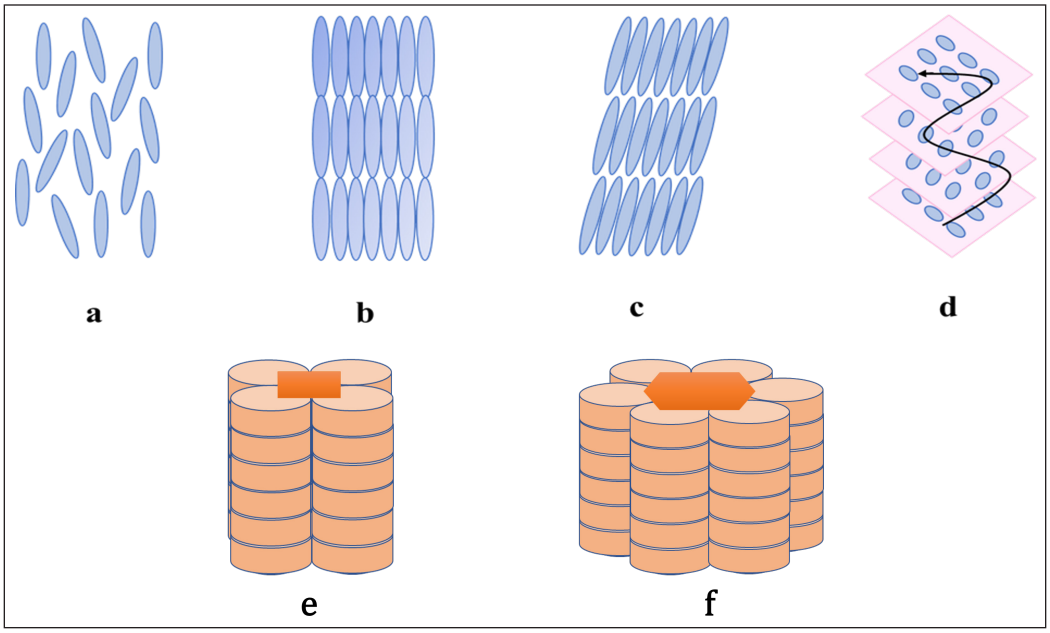


**Figure 7**. Schematic representation of nematic (a), smectic A (b), smectic C (c), cholesteric (d), columnar rectangular (e), and columnar hexagonal (f).



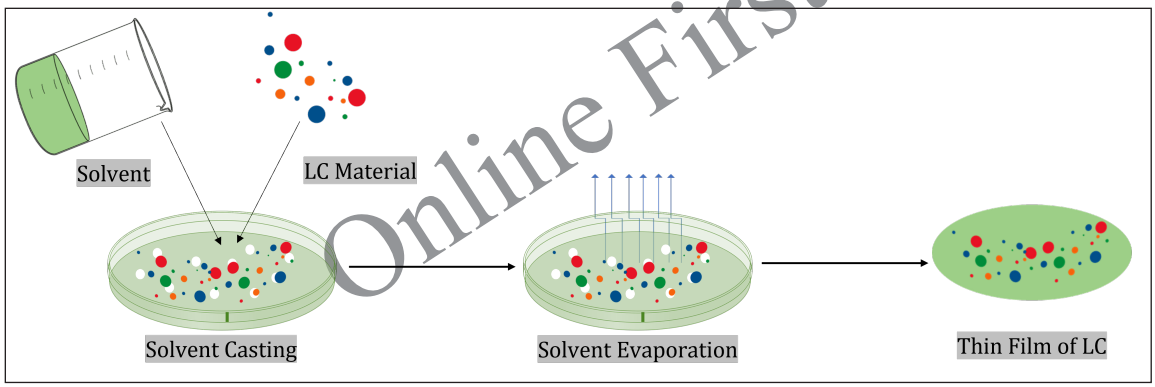


**Figure 8.** Schematic representation of solvent casting.

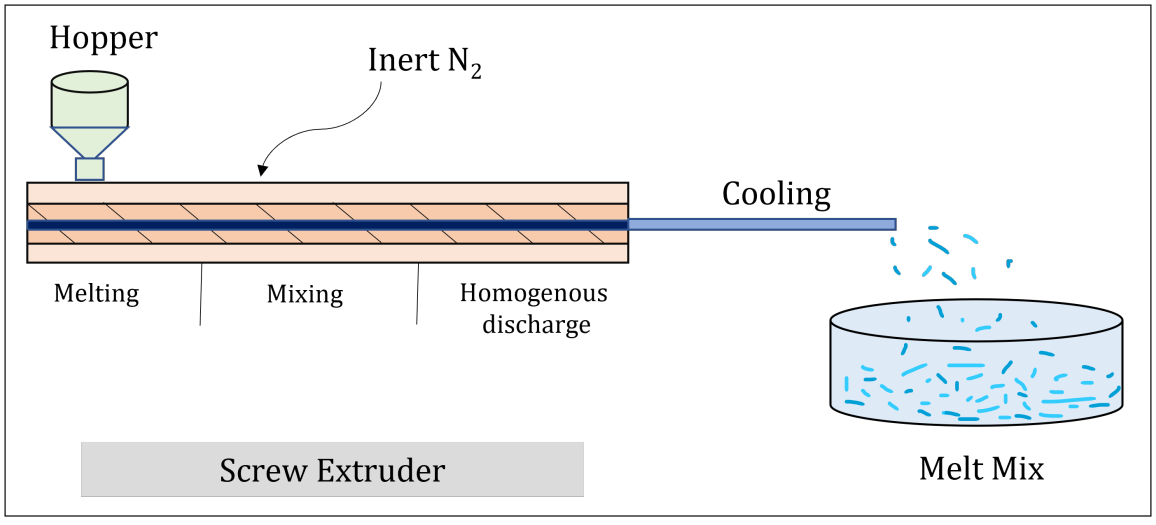


**Figure 9.** Schematic representation of melt mixing.

steps. Proper optimization of these factors is important to ensure complete mixing, prevent phase separation, and achieve the targeted mesophase with high purity and stability. Melt mixing is especially advantageous for preparing TLC blends or incorporating additives (such as nanoparticles or polymers) to create functional composite materials, as it avoids the use of solvents and can be easily scaled up for industrial applications [44].

### Template-induced methods

This method involves directing the arrangement of LC molecules during the preparation stage using a model or scaffold. Techniques like templated self-assembly, nanopatterning, surface topography, or chemical patterning can be used to align or arrange LC molecules using a template [29,45]. Surface topography, wherein surfaces having ridges, grooves, or other surface characteristics that are micro- or nanopatterned, can direct the LCs into an aligned setting and chemical patterning, wherein a substrate can be treated in specific areas using photoalignment methods or patterned with various chemical groups, are the most commonly used methods.

Factors such as the chemical makeup of the LC component, molecular structure, functional groups, and length and stiffness of the molecule influence the synthesis of TLC. These factors also affect the phase behavior and complexity of the LC that is formed. Stabilizing agents, flow characteristics, and the LC's compatibility with other materials, including glass, plastics, coating materials, and coating and encapsulating techniques, are further variables. The transition temperature is crucial since the LC should tolerate high temperatures without degrading. The direction of the LC molecules may be controlled by the director's alignment [46].

## CHARACTERIZATION TECHNIQUES OF TLC

Evaluating LC's optical properties, such as optical anisotropy, birefringence, and polarization effects, is essential, measured using polarized light microscopy (POM), ellipsometry, and spectrophotometry. Identifying the molecular alignment and organization of LC molecules is necessary for predicting their behavior. Electron microscopy, nuclear magnetic resonance (NMR) spectroscopy, and X-ray diffraction (XRD) techniques may all be used to understand molecular structure and orientation [47].

Characterizing LC's viscosity and rheological behavior is essential for flow and processing applications. The flow qualities are assessed under different conditions using rheometry and viscosity measurements [48]. One of the most important steps in the process is figuring out the temperature ranges at which the isotropic, nematic, smectic, cholesteric, and other phases of TLCs shift. These phase transitions are commonly detected using techniques such as differential scanning calorimetry (DSC) and POM [49].

The stability and behavior of LC phases can be understood by analyzing thermodynamic parameters connected to phase transitions, such as entropy, enthalpy, and Gibbs free energy. Techniques like DSC and calorimetry are used for these kinds of measurements. Different characterization techniques used for LC are mentioned in Table 1. The following are the methods used for the characterization of TLC:

POM is a standard instrument for identifying LC phases and phase transitions from a macroscopic perspective. Under crossed polarizers, any material for which the incident polarized light has either parallel or perpendicular polarization alignment to the director itself looks black. As LCs are anisotropic, they propagate polarized light perpendicular to the director at different speeds than light polarized along the director. Therefore, when viewed through crossed polarisers, the LC could be bright. The LC molecules rotate the light's polarization [13,14,50]. This method is extensively used to identify LC phases, but it is very challenging since it needs a lot of expertise to recognize the optical patterns of each phase. Optical transmission in the isotropic phase is zero, and hence, to observe the sample, it is heated and then gradually cooled to detect changes in the LC material's texture inside the cell and to determine the transition temperatures of different phases [51].

DSC is a useful method used with optical methods to help determine the transitions between LC phases. The temperature is raised and lowered to guarantee a full transition to the isotropic phase. This thermoanalytical approach records the rise in sample and reference temperatures as a function of temperature, records the resulting heat, and computes the heat difference [13,52]. The melting temperature shows when the material enters the LC phase, and the crystalline structure is disturbed, resulting in characteristic peaks [49]. The melting temperature shows when the material enters the LC phase, and



**Table 3.** TLCs versus polymeric nanoparticles/liposomes.

| Feature | TLCs | Polymeric nanoparticles | Liposomes |
|---|---|---|---|
| Drug release kinetics | Tunable, temperature-triggered, can achieve extended or on-demand release [50,85] | Controlled, often pH- or enzyme-responsive, sustained release [107] | Controlled, can be rapid or sustained, and modifiable by lipid composition [108] |
| Stability | Sensitive to temperature and composition; some formulations are prone to phase change or aggregation [85] | Generally high; can be engineered for enhanced stability [107] | Moderate; sensitive to oxidation, aggregation, and leakage [108] |
| Biocompatibility | Varies. Cyanobiphenyls are toxic, and fluorinated TLCs show high safety [50,62] | Generally good; depends on polymer type and degradation products [107] | Generally excellent; widely used clinically [108] |
| Clinical translation potential | Emerging, promising, but limited by toxicity and regulatory hurdles [62,85] | Advanced; several formulations approved or in trials [107] | Advanced, multiple products in clinical [108] |

the crystalline structure is disturbed, resulting in characteristic peaks [50,53].

Based on optical patterns, it is difficult to distinguish between various smectic or columnar phases, and enthalpy values might not be distinguishable enough for phase transitions to be identified. To overcome these obstacles and acquire more comprehensive structural data, diffraction investigations become essential [50].

XRD: Mesophase identification can be done more conclusively with XRD. This method not only aids in determining the LC phases' structure but also demonstrates the existence of long-range order [54]. XRD can be used to figure out a material's atomic and molecular structure. The sample material is irradiated with incident X-rays, after which the scattering angles and X-ray intensities are recorded as scattered by the material. The analysis of the intensity profiles so obtained translates to a plot of scattered X-ray intensity against the angle of scattering, which elucidates the material's structure. The diffraction pattern for an LC phase usually displays a widened peak at the base [55].

Small-angle X-ray diffraction (SAXD): The three-dimensional configurations of the various groups in the LC formulation (sample) can be determined using small-angle X-ray scattering [10]. A better method for examining thin-film nanostructures is grazing incidence X-ray diffraction. To determine the order–order transition change, a grazing incidence small-angle X-ray scattering study was performed [13]. Transmission electron microscopy (TEM) determines the shape of the mesophase [10,43].

An instrument that combines viscosity and birefringence measurement is called the fiber wobbling method. This device responds well to birefringence and is highly sensitive to viscosity [13].

Raman spectroscopy: The behavior of the molecules in the distinct LC phases at varying temperatures is explained by the Raman spectra. Furthermore, bond-specific Raman spectroscopy offers insight into the way LCs interact with colloidal networks. The transition temperatures and changes in the molecular bonds of the LC molecules at various temperatures may be seen using Raman analysis. Additionally, Raman analysis offers insight into the molecular vibrations; hence, each substance or material has a unique Raman fingerprint that may be utilized for sensitive identification [56,57].

Infrared thermography (IRT)/thermal imaging: IRT is a method wherein a thermal camera captures an object's IR radiation, which is then used to build a picture. This approach is used to evaluate infrared imaging performance and other temperature monitoring techniques with TLCs. For temperature mapping applications, it aids in assessing the precision and dependability of these materials [58].

## BIOCOMPATIBILITY AND TOXICITY CONCERNS

Evaluation of biocompatibility is necessary for DDS, including those based on nanotechnology. The effect of a drug and its interaction in the biological environment should be studied for its hemocompatibility, cytotoxicity, and irritation [59]. For LLC, usually lipids, which are generally considered safe and fall under the category 'Generally Recognised as Safe' by the FDA, such as glyceryl monooleate, glyceryl trioleate, sodium oleate, phytantriol, are used [60].

For TLC materials to be used safely in biomedical applications, their toxicity and biocompatibility are essential factors. There is growing recognition of the potential uses of TLCs in biological domains, particularly in tissue engineering and DDSs. Since TLC materials' physical characteristics and chemical makeup can directly affect cells and tissues, it is important to properly assess them to ensure they are safe for use *in vivo*.

Cytotoxic effects may be seen with some components employed in producing TLCs. Azo derivatives, for instance, are often utilized in light-responsive materials, although their possible toxicity has raised queries [61]. Compliance with regulatory standards for biocompatibility testing is crucial for the clinical application of TLC materials. This entails assessing their stability and impact on human health and making sure they adhere to safety guidelines before being used in biomedical applications [50].

Studies have shown that commonly used cyanobiphenyl-based TLCs, such as 5CB and related compounds, exhibit significant toxicity toward mammalian cells and can be persistent and bioaccumulative in the environment. For example, exposure of mammalian cell lines to 5CB and E7 resulted in considerable cell death within hours, and these compounds have been associated with high log Kow values, bioaccumulation, and environmental persistence. In contrast, TLCs containing fluorophenyl groups have demonstrated minimal or no cytotoxicity in similar assays, with cell viability and proliferation rates comparable to controls. This suggests that the chemical structure and functional groups of TLCs play a decisive role in their biocompatibility profile [50,62,63]. Bioassay studies conducted using TLC have been summarized in Table 5.

To resolve the conflicting biocompatibility data observed with different TLCs, several strategies can be adopted. Rational design should focus on developing TLCs with non-toxic functional groups, such as fluorinated or biomolecule-derived mesogens, to minimize adverse cellular effects. Comprehensive screening is also essential, involving systematic cytotoxicity and biocompatibility testing across various cell types and exposure durations to establish robust safety profiles. Additionally, engineering TLCs for biodegradability by incorporating natural moieties can help reduce environmental persistence and bioaccumulation. Finally, aligning material selection and testing protocols with regulatory guidelines for medical devices and DDS will facilitate smoother clinical translation and ensure that safety and efficacy standards are consistently met [62].

## APPLICATIONS OF TLCS IN DRUG DELIVERY AND DIAGNOSTICS

While LCs are most well-known for their electro-optical qualities, research into their potential uses for other purposes has been going on for a while [34,64]. TLCs are renowned for their practical significance in laptops, flat-screen televisions, tablet displays, and mobile devices. All these uses depend on the idea that LCs exhibit elastic behavior and may be affected

**Table 4.** TLC types (calamitic, discotic, bent-core) with drug-loading capacities and release profiles.

| TLC type | Molecular shape | Drug-loading capacity | Release profile |
|---|---|---|---|
| Calamitic [5,15,94] | Rod-like (linear) | Moderate to high | Tunable, temperature-responsive; can be sustained or pulsatile depending on phase (nematic, smectic) and formulation |
| Discotic [15,94] | Disc-shaped | Moderate | Sustained, often slower release due to columnar stacking and restricted diffusion |
| Bent core [15,50] | Banana-shaped | Moderate (potentially high for certain drugs) | Responsive and potentially rapid release due to unique molecular packing and high free volume |

by electric or magnetic fields, which change the optic axis's orientation and, consequently, the birefringence [14]. TLCs also make injection molds, fibers, and films [65]. Many LC materials are excellent solvents and are used in chromatography, electron spin resonance, ultraviolet and infrared spectroscopy, and NMR [66]. Furthermore, TLCs are employed in temperature mapping, namely in industrial applications for assessing stress distribution patterns and hot spot detection, as well as in healthcare wound monitoring systems [58].

Liquid crystalline nanoparticles (LCNPs) enhance lipid biodegradability, encapsulation of molecules and can control and precisely target the release of bioactive materials. Like polymeric nanoparticles protect biodegradable materials, the LCNP structure can protect its active components from severe circumstances in the gastrointestinal system [11,12,19]. Drugs incorporated into LCNPs also provide prolonged drug release, which helps in lowering drug toxicity [18].

The use of change in temperature is one of the most important stimuli in modulated DDSs [67,68]. Thermoresponsive DDSs work based on the temperature changes that occur in their environment. It is crucial that the temperatures at which the phase changes occur in the TLCs are close to 37–40°C. Although LLCs have been explored for drug delivery, studies on thermotropic mesogens as DDSs are meager. This review emphasizes exclusively TLCs by exploring their special qualities and possible uses in the field of drug delivery.

LCs employed as drug carriers in a few pharmaceutical application studies are summarized in Table 2. The pharmaceutical, chemical, and cosmetics industries, and other fields have expressed interest in using liquid crystalline systems as delivery methods. LCs can be kept for extended periods without phase separation as they are thermodynamically stable, making them applicable for drug delivery purposes [69–71].

### LC embedded membranes

DDS that can deliver drugs on demand in response to an external signal have received a lot of interest lately. In these systems, release may occur periodically, pulsatile, or diagonally in response to a signal produced by the disease condition [72]. One of its justifications is the potential application of thermoresponsive DDSs in chemotherapy under localized hyperthermia.

Dinarvand *et al.* worked on LCs as "on-and-off" switches for drug delivery using membranes. A thermoresponsive system of this kind was created by sandwiching two layers of poly-HEMA membranes between two LCs, n-pentyl-cyanobiphenyl (K15) and n-heptyl-cyanobiphenyl (K21), that had transition temperatures close to body temperature. The effects of various temperatures on drug penetration across LC membranes were investigated. The study concluded that the disordered state of LC molecules occurred at a higher temperature than the phase transition temperature. Molecules could travel freely as predicted, and hence, the diffusion of drug molecules across the LC membrane was facilitated. Additionally, at temperatures below the phase transition, only a small amount of drug release occurred. This work has been repeated using model drugs methimazole, paracetamol, and hydroxyurea [17,73,74].

### TLCs with cholesteryl carbonate backbone

While cholesteryl esters have been the subject of several studies, very few studies have been conducted on their analogue, cholesteryl carbonate.

Cholesteryl palmityl carbonate ester was dissolved using a methanol–chloroform mixture. Amphotericin B (AmB) was gradually added and continuously stirred, causing evaporation of the organic solvent, resulting in a dry powder. This powder was then analyzed for interactions using DSC, SAXD, PLM, TEM, and the changes in the phase behavior of LC. After being physically mixed with sugar, the AmB formulations in LC showed great content homogeneity and good dry powder form properties. Red blood cell toxicity was also minimal [75].

Cholesteryl cetyl carbonate (CCC) was used to incorporate indomethacin (IDM) for drug delivery. When creating synthetic LC for topical doses, it is essential to consider the transition temperature, which is 32°C, similar to skin temperature. The CCC-IDM combination ought to cause the liquid crystalline system to release IDM at skin temperature. However, the DSC of the CCC-IDM mixture's thermogram revealed an endothermic peak at 73°C, much higher than 32°C [69]. Later, using CCC and lauryl alcohol (LA), IDM was formulated into a transdermal dosage form. Adding LA made the transition temperature nearer to the skin's natural temperature. The penetration of IDM into the skin was also improved by this to an extent of 45% within 24 hours when compared to the IDM-CCC formulation alone [76].

Novel LC technologies provide new opportunities for creating controlled drug release. Work has been done to increase the effectiveness and reduce toxicity by utilizing AmB to formulate CCC LCs. Using a hot melt, AmB was mixed into the LC using CCC as the solvent, made into a dry powder using

**Table 5.** Bioassay studies using TLCs and their research gaps.

| Study/reference | TLC type and composition | Application/ model | Key findings | Gaps/limitations |
|---|---|---|---|---|
| Nesterkina *et al.* [50] | Cholesteryl esters and terpenoids | *Ex vivo* human skin (surgical) | TLC formulations enabled temperature-triggered drug release, well tolerated by skin cells | No *in vivo* animal or human clinical trials; limited to *ex vivo* and cell models |
| Dinarvand *et al.* [73] | Cyanobiphenyl blends (K15/K21) | *In vitro* membrane model | Demonstrated pulsatile, temperature-controlled drug permeation for paracetamol and methimazole | No *in vivo* validation; toxicity concerns with cyanobiphenyls; lacks long-term safety data |
| Nesterkina *et al.*, Rajak *et al.*, Bunjes *et al.* [5,50,94] | Various TLCs (nematic, smectic, cholesteric) | Drug delivery (multiple routes) | TLCs show promise for sustained, controlled release and biocompatibility *in vitro*/*ex vivo* | Scarcity of *in vivo* animal studies and clinical trials; regulatory and scalability challenges |

sugar, and then micronized. LC formation was discovered to have the potential to decrease erythrocyte lysis caused by AmB when pure CCC is melted at body temperature. Adding sugar to formulate a dry powder increased the bulkiness and flowability of the formulation [77].

Another ester, cholesterol oleyl carbonate (COC), was encapsulated in a cellulose nitrate membrane to create a DDS with a thermal stimulation response. Thermoresponsive properties of COC-embedded membranes were studied via stepwise temperature shifts between 10°C and 25°C below and above the transition temperature (gel-LC) of COC. The model drug used for the study was salbutamol sulfate. Temperature variations may be able to precisely regulate how much salbutamol sulfate permeates the membrane, and were analyzed by SEM and other characterization techniques. The outcome implied that an LC-embedded membrane may regulate drug penetration in an "on and off" response to temperature changes. Future research employing the mixed LC, with a phase transition temperature close to body temperature, must be investigated to build a suitable LC-embedded membrane for medical use [78–80].

Katkam *et al.* [81] have reported the incorporation of rifampicin into polyethylene glycol (PEG) 400 and cholesterol-based LC CCC to extend the homogeneity of the drug in the carrier, along with some other LC materials such as dicholesteryl carbonate and sodium cholesteryl carbonate. Dielectric constant and other characterization techniques were determined to analyze the phase behavior. According to the evaluation of rifampicin's phase behavior in a combination containing LCs, the CCC and PEG systems had the greatest ability to solubilize rifampicin [81].

Using *in situ* suspension polymerization, thermotropic cholesteryl LC microcapsules were prepared using Cholesterol LC and poly (methyl methacrylate) (PMMA). This was done to identify the morphology and phase behavior of the formed microcapsules with LC. These CLC/PMMA microcapsules might be used in thermoresponsive drug carriers in pharmaceutics [82].

A thermoresponsive cellulose membrane embedding 36% COC and 64% cholesteryl nonanoate (CN) was successfully used to provide a rate-controlled and time-controlled drug release in response to the body temperature. Using DSC and FT-IR, studies were carried out to examine the temperature-sensitive "on-off" pulsatile drug penetration function across this thermoresponsive membrane. The results indicated that the drug may be given pulsatile via the binary COC–CN mixture-embedded membrane, dependent on skin temperature [83].

Bhageri *et al.* [84] examined the possibility of using liquid crystalline blends of COC and cholesteryl chloride ester (CCE) as a controlled drug delivery technique. Adjusting the COC to CCE ratio produced a mix with a phase transition temperature marginally higher than the body temperature. The COC/CCE combination's phase transition behavior was characterized using DSC and POM. Subsequently, the blend was introduced onto a cellulose nitrate membrane to facilitate *in vitro* studies on drug absorption. The model drugs mesalazine and paracetamol represented hydrophobic and hydrophilic compounds, respectively. At 39°C, the LC phase transition and paracetamol's permeability increased. Drug penetration was impacted by membrane pore size and LC adsorption. Mesalazine did not show any penetration because of potential differences in the hydrophilicity of the drug and the membrane. The study found that, particularly in the case of thermoresponsive systems, the structure of the LC plays a key role in drug release [84].

Using IDM as the model drug, two PP membranes were prepared using monooxyethylene trimethylolpropane tristearate LC through sandwiching and soaking. IDM's penetration through the sandwich membrane was significantly regulated by temperature variations between 32°C and 38°C, indicating the use of TLCs in drug delivery [72].

Thermoresponsive barriers for drug penetration were created using cellulose nitrate and cellulose acetate (CA) monolayer membranes containing n-heptyl-cyanobiphenyl (K21) LC. As hydrophilic and hydrophobic drug models, methimazole and paracetamol were employed. The permeability of LC-embedded membranes changed noticeably above the LC phase transition temperature, indicating temperature-sensitive drug permeation, but the membranes, as such, did not demonstrate any temperature sensitivity for drug permeation. Therefore, it can be concluded that heat can be used to control drug penetration via these LC-embedded membranes [17].

A thermoresponsive system containing Eudragit RL and COC was prepared and analyzed using salbutamol sulfate as the drug. Drug permeation was conducted at 25°C and 37°C, and it was found that the permeability showed an increase above the phase transition temperature of COC [42].

**TLCs based on biomacromolecules**

Studies have shown that by complexing different biomacromolecules with surfactants, such as proteins and nucleic acids, TLCs may be produced. By creating thermotropic phases with low transition temperatures, this technique makes it possible to employ them without causing delicate biomolecular components to degrade thermally. This feature is vital for applications such as medical diagnostics, where temperature control is critical [85]. One innovative approach to sensing technologies is using TLCs to generate fault structures, which can be used to identify changes in biological material [86]. The intrinsic biocompatibility and biodegradability of natural biomacromolecules in TLCs make them suitable drug delivery vehicles. While lowering systemic toxicity, these systems can enhance a drug's pharmacokinetics. Because of their structural properties, biomacromolecule-based carriers are superior to synthetic materials as they permit the controlled and prolonged release of medicinal drugs [87]. Some examples of biomacromolecules which can form LC are chromosomal or phage DNA, plasmids, cellulose, collagen–CLC, phospholipids-lamellar LC, silk, insulin, microtubules–nematic LC, and starch–smectic LC [88].

**Biosensing and cancer detection applications**

Real-time data on biological interactions can be obtained through creative sensing systems utilizing TLCs' capacity to alter their optical characteristics in response to temperature changes. Due to their sensitivity to biologically relevant chemicals, TLC films are being developed for biosensing applications. The ability to functionalize these films to react selectively to pathogens increases their significance in disease detection. In addition to the nematic LC phase, chiral nematic (blue and cholesteric phases) and smectic LCs can also be employed for sensing [86]. Additionally, TLC-based sensors are being developed for food safety applications to identify impurities or signs of spoilage in food items to protect consumers [58].

LC thermography (LCT) is a sophisticated, nonintrusive measurement method that can provide a continuous temperature field measurement with high accuracy, particularly for a complex-structured heat transfer surface [89]. The principle of LCT can be applied to identify temperature variations linked to tumor manifestations. Early cancer detection can be facilitated by the thermal profiles produced by LCT, which can reveal information about tumor growth and metabolism [90–92].

**Temperature mapping applications**

TLCs have shown significant promise in temperature mapping applications, particularly for monitoring physiological states and detecting various medical conditions. Their unique ability to undergo reversible color changes in response to temperature variations makes them highly suitable for visual and quantitative thermal mapping in clinical settings. For instance, TLCs have been investigated for the early detection of cancer and tumors, where abnormal tissue often exhibits elevated temperatures due to increased metabolic activity and blood flow. Similarly, TLC-based sensors can be used for mapping temperature distributions across different parts of the body, aiding in the identification of inflammation in organs such as the lungs or liver, as well as in diagnosing acute appendicitis and bone fractures, where local temperature changes can signal underlying pathology.

A notable advantage of TLC arrays is their sensitivity within the physiological temperature range, particularly between 34°C and 38°C, which encompasses normal and slightly elevated human body temperatures. Devices constructed with TLC arrays can provide rapid, real-time feedback by reflecting visible light in distinct colors corresponding to specific temperature intervals. This feature allows for immediate visual assessment, making TLC-based sensors especially useful for applications such as wound monitoring, where changes in local temperature can indicate infection or healing progress.

According to Miskovic *et al.* [58], TLCs offer a fast response time and high spatial resolution, enabling detailed thermal imaging without the need for complex electronics or invasive procedures. Their biocompatibility and ease of integration into flexible substrates further enhance their potential for wearable or patch-based sensors, which can continuously monitor patient conditions in a non-invasive manner. As research advances, TLC-based temperature mapping devices are expected to become increasingly valuable tools in diagnostics, patient monitoring, and personalized healthcare, offering clinicians a simple yet powerful method for visualizing and interpreting thermal changes associated with various medical conditions.

**TLC in tissue engineering**

LC elastomers (LCEs), a type of TLC, possess orientational anisotropy and mechanical flexibility, making them appropriate for 3D scaffolds in tissue engineering applications. Such scaffolds promote cell growth, differentiation, and extracellular matrix formation, which are similar to the natural surroundings of tissues. Such scaffolds have specific advantages in applications where extended co-culture systems enable neural tissue engineering. The advent of TLC-based bioinks in 3D printing has made it easy to manufacture intricate, responsive scaffolds. These materials facilitate enhanced cell attachment and proliferation while concurrently allowing for the meticulous tuning of the scaffold's mechanical and optical features [58,61,93]. Zhang *et al.* [87] have investigated the development and use of hydrogels that react to environmental stimuli, specifically temperature and pH, allowing for dynamic behavior that is appropriate for tissue engineering. According to their research, these responsive materials can alter their chemical and physical characteristics *in situ* to promote tissue regeneration, cell adhesion, and proliferation. The functional potential of TLC, whose temperature-dependent phase behavior can also be used to produce adaptive scaffolds, is well suited to this strategy. Thus, the incorporation of TLCs in this situation may replicate the responsiveness demonstrated by hydrogels, providing platforms that can be adjusted for guided tissue growth and regeneration [94].

**Thermoresponsiveness and 3D printing**

Three-dimensional printing with TLCs is an emerging field that exploits the unique properties of TLCs to produce

highly anisotropic and mechanically strong structures. These materials are particularly relevant for 3D printing since they can self-organize and form ordered structures that can be used to improve the mechanical properties of printed objects. When the thermoresponsive materials are subjected to temperature, the macroscopic properties of their fabricated components (shapes) change; 3D printing of thermoreactive material has many advantages for drug delivery. Not only does it allow the construction of complex, individually designed therapeutic constructs with temperature-responsive drug release, but it can also be used to manufacture polymer and hydrogel materials that enclose and alter therapeutic release as a function of temperature via phase transitions from solid to liquid or swelling. This process allows for the most exciting applications: controlling drug delivery in response to temperature for targeted drug delivery on demand, which essentially improves the efficacy of treatment and the avoidance of side effects. The 3D printing technology alone allows designing patient-specific devices and dosage forms, thereby personalizing drug therapy. This combination of thermoresponsive materials and additive manufacturing will thus open up entirely new avenues in the future for more advanced, dynamic-responsive DDS. The fact that 3D printing is very flexible and can be configured well with design enables the preparation of biomedical functional prototypes of thermoresponsive polymers. Applications of these polymers include micellization, cell separation, reversible gelators, and controlled drug supply. Their fabrication into biomedical functional prototypes will also be simplified with 3D printing, given the ease of design and flexibility of most configurations in creating final products. Applications include micellization, cell separation, reversible gelators, and controlled drug supply [95]. Preserving the high orientational order of the polymer domains during the printing process is one challenge with utilizing thermotropic LCPs for 3D printing. Research has proven that the initial orientation attained after filament extrusion may be partially lost as a result of printer nozzle phenomena such as director tumbling and thermal relaxation [96,97].

### TLC in wound repair

TLCs show promise for wound healing applications because they exhibit temperature-responsive phase changes that are comparable to smart hydrogels utilized in tendon injury repair. TLCs may form localized scaffolds for sustained drug release at 37°C by undergoing a transition into organized mesophases, similar to thermosensitive hydrogels that gel at body temperature to distribute bioactives. Such hydrogels efficiently released $Mg^{2+}$ and polyphenols in tendon models, which enhanced collagen deposition, reduced inflammation, and encouraged the induction of stem cells. Drugs could also be encapsulated in TLCs and released in a temperature-dependent, regulated manner. Furthermore, by creating protective barriers at physiological temperatures, thermoresponsive hydrogel adhesives avoid post-surgical adhesions. Therefore, by using TLCs' thermoresponsive properties, which mimic those of well-established hydrogel systems, advanced wound therapies can be made possible through improved tissue regeneration, less fibrosis, and controlled release [98]. Notably, thermoresponsive polymers help control infections by creating *in situ* barriers that prevent microbial invasion and release antimicrobials continuously. TLC are excellent candidates for next-generation, infection-responsive wound dressings because they can mimic this function through temperature-induced phase transitions, providing biocompatibility, structural support, and responsive drug delivery [99].

## CHALLENGES

Systems for delivering drugs via TLCs provide special benefits such as prolonged release and improved drug absorption. However, they also present a few difficulties as follows:

Developing TLC formulations requires understanding pharmacology and materials science. Obtaining the necessary drug loading, release kinetics, and stability can be challenging and may require extensive adjustment [5,100,101]. Increasing the output of TLC formulations while maintaining their quality and consistency is difficult in manufacturing. Essential elements of the manufacturing process include pharmacological homogeneity and reproducibility of release kinetics [5,96]. LC phases are impacted by temperature, light, and mechanical stress. Maintaining the stability of these systems throughout storage and administration can be challenging, particularly for complex or long-term formulations [50,58,100].

Even though TLCs may exhibit encouraging *in vitro* drug release patterns, their efficacy *in vivo* may be influenced by physiological factors such as stomach pH, mucosal barriers, and enzyme activity. Ensuring constant drug delivery in physiological situations is essential for therapeutic success [50,100]. Regulating agencies must comprehensively grasp DDS's quality, safety, and effectiveness. Developers of TLC formulations are required to do thorough preclinical and clinical trials to fulfil regulatory criteria for approval [50,86].

Careful evaluation of the safety of LC materials and the by-products of their breakdown is necessary to ensure biocompatibility and minimize possible toxicity. This includes assessing potential harm to tissues and cellular membranes [50,62]. Taking into account factors such as comfort, convenience, and simplicity of administration, how well patients accept LC-based DDSs may influence patient compliance and overall treatment results [86,102].

Besides physiological and safety concerns, developing TLC systems also presents challenges, especially when it comes to maintaining phase stability, ensuring consistent drug loading, and scaling up the process. Some thermolabile drugs may not tolerate the elevated temperatures required for phase transitions in TLC, which is a great challenge as it confines them to some drug groups, which can be overcome by using an additive to reduce the phase transition temperature. As mentioned earlier, the CCC-IDM mixture had a transition peak at 73°C, but with the addition of LA, it was brought back to body temperature [76]. Like this, most of the TLCs available or synthesized have a higher transition temperature, which does not help in delivering the drug when needed. But the CCC-IDM-LA combination sets an example that, with the right choice of moieties or additives,

the temperature can be brought to body temperature and drug delivery can be made possible. The major challenge in this approach is finding the right choice of additive for each TLC.

The chemical nature of TLCs can also result in the production of cytotoxic effects, hemolysis, adverse reactions, and biocompatibility concerns, which need to be taken care of. Many TLC systems, despite promising preclinical outcomes, do not progress to clinical trials because of insufficient long-term stability data and regulatory challenges associated with novel excipients. As a result, only a few have reached human studies. For example, while drugs such as itraconazole and ciclosporin have demonstrated thermotropic mesomorphism and improved solubility in preclinical research, their translation to clinical application remains limited due to these barriers [94,103].

## FUTURE OUTLOOKS

The unique characteristics of TLCs, including their controllable phase transitions, anisotropic, optical, and mechanical behaviors, and temperature responsiveness, have made them extremely promising in the biomedical area. The temperature sensitivity of TLCs may prove useful for temperature imaging in biological entities. Owing to the birefringence and light-modulating properties of TLCs, imaging techniques can be improved with high-contrast resolution [58,86,104]. TLCs can be fused to dressing and bandages to depict visually whether there is an infection or whether the healing process of a wound is improving or deteriorating based on temperature variations. Additionally, TLCs may be used as components in implanted devices designed to constantly check the temperature of human bodies. LC structures could be designed to encapsulate and efficiently deliver genetic materials [58,105,106].

The potential of TLCs in biomedical fields is set to grow significantly through advances in interdisciplinary research and technology. Beyond their established uses in temperature sensing and wound care, TLCs could be integrated with cutting-edge digital health tools, such as wearable devices and continuous biosensors, to enable real-time, non-invasive monitoring of various physiological signals. The development of TLC-based microfluidic systems may also transform point-of-care diagnostics by providing rapid and highly sensitive detection of disease biomarkers with easily interpretable visual outputs. Furthermore, combining TLCs with innovative materials like responsive hydrogels, smart polymers, and biofunctional nanoparticles could lead to multifunctional platforms capable of simultaneous diagnosis, targeted treatment, and dynamic feedback. Advances in molecular design may produce new TLC materials that respond to multiple stimuli—including temperature, pH, light, or specific biomolecules—expanding their applications in personalized medicine and controlled drug release.

Future research should emphasize creating biocompatible, safe, and biodegradable TLC formulations to ensure patient safety and environmental sustainability. Collaborative efforts among chemists, materials scientists, engineers, and healthcare professionals will be crucial to translate these materials from the lab to clinical settings. Additionally, addressing regulatory requirements and ensuring long-term stability will be vital for the successful adoption of TLC-based biomedical devices.

## CONCLUSION

Thermoresponsive or pulsatile delivery of the drug is possible with proper usage of the phase transition knowledge of LC. In-depth research on obtaining LC exhibiting phase transitions near or below the body temperatures is crucial to achieving the principle of thermoresponsiveness. The use of TLC in thermoresponsive DDS is a novel strategy with great promise for targeted and regulated drug release. These systems are appropriate for a range of therapeutic applications because they can precisely control drug release rates by utilizing the temperature-dependent phase transitions of thermotropic LCs. To overcome current obstacles and optimize these systems for clinical use, further study and development are necessary. In conclusion, the distinctive features of TLCs position them as a promising platform for innovation in healthcare. Continued development aimed at enhancing their responsiveness, biocompatibility, and scalable production will enable TLCs to become integral components of next-generation diagnostic, therapeutic, and personalized medicine technologies, ultimately broadening their impact in clinical practice and beyond.

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## AUTHOR CONTRIBUTIONS

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work. All the authors are eligible to be an author as per the International Committee of Medical Journal Editors (ICMJE) requirements/guidelines.

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This study does not involve experiments on animals or human subjects.

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All data generated and analyzed are included in this research article.

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## USE OF ARTIFICIAL INTELLIGENCE (AI)-ASSISTED TECHNOLOGY

The authors declares that they have not used artificial intelligence (AI)-tools for writing and editing of the manuscript, and no images were manipulated using AI.

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