

Liquid Crystalline Phase & its Pharma Applications

*Prajakta P. Gaikwad, Maya T. Desai

Department of Bio pharmaceuticals, Govindrao Nikam College of Pharmacy, Sawarde. Chiplun, Ratnagiri-415 606, India.

ABSTRACT

Liquid crystals are the materials that are in many ways intermediate between the liquid and solid states. Liquid crystals exhibit different molecular arrangements than the liquid and solid states. The liquid crystalline state may result either from the heating of solids (thermotropic liquid crystals) or from the action of certain solvents or solids (lyotropic liquid crystals). The two main types of liquid crystals are: *smectic* (soap like or grease like) or *nematic* (threadlike). LC based systems can provide specific advantages of thermodynamic stability, high solubilisation levels, improved bioavailability, protection against oxidation and controlled release properties to the pharmaceuticals. Thus material characterization and understanding of the liquid crystalline states of active pharmaceuticals can yield wide range of options to enhance formulation performance for drug delivery. Liquid crystal materials are unique in their properties and uses. As research into this field continues and as new applications are developed, liquid crystals will play a vital role in modern technology. The purpose of this review is to focus on types, properties and applications of liquid crystals. LCs based delivery systems such as creams, ointments, gels, liposomes, colloidal dispersions and transdermal patches have been used in pharmaceuticals and cosmetics. Liquid crystals have many applications in fields of science, engineering and device technology.

Keywords: Liquid crystalline phase, mesophase, pharma applications, sub phases

Received 02 Oct 2013

Received in revised form 25 Oct 2013

Accepted 29 Oct 2013

*Address for correspondence:

Prajakta P. Gaikwad

Department of Bio pharmaceuticals, Govindrao Nikam College of Pharmacy, Sawarde.415 606, Chiplun, Ratnagiri, India.

E-mail: prajakta.gaikwad91@gmail.com

INTRODUCTION

The liquid crystalline state combines properties of both liquid and solid states. The liquid state is associated with the ability to flow, whereas the solid state is characterized by an ordered, crystalline structure. Crystalline solids exhibit short as well as long-range order with regard to both position and orientation of the molecules. Liquids are amorphous in general but may show short-range order with respect to position and/or orientation. Liquid crystals show at least orientational long-range order and may show short-range order, whereas positional long-range order disappears. Accordingly, liquid crystalline phases represent intermediate states and are also called mesophases [1]. the formation of liquid crystalline mesophases are categorized by therapeutic

target and molecular size and the analytical means of their identification [2].

Liquid crystals exhibit different molecular arrangements than the liquid and solid states. LCs can be classified as thermotropic and lyotropic crystals. The most common sub phases of LCs are nematics and smectics. Pharmaceutical drugs and excipients have been characterized to show liquid crystalline states which can form the basis for a new class of drug delivery system. The same has found applications in food and dermal products. LC based systems can provide specific advantages of thermodynamic stability, high solubilisation levels, improved bioavailability, protection against oxidation and controlled release properties to the pharmaceuticals. Thus material characterization and understanding of the liquid crystalline

states of active pharmaceuticals can yield wide range of options to enhance formulation performance for drug delivery [3].

Several liquid crystalline phases are bicontinuous cubic (Q2), reversed hexagonal (H2), or reversed cubic phase (I2), and several nanostructure liquid phases. Of the many liquid crystalline structures self-assembled from aqueous surfactant systems, bicontinuous cubic phases possess a special status [4].

Liquid crystal materials are unique in their properties and uses. As research into this field continues and as new applications are developed, liquid crystals will play a vital role in modern technology. This article provides an introduction to the science and applications of these materials [5].

What are Liquid Crystals?

Liquid crystal materials generally have several common characteristics. Among these are rod-like molecular structures, rigidity of the long axis, and strong *dipoles* and/or easily polarizable substituent.

The distinguishing characteristic of the liquid crystalline state is the tendency of the molecules (*mesogens*) to point along a common axis, called the *director*. This is in contrast to molecules in the liquid phase, which have no intrinsic order. In the solid state, molecules are highly ordered and have little translational freedom. The characteristic orientational order of the liquid crystal state is between the traditional solid and liquid phases and this is the origin of the term mesogenic state, used synonymously with liquid crystal state. Note the average alignment of the molecules for each phase in the following diagram.

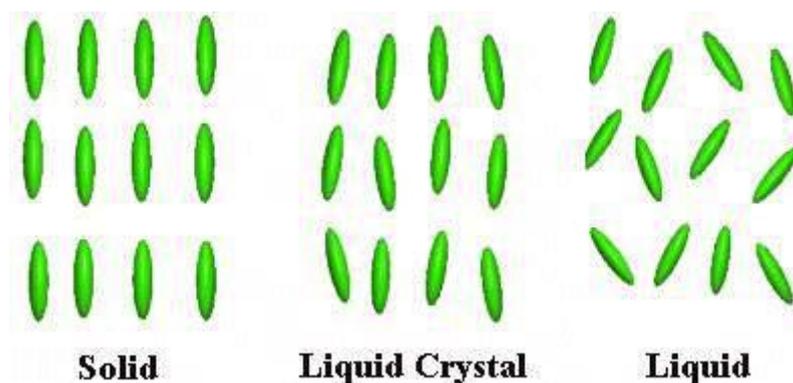


Figure1: Average Alignment Of Molecules For Each Phase

It is sometimes difficult to determine whether a material is in a crystal or liquid crystal state. *Crystalline* materials demonstrate long range periodic order in three dimensions. By definition, *anisotropic* liquid has no orientational order. Substances that aren't as ordered as a solid, yet have some

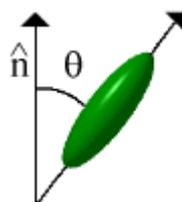
degree of alignment are properly called liquid crystals.

To quantify just how much order is present in a material, an *order parameter* (S) is defined. Traditionally, the order parameter is given as follows:

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

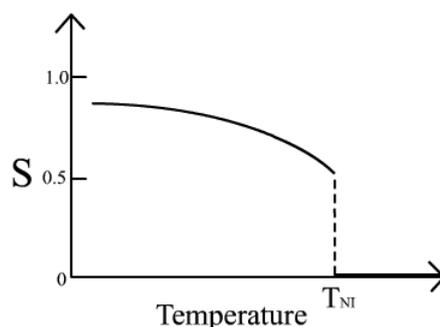
Where, *theta* is the angle between the director and the long axis of each molecule. The brackets denote an average over all of the molecules in the sample. In an isotropic liquid, the average of the cosine terms is

zero, and therefore the order parameter is equal to zero. For a perfect crystal, the order parameter evaluates to one. Typical values for the order parameter of a liquid crystal range between 0.3 and 0.9, with the



exact value a function of temperature, as a result of kinetic molecular motion. This is

illustrated below for a nematic liquid crystal material:



Graph 1. Values for the order parameter of a liquid crystal

The tendency of the liquid crystal molecules to point along the director leads to a condition known as *anisotropy*. This term means that the properties of a material depend on the direction in which they are measured. For example, it is easier to cut a piece of wood along the grain than against it. The anisotropic nature of liquid crystals is responsible for the unique optical properties exploited by scientists and engineers in a variety of applications.

Characterizing Liquid Crystals

The following parameters describe the liquid crystalline structure:

- *Positional Order*
- *Orientalional Order*
- *Bond Orientalional Order*

Each of these parameters describes the extent to which the liquid crystal sample is ordered. *Positional order* refers to the extent to which an average molecule or group of molecules shows translational symmetry (as crystalline material shows). *Orientalional order*, as discussed above, represents a measure of the tendency of the molecules to align along the director on a long-range basis. *Bond Orientalional Order* describes a line joining the centers of nearest-neighbor molecules without requiring a regular spacing along that line. Thus, a relatively long-range order with respect to the line of centers but only short range positional order along that line.

Most liquid crystal compounds exhibit *polymorphism* or a condition where more than one phase is observed in the liquid crystalline state. The term *mesophase* is used to explain the "sub phases" of liquid crystal materials.

Mesophases are formed by changing the amount of order in the sample, either by imposing order in only one or two dimensions, or by allowing the molecules to have a degree of translational motion. The following section describes the mesophases of liquid crystals in greater detail [5].

Plastic Crystals

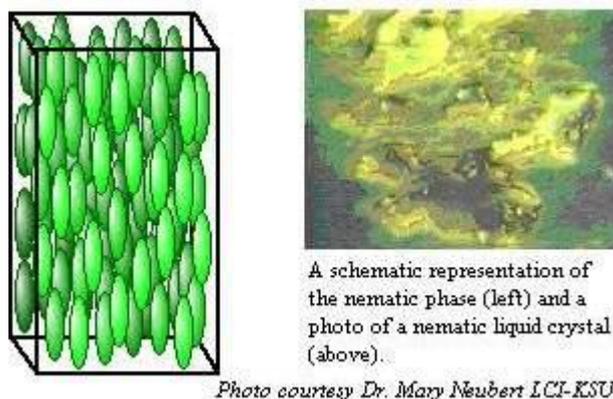
Plastic crystals are not usually incorporated into descriptions of mesogens, however, they are very closely related and therefore worthy of discussion in relation to liquid crystals. *Plastic crystals* usually possess molecules that have spherical shapes, and like the soft crystals associated with liquid crystal systems, the molecules in plastic crystals have long range periodic order and rotate very rapidly about their lattice points. The molecular motion is diffuse and takes place in all directions, unlike the process in liquid crystals which is principally about one major axis. Plastic crystals, therefore, are optically isotropic.

Liquid Crystal Phases:

The liquid crystal state is a distinct phase of matter observed between the crystalline (solid) and isotropic (liquid) states. There are many types of liquid crystal states, depending upon the amount of order in the material. This section will explain the phase behavior of liquid crystal materials.

Nematic Phases

The nematic liquid crystal phase is characterized by molecules that have no positional order but tend to point in the same direction (along the director). In the following diagram, notice that the molecules point vertically but are arranged with no particular order.



A schematic representation of the nematic phase (left) and a photo of a nematic liquid crystal (above).

Photo courtesy Dr. Mary Neubert LCI-KSU

Figure 2: Nematic Phases

Liquid crystals are *anisotropic* materials, and the physical properties of the system vary with the average alignment with the director. If the alignment is large, the material is very anisotropic. Similarly, if the alignment is small, the material is almost isotropic. A special class of nematic liquid crystals is called chiral nematic. *Chiral* refers to the unique ability to selectively reflect one component of circularly polarized light. The term chiral nematic is used interchangeably with cholesteric. Refer to the section on cholesteric liquid crystals for more information about this mesophase.

Smectic Phases - The word "smectic" is derived from the Greek word for soap. This

seemingly ambiguous origin is explained by the fact that the thick, slippery substance often found at the bottom of a soap dish is actually a type of smectic liquid crystal.

The smectic state is another distinct mesophase of liquid crystal substances. Molecules in this phase show a degree of *translational order* not present in the nematic. In the smectic state, the molecules maintain the general orientational order of nematics, but also tend to align themselves in layers or planes. Motion is restricted to within these planes, and separate planes are observed to flow past each other. The increased order means that the smectic state is more "solid-like" than the nematic.



Photo courtesy Dr. Mary Neubert LCI-KSU

Figure 3: Photo of a smectic phase (using polarizing microscope)

Many compounds are observed to form more than one type of smectic phase. As many as 12 of these variations have been identified, however only the most distinct phases are discussed here.

In the smectic-A mesophase, the director is perpendicular to the smectic plane, and there is no particular positional order in the

layer. Similarly, the smectic-B mesophase orients with the director perpendicular to the smectic plane, but the molecules are arranged into a network of hexagons within the layer. In the smectic-C mesophase, molecules are arranged as in the smectic-A mesophase, but the director is at a constant

tilt angle measured normally to the smectic plane.

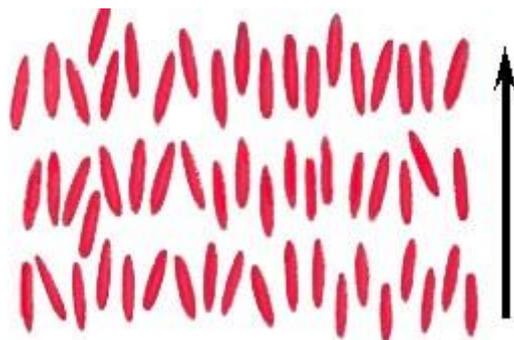


Figure 4: Picture of the smectic A phase



Photo courtesy of Dr. Mary Neubert LCF-KSU

Photo of the smectic A phase (using polarizing microscope)



Figure 5: Picture of the smectic C phase

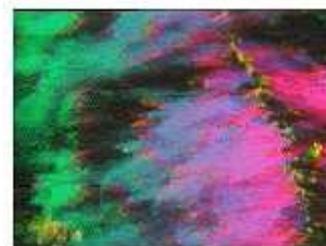


Photo courtesy Dr. Mary Neubert LCI-KSU

Photo of the smectic C phase (using polarizing microscope)

As in the nematic, the smectic-C mesophase has a chiral state designated C*. Consistent with the smectic-C, the *director* makes a tilt angle with respect to the smectic layer. The difference is that this angle rotates from layer to layer forming a helix. In other

words, the director of the smectic-C* mesophase is not parallel or perpendicular to the layers, and it rotates from one layer to the next. Notice the twist of the director, represented by the green arrows, in each layer in the following diagram.

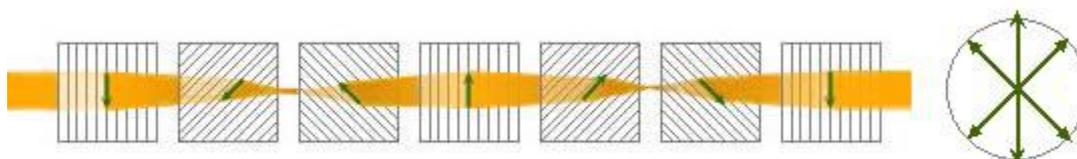


Figure 6: A schematic representation of a smectic C* phase (left), and a view of the same phase, but along the axis (right).

In some smectic mesophases, the molecules are affected by the various layers above and below them. Therefore, a small amount of three dimensional order is observed. Smectic-G is an example demonstrating this type of arrangement.

Cholesteric Phases

The *cholesteric* (or chiral nematic) liquid crystal phase is typically composed of nematic mesogenic molecules containing a

chiral center which produces intermolecular forces that favor alignment between molecules at a slight angle to one another. This leads to the formation of a structure which can be visualized as a stack of very thin 2-D nematic-like layers with the director in each layer twisted with respect to those above and below. In this structure, the directors actually form in a continuous helical pattern about the layer

normal as illustrated by the black arrow in the following figure. The black arrow in the

animation represents director orientation in the succession of layers along the stack.

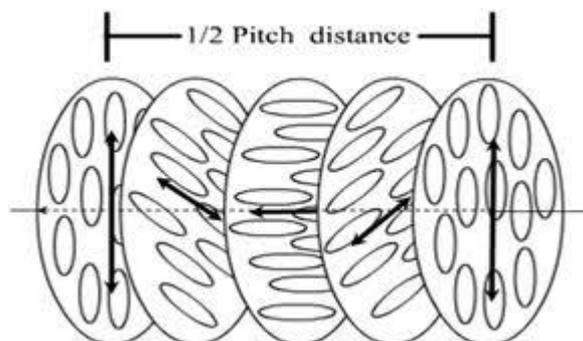


Figure 7: Cholesteric Phases

The molecules shown are merely representations of the many chiral nematic mesogens lying in the slabs of infinitesimal thickness with a distribution of orientation around the director. This is not to be confused with the planar arrangement found in smectic mesophases.

An important characteristic of the cholesteric mesophase is the *pitch*. The pitch, p , is defined as the distance it takes for the director to rotate one full turn in the helix as shown in the above animation. A byproduct of the helical structure of the chiral nematic phase is its ability to selectively reflect light of wavelengths equal to the pitch length, so that a color will be reflected when the pitch is equal to the corresponding wavelength of light in the visible spectrum. The effect is based on the temperature dependence of the gradual change in director orientation between successive layers (as shown above), which modifies the pitch length resulting in an alteration of the wavelength of reflected light according to the temperature. The angle at which the director changes can be made larger, and thus tighten the pitch, by increasing the temperature of the molecules, hence giving them more thermal energy. Similarly, decreasing the temperature of the molecules increases the pitch length of the chiral nematic liquid crystal. This makes it possible to build a liquid crystal thermometer that displays the temperature of its environment by the reflected color. Mixtures of various types of these liquid crystals are often used to create sensors with a wide variety of responses to temperature change. Such

sensors are used for thermometers often in the form of heat sensitive films to detect flaws in circuit board connections, fluid flow patterns, condition of batteries, the presence of radiation, or in the novelties such as "mood" rings.

In the fabrication of films, since putting chiral nematic liquid crystals directly on a black background would lead to degradation and perhaps contamination, the crystals are micro-encapsulated into particles of very small dimensions. The particles are then treated with a binding material that will contract upon curing so as to flatten the microcapsules and produce the best alignment for brighter colors. An application of a class of chiral nematic liquid crystals which are less temperature sensitive is to create materials such as, clothing, inks, dolls and paints.

The wavelength of the reflected light can also be controlled by adjusting the chemical composition, since cholesterics can either consist of exclusively chiral molecules or of nematic molecules with a chiral dopant dispersed throughout. In this case, the dopant concentration is used to adjust the chirality and thus the pitch.

Columnar Phases

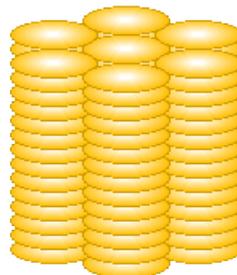


Figure 8: Columnar Phases

Columnar liquid crystals are different from the previous types because they are shaped like disks instead of long rods. This mesophase is characterized by stacked columns of molecules. The columns are packed together to form a two-dimensional crystalline array. The arrangement of the molecules within the columns and the arrangement of the columns themselves leads to new mesophases [5].

Types of Liquid Crystals:

The liquid crystals can be divided into two classes: thermotropic and lyotropic. Thermotropic liquid crystalline phases are exhibited by large number of organic compounds whose molecule has anisotropy of shape. This state can be obtained by raising temperature of solids and/lowering temperature of liquid. If temperature increase is too high, thermal motion will destroy ordering of liquid crystal phase, pushing material into isotropic liquid phase. If temperature is too low, most liquid crystal materials will form conventional crystals. Scientists further subdivided thermotropic liquid crystals based on shape of the molecules itself and different variations in ordering of molecules. These can generally be formed by calamitic (rod like) or discotic (disc like) molecules. Smectic liquid crystals have layered arrangement of orientationally ordered rod-like molecules. The simplest liquid crystals phase is called nematic phase and is close to liquid phase. The molecules float around as in liquid phase, but are still ordered in their orientation. The nematic phase is seen as the marbled structure. Columnar liquid crystals are different from previous types because they are shaped like disks instead of long rods. The columns are packed together to form two-dimensional crystalline array.

Lyotropic liquid crystals have several fundamental characteristics that make them dramatically different than thermotropic liquid crystals. First, these types of liquid crystals form in solution rather than in pure substances. Secondly, individual molecules do not align by themselves to create anisotropy instead, the molecules come together to form anisotropic aggregates which themselves align along director. For these reasons,

additional conditions besides temperature determine whether the liquid crystals phase forms. Temperature still affects phase in the same way as thermotropic liquid crystals but concentration of substance also has strong effect on liquid crystalline behavior. Lyotropic crystals are formed by the amphiphilic molecules, often known as surfactants.

These two types of liquid crystals are distinguished by mechanisms that drive self-organization, but they are also similar in many ways. Thermotropic phases are initiated by changes in temperature, while lyotropic phases can also be initiated by changes in concentration. Lyotropic liquid crystals occur as a result of solvent-induced aggregation of constituent mesogens into micellar structure [6].

Reversed Liquid Crystalline Mesophases: Reversed liquid crystalline mesophases, such as the reversed bicontinuous cubic, reversed hexagonal or reversed micellar cubic phase, are nowadays widely studied due to their potential applications in, for instance, the controlled delivery of functional molecules. In order to design the adequate mesophase delivery system for a specific application, the crystallographic structure of the phase has to be determined and related to the desired function. There are different analytical methods available for investigating the structural features of these mesophases. In the cryo-TEM method, it allows studying the crystallographic structure of single mesophase particles. Moreover, the potential to use rheology as a unique technique to determine in a simple way both the crystallographic structure of the liquid crystalline phases as well as the dynamic processes occurring during relaxation of these mesophases. The dynamic characteristics are significantly determining and controlling the mechanism and kinetics by which guest molecules and active ingredients can be released from their host [7].

Bicontinuous Cubic Liquid Crystalline Phase

Bicontinuous cubic phase liquid crystals are newly discovered exotic materials originally found in the most unassuming

places. The original observations of cubic liquid crystalline phase came during the study of polar lipids, such as monoolein, that are used as food emulsifier. The most studied binary system, monoolein-water, forms at least two types (diamond and gyroid;) of an optically clear, solid-like bicontinuous cubic phase at water contents between 20-40% (w/w) at room

temperature. Other aqueous surfactant systems self-assemble into thermodynamically stable bicontinuous cubic liquid crystalline phases as well [8].

Phase Transition Simulation

The following simulation demonstrates the phase behavior of liquid crystal materials. As has been shown, temperature determines the phase of the material.



Macroscopic View

Optical polarizing microscopy is a standard tool in the identification of liquid crystal phases and phase transitions but requires considerable experience, particularly in the study of new and less familiar materials.

As the material, initially in the nematic state, changes abruptly into the solid crystalline form as the temperature is lowered.

X-Rays provide a much more definitive means for the identification of mesophases.

Differential Scanning Calorimetry

Differential Scanning Calorimetry (DSC) is a useful tool which complements optical methods in the study of liquid crystal phase transitions. Its utilization in determining the heat supplied or extracted during a process such as a phase transition is included in *Thermal Properties of Polymers*.

In the following two figures, furnished by Prof. Charles Rosenblatt (Dept. of Physics, Case Western Reserve University), DSC traces obtained with a small sample of 8

OCB (octyloxy cyanobiphenyl) at a rate of 1° C/min are displayed to illustrate its use with liquid crystals. The lower curve in Figure (i) corresponds to a heating process. This is followed by a cooling process, represented in the upper curve.

A phase diagram bar illustrating the heating process is placed just above the temperature axis (at one atmosphere pressure). This includes a crystal to liquid crystal (smectic A) transition at 55°C followed by a barely detectable smectic A to nematic transition at 67° C and finally the nematic to isotropic (NI) transition near 80°C. The upper, cooling, curve shows a slight displacement of the NI transition, partially due to super cooling and partially instrumental hysteresis attributable to the temperature scan rate. The smectic A to crystal transition is depressed strongly due to super cooling of the smectic A phase. Thus, the phase diagram for the cooling process would not be identical to that for heating.

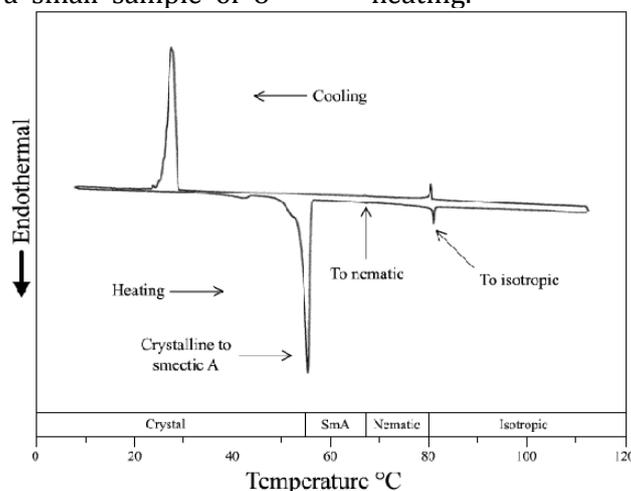


Figure (I): DSC plot with phase diagram

Figure (ii) is a repeat of this run, beginning to heat at a temperature above the crystal to smectic A transition so that greater sensitivity could be employed. This makes

the smectic A to nematic transition more visible and illustrates the capability of the DSC method is detecting subtle effects.

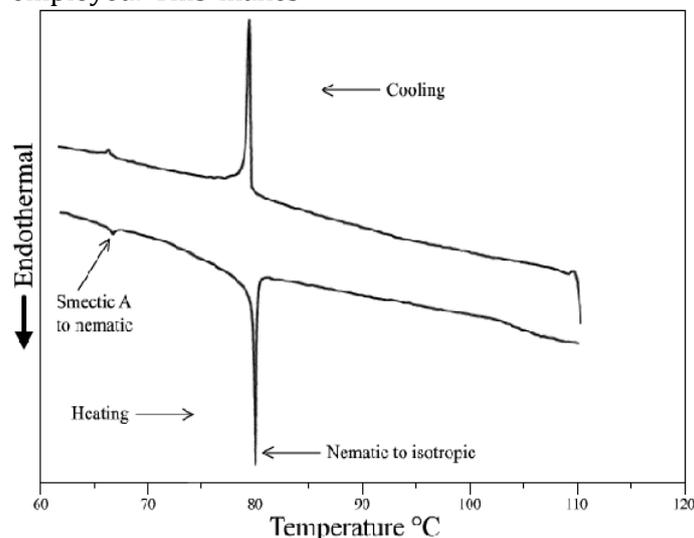


Figure (II): DSC plot

External Influences on Liquid Crystals

Scientists and engineers are able to use liquid crystals in a variety of applications because external *perturbation* can cause significant changes in the macroscopic properties of the liquid crystal system. Both electric and magnetic fields can be used to induce these changes. The magnitudes of the fields, as well as the speed at which the molecules align are important characteristics industry deals with. Finally, special surface treatments can be used in liquid crystal devices to force specific orientations of the *director*.

Electric and Magnetic Field Effects

The response of liquid crystal molecules to an electric field is the major characteristic utilized in industrial applications. The ability of the director to align along an external field is caused by the electric nature of the molecules. *Permanent electric dipoles* result when one end of a molecule has a net positive charge while the other end has a net negative charge. When an external electric field is applied to the liquid crystal, the dipole molecules tend to orient themselves along the direction of the field. Even if a molecule does not form a permanent dipole, it can still be influenced by an electric field. In some cases, the field produces slight re-arrangement of electrons and protons in molecules such

that an *induced electric dipole* results. While not as strong as permanent dipoles, orientation with the external field still occurs.

The effects of magnetic fields on liquid crystal molecules are analogous to electric fields. Because magnetic fields are generated by moving electric charges, permanent magnetic dipoles are produced by electrons moving about atoms. When a magnetic field is applied, the molecules will tend to align with or against the field.

Surface Preparations

In the absence of an external field, the director of a liquid crystal is free to point in any direction. It is possible, however, to force the director to point in a specific direction by introducing an outside agent to the system. For example, when a thin polymer coating (usually a polyimide) is spread on a glass substrate and rubbed in a single direction with a cloth, it is observed that liquid crystal molecules in contact with that surface align with the rubbing direction. The currently accepted mechanism for this is believed to be an epitaxial growth of the liquid crystal layers on the partially aligned polymer chains in the near surface layers of the polyimide.

Freedericksz Transition

The competition between orientation produced by surface anchoring and by electric field effects is often exploited in liquid crystal devices. Consider the case in which liquid crystal molecules are aligned parallel to the surface and an electric field is applied perpendicular to the cell as in the following diagram. At first, as the electric field increases in magnitude, no change in alignment occurs. However at a threshold magnitude of electric field, *deformation* occurs. Deformation occurs where the director changes its orientation from one molecule to the next. The occurrence of such a change from an aligned to a deformed state is called a *Freedericksz transition* and can also be produced by the application of a magnetic field of sufficient strength. The Freedericksz transition is fundamental to the operation of many liquid crystal displays because the director orientation (and thus the properties) can be controlled easily by the application of a field [5].

The study of liquid crystals started in 1888 when an Austrian botanist named Friedrich Reinitzer observed that a material known as cholesteryl benzoate had two distinct melting points. In his experiments, Reinitzer increased the temperature of a solid sample and noted the crystal change into a hazy liquid. As he increased the temperature further, the material changed again into a clear, transparent liquid. Because of this early work, Reinitzer is often credited with discovering a new phase of matter - the *liquid crystal* phase [9].

Function & properties of the liquid crystal system

Because of their intermediate nature, liquid crystals have some of the properties of liquids & some of the properties of solids. For example, liquid crystals are mobile & thus can be considered to have the flow properties of liquids. At the same time, they possess the property of being birefringent, a property associated with crystals. In birefringence, the light passing through a material is divided into two components with different velocities & hence different refractive indices.

Some liquid crystals show consistent color changes with temperature & this characteristic has resulted in their being used to detect areas of the elevated temperature under the skin that may be due to a disease process. Nematic liquid crystals may be sensitive to electric fields, a property used to advantage in developing display systems. The smectic mesophase has application in the solubilization of water-insoluble materials. It also appears that liquid crystalline phases of this type are frequently present in emulsions & may be responsible for enhanced physical stability owing to their highly viscous nature.

The liquid crystalline state is widespread in nature, with lipoidal forms found in nerves, brain tissue & blood vessels. Atherosclerosis may be related to lying down of lipid in the liquid crystalline state on the walls of blood vessels. The three components of bile (cholesterol, a bile acid salt, & water), in the correct proportions, can form a smectic mesophase, & this may be involved in the formation of gallstones. Bogardus applied the principle of liquid crystal formation to the solubilization & dissolution of cholesterol, the major constituent of gallstones. Cholesterol is converted to a liquid crystalline phase in the presence of sodium oleate & water, & the cholesterol rapidly dissolves from the surface of the gallstones.

Nonaqueous liquid crystals may be formed from triethanolamine (TEA) & oleic acid with a series of polyethylene glycol or various organic acids such as isopropyl myristate, squalane, squalene, naphthenic oil as the solvents to replace the water of aqueous mesomorphs. Triangular plots or ternary phase diagrams were used by Friberg et al. to show the regions of the liquid crystalline phase when either polar (polyethylene glycols) or nonpolar (squalene, etc.) compounds were present as the solvent. Friberg wrote a monograph on liquid crystals.

Ibrahim studied the release of salicylic acid as a model drug from lyotropic liquid crystalline systems across lipoidal barriers & into an aqueous buffered solution.

Finally, liquid crystals have structures that are believed to be similar to those in cell

membranes. As such, liquid crystals may function as useful biophysical models for the structure & functionality of cell membranes [9].

APPLICATIONS IN PHARMA

It has been estimated that approximately 5 per cent of all organic molecules are able to exist as thermotropic LCs. Pharmaceutical compounds have been increasingly characterized by their lyotropic liquid crystalline states with relatively fewer examples of thermotropic LC states. LLCs based delivery systems such as creams, ointments, gels, liposomes, colloidal dispersions and transdermal patches have been used in pharmaceuticals and cosmetics.

Pharma drugs as LCs

Many small molecular pharmaceutical active compounds have been demonstrated to form LC mesophases. Nafoxidine hydrochloride is one such example; this cationic drug has amphiphilic properties and gives rise thermotropic (smectic type) and lyotropic liquid crystalline structures. Palmitoyl propranolol hydrochloride is an amphiphilic derivative of the beta-blocker propranolol hydrochloride which forms smectic type liquid crystalline phase. It has been administered as liquid crystalline dispersion for cardiac problems. Itraconazole hydrochloride is an antifungal drug which forms chiral nematic phases. Some of the other examples of small molecular pharmaceuticals which can form LCs are arspenammine, fenoprofen sodium, fenoprofen calcium, penbutolol sulphate, nafcillin, methotrexate, folic acid and tobramycin. Large molecular pharmaceutical active compounds are also known to form LCs; some common examples of them are cyclosporine, calcitonin, amylin, nafarelin, detirelix and leuprolide. Some of the pharmaceutical excipients such as hydroxypropylcellulose, ethyl cellulose and cellulose acetate have also displayed LC phases. Besides this, examples of naturally occurring LCs are DNA, cholesterol and the biological membranes.

LCs for solubility enhancement

Thermotropic liquid crystalline state of fenoprofen calcium (a class II drug from biopharmaceutical classification system)

has demonstrated higher solubility than its crystalline state. Liquid crystalline state of lipids has been used as a model to mimic the biological systems. In various foods, pharmaceutical and biotechnical applications, the liquid crystalline phases formed by surfactants in aqueous medium represent useful host systems for drugs, amino acids, peptides, proteins and vitamins. Various biologically active food additives are soluble in neither aqueous nor oil phase and require environmental protection against hydrolysis or oxidation. Lyotropic liquid crystals meet these requirements mainly due to their high solubilization capacities for hydrophilic, lipophilic and amphiphilic guest molecules. Moreover, recent studies demonstrated controlled and/or sustained release of solubilized molecules from different liquid crystalline matrices.

Colloidal dispersions

The bulk liquid crystalline structure may be dispersed in water in the presence of additional stabilizer/emulsifier to form sub-micrometer soft particles (of 100-500 nm) which retain the internal structure of the liquid crystal bulk phase. In the case of lamellar, hexagonal, and cubic phases, these soft particles have been termed liposomes, hexosomes, and cubosomes, respectively. They have significant advantages in comparison to the bulk phase as these have a high interfacial area (relative to their volume) and low viscosity, thus widening its scope of application.

Smectic nanoparticles

Colloidal smectic nanoparticles are emerging as a carrier system for lipophilic drugs due to their liquid crystalline nature. One such example of this smectic nanoparticulate carrier system is cholesteryl myristate. Colloidal smectic nanoparticles are suitable models to study the crystallization behavior of pharmaceuticals and determining the influence of various parameters for the development of smectic nanoparticles which are resistant to crystallization upon storage.

Dermal application

Drug molecules and pharmaceutical excipients with amphiphilic character can form lyotropic mesophases, this is

particularly for surfactants, which are commonly used as emulsifiers in dermal formulations and associate to form micelles after dissolving in a solvent. With increasing concentration the probability of interaction between the micelles increases and thus liquid crystals form. Liquid crystalline formulations have been used in cosmetics and pharmaceutical controlled release dosage forms. These formulations achieve enhanced penetration of biologically active materials (e.g., vitamin A) into the skin. The delivery systems comprise of cholesteric liquid crystals wherein the active material is retained within the lamellar molecular structure (i.e. between the molecular sheets) of the cholesteric liquid crystal [3].

Drug Delivery Utilizing Liquid Crystal Structures:

Vitamin E TPGS/drug compositions and methods are provided which obviate the need for surfactants or non-evaporated co-solvents because the active drug component is dissolved directly into Vitamin E TPGS to form a true molecular solution--not an emulsion or a micro-emulsion. The invention provides a slowly dissolving TPGS/Drug matrix that absorbs gastrointestinal fluid into the matrix at the dosage form/fluid interface, where a gel-like liquid crystal is formed. This gel front forms a liquid crystal boundary where drug dissolution is highest. At this liquid crystal/GI fluid boundary, synchronization takes place in which the rate of formation of liquid crystals equals the dissolution rate of liquid crystals at the water interface, thereby giving controlled order release of the drug into the GI tract. The rate of dissolution is also controlled by the geometry of the dosage form. The solid Vitamin E TPGS/drug matrices of the invention can be solidified and compressed into tablets or filled into capsules, with other excipients, binders and/or fillers. The solid TPGS/drug solution of the invention also can be made into an immediate release liquid formulation upon addition of water, or into a controlled release system solid tablet by the use of impermeable or semi-permeable barriers or coatings surrounding portions of the tablet [10].

Non-pharma applications of Liquid Crystals

1. Liquid Crystal Displays
2. Liquid Crystal Thermometers
3. Optical Imaging

Liquid crystal technology has had a major effect many areas of science and engineering, as well as device technology. Applications for this special kind of material are still being discovered and continue to provide effective solutions to different problems.

Liquid crystals have a multitude of other uses. They are used for nondestructive mechanical testing of materials under stress. This technique is also used for the visualization of RF (radio frequency) waves in waveguides. They are used in medical applications where, for example, transient pressure transmitted by a walking foot on the ground is measured. Low molar mass (LMM) liquid crystals have applications including erasable optical disks, full color "electronic slides" for computer-aided drawing (CAD), and light modulators for color electronic imaging.

As new properties and types of liquid crystals are investigated and researched, these materials are sure to gain increasing importance in industrial and scientific applications [11].

CONCLUSION

There are three states of matter--gas, liquid and solid. A fourth state of matter is the *liquid crystalline state* or *mesophase*. The term *liquid crystal* is an apparent contradiction, but it is useful in a descriptive sense because materials in this state are in many ways intermediate between the liquid and solid states. The two main types of liquid crystals are termed *smectic* (soap like or grease like) and *nematic* (threadlike). In general, molecules that form mesophases are (a) organic, (b) elongated and rectilinear in shape, (c) rigid and (d) possess strong dipoles and easily polarizable groups. The liquid crystalline state may result either from the heating of solids (thermotropic liquid crystals) or from the action of certain solvents or solids (lyotropic liquid crystals). LLCs based delivery systems such as creams, ointments, gels, liposomes,

colloidal dispersions and transdermal patches have been used in pharmaceuticals and cosmetics. Non-pharma applications of liquid crystals are-liquid crystal displays, liquid crystal thermometers and optical imaging. As research into this field continues and as new applications are developed, liquid crystals will play a vital role in modern technology.

REFERENCES

1. Christel C.Mueller-Goymann, "Drug delivery: Liquid crystals in", Encyclopedia of Pharmaceutical Technology, Chapter 75, Third Edition, October 2006, Informa healthcare
2. Stevenson CL, Bennett DB, Lechuga-Ballesteros D Pharmaceutical liquid crystals: the Relevance of partially ordered systems J PharmSci. 2005 Sep; 94 (9):1861-80.
3. Ganesh shete, Vibha puri, Arvind K Bansal, "Liquid crystals in pharma", India's most comprehensive portal-Pharmabiz, March 25, 2009
4. P. V. Patel, J. B. Patel, R. D. Dangar, K. S. Patel, K. N. Chauhan, " Liquid Crystal Drug Delivery System", Int J. of Pharma.& App.sci./1(1)/2010:118-123
5. "Liquid crystals ½-Anthony Crasto Organic Chemistry +Saxitoxin"
6. Maiti S, "Liquid-crystal and Nano-crystal Technology for Solubilization of Poorly Water Soluble Drugs", Journal of PharmaSciTech 2012;2(1):1-4
7. Laurent Sagalowicz, Raffaele Mezzenga, and Martin E. Leser, "Investigating reversed liquid crystalline mesophases" "Current Opinion in Colloid & Interface Science 11(4): 224-229, 2006"
8. Patrick T. Spicer, "Bicontinuous Cubic Liquid Crystalline Phase and Cubosome Personal Care Delivery Systems" The Procter & Gamble Company Corporate Engineering: 8256 Union Centre Boulevard West Chester, OH 45069:59-62
9. Martin's Physical Pharmacy & Pharmaceutical Sciences, 5th edition: 41-42
10. Garry Myers, Kingsport, Tenn. "Drug delivery system utilizing liquid crystal structure" US 5,891,845/ April 6, 1999
11. Denis Andrienko, "Introduction to liquid crystals "International Max Planck Research School Modelling of soft matter 11-15 September 2006, Bad Marienberg, September 14, 2006:27-29.

Liquid crystals: identification of thermotropic and lyotropic liquid crystalline phases (mesophases). In surfactant systems by low-angle diffraction measurements, for example. XRD solutions for phase ID. AERIS benchtop diffractometer with its intuitive user interface, best-in-class data quality and high sample throughput is an excellent tool for routine phase analyses of powdered and solid samples in both industrial and research environments. The CubiX³ instruments are designed for specific industrial applications with sample changer and automation options to accommodate high sample volumes. HighScore (Plus) is a powerful software package that allows for peak search and easy phase identification, even in complex phase mixtures. Liquid crystalline phase & its pharma applications. P P Gaikwad. M T Desai. Scattering Methods and their Application in Colloid and Interface Science. Book. Mar 2018. Otto Glatter. Liquid crystals in the last two decades have become part of a technological explosion, leading to advances in areas as diverse as oil recovery, the production of temperature sensors--from medical thermograms to "mood rings"--and biological research into nerve conduction and arteriosclerosis. Although they are as fundamental a phase of matter as solids, liquids, and gases, liquid crystals have over the past century puzzled scientists by their very existence.