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## A REVIEW ON LIQUID CRYSTAL

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### ABSTRACT:

Liquid crystal (mesophase) is a state of matter which has properties between those of conventional liquids and those of solid crystals have been recently studied as novel drug delivery systems. The reason behind this is their similarity to colloidal systems in living organisms, they have proven to be advantageous over traditional, dermal, parenteral and oral dosage forms. Liquid crystals are thermodynamically stable and possess long shelf life. Liquid crystals show bio adhesive properties and sustained release effects. Objective of this review paper is to provide in depth information of pharmaceutical liquid crystal technology. It shall deal with cubic and hexagonal liquid crystal and their applications in drug delivery systems.[1]

**KEYWORDS:** Liquid Crystals, Mesophase, Novel Drug Delivery System, Sustained Release etc.

### HISTORY:

The discovery of an intermediate, liquid crystal, state of matter is credited to Friedrich Reinitzer. In 1888, Austrian botanical physiologist Friedrich Reinitzer, working at the Karl-Ferdinands-Universität, examined the physicochemical properties of various derivatives of cholesterol which now belong to the class of materials known as cholesteric liquid crystals. Previously, other researchers had observed distinct color effects when cooling cholesterol derivatives just above the freezing point, but had not associated it with a new phenomenon. Reinitzer perceived that color changes in a derivative cholesteryl benzoate were not the most peculiar feature. He found that cholesteryl benzoate does not melt in the same manner as other compounds, but has two melting points. At 145.5 °C (293.9 °F) it melts into a cloudy liquid, and at 178.5 °C (353.3 °F) it melts again and the cloudy liquid becomes clear. The phenomenon is reversible. Seeking help from a physicist, on March 14, 1888, he wrote to Otto Lehmann, at that time a Privatdozent in Aachen. They exchanged letters and samples. Lehmann examined the intermediate cloudy fluid, and reported seeing crystallites. Reinitzer's Viennese colleague von Zepharovich also indicated that the intermediate "fluid" was

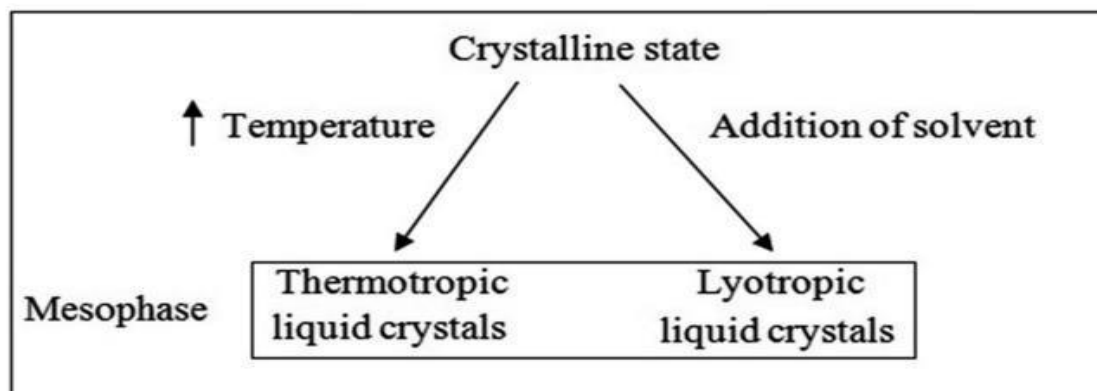
crystalline. The exchange of letters with Lehmann ended on April 24, with many questions unanswered. After this accidental discovery, Reinitzer did not continue studying liquid crystals further. The research was later carried forward by Lehmann, who realized that he had been encountering an entirely new phenomenon and was in a position to investigate it. In his postdoctoral years he had become an expert in crystallography and microscopical studies. Lehmann started a systematic study, first of chemical cholesteryl benzoate, and then of its related compounds which exhibits the double-melting phenomenon. He was then able to make observations in prepolarized light, and his microscope was provided with a hot stage (sample holder equipped with a heater) which enabled high temperature observations. The intermediate cloudy phase may clearly sustained flow, but other features, particularly the signature under a microscope, convinced Lehmann that he was dealing with a solid one. After Lehmann's, his work was continued and scientifically expanded by the German chemist Daniel Vorlander, by whom from the beginning of 20th century until his retirement in 1935, had prepared many of the liquid crystals known. However, liquid crystals were not popular among scientists at that time and the material remained as a pure scientific curiosity for more than 80 years. 1888: Reinitzer observed the two phenomena, birefringence and the occurrence of iridescent colors between the two melting points in a material that we now were cholesteryl benzole. 1889: Lehmann carried out detail investigation and reasoned that the birefringent portions of the liquid must be crystals. He previously referred to these materials as liquid crystals. 1890: Gattermann blended the principal fluid precious crystals of azoxybenzene, with fully known structures. 1908: D. Vorlaender, the first to integrate a thermotropic smectic compound, related liquid crystallinity to chemical structures, detected polymorphism of liquid crystal state. 1922: Freidel identified and named the different microscopic textures (nematic, smectic, and cholesteric), observed the impacts of electric and magnetic fields. 1930: Fredericksz studied the transition from a homogeneous structure at some critical value of applied field strength. 1965: the global liquid crystal society by Glenn Brown at Kent state university. Lehmann and Reinitzer are known as the grandfathers of LCs science. [30]

## INTRODUCTION:

liquid crystals are a state of matter which has properties between those of conventional liquids and those of solid crystals. A liquid crystal may flow like a liquid, but its molecules may be oriented in a crystal-like way. Liquid crystal was been revealed in starting for cholesterol found in incentives by F.Reinitzer. More than 100 years after, examination of biological liquid crystal materials is still interest. However, the focus has shifted from the study of common liquid crystal features to more refined subjects such as their impact on molecular organization relevant for biological living cells carry liquid crystalline environment. In 1888 year, the finding of a mid-liquid crystalline state, is recognized by Friedrich Reinitzer, throughout the experiments on a cholesterol-based matter trying to figure out the correct formula and molecular weight of cholesterol, he was hit by the fact that this matter appeared to have 2 melting points. Solid crystal molten into a heavy liquid at 145.5 degree Celsius which existed until 178.5 degree Celsius where the muddiness unexpectedly went,

giving way to a clear transparent liquid. The liquid crystals called mesophase (intermediate between the crystalline solid state and the amorphous liquid state). Liquid crystals nano carriers are intermediary state between the solid and liquid state. It is mostly named a mesomorphic state from reverse cubic phase colloidal particles are interior aqueous zones also afford certain benefits in technical applications compared by means of droplets of general oil-in-water emulsion (o/w). These surroundings one the one hand carry out a definite molecular organization on other solvated molecules and accumulation. 2) The liquid crystal is a substance that is thermodynamically situated in the middle of the isotropic liquid and the crystalline phase. They show flow properties like a liquid and at same time partly hold the order of a liquid crystal can be deliberated a quarter state of matter following solid, liquid and gas. Liquid crystal phases, as their suggests, be existent between the predictable crystal phase and liquid phase. Typically, liquid crystal molecules keep rod like structure or disc like anisotropic structures. The distinctive characteristic of liquid crystals is the propensity of the molecules to support themselves with long-range direction. The liquid crystal can flow like a liquid, but the molecules in the liquid are recognized and or in favor of in a crystal-like manner. In these two generic classes of liquid crystals: which are changes are driven by thermal processes called thermotropic liquid crystals and lyotropic systems are strongly influenced by solvents and many thermotropic liquid crystals exhibit a diversity of stages as the temperature of system is altered. For example, a specific type of liquid crystal particle may exhibit numerous smectic and nematic phases as the temperature is increased.3) A unique state of matter called liquid crystal exists in case of certain substances that are located between solid and liquid state. Liquid crystals are typically elongated organic molecules with an uneven distribution of electric charges along their axes (dipole). This gives rise to a special physical characteristic to which liquid crystals own their name, between the crystalline and liquid states they possess both structural order and mobility. Liquid crystalline structures exhibit anisotropy, having optical direction and the characteristics properties of solid and liquids. The three distinct states of matter as solid, liquid and gas have been discussed so far. However, there is a state of matter, which does not meet the necessary requirements of any of these three categories. For example, a substance like cholesterol is somewhere between a liquid and a solid. This is not quite liquid or quite solid, but is a phase of matter whose order is intermediate between that of a liquid and crystal. It is called as mesomorphic state which is state of matter in degree of molecular order is intermediate between the perfect three dimensional, long -range positional and orientational order found in solid crystals and the absence of long-range order found in isotropic liquid, gases, and amorphous solid. It is also called intermediate, physically, they are observed to flow like liquids showing some properties of crystalline solids. Hence this state is considered to be the next(fourth) state of matter known as liquid crystal state. Liquid crystals can be considered to be crystals, which have lost some or all of their positional order while maintaining full orientational order. They are free to move, but like to line up in about the same direction. The degree of mobility of the molecules in the liquid crystal is less than that of a liquid. Controlled drug delivery systems are advanced methods for the transport of pharmaceutical compounds within the body, and can be used to overcome many of the limitations of conventional drug formulations, the aim of this approach

is to create a higher concentration of the drug at a specific site relative to that in the rest of the body, as well as to develop controlled release formulations, various types of drug delivery systems have been developed, including hydrogels, nano particulate delivery systems, drug loaded biodegradable microspheres, and drug polymer conjugates. One of the more recent advancements in drug delivery systems are liquid crystals, which have emerged as injectable formulations because of their sustained release properties. Lyotropic liquid crystal phases form a long-range order with the addition of a solvent, and have historically been used to describe materials composed of amphiphilic molecules. Lyotropic liquid crystal phases are formed when dissolving amphiphilic molecules in a solvent, and are influenced by the amphiphilic structure of the molecule, the presence of additives and conditions of the solution. Liquid crystals are class of soft matter, whereby the constituent molecules exhibit positional and or long range orientational order of greatest interest for pharmaceutical applications are lyotropic liquid crystal, which consists of low or more components whereby one acts as a solvent to provide fluidity to the systems, and the other provides an isometric shape. The arrangement of the liquid crystal molecules in a particular solvent depends on various factors, including temperature and concentration as well as the shape of the liquid crystal molecule.[4] Liquid crystals are widely used for drug delivery due to their controlled release and sustained release properties. In this paper, drug crystallization encapsulated liquid crystal emulsion, a novel drug delivery system, was proposed. Controlled drug delivery systems are advanced methods for the transport of pharmaceutical compounds within the body, which has paramount importance to enhance the efficacy of medications. It improves the solubility and bioavailability and reduces the side effects of drugs to achieve the best therapeutic effect. Liquid crystals are one of the most widely used carriers for drug delivery due to their controlled drug release and



sustained drug release properties.[5] Liquid crystal dosage forms, particularly those using lipid based lyotropic liquid crystals have generated considerable interest as potential drug delivery systems. Liquid crystals have the physical properties of liquids but retain some of the structural characteristics of crystalline solids. They are compatible with hydrophobic and hydrophilic compounds of many different classes and can protect even biologicals and nucleic acids from degradation. Designing novel dosage forms to increase efficacy and stability of existing drugs in one of the formulation development processes performed in the pharmaceutical industry. Recently, liquid crystal dosage forms have generated substantial interest because they are applicable to both oil and water-soluble compounds.[6]

Figure No-1

**Advantage of Liquid crystals in emulsions:** LCs (mesophases) provides the following advantages to emulsion.

1. Increased stability
2. Prolonged hydration
3. Controlled drug delivery

**1) Stability:** Emulsion stability of the multilayers around the oil droplets act as a barrier to coalescence. If oil droplets coalesce emulsion breaks. This barrier for coalescence acts as an increased stability property of the emulsion.

**2) Prolonged hydration:** Lamellar liquid crystalline and gel network contain a water layer, which shows that 50% of the water of oil in water (o/w) emulsion can be bound to such structures. Such water is less prone to evaporation when applied to the skin and permits a long-lasting moisturizing / hydrating effect, necessary for drug entry.

**3) Controlled Drug delivery:** Liquid crystals prevent the fast release of the drug dissolved in the oil phase of an emulsion. This is attributed to the lamellar liquid crystalline multilayer, which reduces the interfacial transport of a drug dissolved within the oil droplets. Microscopic observations under polarized light show the exceptional thickness of liquid crystalline lamellar layer around the oil droplets.[27]

## **FUNCTION AND PROPERTIES OF LIQUID**

### **CRYSTAL SYSTEM:**

LCs When present at the oil/water interface, the liquid crystals help give the system rigidity and, by limiting the fluctuation of the components at the interface, give the emulsion great stability. Furthermore, the liquid crystal system enhances the moisturizing ability of the emulsion; in this special network. The quantity of inter-lamellar water can be extremely high and become immediately available when the cream is applied to the skin. For these reasons these emulsions have a shiny surface, a fresh and original feel and they leave a light and pleasant sensation on the skin. In recent years, the moisturizing effect of creams and lotions has become increasingly more important and cosmetic chemists are constantly searching for better methods of retaining water in the superior layers of the skin. The evaporation of the bonding water in emulsions containing anisotropic lamellar phases are slower and permit a hydro retentive action that prolongs the moisturizing effect. The associations that are formed because of the excess water are particularly interesting; in these cases, the ability of the crystalline phase to swell is strictly linked to the stability and the behavior of the emulsion because, in a liquid crystal system, the quantity of inter- lamellar water and of hydrophile elements can amount to 70% of total external phase. [27]



## CLASSIFICATION OF LIQUID CRYSTALS:

Liquid crystalline compounds are differentiated into two types: thermotropic and lyotropic. The liquid crystals which change their phase upon heating or cooling are thermotropic. The mesophase is called enantiotropic when the phase is obtained upon both heating and cooling.

When added in a suitable solvent lyotropic phases are formed and the appearance of the mesophase is dependent on both concentration and temperature.

### 1) Lyotropic liquid crystal

### 2) Thermotropic liquid crystal

#### 1) Lyotropic liquid crystal

Lyotropic liquid crystals form in the presence of solvent. The solute molecules that form these liquid crystal phases are amphiphilic in nature having distinct polar and non-polar units in molecular structures. The solutes could be ionic, non-ionic or cationic. The solvents can be either polar or nonpolar depending upon the solute molecule chosen, however the most commonly studied solvent. When the amphiphilic molecules are dissolved in water, the hydrophilic polar head and the hydrophobic carbon chain tail self-assemble into spherical aggregates called micelles. In a micelle, the hydrophilic heads of each amphiphilic molecule are exposed to surrounding water, and the hydrophobic tails are protected inside the spherical shell created by the head groups. Micelles are essentially an amphiphilic monolayer system and each of the aggregates is distributed randomly in the solvent creating an isotropic micellar solution. [7]

Lyotropic liquid crystal systems composed of amphiphilic can be classified into 1) Lamellar (La) 2) Hexagonal 3) Cubic phases based on their assembly shape. Among them the reversed Hexagonal phase (H<sub>2</sub>) and the reversed cubic phase (Q<sub>2</sub>) have been extensively investigated for their ability to control the release rate of numerous drug substances, from low molecular weight chemicals to macromolecular drugs (Protein, peptides and nucleic acids). Their structure consists of a linear arrangement of alternating lipid bilayers and of aqueous channels arranged in periodic minimal surface geometries. The reversed hexagonal phase consists of an infinite rod type water channel arranged in a two-dimensional lattice and separated by lipid bilayers and the reversed cubic phase comprises a curved water channel and bicontinuous lipid bilayer that extends in their dimensions. The hexagonal and cubic phases are spontaneously formed from the lipid crystal forming system (LLFs) in aqueous fluid.[8]

Lyotropic liquid crystals have a number of beneficial properties from the point of view of pharmaceutical technology. Lyotropic liquid crystals are usually formed of water, one or two tensides and oil in a specified concentration and temperature range; they are suitable carrier systems for hydrophilic, lipophilic or amphiphilic drugs. They are an extremely stable system thermodynamically and can be maintained for a long time without the separation of the phases, so their structure is retained for a long time without structural changes. They also promote the penetration of the active substance through the skin, due to the low surface tension at the water oil interface. Their use through the skin is especially advantageous, given the concentration ratio of the components of lyotropic liquid crystal; the structure of the double liquid layer of

the stratum corneum present a similar Lamellar structure and therefore their application can improve the penetration of the active ingredient. [9]

Lyotropic liquid crystals play an important role in many biological environments, such as Micelle's liposomes and phospholipid bilayers of cell membranes. [10]

Lyotropic liquid crystals form only upon addition of a solvent most often water; moreover, the building blocks of lyotropic phase are often not one but many molecules (typically on the order of 100), organized into an aggregate called a micelle. The micelle formation is a result of the amphiphilic character of the constituent molecules, generally surfactant, anionic and cationic and nonionic respectively. Micelles, in which amphiphiles are organized with the nonpolar tails inwards thus protected from water contact by the outwards directed polar head groups, start forming beyond limiting amphiphile concentration called the critical micelle concentration (CMC). The nematic is the simplex liquid crystal phase, exhibiting long range orientational order but no positional order. If we add 1 D positional order i.e. periodic distribution of the molecules along one specific direction, we get the so-called smectic (thermotropic) or Lamellar (lyotropic) phases, where the molecules (typically rod shaped) are organised into layers. In a smectic the degree of positional order is still not very high and molecules frequently move from one layer to next, but in the Lamellar phases the amphiphiles build up bilayer that are separated by an aqueous region that can be much thicker than bilayer, making the layering much more distinct within the layers the molecules may be on the average perpendicular to the layers or they can be inclined with a certain angle (thermotropic smc or lyotropic L $\beta$ ) the difference between L $\alpha$  and L $\beta$  however goes far beyond the issue of molecule tilt. The next step in a long range positional order in a liquid crystal phases is encountered among the columnar phases, where the building blocks are positioned on 2D lattice, but without long range positional correlation in the third direction. [11]

Lyotropic liquid crystals, on the other hand, are observed when changing the concentration of a shape or property of anisotropic dispersant in an isotropic solvent. Often, lyotropic phases are observed as a function of concentration of amphiphilic molecules in water or other solvents. Below the critical micelle concentration CMC the amphiphiles are molecularly dispersed in the solvent but at larger concentration form micelles which can be of the spherical disk or rod like type, depending on the molecular shape. At even higher concentration these micelles aggregate to ordered structures and can form hexagonal cubic or lamellar phase also of the inverse type. [12]

Water free lyotropic liquid crystalline pre-concentrates which consist of oil and surfactants with good physiological tolerance and spontaneously form lyotropic liquid crystalline phase in aqueous environment. In this way these pre-concentrates having low viscosity can be injected into the periodontal pocket, where they are transformed into highly viscous liquid crystalline phase, so that the preparation is prevented from flowing out of the pocket due to its great viscosity, while drug release is controlled by the liquid crystalline texture. [13]

Lipid based lyotropic liquid crystals or liquid crystalline nanoparticles are highly ordered, thermodynamically stable, internal nanostructures and offer the potential to develop a sustained drug release matrix. The main reason behind lipid based liquid crystals gaining a lot of interest in recent years is the fact that, besides being a potential for controlled drug delivery systems, they also provide us with an alternative for safer and efficacious routes of drug administration with minimum toxicity.

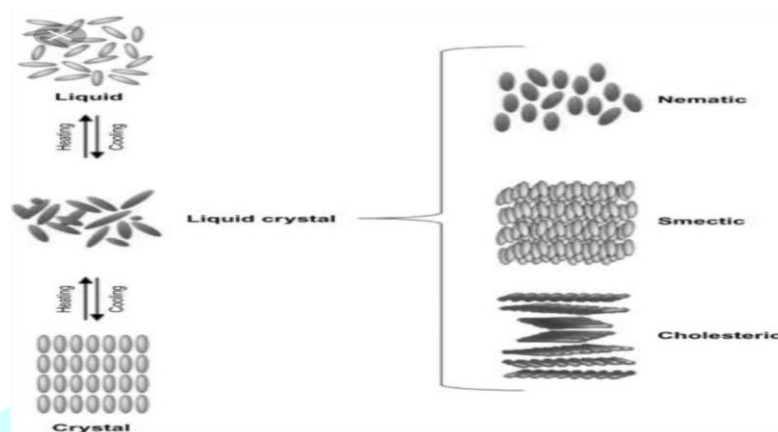


Figure No-2

### SUBCLASSES OF LYOTROPIC LIQUID CRYSTALS:

Lyotropic liquid crystals (LLCs) can be broadly classified into three categories According to their internal structure.

- 1) Lamellar phase(La)
- 2) Cubic phase(V2)
- 3) Hexagonal phase(H2)



Figure No-3 sub classes of Lyotropic liquid crystal

#### 1) Lamellar phase (La)

The lamellar phase extensively exists in organisms. For example, it is the basic building block of cell membranes. The lamellar phase is a planar structure, consisting of lipid bilayers separated by water, where the polar head groups of the amphiphilic molecules associate and are in contact with water directly, while the hydrophobic tails are away from water. The rheology gives the information that the lamellar structure is less viscous compared with the hexagonal structure; furthermore, the lamellar phase can be characterized by crossed polarized light microscopy, exhibiting "streaky" or "mosaic" like texture. In addition, Bragg peaks



with relative positions at the ratios of 1:2:3:4 are obtained from the small-Angle x-ray scattering measurement. [15]



Figure No-4 liquid crystal phases

## 2) Cubic phase

Structure of cubic phase is unique and consists of curved bicontinuous lipid bilayers extending in three dimensions, separating two congruent networks of water channels. The water pore diameter of the fully swelled phase is about 5 nm and the phase is very viscous. The unique curvature of the bilayer as in the cubic phase is associated with an energy known as the curvature elastic energy. Which determines the stability of the cubic phase as a function of composition suggested that the spontaneous formation and thermodynamic stability of cubic phase, consisting of continuous bilayers arranged in geometries of periodic minimal surfaces found in a many lipid/water system, is due to a competition between the two free energy terms the curvature energy of each monolayer versus the stretching energy of the lipid chain. Cubic phase reveals a great flexibility, since drugs of very different polarity and size may be incorporated. Typically, hydrophilic drugs can be dissolved in water and this aqueous drug solution can be used to form a cubic phase. Similarly, lipophilic or lipid soluble drugs can be dissolved in lipid phase such as GMO (glyceryl monooleate), which can then be used to prepare the cubic phase. Since cubic phase can be prepared at water concentration from 55 to 85% with 15 to 45% GMO. Drugs with extremely different polar Nature and wild variety of doses can be incorporated. This great versatility of cubic phase has been very clearly demonstrated by the incorporation and sustained release of drugs with varying molecular weights and solubility in water such as aspirin and vitamin E. [16]

## 3) Hexagonal phase

Hexagonal phase forming lipids: oleyl glycerate (OG) 2,5- Dihydroxy propionic acid octadec -9enyl ester) and phytanyl glycerate (PG, 2,3- Dihydroxy propionic acid 3,7,11,15 tetramethyl hexadecyl esters are found to form hexagonal phase at physiological temperature when exposed to excess water, which further expands the lipid pool to form hexagonal phases. The molecular structure and phase behaviours of OG and PG reported that a series of model hydrophobic and hydrophilic drugs such as paclitaxel irinotecan glucose, histidine and octreotide can be incorporated into OG and PG based hexagonal phases and in vitro drug release was shown to follow the Higuchi diffusion-controlled release profile. Although the understanding of these

new glycerate esters is limited, for example, their long term safety, to terality, the susceptibility to esterases, and local toxicity of their degradation products they are promising materials due to their lower melting point and improved thermal stability compared to GMO.[17]

A hexagonal phase of lyotropic liquid crystal is formed by some amphiphilic molecules when they are mixed with water or another polar solvent. In this phase, the amphiphile molecules are aggregated into cylindrical structures of indefinite length and these cylindrical aggregates are disposed on a hexagonal lattice, giving the phase long - range orientational order. In Normal topology hexagonal phases, which are formed by type 1 amphiphiles, the hydrocarbon chains are contained within the cylindrical aggregates such that the polar-apolar interface has a positive mean curvature. Inverse topology hexagonal phases have water within the cylindrical aggregates and hydrocarbon chains fill the voids between the hexagonally packed cylinders. Normal topology hexagonal phases are denoted by H1 while inverse topology hexagonal phases are denoted by H11. When viewed by polarization microscopy, thin film of both normal and inverse topology hexagonal phases exhibit birefringence, giving rise to characteristic optical textures, typically, these textures are smoke like, fan like or mosaic in appearance. The phase are highly viscous and small air bubbles trapped within the preparation have highly distorted shapes size and shapes of lamellar, micellar and hexagonal phases of lipid bilayer phase behaviour and mixed lipid polymorphism in aqueous dispersions can be easily identified and characterized by negative staining transmission electron microscopy too. The hexagonal phase is composed of cylindrical micellar packed in a hexagonal pattern. In contrast to the cubic phase, the water channels in the hexagonal phase are closed. The distribution of drugs in the hexagonal phase is similar to that in the cubic phase. In recent years, cubic phase and hexagonal phases have received considerable attention because of their potential as drug delivery systems. Cubic and hexagonal phase provide a slow drug release matrix and protect peptides, Proteins and nucleic acids from chemical and physical degradation.[18]

## 2) Thermotropic liquid crystals

Most of the thermotropic liquid crystals are composed of rod-like molecules and classified into three types, nematic, smectic and cholesteric. They are formed by heating and crystalline solid or cooling the isotropic liquid. Nematic phase (thread like) is the simplest liquid crystalline phase. Where the molecules maintain long range orientation. There exists no positional order, liquid crystals used in electronics displays are primarily of the nematic type. When viewed under a polarizing microscope the defect regions linking these domains appear as dark threads. Smectic phase (soap like) a name that was coined by Friedel from a Greek word, meaning 'grease or slime'. The smectic structure is stratified as the molecules are arranged in layers with their long axes approximately Normal to the plane of the layers with well-defined interlayer spacing. Cholesteric phase is also known as chiral nematic liquid crystal. The arrangement of the cholesteric phase can be described as a combination of nematic and smectic, where some layers which resemble the smectic phase are incorporated in the nematic layers. Due to the helical structure, it exhibits an interesting phenomenon like optical rotation, selective reflection and circular polarization.[19]

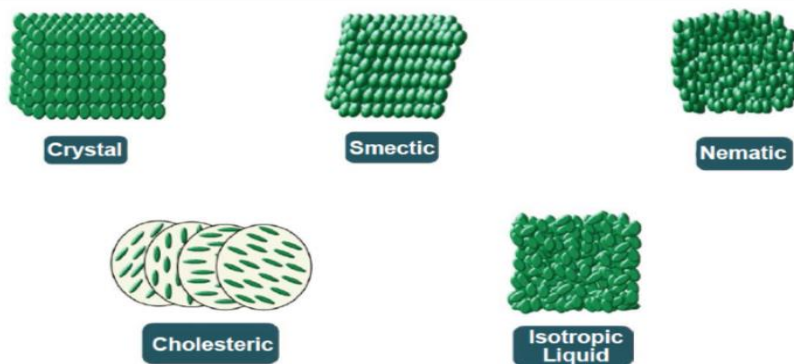


Figure No-5 subclasses of Thermotropic liquid crystal

### PREPARATION OF LIQUID CRYSTAL PHASES AND IT'S DISPERSION:

Preparation of liquid crystals is very simple as compared to their dispersions. Liquid crystal can be prepared by intimately mixing lipid with aqueous phase by vortexing at high speed. The vortexing can be reported to achieve a homogeneous state. The mixture is equilibrated at room temperature for at least 48 hours to obtain the liquid crystal. Depending upon the characteristics of the lipid, other additives may be added into the mixture or the method can be modified e.g if more than one lipid is used both the lipids are mixed and if required melted prior to vortex mixing with aqueous phase. On the other hand, the preparation of liquid crystal dispersion is complex. Two techniques are used to prepare their dispersions. The first one is called the "Top -Down approach" where at first the lipid and stabilizer is hydrated to self-assemble in a viscous bulk and then the bulk is dispersed into an aqueous solution by using high pressure homogenization and Ultrasonication. The second one is called the "Bottom up approach", where the presence of hydrotrope plays the important role by creating liquid precursors and preventing liquid crystal formation at high concentration controlled addition of aqueous medium to the mixture leads to the formation of its dispersion. It is a dilution-based method and does not require any fragmentation procedure.

### CHARACTERIZATION OF LIQUID CRYSTALS:

These are the methods which are used for the identification of liquid crystals.

- 1) Polarized light microscopy
- 2) Transmission electron microscopy
- 3) Differential scanning calorimetry
- 4) X-ray diffraction method
- 5) Rheological method
- 6) High performance liquid chromatography
- 7) Determination of entrapment efficiency
- 8) Viscosity
- 9) Drug content
- 10) Stability studies

**1) Polarized light microscopy:** Polarized light microscopy (PM) is suitable for detection of lyotropic liquid crystals (except cubic mesophases) because liquid crystals show typical black and white texture. In the case of an additional lambda plate with strong birefringent properties. Colour effects of the textures can also be observed. Hexagonal mesophases can be recognised by their typical fan shape texture. Lamellar mesophase typically show oily streaks with inserted maltese crosses. The latter result from defect structures, called confocal domains that arise from concentric rearrangement of plane layers. In some lamellar mesophases these defects prevail. Hence no oily streaks occur but Maltese crosses are the dominant texture.

**Drawback of this process:** it is restricted to particle dimensions in the micron or submicron range, whereas colloidal dispersions of liquid crystals are only resolved by transmission electron microscopy.[20]

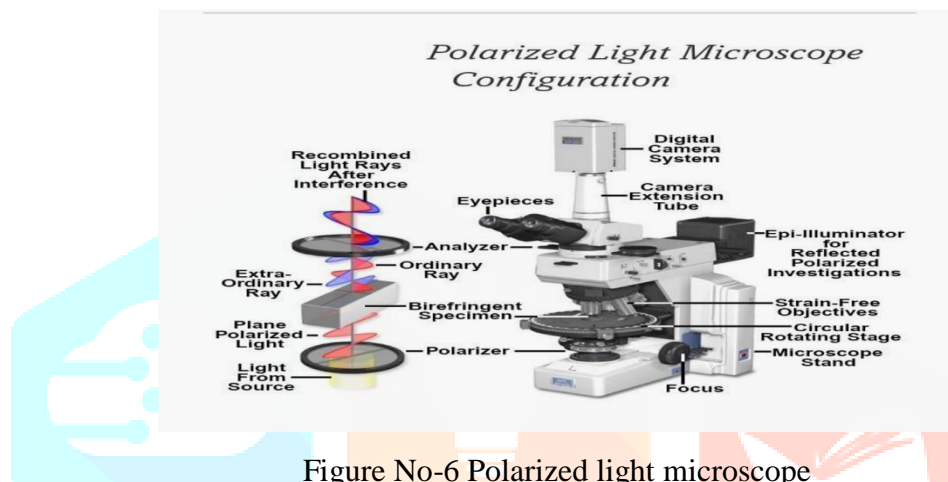


Figure No-6 Polarized light microscope

## 2) Transmission electron microscopy:

Transmission electron microscopy is used to analyze the morphologies of different discotic liquid crystal phases. Particle size distribution, entrapment efficiency is measured for the liquid crystals which are used in drug delivery. [21]

Very few studies have been carried out on this type of composite in transmission electron microscopy, partly because of the fluidity of the liquid crystals, and partly because of the amorphization of the liquid crystal during electron radiation. [22]

Transmission electron microscopy (TEM) and its facilities for electron diffraction has long been a key technique in materials science. Its use for characterization of pharmaceutical samples has, however, been very limited, largely due to the difficulties associated with the preparation of appropriately thin samples, as well as issues with sample damage caused by the electron beam. Transmission electron microscopy is a microscopy technique in which a beam of electrons is transmitted through a specimen to form an image. The specimen is most often an ultra-thin section less than 100nm thick or a suspension on a grid. An image is formed from the interaction of the electrons with the samples as the beam is transmitted through the specimen. The image is then magnified and focus on to an imaging device, such as fluorescent screen, a layer of photographic film, or a sensor such as a scintillator attached to a charge coupled device; transmission electron microscopy are capable of imaging at a significantly higher resolution than light microscope, Owing to the smaller de broglie wavelength of electrons.[23]

The first transmission electron microscopy demonstrated by Max Knoll and Evonst ruska in 1931, with this group developing the first transmission electron microscopy with resolution greater than that of light in 1933 and the first commercial transmission electron microscopy in 1939. In 1986, Ruska was awarded the Nobel prize in physics for the development of the transmission electron microscopy.[24]

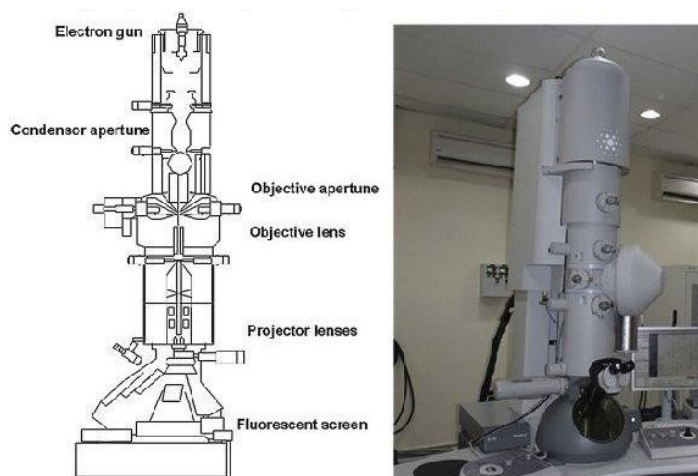
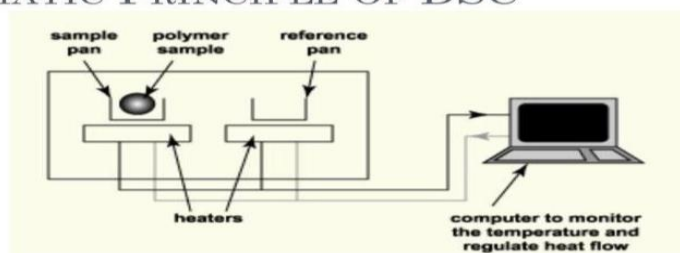


Figure No-7 Transmission electron microscope

### 3) Differential scanning calorimetry:

#### SCHEMATIC PRINCIPLE OF DSC



Sample and reference material are heated by separate heaters in such way that their temperature are kept equal while these temperature are increased or decreased linearly.

Figure No-8 Differential scanning calorimetry

Differential scanning calorimetry is frequently a preferred thermal analytical technique because of its ability to provide detailed information about both the physical and energetic properties of a substance. This is often information that cannot be obtained as accurately, easily, or quickly using any other technique with the development of sophisticated, modulated temperature.

Programs, micro-scale test configuration, robot systems, and combined differential scanning calorimetry spectroscopic instrumentation it is likely that differential scanning calorimetry will retain its place at the



forefront of the pharmaceutical thermal analytical sciences for some time to time to come. Differential scanning calorimetry these instruments provide quantitative information about exothermic, endothermic and heat capacity changes as function of temperature and time (such as melting, purity and glass transition temperature. Differential scanning calorimetry is a thermodynamic technique in which the difference in the amount of heat required to increase the temperature of a sample and reference is measured as a function of temperature.[25]

#### 4) X-ray diffraction method:

In the study of liquid crystals, as in the study of liquids and in the study of crystals, x-ray diffraction is a very useful tool because the wavelength of the x-rays is of the same order of magnitude as the interatomic and intermolecular distances in the material investigated. Thus, from x-ray diffraction data, it is possible to gather information about the local molecular arrangement (conformation and packing), and about the existence and range of order in the molecular orientations and/or positions. In discussing the positions of x-ray diffraction maxima in the diffraction pattern in a plane perpendicular to the incident x-ray beam, we will use the terms “radial position” and “azimuthal position” (see Figure). “Radial position” will refer to the distance of the maximum from the center of the x-ray diffraction pattern, “azimuthal position” will refer to the angle at which a line from the maximum to the center would make a reference line through the center. Similarly, we will use the terms “radial width” and “azimuthal width” to describe the size of the maxima (see Figure). We will limit our discussion to thermotropic liquid crystals.[26]

#### 5) Rheological method:

Rheological properties of various degrees are shown by different forms of liquid crystals. With an increase in the microstructural organization of the liquid crystal, its consistency increases and the flow behaviour become more viscous. The coefficient of dynamic viscosity  $Z$ , although a criterion for the viscosity of ideal viscous flow behaviour (Newtonian systems), hexagonal, and cubic liquid crystals show comparatively higher viscosity than lamellar phase. Moreover, plastic flow behaviour (non-Newtonian) is observed in cubic and hexagonal crystals but pseudo plastic flow behaviour (non-Newtonian) is observed in lamellar phase; which is the key feature to differentiate between these two types. For thermotropic liquid crystals, the viscosity increases in the following sequence: nematic < smectic A < smectic C.[2]

#### 6) High Performance Liquid Chromatography:

The sample concentration was determined with the help of Agilent HPLC 1100 Series (Agilent Technologies, USA) Determination was passed out in a solvent system of formic acid -methanol–water. Data was composed and managed using a Chem Station software version B.01.03. The gained values with standard methanolic sample solutions showed linearity over the concentration range of 0.1–100 µg/g with a correlation coefficient  $r^2$  value of 0.999. The quantification limit in the HPLC assay was 0.1 µg/g and standard deviation under repeatability conditions was no more than 5.6% in all concentrations tested, liquid crystals (LC) phases and

Liquid crystals nanoparticles dispersions were prepared using sample standard with respective lipid compositions.

**7) Determination of Entrapment Efficiency:** Drug loading of Liquid crystals and Entrapment efficiency can be determined with the help of ultrafiltration techniques. In liquid crystals formulation Unloaded drug concentration is finding, which is withdrawn from the total drug added. The amount of drug is analyzed by use of UV spectrophotometer. freshly prepared 1ml of liquid crystals formulation dispersion was diluted upto 10 mL with deionized water and the diluted samples up 3ml was placed in centrifuge tube for specific time (15 min) and centrifuged at specific rate of rotation (4000 rpm). Certain active ingredients are adsorbed to the ultrafiltration membrane to some amount, the drug adsorption to the ultrafiltration membrane was examined by filtration of drug solution of known amount pass through the membrane and determining drug concentrations in the ultrafiltrate. By spectrophotometrically the free drug contained in filtrate was measured at specific  $\lambda_{max}$  of drug. The quantity of entrapped drug was achieved by subtracting the quantity of free drug from the total drug incorporated in 1 ml of LCs dispersion. The total amount of drug incorporated in 1 ml of LCs dispersion was examined after adding 9.0 ml methanol to dissolve the drug-loaded-LCs. The resulting solution was examined for the total drug content spectrophotometrically with methanol as blank. The EE was determined by subtracting the quantity of free drug from the calculated total incorporated drug is weight. The entrapment efficiency i.e.(EE%) is can be calculated as:  $EE\% = WE/ WA\% \dots$ (eq no 1)Where, WE is the mass of CI entrapped in the CI-Cubs, and WA is the weight of CI in the system.

#### 8) Viscosity:

The prepared mesophase gel formulation was evaluated using viscometer named as rotational

Brookfield viscometer of cone and plate structure, with the help of spindle bar CPE- 41 at temperature  $25 \pm 2$  °C. About 0.5 g of the tested sample was applied to the plate and settings the speed ranges from 0.3 to 60 rpm or 0.5 to 100 rpm with 10 s among each 2 successive speeds.

When the torque was within 10–100% the standard range and rheological data were recorded.

#### 9) Drug Contents:

In drug content drug loaded liquid crystals formulation and methanol are used. The mesophase formulation mixed with methanol then sonicated for 10 min to obtain a cleasolution. Concentrations of drug were determined spectrophotometrically at  $\lambda_{max}$  of drug Drug Content = actual yield/Theoretical yield $\times$ 100.

#### 10) Stability studies:

Physical stability can be studied by analysis of organoleptic and morphological characteristics as a function of time. Particle size distribution and drug content can be judged at different time periods or intervals and can also be used to evaluate the possible changes by time. [3]

**APPLICATIONS:****1) Liquid Crystal Emulsion:**

A large part of cosmetic products is made in the form of emulsions, a form that allows the simultaneous use of lipophilic and hydrophilic ingredients in the required dosages. A product in the form of an emulsion also has the advantage of having the most convenient appearance and texture that also facilitates its application. They can be formulated to be liquid, milk type emulsions of variable consistency, creams, or even super liquid spray-able emulsions. Finally, we should also consider the fact that an emulsion is the best carrier for active ingredients and functional substances. The theory of stabilising an emulsion through the formation of a network of liquid crystals is different to the HLB theory or the Schulman couple theory. The gelification of the water phase obtainable with hydrosolvatable polymers or with emulsifiers that are able to form a reticular organised structure in liquid crystal form, eliminates the need to use waxy components in large quantities and consistency factors that are no longer in harmony with the modern conception of light and easy to spread emulsion.[27]

**2) Transdermal Drug Delivery**

Topical drug delivery is emerging as a striking substitute for oral administration. Despite the restricted or limited absorption of drugs through the skin barrier, myriad carrier systems have been screened for the topical delivery of pharmaceuticals. Stratum corneum (SC) is the rate-limiting barrier in topical drug delivery. Liquid crystals are currently explored for topical delivery as highly bioadhesive and physically stable carriers in comparison with solid lipid nanoparticles, liposome, etc., competent for penetrating through stratum corneum, providing sustained release of incorporated drugs and protecting them from physical and enzymatic degradation. Higher surface area and similarity of liquid crystals to biological lipids facilitate drug permeation across the skin, enhance drug interaction with the skin and mucus, thus increasing the potential for topical drug delivery efficiency.[28]

**3) Ability to Enhance the Stability of Drugs:**

The unique structure of the cubic phase is used to incorporate unstable drug substances and protect them from physical and chemical degradation. studied the ability of cubic phase gel to protect insulin from agitation induced aggregation. The results showed that the native conformation of agitated insulin in cubic phase gels was almost unaffected for 2 months at 37°C, while the majority of insulin in solution appeared to aggregate and precipitate only after 8 days. Therefore, the cubic phase gel was able to protect insulin from agitation-induced aggregation and subsequent precipitation. Furthermore, they investigated the effect of agitation on biological activity of insulin in cubic phase gel by subcutaneous injections of the agitated cubic phase gel, non-agitated cubic phase gel, agitated insulin solution, and normal saline to fasted rats and their blood glucose levels were measured. The blood glucose levels given the non-agitated cubic phase gel and the agitated cubic phase gel were significantly lower ( $P < 0.05$ ) than those in the agitated insulin solution or saline from 40 min

to 4 h. The results suggested that insulin was biologically active in both agitated and non-agitated cubic phase gels. However, upon agitation, insulin in solution totally lost its hypoglycemic activity. In summary, GMO-based cubic phase gel can protect insulin from agitation-induced aggregation. Also evaluated the stability of two model drugs, cefazolin and cefuroxime, in a GMO cubic phase gel. The stability of cefazolin was assessed at two different concentrations (200 and 50  $\mu\text{g/g}$ ), at 22 and 37°C. The results showed that the degradation of cefazolin at lower concentration was 3- and 18-fold slower in cubic phase gel than that in solutions at 22 and 37°C, respectively. At 22 and 37°C, the kinetics of degradation at higher concentration of cefazolin was not first order but a lag phase followed by an exponential loss of cefazolin, which may be due to its oxidation. Later on, the oxidation of cefazolin was confirmed by its 18-fold higher stability in the presence of EDTA and nitrogen in solution. In addition, the degradation rate of cefuroxime was 2 times slower in cubic phase gel than that in solution. In summary, this study clearly demonstrated that cubic phase gel enhanced the chemical stability of cefazolin and cefuroxime.[29]

#### 4) Controlled Drug Delivery:

Liquid crystals prevent the fast release of the drug dissolved in the oil phase of an emulsion. This is attributed to the lamellar liquid crystalline multilayer, which reduces the interfacial transport of a drug dissolved within the oil droplets. Microscopic observations under polarized light show the exceptional thickness of liquid crystalline lamellar layer around the oil droplets.[30]

#### 5) Solubility enhancement of poorly soluble drugs:

Many substances are more soluble in lyotropic liquid crystals. One example is hydrocortisone. It is often taken in topical applications, but its uses have been limited because highest concentration possible has been only 1%. When hydrocortisone went up to 4%. In time, liquid crystals may become a primary solvent for topical medications.[30]

#### 6) Ophthalmic drug delivery:

Ophthalmic delivery is also a topic of interest for which LLC NPs are also being considered as effective drug vehicles. Recent studies show that aspects such as improved precorneal retention, reduction of ocular irritancy and enhanced bioavailability can be attained using cubosomes as nanocarriers for ocular drugs. The trans-corneal permeation of dexamethasone (DEX) and flurbiprofen is enhanced when these drugs are formulated in cubosomes. Indeed, the drug loaded cubosomes are retained in the periocular region much longer than that of the corresponding solutions administered through eye drops, and this enhances their ocular bioavailability. Moreover, the DEX-cubosomes formulation is confirmed not to affect the corneal structure and tissue integrity. For flurbiprofen, cubosomes formulation reduces its inherent irritancy.

## 7) Oral drug delivery

Liquid crystals address the different challenges in oral delivery of several promising compounds together with large molecular size, poor aqueous solubility & poor absorption. In a different application large protein have been used for local activity in the gastrointestinal tract. Liquid crystalline Nanoparticle carriers can be combined with targeting release and controlled release. The particles are intended to procedure in situ in a controlled rate, which permits an effective in vivo distribution of the drug from dosage form. Cubosomes carriers can also be released at various absorption sites, for example in the upper / lower intestine, which is important for the drugs that have narrow absorption window<sup>1</sup> In topical and mucosal depositions Cubic phases are more bio adhesive in the nature, so that they can suitably use in topical & mucosal depositions and delivery of different drugs by dosage forms.

## 8) Intravenous drug delivery systems:

Liquid crystals containing internal liquid crystal structures of curved lipid membranes are used for solubilizing, encapsulating and distributing medicines to disease zones within the body. While liposomes and emulsions have found use as intravenous carriers in drug products, liquid crystal nanoparticle structures improved payloads of proteins, peptides and many insoluble small molecules, and are greatest carriers for injection or infusion of many activities.

## 9) Improve drug bioavailability and reduce drug toxicity:

An important application of LLCs has been to increase bioavailability of drug as well as to reduce toxicity. This can be attributed to targeted drug delivery, lipid metabolism, and increased permeation enhancement of the LCNP, as well as LLC. prepared PT-based cubosomes containing Amphotericin B to increase its bioavailability and reduce nephrotoxicity. After oral administration, bioavailability was found to be 285%, compared to control with minimal nephrotoxicity. Similarly, when developed a cyclosporine A containing GMO/F127-based cubosome system to reduce ocular irritancy. The results showed no form of irritation or cornea or iris damage, justifying the reduced toxicity claims. Although solutions are used as topical application in ocular diseases, removal mechanisms, such as blinking, tear drops, and nasolacrimal leakage are considerable challenges for poor bioavailability, as well as efficacy. The high lipophilicity as well as tight conjuncture creates a hurdle in drug delivery via the ophthalmic route. With a view of all the possible considerations that should be made for increasing bioavailability of drugs by ophthalmic administration, as well as reducing any toxic or irritation effect, cubosomes and hexosomes were considered to have great potential as an ophthalmic drug delivery system. performed studies with cubosomes to increase bioavailability of flurbiprofen by ophthalmic delivery. The studies revealed that cubosomes showed low ocular irritation by the Draize test, and simultaneously showed better bioavailability. Studies conducted by. Reflected similar results. It was found that cubosome formulation exhibited a slower rate of clearance and better retention of fluorescence in the ocular region of interest (ROI) (about 40%) when compared to the



solution. The authors attributed this enhanced ocular retention to the lipid bilayer microstructure provided by cubosomes, which enhanced nonspecific interaction between the cubosomes and the oily layer of the tear film. When compared to carbopol gel of high viscosity, cubosomes showed better retention and less irritation, due to low viscosity. Consequently, we can see how low viscosity and hydrophobic interactions make cubosomes valuable as a vehicle for ophthalmic administration. Intranasal administration of drugs has proved to be an effective way of drug delivery directly to the brain, as it bypasses the blood brain barrier (BBB), thus providing a noninvasive way for treatment of CNS disorders. developed a protocol for surface engineering of PEGylated cubosomes with functional molecules of odorrana lectin. It was seen that the relative uptake of odorranalectin cubosomes was 3.46 times higher than that of untreated cubosomes. Further results showed that the effect of Gly14-humanin improved on using odorrana lectin cubosomes.[14]

#### 10) Ability to sustain or control drug release:

Hexagonal and cubosomal LLC and LCNP have a structure which gives them the inherent property of providing sustained drug release, as has been seen in the cases of drugs such as Vitamin E, oxybutynin hydrochloride, metronidazole timolol maleate (TM), pyrimethamine hemoglobin, insulin, and furosemide, among others. The control of the diffusion coefficient by the dimensionality (d) of the structure appears as a most promising lever to efficiently tune the release rate from LLC phases and dispersed particles towards sustained, controlled, and targeted release. In a hexagonal phase, the drug molecules can only move along the cylindrical water channels, therefore  $d = 1$ . In a lamellar phase, they can move along the planar bilayers ( $d = 2$ ). In bicontinuous cubic phases, the diffusion is regarded as a pseudo-3d process, although it is possible to increase the connectivity in the structure and thereby the diffusion rate by inserting pores in the membrane. In a micellar cubic mesophase, the drug is essentially confined in the micelles ( $d = 0$ ). Recently, demonstrated how sustained absorption of the poorly water-soluble drug cinnarizine was achievable when incorporated into PT-based cubosome after oral administration. The plasma profiles showed plasma concentration being maintained at 21.5  $\pm$  1.5 ng/mL within 12 and 48 h, while the plasma concentration of cinnarizine dropped below the limit of quantification after 24 h when treated with suspensions or GMO-based cubosomes. In addition, it was seen that the nanostructure of PT-based cubosome remained stable in both simulated intestinal and gastric fluid for over 18 h, when detected with the help of SAXR. In contrast, GMO-based cubosomes showed faster degradation. Consequently, the fact that more than 10% of cinnarizine and PT remained in the stomach, even after 24 h, compared to that of GMO-based cubosomes, which went below quantification levels after 4 h. Therefore, it was concluded from the study that it was the non-digestible nature of PT and the ability to maintain the cubosome structure which contributed to the sustained release and absorption of cinnarizine in the stomach. Similar studies were conducted by using GMO and different solubility modifiers in order to formulate a sustained-release oral formulation of furosemide and increased bioavailability of the drug, utilizing inherent properties of the resultant cubic phase of the LCNP. This is also due to increased residence time due to the bioadhesive nature of formulation. Hydrophobic interactions can

also be used to control the transport rates of drugs within lipid mesophases and, as a consequence, control the release rate. used this alternative approach to prolong the drug release from liquid crystalline matrix. The presence of both polar or apolar interface of the cubic phase and the hydrophobic interior of the lipid bilayers was exploited to achieve the slower drug release. Selective alkylation of the model hydrophilic drug tryptophan demonstrated that the length of hydrophobic alkyl chain played a direct role in the degree of drug immobilization within the cubic phase, through anchoring mechanism of the molecule into the interface. This strategy helped in developing formulations of controlled release for amphiphilic drugs, which show a significant partitioning at the lipid-water interface. Another breakthrough in drug delivery systems came with the advent of formulation studies related to LLCs, whereby suitable carriers for delivery and controlled release of bioactive materials were developed. developed two distinct systems, based on a columnar, reverse hexagonal liquid crystalline symmetry for encapsulation, transfection, and controlled delivery of DNA, the choice of symmetry for this class of bioactives is suitable as it provided the thermodynamic stability in excess physiological conditions with 1D symmetry of long water-filled cylinders, particularly suited to encapsulate the long, rigid DNA molecules. The two developed carriers were prepared using either a nonionic lipid (MO) or a mixture of MO and cationic surfactant oleyl amine. The characteristic difference in charge of the developed carriers helped in distinguishing how ionic interactions played a role in the embedment and consequently the controlled release rate of DNA molecules. The neutral mesophase showed it to be an effective carrier as it was seen that hydrogen bonding stabilized the double-stranded DNA and allowed unhindered diffusion of the molecules within the system. In contrast, the ionic interactions between DNA molecules and oleyl amine head groups resulted in quenching of the DNA release in excess water. This strategy may prove useful in designing technologies and formulations for transfection and gene delivery, the impact of ionic interactions to modulate the diffusive properties of the liquid crystalline matrix. In the study, negatively charged distearoyl glycerol (DSPG) was incorporated in neutral MO containing model cationic drug TM. The authors varied the ionic strength within the bilayer lipid mesophase and it was observed that, at low ionic interactions, sustained release of TM over a few days was achievable. However, the same was not achievable on increasing the ionic strength, which triggered a faster release of drugs from the liquid crystal matrix. Consequently, we can conclude from the study that, by controlling the ionic interactions between the lipid bilayer and the drug, we can achieve a desired release rate. used this idea for using ionic interactions to transform small-sized vehicles into cubic phases.[14]

### **11) Melanoma (cancer) therapy:**

Newly same anticancer compounds have been successfully incorporated in liquid crystals and considered physico chemically. The unique structure of this favorable nano carrier recommends its application in melanoma treatment. An object for size does' pass by the tight junctions that exist between the endothelial cell lining of the vessels. Passive targeting is largely reliant on the capability of a drug nanocarrier size to exhibit an improved circulation lifetime resulting in improved accumulation at the specific targeted site.

Circulation time is dictated by nanoparticle physicochemical characters (size, solubility, charge, biodegradability, shape, rigidity), which can be simply manipulated in the majority of the delivery systems defined.

### **12) Drug delivery vehicle:**

The drug delivery vehicle is a general application for such new materials. The rapid development of the life-sciences industry is predictable to drive earlier “exotic” delivery vehicles and excipients into wider market places, such as personal care and consumer products. Therefore, self-assembled surfactant phases have been widely inspected for compatibility with many medical active ingredients & their applications.

### **13) Sustained release behaviour:**

Even more current patent achievement points to liquid crystals use in personal care product areas such as hair care, skin care, cosmetics, and antiperspirants. A wide variety of drugs with different physico-chemical characters have been added in liquid crystals and their sustained release performance was also studied. Sustained behavior of cubosomes was because of cubosome residue particles. Monoglyceride based cubosomes dispersion can be introduced for topical use, as like for percutaneous or mucosal applications. In treatment of viral diseases: Since of the microbicidal stuffs of monoglycerides, can be used to in intravaginal therapy of sexually transferred diseases caused due to viruses (e.g. HSV, HIV) or due to bacterias (e.g. Neisseria gonorrhoeae and Chlamydia trachomatis). Because of similarity between the structure of the stratum corneum and the cubic phase structure, it is judicious to suppose the construction of a mixture of stratum corneum lipids with ribosomal monoolein. This type of interaction may lead to the formation of a cubosomes goods yard in this layer, from which medication can be released in a controlled manner. In topical and mucosal depositions Cubic phases are most bioadhesive by nature, so that they can suitably be used for topical and mucosal depositions and conveyance of different drugs.

### **14) Controlled-Release Drug Delivery**

Controlled release of solubilized actives compounds is the widely used application followed by LCs researchers, and outstanding evaluations occur for delivery applications as well as pharmaceutical active ingredients that have been solubilized in bulk cubic phase and LCs. Cubic phase is most suitable for controlled release because of its very small pore size (5–10 nm); its capability to solubilize hydrophobic, hydrophilic & amphiphilic molecules; in addition, its biodegradability by simple enzyme action. Cubic phase is intensely bioadhesive and it be a skin penetration enhancer, suggestive of good compatibility with topical and mucosal admission and delivery of active ingredients.[31]

**DISCUSSION:**

The discovery of an intermediate, liquid crystal, state of matter is credited to Friedrich Reinitzer

In 1888, Austrian botanical physiologist Friedrich Reinitzer, working at the Karl-Ferdinands-Universität, examined the physicochemical properties of various derivatives of cholesterol which now belong to the class of materials known as cholesteric liquid crystals. Previously, other researchers had observed distinct color effects when cooling cholesterol derivatives just above the freezing point, but had not associated it with a new phenomenon. Reinitzer perceived that color changes in a derivative cholesteryl benzoate were not the most peculiar feature. He found that cholesteryl benzoate does not melt in the same manner as other compounds, but has two melting points. At 145.5 °C (293.9 °F) it melts into a cloudy liquid, and at 178.5 °C (353.3°F) it melts again and the cloudy liquid becomes clear. The phenomenon is reversible. Seeking help from a physicist, on March 14, 1888, he wrote to Otto Lehmann, at that time a Privatdozent in Aachen. They exchanged letters and samples. Lehmann examined the intermediate cloudy fluid, and reported seeing crystallites. Reinitzer's Viennese colleague von Zepharovich also indicated that the intermediate "fluid" was crystalline. The exchange of letters with Lehmann ended on April 24, with many questions unanswered. After this accidental discovery, Reinitzer did not continue studying liquid crystals further. The research was later carried forward by Lehmann, who realized that he had been encountering an entirely new phenomenon and was in a position to investigate it. In his postdoctoral years he had become an expert in crystallography and microscopical studies. Lehmann started a systematic study, first of chemical cholesteryl benzoate, and then of its related compounds which exhibits the double-melting phenomenon. He was then able to make observations in prepolarized light, and his microscope was provided with a hot stage (sample holder equipped with a heater) which enabled high temperature observations. The intermediate cloudy phase may clearly sustain flow, but other features, particularly the signature under a microscope, convinced Lehmann that he was dealing with a solid one. After Lehmann's, his work was continued and scientifically expanded by the German chemist Daniel Vorländer, by whom from the beginning of the 20th century until his retirement in 1935, had prepared many of the liquid crystals known. However, liquid crystals were not popular among scientists at that time and the material remained as a pure scientific curiosity for more than 80 years.

1888: Reinitzer observed the two phenomena, birefringence and the occurrence of iridescent colors between the two melting points in a material that we now were cholesteryl benzole.

1889: Lehmann carried out detail investigation and reasoned that the birefringent portions of the liquid must be crystals. He previously referred to these materials as liquid crystals.

1890: Gattermann blended the principal fluid precious crystals of azoxybenzene, with fully known structures.

1908: D. Vorländer, the first to integrate a thermotropic smectic compound, related liquid crystallinity to chemical structures, detected polymorphism of liquid crystal state.

1922: Freidel identified and named the different microscopic textures (nematic, smectic, and cholesteric), observed the impacts of electric and magnetic fields.

1930: Fredericksz studied the transition from a homogeneous structure at some critical value of applied field strength.

1965: the global liquid crystal society by Glenn Brown at Kent state university. Lehmann and Reinitzer are known as the grandfathers of LCs

science. Liquid crystals are substances that flow like liquid but maintain some of the ordered structure characteristic of crystalline solid. Liquid crystals can be divided into thermotropic and lyotropic phases. The thermotropic is generated by temperature variation in the liquid state, whereas lyotropic is formed by dissolving the compound in certain solvents. The liquid crystal systems have some advantages such as drug solubilization level, drug degradation, biological and chemical sensing, stability of drug, control drug release, light, thin, sustained and controlled release pharmaceutical properties. Liquid crystal technology has had a major effect in many areas of science pharmacy and engineering, as well as device technology. The drug delivery to the site of the target can be achieved by using liquid crystal systems.

## CONCLUSION:

Liquid crystals technique for drug delivery can be effective and useful for delivering the drug with desired target. This technique can be utilized largely in topical delivery of the drug as it possesses the advantages of smooth feel and drug loading of incompatible molecules. Day by day various patents are coming in this liquid crystal's technique. This technique of drug loading is a new & emerging technique that requires attention further for its practice in real scientific industries to deliver a quality outcome for a society. Liquid crystalline structures furnish a broad range of structural and functional characteristics. They hold power to vehicle hydrophobic and hydrophilic drug(s). It seems that these assigns can be well employed in drug delivery gainsays, constructing surfactant established drug delivery systems is a productive approach. This review mainly discusses the investigation of current status of lipid-based liquid crystalline phases as drug delivery systems. Although the cubic and hexagonal phases have been extensively investigated as potential sustained release systems for nearly 30 years, more work needs to be done to further evaluate them in drug delivery systems. Studies with respect to the interactions between the drug and The liquid crystalline phases in vivo are very limited, and the impact of the biological environment on drug release kinetics and biodegradation is also not well understood. The commercialization of these systems in clinical application are challenging, primarily due to the lack of a suitable, scalable manufacturing method. In addition, the choice of commercially available lipids with a desired phase behavior is limited. Nevertheless, the future of lipid-based liquid crystalline delivery systems remains exciting in both academic and industrial sectors.



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