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REVIEW ARTICLE

LIQUID CRYSTALLINE SYSTEM: A NOVEL APPROACH FOR DRUG DELIVERY

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ABSTRACT
Liquid crystaline system is a thermodynamically stable phase which is characterized by anisotropy. LC's are also termed as mesophase as they exhibit isotropic properties and fluid-like behavior under some conditions (change in temperature). LC'S are influenced by number of factors such as concentration, temperature, pH, and presence of salt. Liquid crystals are divided on the basis of shape of the molecules into two groups one is calmitic and other is discotic. The various liquid-crystal phases (called mesophases) can be characterized by the type of ordering. The ordering of liquid crystalline phases is extensive on the molecular scale. The Liquid Crystals are the only holistic representations of the mineral kingdom and most potent form of crystalline energy on earth. Liquid crystal technology has had a major effect many areas of science pharmacy and engineering, as well as device technology. Liquid crystals have a multitude of other uses. They are used for non destructive mechanical testing of materials under stress. 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 such as optical imaging.

Keywords: Liquid crystalline system, crystal technology, mesophase and optical imaging

INTRODUCTION:

a) History

In 1888, Austrian botanical physiologist Friedrich Reinitzer, working at the Karl-Ferdinands-Universität, examined the physico-chemical 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.

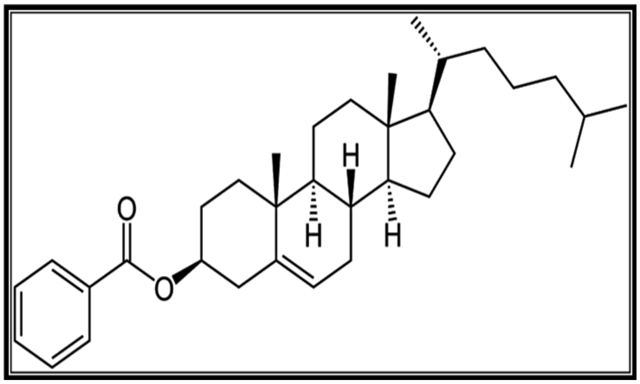

Figure 1: Chemical structure of cholesteryl benzoate molecule

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. Reinitzer presented his results, with credits to Lehmann and von Zepharovich, at a meeting of the Vienna Chemical Society on May 3, 1888.[1]

By that time, Reinitzer had discovered and described three important features of cholesteric liquid crystals (the name coined by Otto Lehmann in 1904): the existence of two melting points, the reflection of circularly polarized light, and the ability to rotate the polarization direction of light.

After his accidental discovery, Reinitzer did not pursue studying liquid crystals further. The research was continued by Lehmann, who realized that he had encountered a new phenomenon and was in a position to

Corresponding author: *Shaikh Zeba* | *E-mail:* *zebashaikh377@gmail.com* investigate it: In his postdoctoral years he had acquired expertise in crystallography and microscopy. Lehmann started a systematic study, first of cholesteryl benzoate, and then of related compounds which exhibited the double-melting phenomenon. He was able to make observations in polarized light, and his microscope was equipped with a hot stage (sample holder equipped with a heater) enabling high temperature observations. The intermediate cloudy phase clearly sustained flow, but other features, particularly the signature under a microscope, convinced Lehmann that he was dealing with a solid. By the end of August 1889 he had published his results in the ZeitschriftfürPhysikalischeChemie.[2]

Lehmann's work was continued and significantly expanded by the German chemist Daniel Vorländer, who from the beginning of 20th century until his retirement in 1935, had synthesized most of the liquid crystals known. However, liquid crystals were not popular among scientists and the material remained a pure scientific curiosity for about 80 years.[3]

b) Defination [4,5]

A liquid crystal is a thermodynamic stable phase characterized by anisotropy of properties without the existence of a three-dimensional crystal lattice, generally lying in the temperature range between the solid and isotropic liquid phase, hence the term mesophase.

Liquid crystals are a class of molecules that, under some conditions, inhabit a phase in which they exhibit isotropic, fluid-like behavior – that is, with little long-range ordering – but which under other conditions inhabit one or more phases with significant anisotropic structure and long-range ordering while still having an ability to flow.

Liquid crystals find wide use in liquid crystal displays, which rely on the optical properties of certain liquid crystalline molecules in the presence or absence of an electric field. In the presence of electric field, these molecules align with the electric field, altering polarization of the light in a certain way.

The ordering of liquid crystalline phases is extensive on the molecular scale but does not extend to the macroscopic scale as might be found in classical crystalline solids. The ordering in a liquid crystal might extend along one dimension, but along another dimension it might have significant disorder.

Liquid crystals are divided into two groups depending on the shape of the molecules. Calamitic liquid crystal consists of rod-like molecules and has order in the direction of the longer axes of the molecules. In contrast, discotic liquid crystals are composed of flat-shaped molecules which align in the direction of the shorter axes of the molecules.

c) Classification

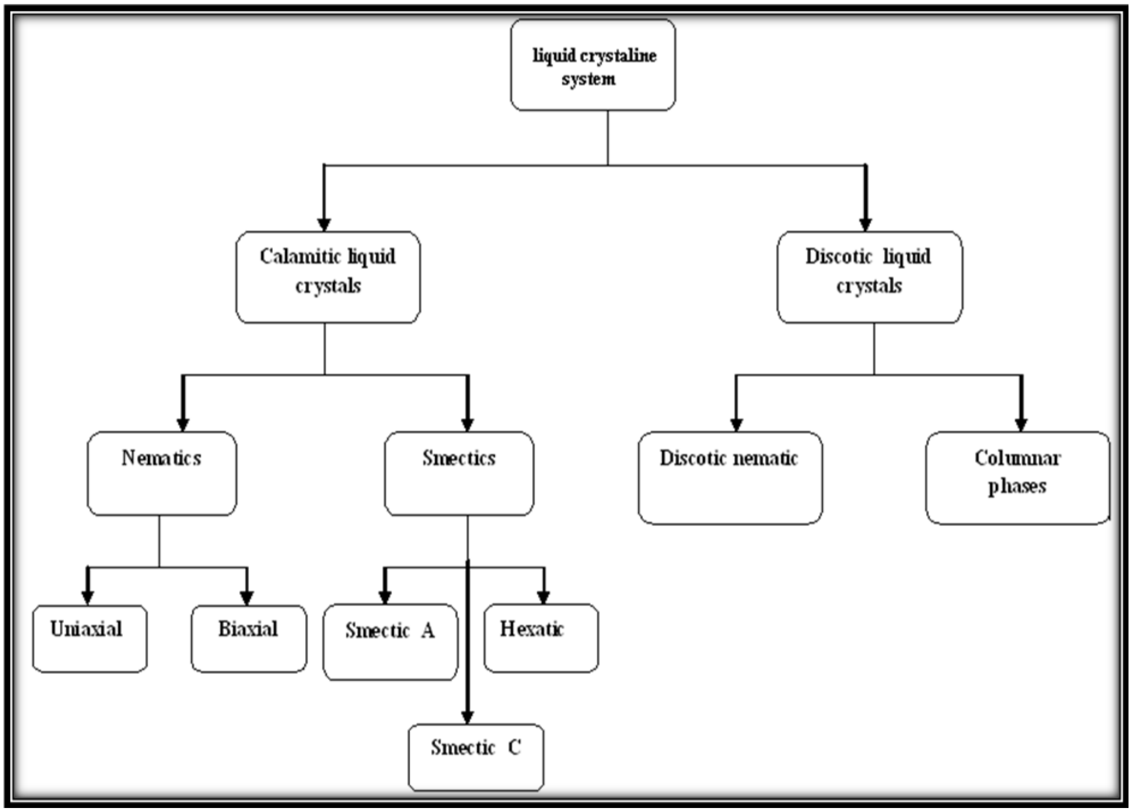

Figure 2: Classification of liquid crystalline system

d) Phases of liquid-crystals

The various liquid-crystal phases (called mesophases) can be characterized by the type of ordering. One can distinguish positional order (whether molecules are arranged in any sort of ordered lattice) and orientational order (whether molecules are mostly pointing in the same direction), and moreover order can be either short-range (only between molecules close to each other) or long-range (extending to larger, sometimes macroscopic, dimensions). Most thermotropic LCs will have an isotropic phase at high temperature. That is that heating will eventually drive them into a conventional liquid phase characterized by random and isotropic molecular ordering (little to no long-range order), and fluid-like flow behavior. Under other conditions (for instance, lower temperature), a LC might inhabit one or more phases with significant anisotropic orientation structure and short-range orientation order while still having an ability to flow[5,6].

The ordering of liquid crystalline phases is extensive on the molecular scale. This order extends up to the entire domain size, which may be on the order of micrometers, but usually does not extend to the macroscopic scale as often occurs in classical crystalline solids. However some techniques, such as the use of boundaries or an applied electric field, can be used to enforce a single ordered domain in a macroscopic liquid crystal sample. The ordering in a liquid crystal might extend along only one dimension, with the material being essentially disordered in the other two directions[7,8].

1) Thermotropic liquid crystals

Thermotropic phases are those that occur in a certain temperature range. If the temperature rise is too high, thermal motion will destroy the delicate cooperative ordering of the LC phase, pushing the material into a conventional isotropic liquid phase. At too low temperature, most LC materials will form a conventional crystal[5,6]. Many thermotropic LCs exhibit a variety of phases as temperature is changed. For instance, a particular type of LC molecule (called mesogen) may exhibit various smectic and nematic (and finally isotropic) phases as temperature is increased.

Example: para-azoxyanisole[9]

a) Nematic phase

One of the most common LC phases is the nematic. The word *nematic* comes from the Greekνήμα (*nema*), which means "thread". This term originates from the thread-like topological defects observed in nematics, which are formally called 'disclinations'. Nematics also exhibit so-called "hedgehog" topological defects. In a nematic phase, the *calamitic* or rod-shaped organic molecules have no positional order, but they self-align to have long-range directional order with their long axes roughly parallel.[10]

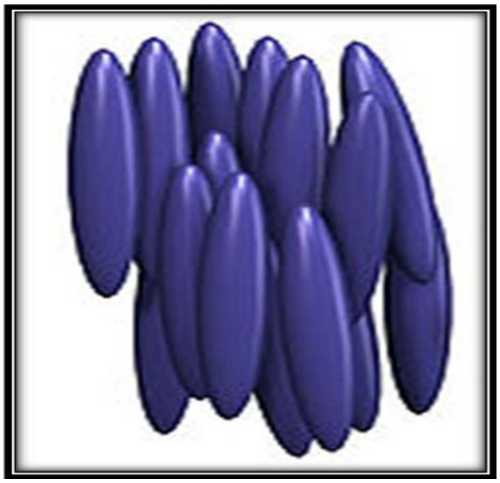

Figure 3: Alignment in a nematic phase

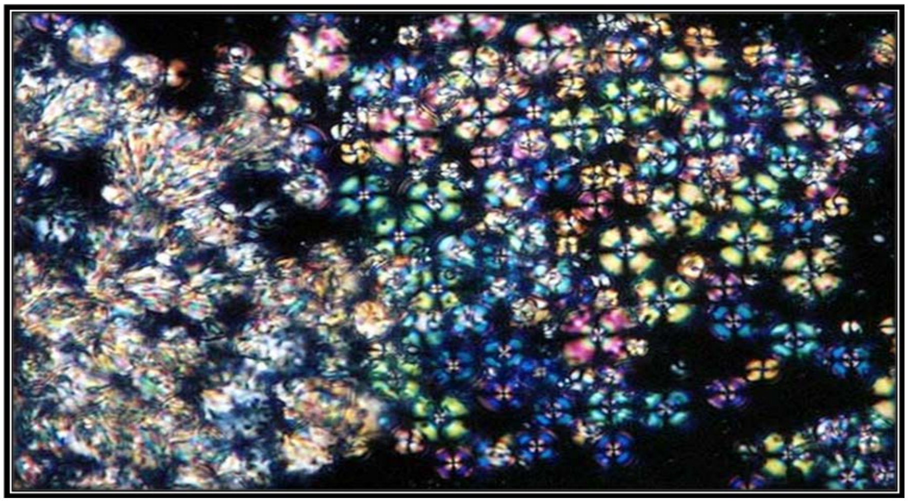

Figure 4: Phase transition between a nematic (left) and smectic A (right) phases observed between crossed polarizer and the black colour corresponds to isotropic medium.

b) Smectic phases

The smectic phases, which are found at lower temperatures than the nematic, form well-defined layers that can slide over one another in a manner similar to that of soap. The word "smetic" originates from the Latin word "smecticus", meaning cleaning, or having soap like properties.[11] The smectics are thus positionally ordered along one direction. In the Smectic A phase, the molecules are oriented along the layer normal, while in the Smectic C phase they are tilted away from the layer normal. These phases are liquid-like within the layers. There are many different smectic phases, all characterized by different types and degrees of positional and orientational order.[5,6]

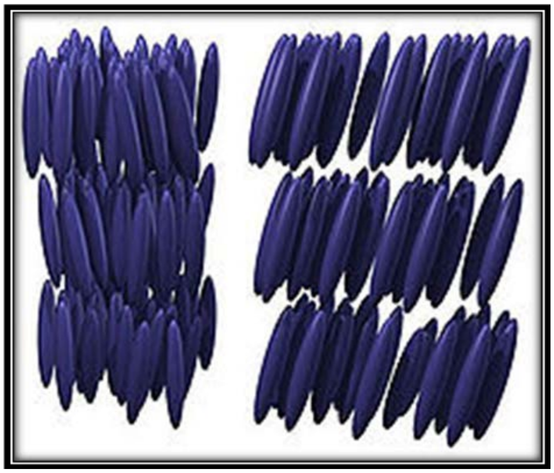

Figure 5: Schematic of alignment in the smectic phases.

The smecticA phase (left) has molecules organized into layers. In the smectic C phase (right), the molecules are tilted inside the layers.

c) Chiral phases

The chiral nematic phase exhibits chirality (handedness). This phase is often called the *cholesteric* phase because it was first observed for cholesterol derivatives. Only chiral molecules (i.e., those that have no internal planes of symmetry) can give rise to such a phase. This phase exhibits a twisting of the molecules perpendicular to the director, with the molecular axis parallelto the director. The finite twist angle between adjacent molecules is due to their asymmetric packing, which results in longer-range chiral order. In the smectic C* phase (an asterisk denotes a chiral phase), the molecules have positional ordering in a layered structure (as in the other smectic phases), with the molecules tilted by a finite angle with respect to the layer normal. The chirality induces a finite azimuthal twist from one layer to the next, producing a spiral twisting of the molecular axis along the layer normal[6,7,8].

Figure 6: Schematic of ordering in chiral liquid crystal phases.

The chiral nematic phase (left), also called the cholesteric phase, and the smectic C* phase (right).

The *chiral pitch*, p, refers to the distance over which the LC molecules undergo a full 360° twist (but note that the structure of the chiral nematic phase repeats itself every half-pitch, since in this phase directors at 0° and ±180° are equivalent). The pitch, p, typically

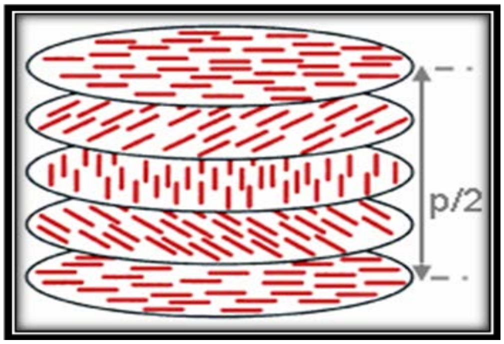

Figure 7: Chiral nematic phase; p refers to the chiral pitch

d) Blue phases

Blue phases are liquid crystal phases that appear in the temperature range between a chiral nematic phase and an isotropic liquid phase. Blue phases have a regular three-dimensional cubic structure of defects with lattice periods of several hundred nanometers, and thus they exhibit selective Bragg reflections in the wavelength range of visible light corresponding to the cubic lattice. It was theoretically predicted in 1981 that these phases can possess icosahedral symmetry similar to quasicrystals.[12,13]

Although blue phases are of interest for fast light modulators or tunable photonic crystals, they exist in a very narrow temperature range, usually less than a few kelvin. Recently the stabilization of blue phases over a temperature range of more than 60 K including room temperature (260–326 K) has been demonstrated.[14][15] Blue phases stabilized at room temperature allow electro-optical switching with response times of the order of 10^{-4} s.[16]

e) Discotic phases

Disk-shaped LC molecules can orient themselves in a layer-like fashion known as the discoticnematic phase. If the disks pack into stacks, the phase is called a discotic columnar. The columns themselves may be organized into rectangular or hexagonal arrays. Chiral discotic phases, similar to the chiral nematic phase, are also known.

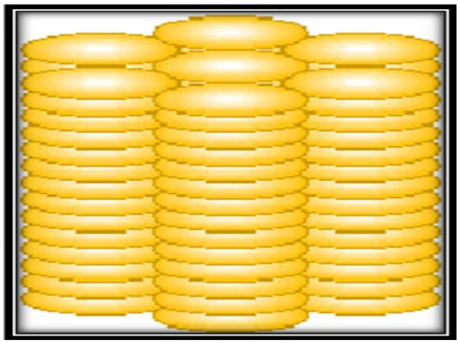

Figure 8: Schematic of Columnar phases

2) Lyotropic liquid crystals

A lyotropic liquid crystal consists of two or more components that exhibit liquid-crystalline properties in certain concentration ranges. In the lyotropic phases, solvent molecules fill the space around the compounds to provide fluidity to the system.[17] In contrast to Thermotropic liquid crystals, these lyotropics have another degree of freedom of concentration that enables them to induce a variety of different phases.

A compound that has two immiscible hydrophilic and hydrophobic parts within the same molecule is called an amphiphilic molecule. Many amphiphilic molecules show lyotropic liquid-crystalline phase sequences depending on the volume balances between the hydrophilic part and hydrophobic part. These structures are formed through the micro-phase segregation of two incompatible components on a nanometer scale. Soap is an everyday example of a lyotropic liquid crystal.

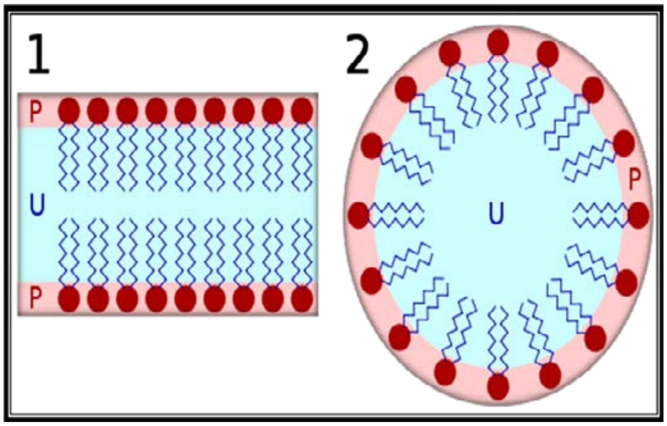

Figure 9 (1) & 9 (2): Structure of lyotropic liquid crystal.

The red heads of surfactant molecules are in contact with water, whereas the tails are immersed in oil (blue): bilayer (left) and micelle (right).

A generic progression of phases, going from low to high amphiphile concentration, is:

- Discontinuous cubic phase (micellar cubic phase)
- Hexagonal phase (hexagonal columnar phase) (middle phase)
- Lamellar phase
- Bicontinuouscubic phase
- Reverse hexagonal columnar phase
- Inverse cubic phase (Inverse micellar phase)

3) Metallotropic liquid crystals

Liquid crystal phases can also be based on low-melting *inorganic* phases like $ZnCl_2$ that have a structure formed of linked tetrahedra and easily form glasses. The addition of long chain soap-like molecules leads to a series of new phases that show a variety of liquid crystalline behavior both as a function of the inorganic-organic composition ratio and of temperature. This class of materials has been named metallotropic.[18]

e) Physical properties of liquid crystal

1) Optical property:

Optical property (Birefringence)of liquid crystalline system can be defined as the resolution or splitting of a light wave into two unequally reflected or transmitted waves by an optically anisotropic medium such as calcite or quartz.

2) Dielectric property:

Dielectric property of liquid crystalline system can be defined as the material that does not conduct electicity readily.

3) Diamagnetic property:

Diamagnetic property of liquid crystalline system can be defined as the property exhibited by substances with a negative magnetic susceptibility, that is, by substances which magnetize in a direction opposite to that of an applied magnetic field.

f) Factors affecting on properties of liquid crystals

1) Effect of concentration:

Concentration of ampiphillic molecules is directly proportional to the properties of Liquid crystal [23].

2) Effect of temperature:

Temperature of ampiphillic moleculesis directly proportional to the properties of Liquid Crystal [24].

3) Effect of salt addition:

The addition of sodium &potassium salts shifts the isotropic-nematic phase boundary upward by more than 10^0C, so that were isotropic at room temperature are transformed into nematic phases [25].

4) Effect of pH:

With addition of salt to the solution or lowering the pH, hydrophilic interaction of head is reduced and optimal interface area is lowered[26].

g) Chemical properties of liquid crystals

Liquid crystals can be classified into two main categories: thermotropic liquid crystals,and lyotropic liquid crystals. These two types of liquid crystals are distinguished by the mechanisms that drive their self-organization, but they are also similar in many ways. Thermotropic transactions occur in most liquid crystals, and they are defined by the fact that the transitions to the liquid crystalline state are induced thermally. That is, one can arrive at the liquid crystalline state by raising the temperature of a solid and/or lowering the temperature of a liquid. Thermotropic liquid crystals can be classified into two types: enantiotropic liquid crystals, which can be changed into the liquid crystal state from either lowering the temperature of a liquid or raising of the temperature of a solid, and monotropic liquid crystals, which can only be changed into the liquid crystal state from either an increase in the temperature of a solid or a decrease in the temperature of a liquid, but not both. In general, thermotropic mesophases occur because of anisotropic dispersion forces between the molecules and because of packing interactions.

A very large number of chemical compounds are known to exhibit one or several liquid crystalline phases. Despite significant differences in chemical composition, these molecules have some common features in chemical and physical properties. There are two types of thermotropic liquid crystals: discotics and rod-shaped molecules. Discotics are flat disc-like molecules consisting of a core of adjacent aromatic rings. This allows for two dimensional columnar ordering. Rod-shaped molecules have an elongated, anisotropic geometry which allows for preferential alignment along one spatial direction. The 5CB is rod-like low molar mass (LMM) liquid crystal.

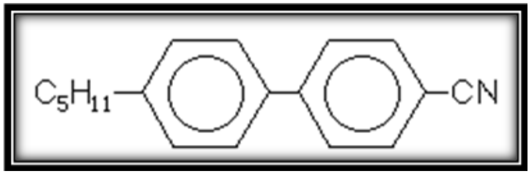

Figure 10: 5CB P-N pentyl-p-cyanobiphenyl (PCB)

That is, in order for a molecule to display the characteristics of a liquid crystal, it must be rigid and rod-shaped. This is accomplished by the interconnection of two rigid cyclic units. The interconnecting group should cause the resulting compound to have a linear planar conformation. Linking units containing multiple bonds such as - (CH=N)-, -N=N-, -(CH=CH)n-, -CH=N-N=CH-, etc. are used since they restrict the freedom of rotation. These groups can conjugate with phenylene rings, enhancing the anisotropic polarizability. This increases the molecular length and maintains the rigidity[19].

B) POLYMERS USED IN LIQUID CRYSTALLINE SYSTEM

Main Chain Polymer Liquid Crystals are formed when rigid elements are incorporated into the backbone of normally flexible polymers. These stiff regions along the chain allow the polymer to orient in a manner similar to ordinary liquid crystals, and thus display liquid crystal characteristics. There are two distinct groups of MC-PLCs, differentiated by the manner in which the stiff regions are formed.

The first group of main chain polymer liquid crystals is characterized by stiff, rod-like monomers. These monomers are typically made up of several *aromatic* rings which provide the necessary size. The following diagram shows an example of this kind of MC-PLC.

The second and more prevalent group of main chain polymer liquid crystals is different because it incorporates a mesogen directly into the chain. The mesogen acts just like the stiff areas in the first group. Generally, the mesogenic units are made up of two or more aromatic rings which provide the necessary restriction on movement that allow the polymer to display liquid crystal properties. The stiffness necessary for liquid crystallinity results from restrictions on rotation caused by steric hindrance and resonance. Another characteristic of the mesogen is its axial ratio. The axial ratio is defined to be the length of the molecule divided by the diameter (x = L/d). Experimental results have concluded that these molecules must be at least three times long as they are wide. Otherwise, the molecules are not rod-like enough to display the characteristics of liquid crystals.

This group is different from the first in that the mesogens are separated or "decoupled" by a flexible bridge called a spacer. Decoupling of the mesogens provides for independent movement of the molecules which facilitates proper alignment. The following is a diagram of this type of main chain polymer liquid crystal. Notice the flexible spacer (methylene groups) and the stiff mesogen (aromatic ring and double bonds).

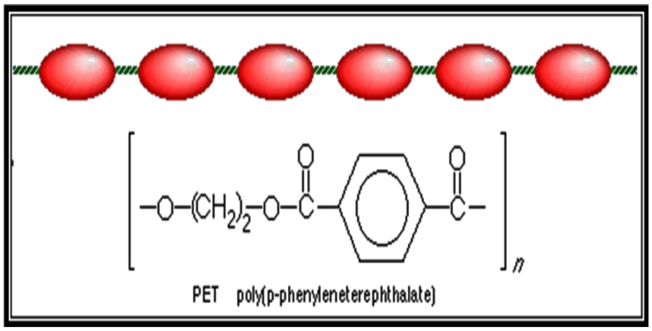

Figure 11: Ply (p-phenyleneterephthalate)

C) ADVANTAGES

- Direct internal contact with the crystals healing energies and Geometric structures allows the biggest advantage for many people concerning the liquid crystals will be cost; it is my intention, that everyone will have the ability to experience the energies of the mineral kingdom, including the more expensive minerals such as Diamond.
- The physical crystals within the earth are resources and will run out one day, the Liquid Crystals, won't and we don't even need to destroy the Earth to get them.
- Via the Liquid Crystals, one can open to the highest aspects of the mineral kingdom, The Master Devas, a door rendered hidden at the fall of ancient Atlantis when the individual minerals were last separated across Earth.
- Although in liquid form a Liquid Crystal retains all its programmability allowing us to get it to work, how and where we need it, even within the body.
- The Master Deva of the crystal becomes an over-lighting force for the patient for the course of treatment, an extra form of guidance.
- By reuniting crystals from every part of the world into oneness, The Liquid Crystals are the only holistic representations of the mineral kingdom and most potent form of crystalline energy on earth.
- Due to the holistic nature of the liquid crystals we have a consistent frequency not dependant on one or several Crystals, but hundreds and sometimes thousands of individuals united in Oneness.
- The Liquid Crystals utilize the healing and energy conducting ability of Water which magnifies the effects of the remedy.

D) GENERAL METHOD FOR THE PREPRATION OF LIQUID CRYSTALLINE SYSTEM:

A liquid can be converted into a liquisolid system without being further modified. On the other hand, if a solid water-insoluble drug (e.g. hydrochlorothiazide, prednisone, etc,) is formulated, it should be initially dissolved or suspended in a suitable non-volatile solvent system to produce a drug solution or drug suspension of desired concentration. Next, a certain amount of the prepared drug solution or suspension, or the liquid drug itself, is incorporated into a specific quantity of carrier material which should be preferably of a porous nature and possessing sufficient absorption properties, such as powder and granular grades of microcrystalline and amorphous cellulose are most preferred as carriers. The resulting wet mixture is then converted into a dry-looking, non adherent, free flowing and readily compressible powder by the simple addition and mixing of a calculated amount of coating material.

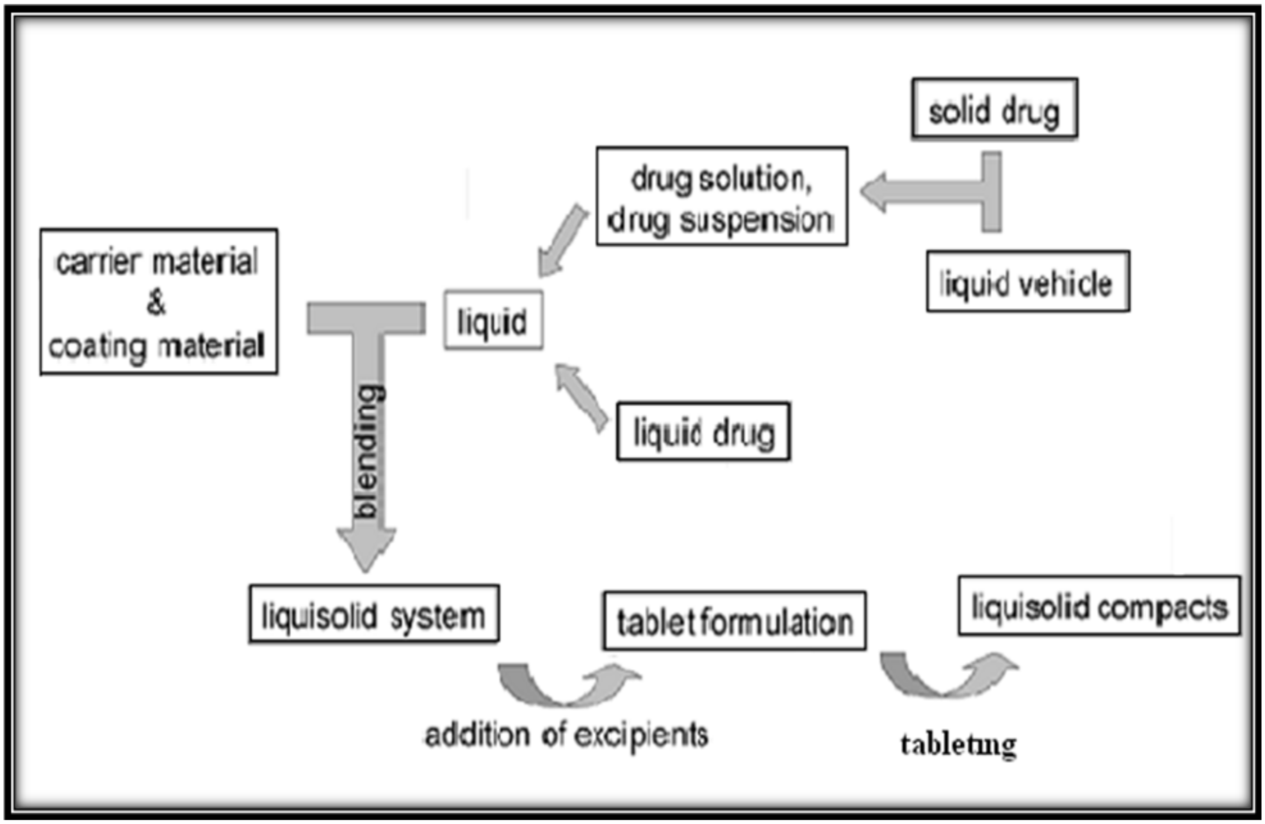

Figure 12: General method of preparation of the liquisolid compact Components of Liquisolid compacts for sustained release

E) EVALUATION PARAMETERS OF LIQUID CRYSTALLINE SYSTEM

1) Macroscopic view

Optical polarizing microscopy is standard tool in identification of liquid crystal phases and transition but requires considerable experience, partcularly in study of less familiar materials.

2) X-Ray diffraction

X-Ray diffraction is very useful tool in identification of liquid crystal phases and phase transitions. It is useful in determining surface texture of liquid crystal during phase transition process [35].

3) Differential scanning calorimetry

Differential scanning calorimetry is useful tool which complements optical methods in study of liquid crystal phase transitions. Its utilization in determining heat supplied or extracted drug during process such as phase transition[35].

4) Content uniformity

Ten tablets from each batch were taken randomly to examine its content uniformity. Each tablet was weighed and crushed individually. The crushed tablet powders were dissolved in acetonitrile water system. The solution was filtered using Whatman filter paper. The drug content was measured using UV spectrophotometer (Shimadzu corporation Pvt. Ltd Nishinokyo-Kuwabara-cho, Nakagyo-ku, Kyoto 604-8511, Japan) at 241 nm.

5) Flow properties of the liquisolid system

The flow properties of the liquisolid systems were estimated by determining the angle of repose, Carr's index and Hausner's ratio. The angle of repose was measured by the fixed funnel method. The bulk density and tap density were determined for the calculation of Hausner's ratio and Carr's index.[36]

6) Infra red spectra analysis

IR spectrum of optimized formulation was recorded by KBr method using Jasco M4100 Fourier Transform InfraRed spectrophotometer. A baseline correction was made by using dried potassium bromide and then the spectrum of powder with potassium bromide was recorded. Sample was scanned from 4000 to 400 cm^{-1}. The compatibility of drug and other excipients in formulation was confirmed by comparing drug and formulation spectra.

F) APPLICATIONS

Liquid crystal technology has had a major effect many areas of science pharmacy 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 many different problems.

A) Pharmaceutical application

1) 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[27].

2) Controlled/sustained release of drug

Application of mesophases (liquid crystal) in pharmaceutical drug delivery systems depend upon their properties. Lipid-based liquid crystalline materials, formed by swelling of certain polar lipids when exposed to aqueous environments, have received much recent attention in drug delivery field for their ability to sustain the release of a wide range of molecules[28].

E.g. Lyotropic liquid crystal per-concentrates for treatment of periodontal disease

This study was done for development of water-free lyotropic liquid crystalline perconcentrates, whichcosist of oils and surfactants with good physiological tolerance and spontaneously formlyotropic liquid crystalline phase in aqueous environment. In this way these perconcentrates 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 pocket due to its great viscosity, while drug release is controlled by liquid crystalline texture. Lyotropic liquid crystal was formed by using mixture of surfactants (Cremophor EL, Cremophor RH40) and oil (Miglyol 801) up on addition of water [29].

Example of Lamellar Liquid Crystals containing Glycerol:-

Lamellar lyotropic liquid crystal was formed by using Brij 96 (poly-oxyethylene-10-oleyl ether) with water, liquid petrolatum (LP) and glycerol.

3) Stability of drug:

Lyotropic liquid crystals have been used to make stable hydrocarbon foam. Hydrocarbon foams have been difficult to produce in the past because surface tension of hydrocarbon is low enough that adsorption to an oil-soluble surfactant would have no significant effect. Without adsorption, hydrocarbon simply behaves as liquid. When lyotropic liquid crystal molecules change from inverse micelles to form. The hydrocarbon and surfactant can dissolve in each other, and surfactant cannot dissolve in water, although water can dissolve in the surfactant and mix into the liquid crystal [30].

4) Effect of base and salts from different liquid crystalline structures on drug release profile:

This study was done for investigate the influence of two types of chlorhexidine species, chlorhexidine base and its salts, on physicochemical features of liquid crystalline systems and on drug transport through liophilicmembranes. For this non-ionic surfactant, Synperonic A7(PEG7-C13-15)was selected for the liquid crystal formulation. Chlorhexidine species was modified liquid crystalline system. As a result of changes of liquid crystalline structures, drug release of various types of chlorhexidine could be also modified[31].

5) Photopolymerization of lyotropic liquid crystalline systems: A new route to nano structured materials:

A novel route to fabricating such materials is through the use of lyotropic liquid crystals (LLCs)that possess highly ordered nano structures. However, LLC phases lack necessary physical robustness.So, templating LLC phase morphology onto other materials such as organic polymers would give a nanostructure retained as part of a robust polymeric matrix.This study focuses on photopolymerization behavior and structure reteintion of hydroxyethyl acrylate (HEA)/dodecyltrimethyl ammonium bromide(DTAB)/water system in a select liquid crystal phase.

6) Nanosrtucture hexosome for injectable drug delivery:

A new class of amphiphiles with a glycerateshead group, recently shown to form reverse hexagonal phase in excess water,have been dispersed to form Hexosome dispersions comparising sub-200 nm particles retaining the internal nanostructure of parent Hexosomephase. The application of these novel materials to development of a new injectable formulation of irinotecan was investigated. The formulation of irinotecan with a small percentage of oleic acid in oleylglycerate permitted a clinically relevant dose of irinotecan to be dissolved in glycerate surfactant and dispersed in aqueous medium to form an injectable particle-base dose form of irinotecan[32].

7) Tempereture modulated drug permeation through liquid crystal embedded cellulose membranes

Stimuli-sensitive membranes may act as “on-off switches” or “permeability valves”, producing patterns of pulsatile release, where the period and rate of mass transfer can be cotrolled by external or environmental triggers.Cellulose nitrate(CN)and cellulose acetate(CA) monolayer membranes containing thermotropic liquid crystals(LC)were developed as thermoresponsivebarriers for drug permeation. A low molecular thermotropic liquid crystal, n-heptyl-cyanobiphenyl, with nematic to isotropic phase transition temperature of 41.5^{0}C was chosen to modulate drug permeation. It was found that upon changing temperature, both cellulose membrane without liquid crystal showed no temperature sensitivity to drugpermeation, whereas the results for liquid crystal entrapped membranes exhibited a distinct jump in permeability when temeperature was raised to above transition temeperature of liquid crystal for drug[33].

8) Liquid crystal for treatment of cancer and other disease

The most recent research involving LCPs has yielded new investigational anti-tumor drug called Tolecine, compound that also has antiviral and antibacterial application. Created by Tsai, it has been shown to be even more effective than the current standard of care for herpes.

The patent application involves formulation that combines Tolecine and Aoatone®, which attacks cancer cells via multiple pathways to offer improved efficacy. Apatone® has been successfully tested in more than 30 human tumor cell lines at Summa and in phase I/IIa clinical trial, which demonstrated delaying effect in progression of end-stage cancer patients. In addition, FDA granted Apatone® orphan-drug status for treatment of metastatic, or locally advanced inoperable bladder cancer in Augast 2007[34].

B) In technical field:

1) Liquid Crystal Displays

The most common application of liquid crystal technology is liquid crystal displays (LCDs). This field has grown into a multi-billion dollar industry, and many significant scientific and engineering discoveries have been made. Please refer to the LCD chapter for more detail.

2) Liquid crystal thermometers

As demonstrated earlier, chiral nematic (cholesteric) liquid crystals reflect light with a wavelength equal to the pitch. Because the pitch is dependent upon temperature, the colour reflected also is dependent upon temperature. Liquid crystals make it possible to accurately gauge temperature just by looking at the colour of the thermometer. By mixing different compounds, a device for practically any temperature range can be built.

The "mood ring", a popular novelty a few years ago, took advantage of the unique ability of the chiral nematic liquid crystal. More important and practical applications have been developed in such diverse areas as medicine and electronics. Special liquid crystal devices can be attached to the skin to show a "map" of temperatures. This is useful because often physical problems, such as tumours, have a different temperature than the surrounding tissue. Liquid crystal temperature sensors can also be used to find bad connections on a circuit board by detecting the characteristic higher temperature.

3) Optical imaging

An application of liquid crystals that is only now being explored is optical imaging and recording. In this technology, a liquid crystal cell is placed between two layers of photoconductor. Light is applied to the photoconductor, which increases the material's conductivity. This causes an electric field to develop in the liquid crystal corresponding to the intensity of the light. The electric pattern can be transmitted by an electrode, which enables the image to be recorded. This technology is still being developed and is one of the most promising areas of liquid crystal research.

C) Other liquid crystal applications

Liquid crystals have a multitude of other uses. They are used for non destructive 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.

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