LIQUID CRYSTALS: - A NOVEL APPROACH DRUG DELIVERY SYSTEM

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ABSTRACT:-

The liquid crystal system have approach towards physical and chemical properties. Now a days liquid crystal are becoming a choice for the research and development process in the pharmaceutical field. The liquid crystal systems have some advantages such as drug solubilisation level, drug degradation, control drug release, light, thin, sustained and controlled release pharmaceutical properties. The drug delivery to site of target can be achieved by using liquid crystal systems. Depending on the composition of polar lipids and surfactants they exhibit a phase behaviour in aqueous environment.

This review will give us information regarding about liquid crystals, their types, phases involved, methods of preparation, evaluation parameters.

KEYWORDS :- Crystal, target site, pharmaceuticals uses, evaluation.

I. INTRODUCTION: -

Liquid crystal name was given by Lehmann (1899) to characterise the state of matter. It is also known as mesophase which explains a state of matter that is intermediate between the crystalline solid and the amorphous liquid. They have properties in between liquid and solids, which makes a new form of state. Liquid crystal have property of solid and liquid, which have anisotropy effect. Depending on the order and symmetry the molecule have to pass one or many phases. They are found birefringent due to anisotropic nature. Liquid crystals are classified into two i.e. lyotropic and thermotropic mesophases.

Mesophase is called a thermodynamic stable phases having anisotropy property without the existence of a three-dimensional crystal lattice, which generally lyes in the temperature range between the solid and isotropic liquid phase. Liquid crystal of thermotropic can be formed by temperature, when the lyotropic phases are formed they get mix in the aqueous phase. They have many properties of liquid e.g. formation of droplets, fluidity is high, inability to shear. It has various properties. (a) comparative energy of intermolecular forces in the liquid crystal.(b) less intermolecular interaction in liquid crystal. It has properties of cubic and hexagonal phases which makes them important to deliver for the scientists through various routes such as buccal, gastrointestinal, rectal, vaginal, lung. The liquid crystal has strong adhesion molecule in liquid crystal and it was weak.

II. TYPES OF LIQUID CRYSTAL:-

1. Lyotropic liquid crystal:-

It is also called as lyomesophases or lyotropics which is mixture of amphiphilic molecules in solvent at given tempaerature and concentration. It can be classified as lamellar, cubic and hexagonal. In this solvent molecules will fill space around the compound to have fluidity in system.

A compound which has two immiscible hydrophilic and hydrophobic within molecule is called amphiphilic molecule. Those molecules show lyotropic liquid crystalline property which depend on hydrophilic and hydrophobic part. These structure formed through micro-phase segregation of two incompatible components.

2. Thermotropic Liquid Crystal:-

In the thermotropic liquid crystal it has a particular range of temperature. When there is rise in temperature which is too high the thermal motion may destroy the duplicate cooperative phases of order.

a. Nematic phase:-

In this molecules have a long-range orientational order with molecular axes aligned in a direction. In the positions of centres of mass there is no long-range order. It is also called "hedgehog" topological defects.

b. Sematic phase:-

It can be distinguished into type and degree of orientation and position. The most important feature of sematic phase is different from nematic phase. The molecules are arranged in form of layers and have similarity in position to the addition of order.

c. Chiral phase:-

The chiral phase exhibit chirality. It is also called as cholesteric phase because it was 1st observed for cholesterol derivatives. Only chiral molecules give raise to such phase. They exhibit changes in its director having molecular axis parallel.

d. Blue phase:-

This liquid crystal phases are produced by the temperature range between an isotropic liquid phase and chiral nematic phase. Blue phases have a 3 dimensional cubic structure with some defects and lattice periods of few hundred nanometers.

e. Discotic phase:-

Discotic phase is having disc- shaped compound of liquid crystal which get involve in fashion which is layer-like. The discotic phase is the discks which is pack into stacks. Discotic columnar is called as chiral discotic phases which is similar to chiral nematic phase. Rectangular or hexagonal arrays both of them get involved in the column.

III. IDEAL CHARACTERISTICS OF LIQUID CRYSTAL:-

1. There are two types of liquid crystal such as lyotropic and thermotropic liquid crystal.
2. The liquid crystal can flow similar to liquid due to transtition phase.
3. Discotics phases are flat having disc-like molecules which has core adjacent to aromatic rings.
4. A large number of chemical compounds are known which can exhibit one or several liquid crystal phases.
5. Liquid crystal phases are mostly cloudy in appearance that they scatter light in same way as colloids.

IV. METHODS:-

1. Top-Down Approach:-

In 1966 the approach was given by Ljusberg-Wahren. By mixing lipid and stabilizer the viscous bulk phase was prepared and then poured into aqueous phase which has more energy (high pressure homogenization [HPH], sonication or shearing.

Worle et al. investigated the parameters having properties glyceryl monooleate based cubosomes. The observed results in which the temperature of F-127 concentration during the process was having important parameter. Now a days to prepare nanoparticles of liquid crystal the approach was used in a laboratory shearing apparatus.

2. Bottom-Up Approach:-

In this approach the factor is hydroptope, which can dissolve water-insoluble lipids to form liquid precursors and can prevent the concentration. Compared with the top-down approach,, the dilution based approach can be produce through cubosomes without fragmentation. It has less input. The top-down approach is similar of bigger particles. The dilution based approach having larger or greater particles aggregation. Which is similar to use for precipitation process to produce nanoparticle.

The bottom-up approach cannot be effectively avoid by forming vesicles. The addition of hydrotope has many issues such as effects of varying concentration of hydrotope on possible allergic problems and nanoparticle which is having chemical and physical properties when the whole formulation is administered into the mesophase. Cubosomes by dilution process has long term stability, which may affect to homodisperse stabilizer into cubosomes.

3. Spray drying:-

To have more effect in cubosomes in field of pharmaceutical, dry powder precursor was prepared by spray drying and used in preparation of solid oral fomulations and inhalants. It was given by Spicer et al. In his research dry powder precursor was prepared by drying a pre-dispersed aqueous solution which consists of GMO, hydrophobically starch and water, water and ethanol and the colloidal stable dispersions of nanostructured cubosomes obtained by hydration of precursors.

After Shah et al. prepared with the help of spray drying they have prepared cubosomes of glycerylmonooleate which has diclofenac sodium. Cubosomes prepared through dilution show long term stability, which might be attributed to homodisperse stabilizer into cubosomes. The addition of hydrotope has many issues such as effect of varying concentration of hydrotope which effect on allergy when the formulation of mesophase are to be administered. When pure drug is orally administered it has effect on analgesic and anti-inflammatory effect on drug. While there was a problem in the solvent residue which can't be ignored.

4. Solvent Displacement:-

In fast diffusion of organic solvent it contains surfactant to get the nanoemulsion preparation by adding oil phase and was dissolved in water organic solvent which is miscible it contains solvent such as ethanol, acetone which was poured into the aqueous phase. The solvent was removed from emulsion by vaccum evaporation. By this method can get yield of nanoemulsion at room temperature which require stirring for production. This technique is mainly used for parenteral purpose. The method drawback is use of solvent which has contribution for removal of emulsion.

5. Heat treatment:-

To provide the effect of drug release of sustained of more component of cubosomes which consists of vesicles. Hence, to have better release behaviour of mesophase, vesicles should be perminated as possible. The heat-treatment step and homogenization of dispersed particles could be prepared by simple process. Good result was obtained in this approach by the heat. The studies shows that treatment of heating have a small decrease in size of particle fraction which correspond to vesicles which has good effect on colloidal stability and which has multi cubic phases with the broader distribution of particle.

The whole process tells about the transtition takes place during the process. The reason is temperature is removed which results reduction in solution and stability. The surfactant which has more solubility when the temperature is below, so particle has effect on the stability was observed. The system loading drug such as protein and temperature sensible drug which are not suitable and can't provide effect on stability under a more temperature.

6. Phase Inversion Method(Self-Nanoemulsion Method):-

It has more application in many fields from expert in pharmaceutical science as it generates formulation of nanoemulsion at a room temperature by any effect on heat and organic solvent. Nanoemulsion which is stable and has droplet size small 50nm could be achieved. It is thermodynamically stable and have high energy. Addition of water stepwise in the solution of surfactant in oil which has more stirring at a temperature which is constant. Nanoemulsification is a automatic process which may be related to phase transtition when the process of emulsification has involved D-type bicontinuous microemulsion or lamellar liquid crystalline phases.

7. Microfluidization:-

Micofluidizer is a technology of mixing it uses this device. The device used is high-pressure displacement pump about 500-20,000psi, which force the residue in the chamber of interaction which consist of channels which is small called "microchannels". The content which moves through a channel into area which result in small particle micron range. The oily phase and aqueous phase are complied with each other so process takes place to have coarse emulsion. Nanoemulsion is a stable and the emulsion in microfluidizer. To remove large droplets which result in nanoemulsion which is uniform and was filtered by filter under nitrogen. This device which uses nanoemulsion for fabrication at industrial scale and laboratory.

V. EVALUATION PARAMETERS:-

1. Morphology:-

The morphology can be determined by transmission electron microscopy and scanning electron microscopy. In the scanning electron microscopy it gives a three dimensional images of globules. The samples are examined at accelerating voltage usually 20kV, at different magnification. A good analysis of surface morphology of dispersed phase in the formulation is obtained through SEM. In TEM, higher resolution images of the dispersed phase can be obtained. The sample is negatively stained with one percentage aqueous solution of phosphotungistic acid or by dropping 2% uranyl acetate solutions onto a 200ml mesh size Pioloform^{TM} coated copper grid ora microscopic car-boncoated grid using a micropipette and the sample can be examined under the transmission electron microscope at 80 kV.

2. Internal morphology:-

Nanoemulsion characteristics can be studied including internal morphology (confocal microscopy), crystalinity by encapsulation efficiency and stability using spectrofluorometry of chosen drugs.

3. Nuclear resonance spectroscopy (NMR):-

It investigated liquid crystalline phases has many possibilities over a range. Deuterium Nuclear Resonance Spectroscopy has a new technique for equilibrium phase to investigate so some of different phases can be forward straight and identified by this method. This method has isotropic phase which has signal resonance of singlet signal of quadrapolar such as ^{2}H, where as of anisotropic phases called quadrupolar splitting there by yields a double signal of resonance. Since, it may be separated by splitting of magnitude of anisotropic phases.

4. Drug content:-

Drug content can be evaluated by taking small amount of formulation and measures its spectrometrically by proper dilution. Cumulative percentage drug release from the formulation can be calculated using dialysis or cellulose membrane filled with it and dipped in a suitable medium.

5. Differential scanning calorimetry:-

The phase transtition occur which changes in energy content of the system. Depending on the type of transition i.e. consumption of energy in which melting of solid or emission of energy occurs due to recrystallization, endothermic or exothermic signals can be observed. The necessary care has to be taken about the sensitivity and detection limit of the measuring device. The consumption of energy decreases from crystalline to amorphous, between the transtition from crystalline to amorphous phase. The liquid crystalline phase occurs and the energy consumption among liquid crystalline phase transitions consume less energy. Change of baseline slope with a change in specific heat capacity is an indicator of entropy change during the phase transition. However phase transtition in liquid crystalline polymers result from entropic the reason is considered as seconder order of transtition.

6. Viscosity:-

The viscosity of several compositions can be measured at different shear rates at different temperatures using Brookfield type rotary viscometer. The sample room of the instrument viscometer. The sample room of the instrument must be maintained at 37°C ± 0.2°C by a thermobath, and the samples for the measurement are to be immersed in it before testing.

7. Polydispersity index and zeta-potential:-

By using particle size analyser polydispersed index and zeta-potential can be detected. It measures The size distribution from cumulative analysis of dynamic light scattering. Polydispersity index checks the quality or homogeneity of dispersion. Particle size distribution derived by this technique is volume based and is expressed in terms of the volume of equivalent spheres and weighted mean of the volume distribution. The laser diffraction system is used for this analysis, a rough equivalent of particle polydispersity could be given by two factors value namely, uniformity and span value is defined by the formula,

Span = (D90%- D10%) D50%

Where, DN% it means percentage volume of particles with diameter of DN% equals to N%. The particle size distribution is narrow and has smaller the span value.

8. In vitro-skin permeation studies:-

Franz diffusion cell is used to get the drug release of nano-emulsion formulation for transdermal application. The release can be visualized by confocal laser microscopy to get depth of skin penetration. In vitro drug release can be obtained by addition of preparation in donor compartment of a Franz cell which is having a membrane as barrier and maintain the appearance of encapsulated drug in receptor medium. It usually contains phosphate buffer solution (PBS) and stirred on magnetic stirrer at 100rpm at 37°C ± 1˚C .1ml sample was withdrawn from medium and replaced with an equivalent amount of medium at definite intervals. The sample withdrawn is filtered through 0.22 - 50 µm filter. The drug release was analysed through ultraviolet spectroscopy (UV) at wavelength of peak absorption of drug.

9. Particle size:-

The particle size of nano formulation was checked by using Malvern Zetasizer. DLS measurement are taken at 90^0 to detect particle size by dynamic light scattering spectrophometer, which uses a neon laser of 632nm wavelength.

10. Exvivo permeation study:-

This is performed by using diffusion cell. The skin is cut from ear or abdomen and fats are carefully removed. Skin is cut at a appropriate size and kept on diffusion cell which was filled with receptor solution. Samples are prepared with vesicular and applied on dorsal surface of skin and then instrument was started. At certain time or intervals the sample is withdrawn from the receptor medium and the fresh medium was put in the receptor. The sample was then analysed by ultraviolet (UV) or high performance liquid chromatography (HPLC). Semi-permeable membrane such as cellulose used in place of skin for in-vitro release studies. The flux (J) of the drug across skin or membrane can be calculated by the formula,

$$J = D\, dc/dx$$

Where, D is diffusion coefficient and is function of size, shape and flexibility of the diffusing molecule as well as the membrane resistance, c is the concentration of diffusion studies, x is spatial coordinate.

11. X-ray diffraction:-

The most used method for investigating liquid crystal phases formed by surfactant and copolymers system is having no doubt in X-ray diffraction. The X-ray scattering experiments were characteritics interferences are generated from microstructure. There are two methods to detect interferences utilizing position-sensitive detectors or scintillation counters i.e. registration of X-ray counts and film detection. Due to the presence of long range structural order in liquid crystals, generation of diffraction patterns are possible as electromagnetic radiation of a suitable wavelength.

12. Stability:-

Stability is the dosage form which refer to the chemical and physical integrity of dosage form and where it is accurate. The ability of the dosage unit maintain microbiological contamination and protect. The drug is one of the product related to problems such as microemulsion and nanoemulsion. The nanoemulsion formulation have the physical and chemical stability of drug. The nanoemulsion formulation are kept at room temperature over a month. During storage condition droplet size, refractive index and viscocity are determined. The changes during this indicates formulation stability. The amount of drug release in nanoformulation is maintained at each interval of time.

VI. CONCLUSION:-

The liquid Crystal help to control the behaviour of drugs in-vivo and maximize the efficiency of drugs medical practice. Liquid crystal formulations have exhibited significant entrapment efficiency, sustained drug release and improved stability. Non-pharmaceutical applications of liquid crystals involves-liquid crystal displays, liquid crystal thermometers and optical imaging. The liquid crystal systems deliver such as gels, cream, ointment, liposomes, colloidal dispersions and transdermal patches have been used in pharmaceuticals and cosmetics. As research field has new development so liquid crystal plays a vital role in pharmaceutical field and modern technology.

VII. ABBREVATIONS:-

Liquid Crystal, pharmaceutical field.

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