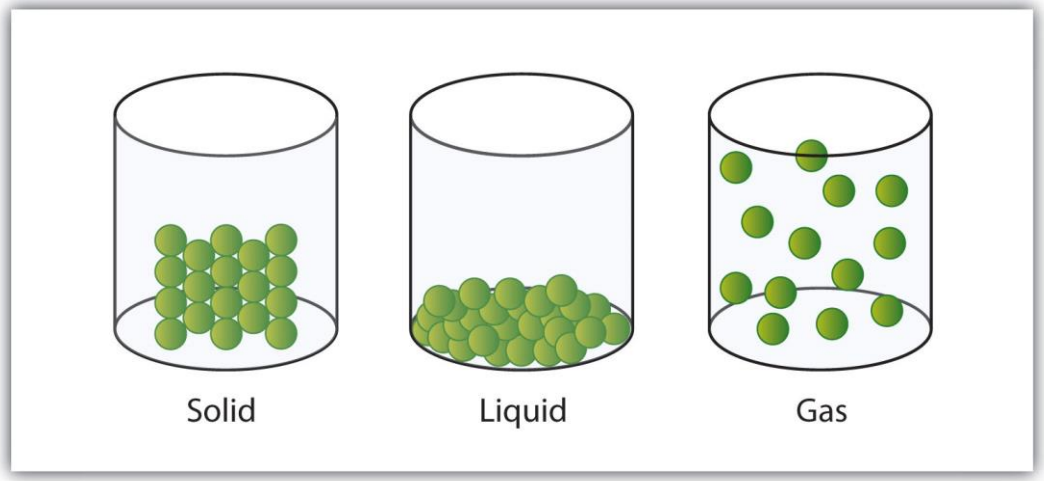
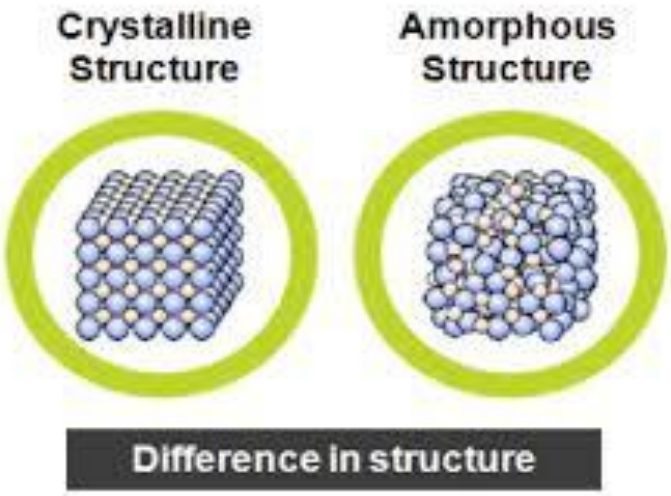
LIQUID CYSTALS

LIQUID CRYSTALS



LIQUID CRYSTALS (MESOPHASE)



The phase transition from the solid phase to liquid is formed via an intermediate path known as mesophase (liquid crystal). It is a thermodynamically stable, special transition structure.

HISTORY

- 1888: Friedrich Reinitzer, an Austrian botanist observed that there was two melting points for a certain material while he was making esters of cholesterol for studying cholesterol in plant.

- Later, German physicist D. Lehmann showed that the phase that is blurred has an anisotropic character as a result of examinations made under polarized microscope. This thermodynamically stable phase was later called liquid crystal phase

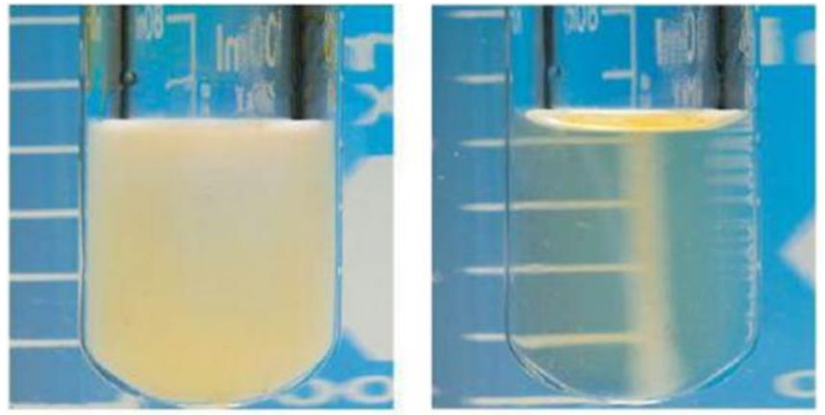
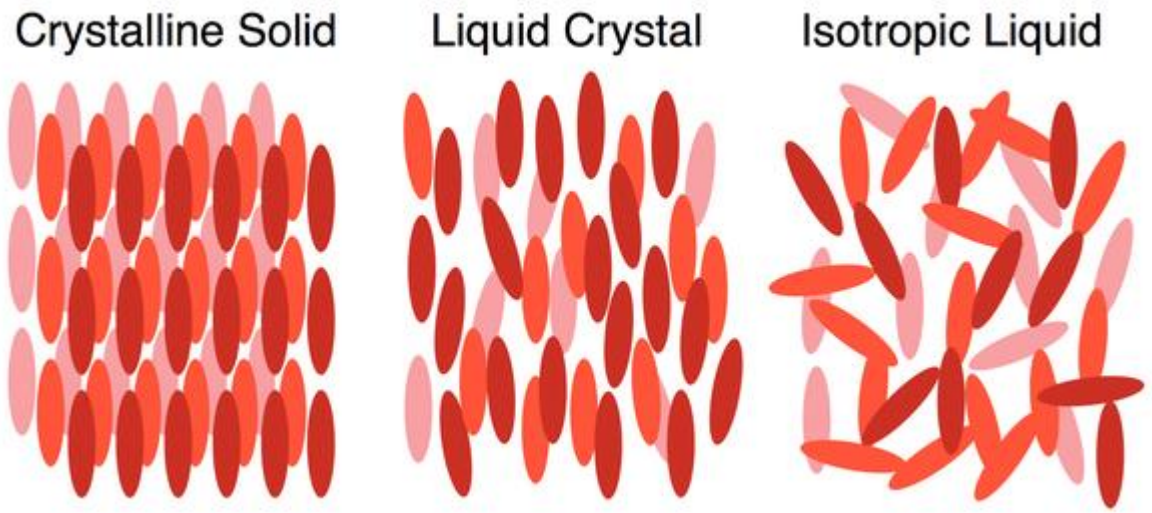


FIGURE 11.31 Cholesteryl benzoate in its liquid and liquid crystalline states.

LIQUID CRYSTALS

DEFINITION

Liquid crystals are substances that flow like liquids but maintain some of the ordered structure characteristics of crystalline solids. They have optical properties of solid crystals and flow properties of viscous fluids.



"ISOTROPIC" AND "ANISOTROPIC

- When the properties of a material vary with different crystallographic orientations, the material is said to be **anisotropic**.
- Alternately, when the properties of a material are the same in all directions, the material is said to be **isotropic**.

  - Some materials found in nature can change the polarization plane of incoming rays.

MESOGENS

- The molecules that form the liquid crystal phase are called MESOGENS:

Excipients
(Eg. Surfactants)
Anisometric molecules such as salts of organic acids or bases

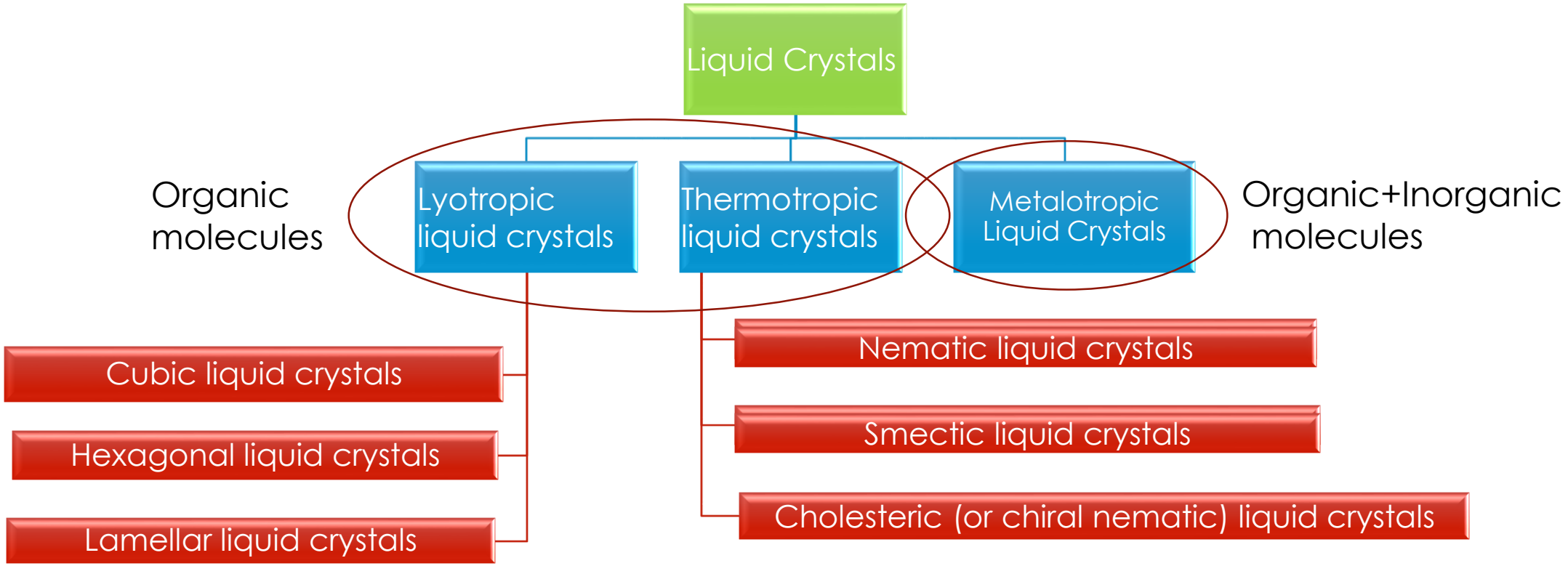
Hydrophilic / Hydrophobic
Lipophilic / Lipophobic

- Amphiphilic mesogens → These molecules are formed of two distinct parts with totally different properties. At certain temperature and concentration, certain fractions of amphiphilic molecules come together to form micelles or aggregates.

Soap, some detergents, block copolymers

-Non-amphiphilic mesogens
calamitic, discotic, pyramidal, sanidic, side-chain, banana mesogenes etc.

CLASSIFICATION



LYOTROPIC LIQUID CRYSTALS

Lyotropic liquid crystals are obtained by dissolving amphiphilic mesogens in a suitable solvent at a suitable concentration, temperature and pressure. (Eg soap and water mixture)

The liquid crystalline phases that occur on increasing the concentration of surfactant solutions are referred to as *lyotropic* liquid crystals.

Both amphiphilic drugs and amphiphilic excipients (especially surfactants) in drug formulations form lyotropic liquid crystals. Lyotropic liquid crystals are usually present in the presence of a solvent such as water.

EXAMPLE: Fatty Acid Salts, Phospholipids, Fibrous Proteins

- Increase of concentration of a surfactant solution frequently causes a transition from the typical spherical micellar structure to a more elongated or rod-like micelle. Further increase in concentration may cause the orientation and close packing of the elongated micelles into hexagonal arrays; this is a liquid crystalline state termed the *middle phase or hexagonal phase*.
- With some surfactants, further increase of concentration results in the separation of a second liquid crystalline state – the *neat phase or lamellar phase*.
- In some surfactant systems another liquid crystalline state, the *cubic phase*, occurs between the middle and neat phases.

- The lyotropic liquid crystals are anisotropic, that is, their physical properties vary with direction of measurement.

THERMOTROPIC LIQUID CRYSTALS

Thermotropic liquid crystals are formed when certain materials (for example the esters of cholesterol) are heated. The materials may form liquid crystals in the presence or absence of solvents. Without the solvent, the solid crystal phase may shift from solid phase to liquid crystal phase via heating; this is called thermotropic mesomorphism.

The thermotropic liquid crystals are generally in three different forms

- Nematic liquid crystals
- Smectic liquid crystals
- Cholesteric (or chiral nematic) liquid crystals

1.Nematic liquid crystals:

- Groups of molecules orientate spontaneously with their long axes parallel, but they are not ordered into layers.
- Because the molecules have freedom of rotation about their long axis, the nematic liquid crystals are quite mobile and are readily orientated by electric or magnetic fields.
- Their flow properties are similar to those of normal liquids, except for the anisotropy they have, due to the orientation of the molecules.

***2.Smectic liquid crystals*:**

– Groups of molecules are arranged with their long axes parallel, and are also arranged into distinct layers.

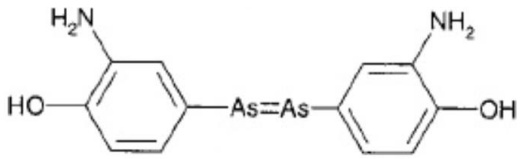
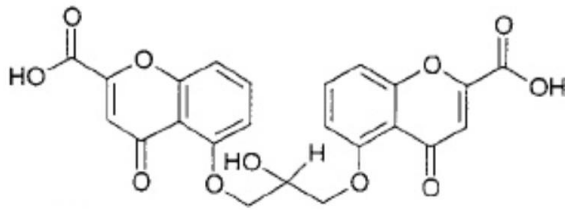
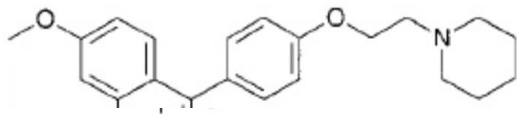
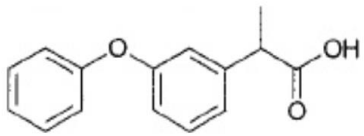
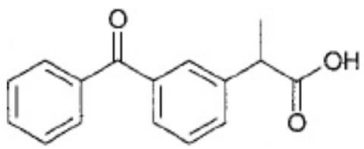
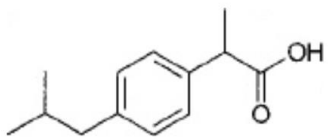
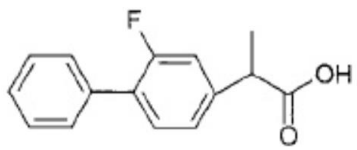
– As a result of their two-dimensional order the smectic liquid crystals are viscous and are not orientated by magnetic fields.

3. *Cholesteric (or chiral nematic) liquid crystals*:

– They consist of various cholesteryl esters. This structure was observed in liquid crystals containing cholesterol for this reason they have been named cholesteric.

- They appear as thin and a bulk of two-dimensional nematic-like layer.
- very sensitive to small changes in temperature and pressure, and depending on them the color changes
- Characteristically form an iridescent appearance of the cholesteric phase when white light is applied

TABLE 1 Liquid Crystalline Drug Substances

Drug	Crystal Type	Formula	Reference
Arsphenamine	Nematic		19
Disodium cromoglycinate	Nematic, hexagonal		20
Nafoxidin HCl[a]	Hexagonal, cubic, lamellar		21
NSAID salts			
Fenoprofen	Lamellar		23
Ketoprofen	Lamellar		23
Ibuprofen	Lamellar		23
Flurbiprofen	Lamellar		23

LIQUID CRYSTALLINE FORMULATIONS FOR DERMAL APPLICATION

- Surfactant Gels
  - Contrheuma Gel Forte N™
  - Trauma-Dolgit™Gel
  - Dolgit Mikrogel™

- Ointments and Creams
- Commonly the surfactant concentration in ointments and creams is significantly lower than in surfactant gels. Ointments are nonaqueous preparations, whereas creams derive from ointments by adding water. The microstructure of both ointments and creams may consist of liquid crystals, as far as a liquid crystalline network or matrix is formed by amphiphilic molecules.

TRANSDERMAL PATCHES

- Transdermal patchs has to remain for up to one week at the appropriate body site. In this case the drug amount in the reservoir is rather high. Since liquid crystalline vehicles with lamellar microstructure have high solubilization capacities, they are recommended as reservoirs for transdermal patches

SUSTAINED DRUG RELEASE FROM SOLID, SEMISOLID, AND LIQUID FORMULATIONS

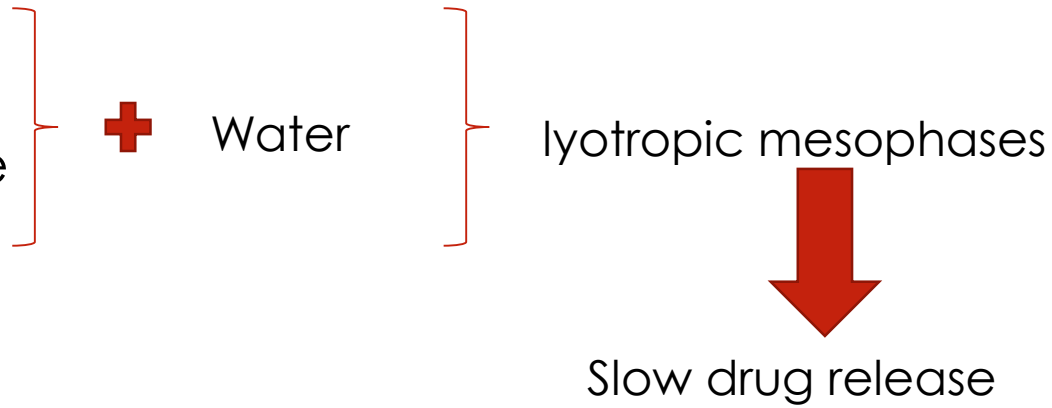
- The therapy of a chronic disease requires repeated drug dosing. In the case of a short biological half-life, the drug has to be administered up to several times daily within short intervals. To reduce the application frequency, sustained formulations have been developed.

  - liquid crystalline excipients

SOLID DOSAGE FORMS

- Solid formulations for sustained drug release may contain mesogenic polymers as excipients forming a matrix which is usually compressed into tablets. Some of the most frequently used excipients for sustained release matrices include cellulose derivatives belonging to the group of lyotropic liquid crystals which gradually dissolve in aqueous media.

- Cellulose Derivates:
  - Hydroxypropyl Cellulose
    Hydroxy Propyl Methyl Cellulose



LIQUID DOSAGE FORMS

Emulsion / Suspension → adsorption of mesogenic materials to the interface → Slow drug release via diffusion

Liquid Dosage Forms (E.g., oily solutions of phospholipids in the form of inverted micelles) + body fluids (plasma, tear or skin lipids) → LIQUID CRYSTALS → Slow drug release via diffusion

LIQUID CRYSTALS IN COSMETICS

- Liquid crystals are mainly used for decorative purposes in cosmetics.
- Cholesteric liquid crystals are particularly suitable because of their iridescent color effects, and find applications in nail polish, eye shadow, and lipsticks.
- The structure of these thermotropic liquid crystals changes as a result of body temperature, resulting in the desired color effect.
- In recent times, such thermotropic cholesteric liquid crystals have been included in body care cosmetics, where they are dispersed in a hydrogel.

OTHER EXAMPLES OF LIQUID CRYSTALS

- Water+ Bile Salt + Cholesterol at certain ratios, resulting in the formation of a smectic mesophase, which can lead to the formation of **gallstones**.
- Liquid crystal structure is found in many structures such as nerves, brain tissue and veins. As the lipids form liquid crystals they accumulate in the vessels and cause **ARTERIOSCLEROSIS**.
- Some liquid crystals can change color depending on the temperature change. With this feature it is possible to determine high temperature regions under the skin due to diseases.
- Can be used as a cell membrane model

BASIC ADVANTAGES

- The phase transitions can be regulated via externally applied magnetic, electrical, mechanical forces, and changing factors such as temperature and pH
- Active agents may spontenously form liquid crystals or some active agents can be loaded into liquid crystals
- Modification of drug release profile (extended release)
- Improvement of drug transport through dermal, mucosal, vaginal, periodontal and oral routes
- İmprove the stability of emulsions
- Improve the solubility of poorly water soluble drugs
- Easy to prepare

DISADVANTAGES

- They are affected by environmental factors (such as temperature, mechanical pressure, electric and magnetic fields)
- They may cause toxic effect and irritation depending on the surfactant concentration
- Limited active agent loading capacity