

المرحلة الثالثة

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تقنيات حبر لينة

م. م. م.

Pharmaceutical Technology

Lotions; liniments and collodions.

Liniments: an alcoholic or oleaginous solution or emulsion applied by rubbing on the skin for treating pain and stiffness of underlying musculature.

Liniments with an alcoholic or hydro alcoholic vehicle are useful when rubefacient, counter irritant, or penetrating action is desired; oleaginous liniments are less irritating to the skin than alcoholic liniments. Liniments are not applied to the skin areas that are broken or bruised because excessive irritation might result. The vehicle for a liniment should therefore be selected for type of action desired (rubefacient, counterirritant, or massage) and also on solubility of the desired components in various solvent. For oleaginous liniments, the solvent may be fixed oil such as almond oil, peanut oil, sesame oil, or cottonseed oil or a volatile substance such as wintergreen oil or turpentine, or it may be a combination of fixed and volatile oils.

All liniments should bear a label indicating that they are suitable only for external use and must never be taken internally. Liniments that are emulsions or that contain insoluble matter must be shaken thoroughly before use to ensure even distribution of the dispersed phase, and these preparation should be labeled SHAKE WELL. Liniments should be stored in tight containers. Depending on their individual ingredients, liniments are prepared in the same manner as solutions, emulsions, or suspension.

Collodion

PCA

Collodion is a clear or slightly opalescent viscous liquid prepared by dissolving pyroxylin (4%w/v) in a 3:1 mixture of ether and alcohol. The resulting solution is highly volatile and flammable and should be preserved in a tight container remote from fire at a temperature not exceeding 30°C.

The product is capable of forming a protective film on application to the skin and the volatilization of the solvent. The film is useful in holding the edges of an incised wound together. However, its presence on the skin is uncomfortable because of its inflexible nature.

The following product, which is flexible, has a greater appeal when a pliable film is acceptable.

Flexible collodion

cc

Flexible collodion is prepared by adding 2% camphor and 3% castor oil to collodion. The castor oil renders the product flexible, permitting its comfortable use over skin areas that are normally moved, such as fingers and toes. The camphor makes the product waterproof. Physicians frequently apply the coating over bandages to make them water proof and to protect them from external stress.

Salicylic acid collodion

Salicylic acid collodion is a 10% solution of salicylic acid in flexible collodion. It is used for its keratolytic effects, especially in the removal of corns from the toes. Patients who use such products should be advised about their proper use. the product should be applied one drop at a time on the corn or warts, allowing time to dry before the next drop is added. Because salicylic acid can irritant normal, healthy skin, every attempt must be made to ensure application directly on the corn or wart. A useful preventive measure is to line the adjacent healthy skin with some white petrolatum prior to application of the product. Proper tightening and storage of the product after use are absolutely necessary because of the volatility of the vehicle.

Stability of Emulsions

A very important parameter for emulsion products is their stability; however, the evaluation of emulsion is not easy. Pharmaceutical emulsion stability is characterized by the absence of coalescence of dispersed phase, ²absence of creaming and retaining its physical characters like elegance, odor, color and appearance.

Generally speaking, an emulsion is considered to be physically unstable if:

- 1- The internal or dispersed phase upon standing tends to form aggregates of globules.
- 2- Large globules or aggregates rise to the top or fall to the bottom of the emulsion to form a concentrated layer of the internal phase.
- 3- If all or part of the liquid of the internal phase becomes "unemulsified" and forms a distinct layer on the top or bottom of the emulsion as a result of the coalescing of the globules of the internal phase.

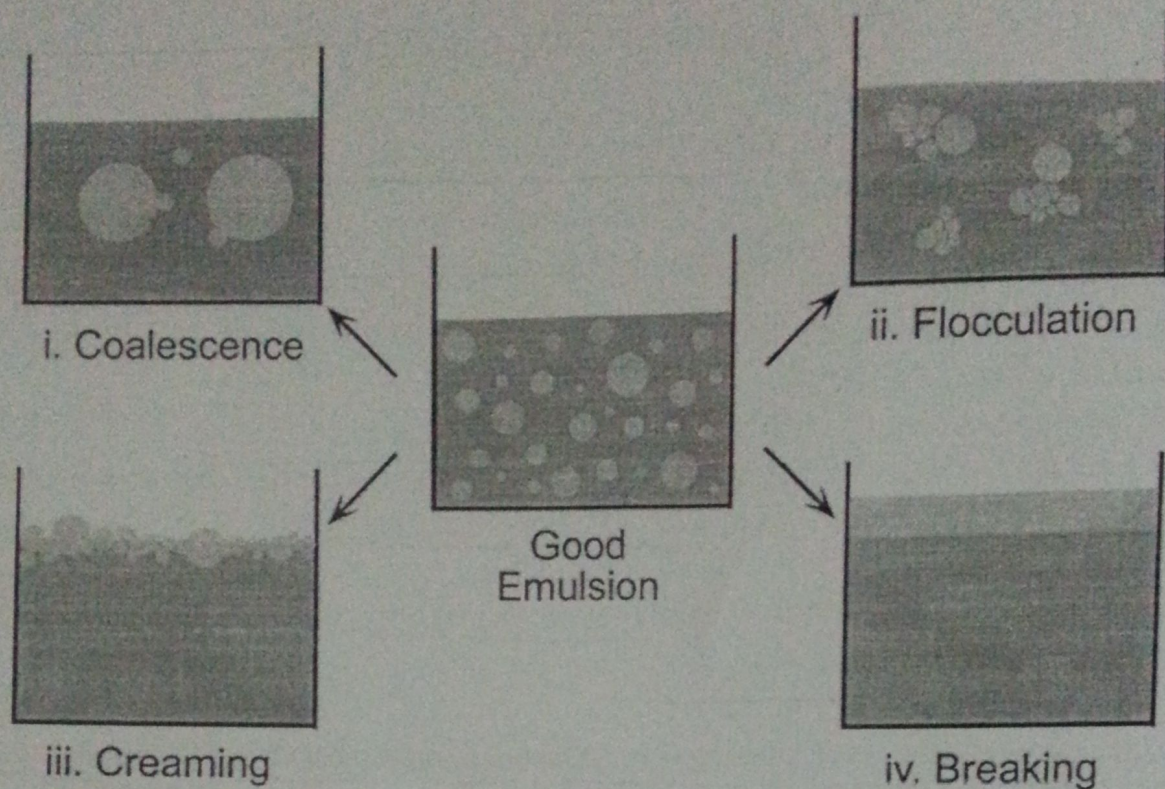
In addition, an emulsion may be adversely affected by microbial contamination and growth and by other chemical & physical alterations.

The instability of emulsion may be classified into four phenomena: *Flocculation*, *creaming*, *coalescence* and *breaking* as shown in the figure.

♣ *Flocculation*

It is the joining together of globules to form large clumps or floccules which rise or settle in the emulsion more rapidly than individual particles.

I.e. it is the association of small emulsion particles to form large aggregate which is re-dispersible upon shaking. It is a reversible process in which the droplets remain intact. Flocculation is considered as the precursor of coalescence. This is because the presence of excess surfactant in the continuous phase of an emulsion can lead to flocculation of emulsion droplets.



♣ Creaming

The term is taken from the dairy industry & is analogous to the creaming or the rising to the top of cream in milk that is allowed to stand. Creaming is the phenomenon in which the dispersed phase separates out, resulting in rising (up-ward creaming) or settling (down-ward creaming) of globules or floccules to form a concentrated layer at the surface or at the bottom of the emulsion.

It is not able that in creaming, the dispersed phase remains in globules state so that it can be re-dispersed on shaking; thus, it is a reversible process. Creaming causes a loss in dose's uniformity and a change in the appearance of emulsion. The rate of creaming is determined by Stoke's law as follows:

$$V = \frac{D^2(\rho^d - \rho^o)g}{18\eta}$$

$\xleftarrow{\text{gravitational acceleration}}$
 diameter density
 velocity viscosity

Where V is the velocity in cm/s (rate of creaming), D is the diameter of particles of dispersed phase in cm, ρ is the dispersed phase density, ρ_0 is the continuous phase density, η is the continuous phase viscosity and g is the gravitational acceleration.

The rate of separation of the dispersed phase of an emulsion may be related to such factors as the particle size of the dispersed phase, the difference in the density between phases and the viscosity of the external phase.

It is important to recall that the rate of separation is increased by increased particle size of the internal phase, a larger density difference between the two phases, and a decreased viscosity of the external phase.

Therefore, to increase the stability of an emulsion, the globule or particle size should be reduced as fine as is practically possible, the density difference between the internal and external phases should be minimal, and the viscosity of the external phase should be reasonably high.

The most important factor is the diameter of globules because it is rise to the power of two. Thus, doubling the D increases the velocity of settling or creaming. So reducing the particle size by passing the emulsion through a homogenizer will decrease the rate of creaming.

Adding suitable thickeners such as tragacanth & microcrystalline cellulose are frequently used to increase the viscosity of the external phase since other thickening agents can cause clumping & coursing of emulsion (unstable emulsion).

The density differences show that, when the density of the internal and external phases are equal ($\rho = \rho_0$), the velocity of creaming is zero (impossible to reach this state practically). When the internal phase is less than the continuous liquid which is generally the case in o/w emulsion (i.e. $\rho < \rho_0$) then V is negative. This expresses the fact that creaming occurs in an up-ward creaming. When $\rho > \rho_0$ then $\rho - \rho_0$ is positive and V is positive too. This condition generally occurs in w/o emulsion, resulting in a settling of the globules (down-ward creaming).

In conclusion: o/w emulsions generally face up-ward creaming when the globules of the dispersed phase are less dense than the continuous phase. In contrast, w/o emulsions face down-ward creaming when the globules of the dispersed phase are denser than the continuous phase.

The gravity factor is essentially constant under ordinary conditions, but creaming may be accelerated by centrifugation.

♣ Coalescence (synonyms: breaking or cracking)

Of greater destruction to an emulsion than creaming is coalescence of the globules of the internal phase and the separation of that phase into a layer. The separation of the internal phase from the emulsion is called the "breaking" of the emulsion, and the emulsion is described as being "cracked or broken".

As noted earlier, flocculation & creaming are reversible because the globules are still surrounded by protective sheath of emulsifying agents and may be re-dispersed simply by agitating the product, while coalescence & breaking are irreversible because the protective sheath about the globules of the internal phase no longer exists (destroyed).

So attempts to re-establish the emulsion by the agitation of the two separate layers are generally unsuccessful. Additional emulsifying agent and passing the product through the proper emulsifying machinery are usually the solution to such problems.

♣ Deterioration by microorganisms (molds, yeasts and bacteria)

Many molds, yeasts and bacteria can bring about decomposition, thereby causing the disruption of the system. In cases in which the emulsifier is not affected by the microbes, the product can be rendered unsightly by their presence and growth and will of course not be efficacious from a pharmaceutical and therapeutic standpoint.

Fungistatic preservatives are generally included in the aqueous phase of an o/w emulsion, since fungi (molds & yeasts) are more likely to contaminate emulsions than are bacteria.

Properties of preservatives in emulsion:

1. They should be potent against molds, yeasts and bacteria.
2. They should not interact with any one of the constituents of emulsion.
3. They should be present in enough concentration to protect both phases.
4. They should have a good solubility in both phases.

Combinations of methylparaben and propylparaben are frequently employed to serve this function. Alcohol in the amount of 12-15% based on the external phase volume is frequently added to orally used o/w emulsion for preservation.

♣ Miscellaneous Physical and Chemical Changes

These include light, extreme temperature & cold, oxidation, hydrolytic rancidity of the oil and phase inversion.

- 1- Extreme heat and cold will result in coarsening and breaking of emulsion and this can be protected by using a strong synthetic emulsifying agents.
- 2- Light, for light-sensitive emulsion, light-resistant containers are used. For emulsion susceptible to oxidative decomposition and rancidity (effect on the color and odor may destroy the vitamin activity), antioxidant should be added, and adequate label warning provided to ensure that the container is tightly closed to air after each use.
- 3- Phase inversion- a physical process (change in the type of emulsion). Inversion in the type of emulsion is a sign of instability except in dry-gum method where it is desired.