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Pharmaceutical Dosage Forms *and* Drug Delivery

SECOND EDITION

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14 Emulsions

LEARNING OBJECTIVES

On completion of this chapter, the reader should be able to

1. Define pharmaceutical emulsions
2. Identify different types of emulsions
3. Define emulsifying agents
4. Describe different types of emulsifying agents
5. Describe the role of hydrophile–lipophile balance (HLB) in the selection of emulsifying agents
6. Discuss different types of physical instability of pharmaceutical emulsions
7. Describe the strategies that may be utilized to stabilize emulsions

14.1 INTRODUCTION

An emulsion consists of at least two immiscible liquid phases, one of which is dispersed as globules (dispersed phase) in the other liquid phase (continuous phase). Emulsions are thermodynamically unstable and are usually stabilized by the presence of an emulsifying agent. The process of formation of an emulsion is termed emulsification. The diameter of the dispersed phase globules is generally in the range of about 0.1–10 μm, although it can be as small as 0.01 μm or as large as 100 μm. Emulsified systems range from lotions of relatively low viscosity, to ointments and creams, which are semisolid in nature. Pharmaceutical emulsions are used for the administration of nutrients, drugs, and diagnostic agents. Topical creams and lotions are popular forms of emulsions for external use.

The main advantages of emulsions as drug delivery systems include

1. *Increased drug bioavailability.* Many drugs are highly hydrophobic, with high logP values (partition coefficient between oil and water). These drugs are usually poorly soluble in water but readily soluble in oils. Formulation of a drug dosage form as an emulsion allows the administration of a hydrophobic drug in a soluble/dissolved state. This can improve the oral bioavailability of a biopharmaceutics classification system class II (low solubility, high permeability) and class IV (low solubility, low permeability) drug since absorption from an emulsion does not require the dissolution step.
2. *Increased drug stability.* Drugs that are more stable in an oily compared to an aqueous medium can show improved stability in an emulsion dosage form.

3. *Prolonged drug action*. The oily phase can serve as a reservoir of the drug, which slowly partitions into the aqueous phase for absorption. This phenomenon, especially with semisolid emulsions, can help prolong drug action. For example, intramuscular injection of an emulsion can result in long drug absorption time.

14.2 TYPES OF EMULSIONS

Emulsions typically consist of a polar (e.g., aqueous) and a relatively nonpolar (e.g., an oil) liquid phase. Based on the nature of the internal and/or external phase, emulsions can be classified into different types (Figure 14.1).

14.2.1 Oil-in-Water Emulsion

When the oil phase is dispersed as globules throughout an aqueous continuous phase, the system is referred to as an oil-in-water (o/w) emulsion. An o/w emulsion is generally formed if the aqueous phase constitutes more than 45% of the total weight and a hydrophilic emulsifier, such as sodium lauryl sulfate, triethanolamine stearate, sodium oleate, and glyceryl monostearate is used.

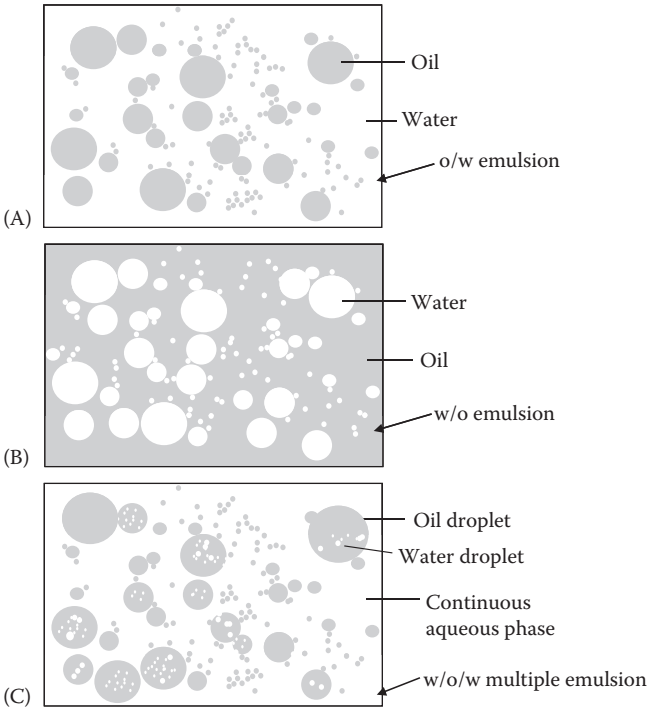

FIGURE 14.1 Types of emulsions: (A) o/w emulsions, (B) w/o emulsion, and (C) w/o/w multiple emulsion.

14.2.2 Water-in-Oil Emulsion

When the aqueous phase is dispersed and the oil phase is the continuous phase, the emulsion is termed as water-in-oil (w/o) emulsion. Generally a lipophilic emulsifier is used for preparing w/o emulsions. The w/o emulsions are used mainly for external applications and may contain one or several of the following emulsifiers: calcium palmitate, sorbitan esters (Spans), cholesterol, and wool fats.

14.2.3 Multiple Emulsions

Multiple emulsions are emulsions whose dispersed phase contains droplets of another emulsion. Both water-in-oil-in-water (w/o/w) and oil-in-water-in-oil (o/w/o) multiple emulsions are of interest as delayed- and/or sustained-action drug delivery systems. Emulsifying a w/o emulsion using surfactants which stabilize an oily dispersed phase can produce w/o/w emulsions with an external aqueous phase and lower viscosity than the primary emulsion. They also have applications in cosmetics. Multiple emulsions are often used for microencapsulation of peptides/proteins and hydrophilic drugs.

14.2.4 Microemulsions

Microemulsions are visually homogeneous, transparent systems of low viscosity. These emulsions have a very finely subdivided dispersed phase, and often contain a high concentration of the emulsifier(s) and a cosolvent (such as ethanol). Microemulsions form spontaneously when the components are mixed in the appropriate ratios. Microemulsions are thermodynamically stable for prolonged periods of time. In their simplest form, microemulsions are small droplets (diameter 5–140 nm) of one liquid dispersed throughout another by virtue of the presence of a fairly large amount of surfactant(s) and cosolvent(s). They can be dispersions of oil droplets in water (o/w) or water droplets in oil (w/o). The types of microemulsion (w/o or o/w) formed is determined largely by the nature of the surfactants. Microemulsions can be used to increase the bioavailability of poorly water soluble drugs by incorporating them into the oily phase. Incorporation of etoposide and methotrexate diester derivative into w/o microemulsion has been suggested as a potential carrier for cancer therapy.

14.2.5 Self-Emulsifying Drug Delivery Systems and Self-Microemulsifying Drug Delivery Systems

A solution of drug in the oil-surfactant-cosolvent mixture can spontaneously form an emulsion or microemulsion with minimal agitation at room temperature. Whether this mixture forms an emulsion or a microemulsion depends on the composition of this mixture and the amount of water added. A higher proportion of oil and lower proportion of cosolvent leads to the formation of an emulsion. Self-microemulsifying mixtures typically contain a higher proportion of the cosolvent and the surfactant, while the proportion of oil is lower. These mixtures are termed as self-emulsifying

drug delivery system (SEDDS) or self-microemulsifying drug delivery system (SMEDDS). The SEDDS and SMEDDS can be administered orally for *in vivo* emulsion or microemulsion formation in the patient's gastrointestinal tract. For example, cyclosporine microemulsion (Neoral) is a self-microemulsifying preconcentrate of cyclosporine, which is more rapidly and consistently absorbed than the original self-emulsifying formulation of cyclosporine (Sandimmune).

14.3 QUALITY ATTRIBUTES

Emulsion dosage forms are designed to meet the following quality attributes:

1. *Uniformity of content* (dose-to-dose within the same bottle and bottle-to-bottle). All the doses dispensed from a given multi-dose container should have acceptable uniformity of drug content. In addition, the drug content must be uniform between different bottles of a given batch of emulsion.
2. *Separation volume*. Once an emulsion has been left undisturbed for a sufficient period of time, it is likely to show some degree of separation of the dispersed phase from the dispersion medium. For example, in the case of an o/w emulsion, "creaming" of an emulsion is sometimes observed, which indicates higher concentration of the oil phase in the top layer of the emulsion which is visually distinguishable from the bottom layer. The proportion of the volume occupied by the separated phase which contains a higher concentration of the dispersed globules is an indicator of physical stability of the emulsion. Higher this volume, more stable is the emulsion.
3. *Absence of dispersed phase globule size change and active pharmaceutical ingredient (API) crystallization*. Particle size distribution of dispersed phase should remain fairly constant. Brownian and gravitational motion of the dispersed phase leads to collisions of globules with each other, which can lead to agglomeration and increase in the size of certain granules. A change in the dispersed phase globule size could be indicative of inherent physical instability of the emulsion. In cases where drug concentration in the emulsion is close to the drug solubility, crystallization can sometimes occur due to temperature fluctuations during storage, preferential evaporative loss of one phase, incompatibility with packaging components, or unintended nucleation. Crystal growth can be inhibited by the use of appropriate solubilizers and surfactants, and by formulating an emulsion at lower concentration than its thermodynamic solubility.
4. *Palatability*. Palatability of an oral dosage form is usually enhanced by the use of sweeteners, flavors, and colorants. For especially bitter or otherwise unpleasant tasting drugs, incorporation of the drug in the oil phase may not be adequate since some drug would inadvertently partition into the aqueous phase. In certain cases, taste masking approaches may be needed. These considerations, of course, are not pertinent for parenteral administration. In the case of parenteral emulsions, tissue irritability and osmotic pressure are important considerations.

5. *Redispersibility.* A separated or creamed emulsion should readily redisperse upon gentle shaking of the container.
6. *Absence of phase separation.* While creaming of an emulsion is, to some extent, unavoidable, the dispersed phase should not coalesce and separate from the dispersion medium.
7. *Deliverability.* The labeled number of doses and the labeled amount of emulsion should be deliverable from a bottle under the normal dispensing conditions by a patient.
8. *Flow.* The emulsion must not be too viscous to pour freely from a bottle or to flow through a needle syringe or an IV infusion set (for parenteral emulsions).
9. *Lack of microbial growth.* Use of antimicrobial preservatives could be sufficient for oral and topical emulsions, whereas parenteral, nasal, and ophthalmic suspensions must be sterile.
10. *Physical integrity.* The dosage form should not show any unexpected change in color, or any other change in physical appearance or perception of the dosage form, such as odor that may alarm the patient and/or the health care provider with respect to the physical integrity of the emulsion.
11. *Adhesion to the package.* Preferential adsorption or adhesion of one phase or component of the emulsion, such as the drug, the chelating agent, or the emulsifier, can adversely affect the uniformity and stability of an emulsion.
12. *Chemical stability.* There should not be any unacceptable chemical degradation of the drug during the shelf life of the product under recommended packaging and storage conditions. The drug product must meet the predetermined requirements of minimum potency of the API and maximum levels of known and unknown impurities.
13. *Drug release.* Since an emulsion contains the drug in the dispersed phase, the release of drug from the dispersed phase of a semisolid emulsion into an aqueous solution in an appropriate dissolution vessel is quantified and controlled as an indicator of its bioavailability.

In addition, topical emulsions should be fluid enough to spread easily but not so fluid that it runs off the surface too quickly. They must dry quickly and provide an elastic film that should not be too oily. In addition, the dosage form must have pleasant color and odor, although sweetener is not needed.

14.4 FORMULATION

Emulsions are inherently *thermodynamically unstable* due to the differences in the molecular forces of interaction between the molecules of the two liquid phases. The oxygen and hydrogen atoms in the water molecules in the aqueous phase bond with surrounding water molecules through diploar and hydrogen bonding interactions, whereas the carbon atoms in the oil phase bond with the surrounding molecules predominantly through weak hydrophobic and Van der Waals interactions. Thus, creation of greater surface of interaction between the two phases is thermodynamically unfavorable. Therefore, production of emulsions requires introduction of energy into

the system. This is accomplished by trituration on the small scale and homogenization on the pilot and large scale.

14.4.1 Interfacial Free Energy

From a thermodynamic standpoint, emulsions are unstable systems. This is due to the fact dispersion of an insoluble material in another leads to increase in total energy of the system. Since every system tends to spontaneously reduce its energy to a minimum, all emulsions will tend to separate into two phases with time. When one liquid is broken into small particles, the interfacial area of the globules constituted is much greater than the minimum surface area of that liquid in a phase separated system. The phase separation is driven by greater cohesive (interaction between molecules of the same type) force between the molecules of each liquid phase than the adhesive (mutual molecular interaction) force between the two liquids. A phase separated system represents the state of minimum surface free energy.

The surface free energy of an emulsion is evident in terms of the *interfacial tension* between the two phases. The adsorption of a surfactant or other emulsifying agent at the interface of dispersed phase globules lowers the interfacial tension. Reducing the interfacial tension delays the kinetics of coalescence of the two phases. Frequently, combinations of two or more emulsifying agents are used to adequately reduce the interfacial tension, produce a rigid interfacial film, and achieve the most suitable viscosity of the internal phase.

14.4.2 Phase Ratio

The ratio of volume of disperse phase to volume of the dispersion medium (phase ratio) greatly influences the characteristics of an emulsion. It is generally difficult to formulate a conventional emulsion containing less than 25% of disperse phase, due to their high susceptibility to creaming or sedimentation. The optimum phase–volume ratio is generally obtained when the internal phase is about 40%–60% of the total quantity of the product.

Nevertheless, a combination of proper emulsifiers and suitable processing technology makes it possible to prepare emulsion with only 10% disperse phase without stability problems. Such a combination of emulsifiers includes the use of a hydrophilic emulsifier in the aqueous phase and a hydrophobic emulsifier in the oil phase, leading to the formation of a complex surfactant film at the interface. For example, a combination of sodium cetyl sulfate and cholesterol leads to a closely packed film at the interface that produces an excellent emulsion. On the other hand, sodium cetyl sulfate and oleyl alcohol do not form a closely packed or condensed film, and consequently this combination results in a poor emulsion.

14.4.3 Stoke's Law

Creaming or sedimentation of the dispersed phase in an emulsion is modeled by Stoke's law (see Chapter 13), which indicates that the physical stability of an emulsion can be enhanced by

TABLE 14.1
Examples of Emulsion Formulations

Ingredients	Amount	Role
A. Protective emulsion of calamine		
Calamine	1 g	Protective
Zinc oxide	1 g	Protective
Olive oil	15 mL	External phase
Lime water	15 mL	Internal phase
B. Benzoyl benzoate emulsion		
Benzoyl benzoate	25 mL	Drug and internal phase
Emulsifying wax	2 g	Emulsifier
Water qs	100 mL	External phase

1. Decreasing the globule size of the internal phase. The dispersed globule size (diameter) is preferred to be less than 5 μm for good physical stability and dispersion of the emulsion.
2. Increasing the viscosity of the system. Gums and hydrophilic polymers are frequently added to the external phase of an o/w emulsion to increase viscosity, in addition to reducing the interfacial tension and forming a thin film at the interface.
3. Reducing the density difference between the dispersed phase and the dispersion medium.

14.4.4 Zeta Potential

Emulsions can be stabilized by electrostatic repulsion between the droplets. High *zeta potential* (see Chapter 13) on the surface of the droplets causes the dispersed phase droplets to repel each other and thereby resist collisions due to motion caused by Brownian and gravitational forces. Thus, the droplets remain suspended for a prolonged period of time. For example, if negatively charged lecithin is adsorbed at the droplet surface it creates a negative charge. Addition of positively charged electrolytes to the outer, continuous phase of this system reduces zeta potential on the dispersed phase and can facilitate *flocculation*. Table 14.1 lists the composition of two typical o/w pharmaceutical emulsions.

14.5 EMULSIFICATION

Emulsification can be facilitated by three mechanisms:

1. Reduction of interfacial tension
2. Formation of monomolecular surface film that physically inhibits coalescence of dispersed phase granules
3. Changing the zeta potential of the dispersed phase

TABLE 14.2
Typical Emulsifying Agents

Type	Examples
Surfactants	
Nonionic	Sorbitan oleate (Span 80)
	Polyoxyethylene sorbitan oleate (Tween 80)
Anionic	Potassium laurate
	Triethanolamine stearate
	Sodium lauryl sulfate
Cationic	Quaternary ammonium compounds
	Benzylkonium chloride
Hydrophilic colloids	
Polysaccharides	Acacia
Phospholipids	Lecithin
Sterols	Cholesterol
Finely divided solid particles	
Colloidal clays	Bentonite
Metallic hydroxides	Magnesium hydroxide

Emulsifying agents can be surfactants, hydrophilic colloids, or finely divided solid particles. Table 14.2 lists some of the commonly used emulsifying agents.

14.5.1 Surfactants

Surfactants are amphiphilic molecules, which contain a polar hydrophilic region and a nonpolar hydrophobic region. Depending on the functional groups and relative surface areas of the two regions, surfactants could have a range of hydrophilic/hydrophobic properties. The use of a predominantly hydrophilic emulsifying agent leads to the formation of an o/w emulsion since it has greater area in and/or strongly interacts with the aqueous phase. Conversely, the use of a predominantly hydrophobic emulsifying agent tends to form a w/o emulsion because it has greater area in and/or strongly interacts with the oil phase. Surfactants are adsorbed at oil-water interfaces to form *monomolecular films*, resulting in a decrease in interfacial tension and physical hindrance to collisions. Often, simultaneous use of a hydrophilic with a hydrophobic surfactant is used to form more stable emulsions, which is partly attributable to the strength and flexibility of the interfacial layer. Charged surfactants can further help an increase in negative or positive *zeta potential* and will thus help to maintain stability by increasing or decreasing electrostatic repulsive forces and facilitating flocculation.

14.5.1.1 Ionic and Nonionic Surfactants

Surfactants could be anionic (negatively charged), cationic (positively charged), amphoteric (both positively and negatively charged, depending on the pH), and nonionic (without any charge). Surfactants that bear a permanent positive or negative

charge such as due to the presence of a quaternary ammonium or a phosphate group, respectively, are termed ionic surfactants. In contrast, nonionic surfactants do not bear a permanent charge but may contain electronegative atoms and ionizable groups. Ionic surfactants tend to have strong and specific interactions with a variety of molecules and are, consequently, more toxic than nonionic surfactants. Nonionic surfactants that do not contain an ionizable group are also less sensitive to variations in the electrolyte content and pH of the formulation. Nonionic surfactants, such as the alkyl or aryl polyoxyethylene ethers, sorbitan polyoxyethylene derivatives, and sorbitan are widely used for producing stable emulsions.

14.5.1.2 HLB Value

The relative hydrophobicity/hydrophilicity of a surfactant is indicated by its hydrophile–lipophile balance (HLB) value. An emulsifying agent with high HLB (~9–12) is preferentially soluble in water and favors the formation of an o/w emulsion. The reverse situation is true with surfactants of low HLB (~3–6), which tend to form w/o emulsions.

The HLB system applies to nonionic surfactants only, although there are HLB values reported in literature for ionic surfactants as well for comparison. This system assumes the hydrophilic contribution of the surfactant from a polyhydric alcohol or ethylene oxide group, and the lipophilic contribution from a fatty acid or fatty alcohol group. The hydrophilic portion of a molecule is calculated on a molecular weight basis and divided by 5 to arrive at the HLB value, whose typical scale is 0.5–19.5. In general, surfactants with an HLB value of 1–3 can be used for mixing oils, 4–6 for making w/o emulsions, 7–9 for wetting powders into oils, 7–10 for making self-emulsifying systems, 8–16 for making o/w emulsions, 13–15 for making detergents, and 13–18 for making self-microemulsifying systems.

14.5.2 Hydrophilic Colloids

Hydrophilic colloids are polymeric materials that bear several electronegative atoms, such as oxygen and nitrogen, thus having strong hydrophilicity through dipole-dipole interactions and hydrogen bond formation. Several hydrophilic colloids, such as gelatin, casein, acacia, cellulose derivatives, and alginates, are used as emulsifying agents. These materials adsorb at the oil-water interface and form multilayer films around the dispersed droplets of oil in an o/w emulsion.

Hydrated lyophilic colloids differ from surfactants since they do not cause an appreciable lowering in interfacial tension. They stabilize emulsions by the formation of multilayer films that are strong and resist coalescence. Additionally, they increase the viscosity of the dispersion medium. Hydrophilic colloids are used for formation of o/w emulsions since the films are hydrophilic. Most cellulose derivatives are not charged, but can sterically stabilize the systems.

14.5.3 Finely Divided Solid Particles

Finely divided solid particles that are wetted to some degree by both oil and water can act as emulsifying agents. They are concentrated at the interface where they

produce a film of particles around the dispersed droplets so as to prevent coalescence. Finely divided solid particles that are predominantly wetted by water form o/w emulsions, while those that are predominantly wetted by oil form w/o emulsions. Examples include bentonite, magnesium hydroxide, and aluminum hydroxide.

14.6 MANUFACTURING PROCESS

Emulsions are manufactured by homogenization or another high shear mixing process. The two phases of the emulsion are assembled separately, by dissolving and mixing of the ingredients to form appropriate solutions. Then, the phases are combined by slow addition of the dispersed phase into the continuous phase with continuous mixing. An optimum amount of mixing shear and time are determined based on the change in the size distribution of the dispersed phase with mixing. The resulting emulsion can then be packaged and/or dispensed.

Sequence of addition of formulation ingredients to the emulsion can be critical for the stability of the emulsion. For example, if an o/w emulsion is desired and the system contains two surfactants with different HLB values, the surfactant with the higher HLB value should be added first. Also, volatile ingredients, such as flavors, can be added after the emulsion has been formed to minimize loss during processing. Similarly, thermosensitive ingredients may be added last. The API may be predissolved in one of the phases or added last depending on drug's solubility, stability, and partitioning properties.

SEDDS and SMEDDS are manufactured by simple mixing to dissolve all ingredients. The resulting formulations can then be packaged in single or multi-dose containers for distribution. In cases where the SEDDS or the SMEDDS is to be administered as a unit dose without dilution prior to administration, the dosage form can be packaged in a soft gelatin capsule.

14.7 STABILITY

Emulsions must demonstrate physical, chemical, and microbial stability throughout their shelf life under recommended packaging and storage conditions.

14.7.1 Physical Instability

Physical stability of an emulsion is characterized by the maintenance of elegance with respect to appearance, odor, color, taste, opacity, and viscosity. Four major phenomena are associated with the physical instability of emulsions: flocculation, creaming, coalescence, and breaking. These phenomena are schematically illustrated in Figure 14.2. Flocculation is discussed in Chapter 13.

14.7.1.1 Creaming and Sedimentation

Creaming is the upward movement of dispersed droplets relative to the continuous phase, while *sedimentation*, the reverse process, is the downward movement of particles. Creaming involves visually evident separation of two layers that differ primarily in the number density of the dispersed phase, and, thus, show optical differences.

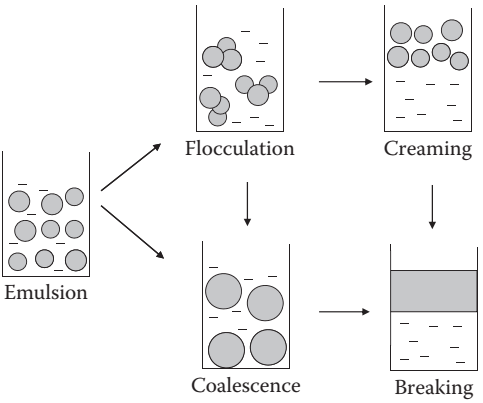

FIGURE 14.2 Schematic illustrations of different types of instability of emulsions.

These processes take place due to the density differences in the two phases and can be reversed by shaking. Creaming is undesirable, because a creamed emulsion increases the likelihood of coalescence due to the closer proximity of the globules in the cream.

Factors which influence the rate of creaming are similar to those involved in the rate of sedimentation of suspension particles and are indicated by the Stoke's law. The rate of creaming is decreased by (1) reduction of the dispersed phase globule size, (2) decrease in the density difference between the two phases, and (3) increase in the viscosity of the continuous phase.

Reduction in globule size is achieved by homogenizing the emulsion. Viscosity of the continuous phase can be increased by the use of thickening agents such as tragacanth or methylcellulose for o/w emulsions, and soft paraffin for w/o emulsions.

14.7.1.2 Aggregation, Coalescence, and Breaking

Aggregation involves close packaging/contact of the dispersed phase droplets, but the droplets do not fuse. Aggregation is to some extent reversible. Coalescence is the process by which emulsified particles merge with each other to form large particles. Coalescence is an irreversible process because the film that surrounds the individual globules is destroyed. It leads to progressive increase in the size of the dispersed phase, ultimately leading to breaking of the emulsion. Breaking of an emulsion refers to complete separation of the two liquid phases. Creaming is a reversible process, whereas breaking is irreversible. When breaking occurs, simple mixing fails to resuspend the globules in a stable emulsified form, since the film surrounding the particles has been destroyed and the oil tends to coalesce.

Coalescence can be prevented by higher mechanical strength of the interfacial barrier. Altering the viscosity may help to stabilize globules and to minimize their tendency to coalesce. Formation of a thick interfacial film is essential to minimize coalescence. Particle size does not correlate well with increased/decreased breaking, nor does viscosity. Phase-volume ratio (relative volumes of oil and water in an emulsion) does contribute to stability (prevention of breaking) of an emulsion.

For example, at greater than ~74% of oil in an o/w emulsion, the oil globules often coalesce and breaking occurs. Thus, a critical concentration is defined in terms of the concentration of the internal phase above which the emulsifying agent cannot produce a stable emulsion of the desired type. Generally, a phase-volume ratio of 50:50 results in the most stable emulsion.

14.7.1.3 Phase Inversion

An emulsion is said to invert when it changes from an o/w to a w/o emulsion, or vice versa. Phase inversion can occur by the addition of an electrolyte or by changing the phase-volume ratio. Monovalent cations tend to form o/w emulsions, whereas divalent cations tend to form w/o emulsions. An o/w emulsion stabilized with sodium stearate can be inverted to a w/o emulsion by adding calcium chloride to form calcium stearate.

14.7.2 Chemical Instability

The API must be chemically stable in the dosage form throughout the shelf life of the product under recommended packaging and storage conditions in terms of both potency and impurities. The drug product must meet predetermined requirements of minimum potency of the API and maximum levels of known and unknown impurities.

14.7.3 Microbial Growth

In addition to the health risks of microbial growth, microorganisms in an emulsion can cause physical separation of the phases. Bacteria can degrade certain nonionic and anionic emulsifying agents. Therefore, preservatives must be added in adequate concentrations in the formulations to resist microbial growth. The preservative should be concentrated in the aqueous phase because bacterial growth will normally occur there. The parabens (methylparaben, propylparaben, and butylparaben) are the commonly used preservatives in emulsions.

REVIEW QUESTIONS

14.1 Coalescence can be reduced by
- A. Decreasing the difference between the density of the dispersed phase and the density of the medium
- B. Adding an agent that reduces the viscosity of the medium
- C. Increasing the droplet size of the dispersed phase
- D. All of the above

14.2 When compounding an emulsion that contains a flavoring agent, the flavoring agent should be in the
- A. Continuous phase
- B. Discontinuous phase
- C. Aqueous phase
- D. Oil phase
- E. Emulsifier

14.3 Define and differentiate between the following:
A. Creaming and breaking
B. Creaming and sedimentation
C. Coalescence and aggregation
D. Phase inversion and self-emulsification
E. Multiple emulsions and microemulsions
F. SEDDS and SMEDDS

14.4 Using the Stoke's law equation, explain how sedimentation and creaming in emulsions can be minimized.

14.5 Why is a surfactant needed to make stable emulsions? Explain which properties of a surfactant are important in formulating emulsions. Enlist two factors that determine whether an emulsion is o/w or w/o.

14.6 List the three mechanisms of emulsification.

14.7 What are emulsifying agents? List the three types of emulsifying agents and differences in their mechanism of stabilization of an emulsion, e.g., in terms of the type of film formed around the dispersed phase and the zeta potential on the dispersed phase.

14.8 Which surfactants will you select for o/w and w/o emulsification?

14.9 Identify the type of self-emulsifying system most appropriate for the following statements (SEDDS or SMEDDS):
A. Has lower dispersed phase globule size after emulsification
B. Has higher content of oil
C. Has higher content of cosolvent
D. Is transparent in appearance after emulsification
E. Is likely to have higher oral bioavailability

14.10 Which of the following surfactants is suitable for the formulation of an o/w emulsion?
A. Surfactant with an HLB value of 1–3
B. Surfactant with an HLB value of 3–6
C. Surfactant with an HLB value of 6–9
D. Surfactant with an HLB value of 9–12
E. Surfactant with an HLB value of 12–15
F. Surfactant with an HLB value of 15–18

14.11 Which of the following surfactants is suitable for the formulation of a w/o emulsion?
A. Surfactant with an HLB value of 1–3
B. Surfactant with an HLB value of 3–6
C. Surfactant with an HLB value of 6–9
D. Surfactant with an HLB value of 9–12
E. Surfactant with an HLB value of 12–15
F. Surfactant with an HLB value of 15–18

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