



## **Physical Stability of Emulsions – An Overview**

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### **ABSTRACT**

*Emulsion stability can be defined as the system's ability to resist changes in its physicochemical properties over time. Emulsion stability is important in many industrial applications, including coatings, food products, agriculture formulations, personal care and petroleum. Several mechanisms such as creaming, flocculation and coalescence cause emulsion breakdown. Emulsions have several advantages as drug delivery systems, especially in the case of hydrophobic drugs. The role of physicochemical characteristics such as droplet size and zeta potential on in vivo behaviour of emulsified systems is very critical. The effect of these parameters on the biodistribution of emulsified drugs after oral or parenteral administration has been placed in context of the altered disposition in different tissues. The stability of emulsions is very important during storage. To administer the emulsion in the body, it is necessary to have good stability. Instability of emulsions leads to floating of droplets to the surface, cohesion between droplets, and finally to creaming and separation. In this review article, we have discussed all possible factors related to stability and instability of all types of emulsions.*

**Key words:** *creaming, flocculation, cohesion, zeta potential, etc.*

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### **INTRODUCTION**

Traditionally, emulsion systems are very popular formulations for topical delivery (pharmaceutical and cosmetic). Since the structure of these systems is responsible for its physical and sensorial properties, investigations of systems structure are essential [1].

In most topical pharmaceutical and cosmetic formulations, primary emulsifiers are low molecular weight surfactants. The use of polymeric emulsifiers (associative thickeners) has been recently suggested as a non irritant alternative to low molecular weight surfactants [2].

Due to their large molecules, Polymeric emulsifiers do not penetrate the skin nor do they enhance an unwanted penetration of other formulation compounds. Thanks to their excellent emulsifying and thickening properties. They also fulfill the need of industry to lower low molecular weight emulsifier concentration without any impact on the stability or flexibility of formulation.

Liquid dispersion polymers (LDPs) recently have been used for emulsions stabilization. The system (LDPs) consists of a polymer phase, a carrier phase (carrier oil), and an activator. The polymer phase can be of anionic or cationic nature. The carrier oil can be a mineral oil, cosmetic ester, or natural oil. The activator functions in the same way as the emulsifier. The emulsifier is nonionic with a high HLB. The activator enables water molecules to move through the small polymer particles by osmosis and allows them to swell [3].

Polymeric emulsifier Simulgel<sup>®</sup> A (INCL: Ammonium polyacrylate / isohexadecane / PEG-40 castor oil) is a new polymer based on inverse latex technology with rapid gelling action and can be used at room temperature. Neither neutralization nor preswelling operations are required, making it very safe for use in production. Just by adding water to Simulgel<sup>®</sup> A, the emulsifier inverts and the polymeric network expands instantly to form stable gel in a few seconds. These special properties are above and beyond its thickening activity, common to all polyacrylates [4].

### **STABILITY OF PARENTERAL EMULSIONS:**

Emulsions are dispersions of one immiscible liquid in another that are typically stabilized with emulsifiers. Parenteral emulsions typically are prepared with phospholipids and used to provide nutrition. In the past 20 years, phospholipid-based emulsions have been investigated as vehicles for enteral and parenteral drug delivery [1-5]. For intravenous use, drugs may be incorporated in highly purified vegetable oil, which is emulsified by phospholipids as an oil-in-water (O/W) emulsion. The potential advantages of these

emulsions are that they are carriers for lipophilic and hydrolytic drugs; can be used to reduce toxicity; and are biodegradable, and relatively easy to produce on a large scale. Emulsions may also have a potential for use in sustained- release <sup>(6)</sup> and targeted delivery systems [6].

#### **Instability of Parenteral Emulsions :**

O/W emulsions are composed of oil droplets as the internal phase dispersed in an external aqueous phase. For use as injectable drug delivery systems, emulsions must be sufficiently stable throughout manufacturing, shipping, storage, and clinical administration. They should be capable of withstanding terminal sterilization, and, for intravenous use, the maximum diameter of the internal phase of the oil droplets needs to be <2  $\mu\text{m}$ . However, the oil droplets tend to coalesce with time at ambient or stressed conditions. Thus, the physical stability of the emulsions is critical in their use as drug delivery systems. The physical instability process may progress from creaming, flocculation, and coalescence to complete phase separation. The primary mechanisms of emulsion instability are coalescence and Ostwald ripening.

Creaming occurs as a result of the application of an external force such as gravitation, centrifugation, and electricity. There is no change in droplet size or size distribution during creaming. Creaming takes place if the two phases of emulsion are not of equal density. The droplets either rise to the top of the emulsion (cream), or they settle to the bottom (sediment). A creamed system redisperses on shaking. However, since the droplets are in close proximity to one another, there is the possibility of flocculation and/or coalescence of the creamed droplets. Flocculated systems cream faster, due to the large size of the flocs. These systems are also easier to re-disperse. Occurrence of coalescence in the creamed layer depends on the probability of the interfacial layer to rupture. Practically, the creaming rate can be reduced by decreasing the emulsion droplet size, equalizing the densities of two phases, and increasing the viscosity of continuous phase [7].

Flocculation is the process in which emulsion droplets aggregate as a result of collisions and adhesive inter droplet forces without rupture of the emulsifier layer. In flocculation, two droplets are associated but still separated by an interfacial layer. They retain their individual identities in the clusters (or flocs) and re-disperse on shaking. Moreover; there is no change in droplet size and/or size distribution. Flocculation is enhanced by polydispersity of the emulsion droplets because the differential creaming rates of small and large droplets cause them to pack more closely than in a monodisperse system. Flocculation may lead to coalescence if the interfacial film ruptures.

Coalescence is the process by which the interfacial liquid film between two droplets ruptures and they converge to form one large droplet. Unlike flocculation, coalescence is considered irreversible. The coalescence process begins when two droplets undergo adhesive contact. The liquid film between the droplets drains. The rate of the drainage is related to the rigidity or micro viscosity of the interfacial layer. Next the interfacial layers rupture and the two droplets merge into one, thereby increasing droplet size [8].

#### **Methods of Measuring Instability:**

The droplet size change is the primary physical stability determinant. Obtaining a reliable value and understanding the limitations associated with its measurement are crucial for the investigation of emulsion stability. The droplet size range in parenteral emulsions is between 25  $\mu\text{m}$  to 1mm, which is near or below the resolution limit for optical microscopy and imaging methods. Although the Brownian motion of such small droplets can be reduced using a viscous media, the low light levels encountered at the high magnifications (typically 800x) needed to see such droplets make traditional photographic methods unrealistic. Droplet sizing instruments based on measurements of changes in electrical resistance (e.g., the Coulter Counter) or light transmission of supporting electrolytes, which may change the size and physical stability of the droplets [9].

Photon correlation spectroscopy (PCS) is a light-scattering technique that uses fluctuation in scattered light intensity to measure the velocity of the Brownian motion of the droplets and hence infers their diameter. The instrument measures the scattered light intensity as a function of time. The smaller the droplets, the higher the intensity. However, quantitative information about droplet size cannot be obtained from the scattered light intensity alone. Thus, the autocorrelation function of decaying (or fluctuating) light intensity is used in size determination.

PCS depends on Brownian motion and typically allows a reliable determination of the mean droplets of diameter in the range of 0.1 to 2.0  $\mu\text{m}$  with the underlying assumption of a Gaussian distribution [8]. This size range typically constitutes the majority of the droplets in parenteral emulsions. PCS provides an accurate measure of the mean droplet diameter but fails to give information on the droplet size distribution. Light obscuration particle counting is a technique by which droplets may be counted and sized as they flow, one at a time, in a fluid past a sensor capable of responding to the obscuration created by each droplet. Droplets can be counted at rates of up to several thousand per second. The minimum measurable diameter is about 0.4  $\mu\text{m}$ . Size standards with narrow size distributions are employed in calibration. If enough droplets are sampled, a complete droplet size distribution can be determined. This technique has been

applied to monitor contaminating particles in parenteral products and to determine large droplets in phospholipid-based parenteral emulsions [9].

Electron microscopy is useful for the size measurement of submicron droplets. It permits direct measurement of individual droplets, providing size distribution and mean diameter. Considerable sample preparation is required. Du plessis and colleagues developed a transmission electron microscopy (TEM) method for the determination of droplet size of parenteral fat emulsions.

#### **STABILITY OF MULTIPLE EMULSIONS:**

The complex nature of multiple emulsion systems has hindered the study of their stability. Over the past few years, a number of new techniques have been developed to detect and quantify breakdown. This section describes some of these techniques and discusses some of the advantages and problems associated with the various methods.

Measurement of the number and size of the multiple drops over a period of time gives a good indication of stability. The simplest and most direct method of achieving this is by photomicrography. There are many problems associated with this method, not the least being the tedium of the process which involves the observation of random samples under the microscope and comparing the size of the observed multiple, internal and simple drops with standard size circles on an eyepiece graticule. In many cases, the number of internal droplets entrapped can also be monitored.

#### **Mechanism of Instability:**

The mechanisms of instability in multiple emulsions are complex and difficult to study. Florence and Whitehill (1981) have attempted an analysis of the possible mechanisms of instability. Theoretical predictions appear to agree with experimental results. W/o/w multiple drops, for example, may coalesce with other oil drops (simple or multiple) or they may lose their internal droplets by rupture of the oil layer on the surface of the internal droplets, leaving simple oil drops. Under the influence of an osmotic gradient, the passage of water across the oil phase. This leads to either swelling or shrinkage of the internal droplets, depending on the direction of the osmotic gradient. Another possible breakdown mechanism may be coalescence of the internal aqueous droplets within the oil phase. A combination of these mechanisms may take place and the exact breakdown mechanisms remain unclear. The likelihood of events taking place may be predicted by analysis of the Van der Waals attractive forces and free-energy changes in these systems [10].

The ability of multiple emulsions to entrap materials is one of their most useful assets and so the passage of materials from the internal to external phase, across the middle phase, is important. This is particularly so in pharmaceutical systems where multiple emulsions are envisaged as possible controlled-release drug delivery systems. The stability and release characteristics of emulsion systems are influenced by a number of factors such as the composition of the emulsion, droplet size, viscosity, phase volumes, pH, etc. This becomes even more complex in multiple systems because there are two dispersed phases, two phase volumes, at least two surfactants, and 3 different droplet size distributions. The release of materials from complex systems will be influenced by the factors controlling the stability and properties of simple emulsion systems but also by a number of factors specific to multiple emulsion systems [11].

#### **SPECIFIC FACTORS CONTROLLING THE STABILITY:**

##### **Effect of Electrolytes:**

Electrolyte presence appears to be one of the most important factors in determining the stability and release of materials from the internal droplets. The effects of electrolytes are two-fold: (a) osmotic; and (b) interfacial, the former being peculiar to multiple systems. The effects of electrolytes on electrical double layers, etc., have not been considered as they are not specific to multiple systems [12].

##### **Mechanism of Passage of Materials across the 'MEMBRANE' Phase:**

There are several possible mechanisms by which materials may be transferred across the oil layer in a w/o/w system. The most obvious is by diffusion for unionized lipid-soluble materials. This will be dependent on the nature of the material (including its dissociation constant) and the oil and the pH of the aqueous phase. In this respect, liquid membranes have been proposed as possible treatments for drug over dosage [13].

##### **Properties of the Membrane Phase :**

The properties of the membrane phase will be of prime importance in determining the stability of the system and mass transfer rates. Of these properties, the most important is viscosity. The thickness of the membrane phase and the type of surfactant used may also be important in determining stability and transport rates.

### Properties of the Interfacial Films :

In a second-order multiple emulsion system, there are two separate interfacial films to be considered. The nature of each film will depend on the nature of the primary and secondary surfactants, used to prepare the primary and multiple emulsions, respectively, and also on the presence of materials in the internal and continuous phases. The viscosity and elasticity of the o-w and w-o interfacial films are particularly important in determining the stability of both the primary and secondary emulsions by, for example, hindering the close approach of drops (by surfactant chain effects) and preventing coalescence (by acting as a mechanical barrier). They will also determine the transport of materials across the interface as through the different phases of the emulsion.

### Properties of the Primary Emulsion:

Instability of the primary emulsion will result in coalescence of the internal droplets within the membrane phase resulting in increased breakup of the multiple drops due to rupture. The internal aqueous phase volume (w/o) may influence the release of materials from the internal aqueous phase.

### DISCUSSION

It is clear that on purely thermodynamic grounds, emulsions are physically unstable. A reduction of the interfacial area by coalescence reduces the systems energy and this process is thermodynamically favored. For this reason, Garrett defined a stable emulsion as one that “would maintain the same number of sizes of particles of the dispersed phase per unit volume of weight of continuous phase. Thermodynamic stability of emulsions differs from stability as defined by the formulator or the consumer on the basis of entirely subjective judgment – A products shelf life may be directly related to its kinetic stability. Kinetic stability means that the physicochemical properties of an emulsion do not change appreciably long period of time.

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