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Advancements in Stabilization of Multiple Emulsions

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Abstract : Multiple emulsions are those polydispersed systems where the drops of dispersed phase themselves contain even smaller droplets. Based on dispersed medium they are of water in-oil-in water or oil-in-water in oil type with former having wide application in encapsulating active ingredient and as novel carrier for drug delivery. Stabilization can be brought about by use of high viscous oils, gelation of phases, liquid crystal formation or stabilization in presence of electrolytes. New method of formulation of emulsion using mono fabricated channel array i.e. Micro Channel (MC) emulsification which exploits interfacial tension on micrometer scale.

Keywords: Mono dispersity, Micro capillary technique, Micro channel emulsification.

Introduction

Depending upon the equilibrium between oil, water and surfactant phase the stabilization takes place . Interphase also contributes a huge part in stabilization. The drug release mechanism, formulation of emulsions comprises major part in these type of emulsions. Several properties are shown by multiple emulsions like flow characteristics. Also the uses of these type of emulsions (after the stabilization) are in a wider range. Multiple emulsions are nothing but the new carrier systems which are complex, poly dispersed, containing more than a single phase systems which consist of at least two immiscible liquids that is both w/o and o/w emulsions exist at the same time in a single system. Lipophilic and hydrophilic surfactants contribute a great part in stabilization. The droplets of dispersed phase contain finer dispersed droplets in inner part of it .Therefore they are called as “emulsions of emulsions”. The inner droplets which are dispersed in multiple emulsions are separated from outer liquid phase. This separation is done by a layer of another phase.

1. Stabilization :

It is a phenomenon which depends upon equilibrium between three phases; water, oil and surfactant. Nevertheless, multiple emulsions are thermodynamically unstable. A little emulsifier may result in unstable systems, whereas too much emulsifier may lead to toxic effects and can cause destabilization.Some mechanisms have been identified which leads to instability of multiple emulsions:

1. Coalescence of multiple emulsion droplets or internal droplets.
2. Rupture of oil layer on surface of internal drops.
3. Shrinkage and swelling of internal droplets due to osmotic gradient across the oil membrane.
4. Flocculation of internal aqueous phase and multiple emulsion droplets and Phase separation.

The main problem in regards to stability is the presence of two interfaces which are thermodynamically unstable. So,Two different emulsifiers are necessary for their stabilization; one with a low HLB (Hydrophile-Lipophile Balance) value for W/O interface and the another one with a high HLB value for O/W interface. We can stabilize the emulsions by using electrolytes, by forming polymeric film,by interfacial complexation between non-ionic surfactant and macro molecules .

Following approaches we can use to overcome instability in multiple emulsions:

1.1 The inner phase: We can stabilize the inner W/O emulsion mechanically, or in presence of better emulsifiers, reducing its droplet size. Also we can achieve our aim by Preparing microspheres and Increasing the viscosity of inner water. [1]

1.2 The oil phase: By modifying nature of oil phase by increasing its viscosity or by adding carriers or by adding complexing agents to the oil.

1.3 The interfaces: This can be done by stabilizing inner and/or outer emulsion by using polymeric emulsifiers, macro molecular amphiphiles or colloidal solid particles to form strong as well as more rigid film at the interface; also by in-situ polymerization at the interface. Hence, stability of multiple emulsions can be improved by forming a polymeric film or macro molecular complex across the oil/water interfaces

2. Drug Release Mechanisms :

Drug release in multiple emulsions from internal to external phase occurs via the middle layer. The release rates are affected by various factors such as droplet size, pH, phase volume ratios, viscosity, nature of entrapped material etc.Some of the mechanisms of drug release are as follows:

2.1 Diffusion mechanism :

Most common transport mechanism where unionized drug (hydrophobic moieties) diffuses via oil layer (semipermeable liquid membrane), especially in stable multiple emulsions. Drug transport has been found to follow first order kinetics and obeyed Fick’s law of diffusion. [2]

2.2 Carrier mediated transport :

It involves a special molecule (carrier) which combines with drug and makes it compatible to permeate via the oil membrane. This involves either incorporation of some material into internal aqueous phase of membrane phase, which reacts with permeating compound to render it liposoluble. Carrier compounds effectively pump the permeating compound across membrane; e.g.,stearic acid facilitated diffusion of Cu^{2+} ions. This mechanism is especially effective for transport of highly hydrophilic compounds.

2.3 Micelle transport:

Since outer lipophilic nature, in this mechanism inverse micelles consisting of non-polar part of surfactant lying outside and polar part lying inside encapsulate hydrophilic drug in core and permeate via the oil membrane.. Inverse micelle can epitomize both ionized and Non ionized drugs. The presence of both lipophilic and hydrophilic surfactants in the oil phase helps in the formation of water swollen inverse micelles, which may act as a mobile carrier for both ionized and unionized drug.

2.4 Thinning of oil membrane:

Due to osmotic pressure difference oil membrane become thin, so water and drug easily diffuses. This mechanism comes into existence when there is an osmotic pressure difference between two aqueous phases, which also provides force for transverse of molecule. Rupturing of oil membrane can unite both aqueous phases and thus drug could be released easily. Solubilization of minute amounts of internal phase in membrane phase results in transport of very small quantities of materials.

3. Formulation Technique

Emulsions are thermodynamically unstable and thus we add emulsifier like surfactant, co polymer to maintain its stability. So two surfactants of opposite nature are added to the system. One stabilizes the w/o (lipophilic) emulsion while the other stabilizes the o/w (hydrophilic) emulsion. When emulsion formation takes place, these emulsifiers are adsorbed on the surface of the droplets which prevents them from aggregating.

3.1 Double emulsification technique :

The first step is formation of a simple w/o or o/w emulsion. In presence of an emulsifier, this is again re- emulsified with excess of water or oil phase to get a multiple emulsion of o/w/o or w/o/w type.[3] Second step is very crucial because fracturing of the internal globules forming simple emulsion of o/w or w/o type may take place depending on various factors. It has a advantage that this technique is easier and gives a high yield.

3.2 Phase inversion technique :

It is a one step mechanism. In this ,the continuous phase become the dispersed phase and vice-versa, could be considered a good path to produce emulsion which are made up of very small droplets**.** Phase inversion could be accompanied by altering the temperature and volume fractions of the system and phases respectively and by adding salts or by imposing the flow rates. It has been founded that, if we raise the temperature, non-ionic surfactants become more hydrophilic. As a result of this ,they change their chemical configuration and phase inversion is done..

3.3 Membrane emulsification technique:

In this technique the emulsifier used is a glass membrane. The principle which is used is dispersing one phase which is not miscible (dispersing phase) into continuous phase by applying pressure. The particle size of the w/o/w emulsion can be restrained by selecting perfect porous glass membrane.

4. Methods to stabilize Multiple Emulsions:

4.1 Stabilization in presence of electrolyte:

Addition of electrolyte resulted in improvement of emulsion stability with respect to coalescence. So, when electrolytes are added in inner layer or outer aqueous layer multiple emulsions migrate across the oils layer and thus migrate to some other aqueous layer. This migration induces changes in osmotic pressure with time and thus alters the stability of multiple emulsions.

4.2 Stabilization by forming polymeric gels:

In order to improve stability of multiple emulsion, either internal phase (aqueous) or secondary aqueous phase needs to be gelled. Production of gels in aqueous phase leads to system which has greater stability. If the internal aqueous phase is gelled, it will prevent coalescence. And when the outer continues phase is gelled, an opaque emulsion is produced in which the dispersed droplets are held in a network of polymer from where the droplets are released on contact with water.

4.3 Steric Stabilization:

Emulsion can be stabilized by increasing the repulsion between the dispersed phases that is by increasing the electrostatic or steric repulsion. This can be done by adding an emulsifier. emulsifier are amphiphiles which reduce the interfacial tension between the two phases and contribute to stabilization of dispersed droplet. Both electrostatic and steric forces can prevent aggregation or coalescence and thus stabilize emulsions.

4.4 Liquid crystal stabilized multiple emulsions:

Liquid crystal at the periphery of multiple emulsion droplets prevents the diffusion of water between inner and outer aqueous system. Liquid structure has a mesomorphic structure between solid and liquid. When a liquid crystal is present at interface, it acts as emulsion stabilizer as it provides rigidity and less composition fluctuation at interphase.

5. Micro channel Emulsification :

For the production of monodisperse emulsions , straight-through microchannel (MC) emulsification is a new technique. It uses a silicon array of micro machined through-holes, known as a straight-through micro-channel.[4] The oblong straight-through MC have channel lengths of 48.7 and 9.6 μm. In contradiction, the systems containing cationic surfactants resulted in the manufacturing of polydispersed O/W emulsions and complete wetting of the dispersed phase on the surface of plate. This showed that a repulsive surfactant–plate surface interaction and a high contact angle value have to be there to achieve a successful straight-through microchannel emulsification. It also showed that it is necessary to keep the negatively charged plate surface hydrophilic when the emulsification process is occurring .Because of the the dispersed-phase flux the straight-through MC emulsification behavior gets affected. [5].

The effect of different concentrations of Sodium Caseinate (0.5, 1, 1.5 gr) in the external aqueous, different portions of primary emulsion (25%, 40%, 50%) and type of hydrophilic emulsifiers in the making and stability of W/O/W emulsions prepared. Sodium caseinate which is a milk protein is a stabilizer at oil-water interfaces is well documented. NaCN is amphiphilic proteins having a strong tendency to adsorb at oil-water interfaces during emulsification thereby reducing interfacial tension.

Conclusion:

Multiple emulsions have shown good applications in pharmaceutical research and development recntly . Use of amphiphilic macromolecules and give up on surfactants having low molecular weight has shown improvement in their stability. Nowadays, the ideal multiple emulsions are likely to be prepared by membrane separation technique using polymeric amphiphiles as emulsifiers with viscosity modifiers and electrolytes to control the osmotic pressure .Newer methods formulation like MC emulsification thus has the advantage of a high yield, which are the results of mild action during droplet formation. In multiple emulsion formulations interior emulsion are replaced by thermodynamically stable nanostructures or micro emulsions in coming years.

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