Introduction

Dispersions of oil and water are commonly employed in the pharmaceutical industry. These dispersions can be classified in three major categories \(^1\) (fig. 1)

- Conventional Emulsions (or) macroemulsions
- Micellare Solutions
- Microemulsions

Figure 1: Emulsion Structure of Micellare solution, Microemulsion

Macroemulsion :

An emulsion (macroemulsion) is a heterogenous system consisting of at least one immiscible liquid dispersed in another in the form of droplets, whose diameter in general exceeds 0.1\(\mu\)m. Such systems possess a minimum stability, which may be accentuated by such additives as surface active agents, finely dividing solids etc. \(^2\)

Micellar Solution :

Micelles are microscopically organized chemical assemblies formed by self-aggregation of individual surfactant molecule. Micelles exist as monomers in very dilute solutions but when their concentration exceeds the critical micellar concentration (CMC) of the surfactant, the monomers associate spontaneously, forming aggregates of colloidal dimensions called micelles. In reverse micelles the polar head of the amphiphile are orientated inward and the non-polar tails are oriented toward the oil continuum. \(^3\)
1.1 Microemulsion:

The term “Microemulsion” refers to a thermodynamically stable isotropically clear dispersion of two immiscible liquids, such as oil and water, stabilized by an interfacial film of surfactant molecules. The dispersed phase typically comprises small particles of droplets, with a size range of 5 nm – 200 nm, and has very low oil/water interfacial tension. Because the droplet size is less than 25% of the wavelength of visible light, microemulsions are transparent. The Microemulsion is formed readily and sometimes spontaneously, generally without high-energy input.4

![Microemulsion Structure](image)

Three types of microemulsions are most likely to be formed depending on the composition

1) Oil in water microemulsions
2) Water in oil microemulsions
3) Bi-continuous microemulsions

In all three types of microemulsions, the interface is stabilized by an appropriate combination of surfactants and/or co-surfactants.
Discrete microemulsions (w/o or o/w microemulsion) consist of domains of one of the pseudo phases (water or oil) dispersed in the other pseudo phase. These microemulsions are generally found when the main component of the other pseudophase and little surfactant is present. The structure of this type microemulsion resembles that of emulsions in that one phase is dispersed in another phase.

1.2 Structure of Microemulsion

Microemulsions are the simple spherical or cylindrical structures formed by the aggregates of miscelles that are formed by surfactants at the oil/water interface. Other structures are lamellar, spherulite, vesicles, interconnected rod-like micelles, bicontinuous structures. Both spherical and non-spherical forms of the dispersed state may aggregate forming chains, lamellae, liquid crystalline etc. Gels of varying consistency may also be formed.

1.3 Important characteristics of Microemulsions

- Particle size : 200nm
- Thermodynamically stable
- Optically clear
- Surface area increased
- High solubilising capabilities
1.4 Factors to be considered during preparation of Microemulsion

Three important conditions:

- Surfactants must be carefully chosen so that an ultra low interfacial tension ($<10^{-3}$ mN/m) can be attained at the oil/water interface which is a prime requirement to produce microemulsions.
- Concentration of surfactant must be high enough to provide the number of surfactant molecules needed to stabilize the micro droplets to be produced by an ultra low interfacial tension.
- The interface must be flexible or fluid enough to promote the formation of microemulsions.

1.5 Comparison with Emulsions\(^1\)

Table 1.1 Comparison of emulsions and microemulsions

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Emulsions</th>
<th>Microemulsions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1" alt="Figure 4: Emulsion" /></td>
<td><img src="image2" alt="Figure 5: Microemulsion" /></td>
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<tr>
<td>2</td>
<td>Emulsions consist of roughly spherical droplets of one phase dispersed into the other.</td>
<td>They constantly evolve between various structures ranging from droplet like swollen micelles to Bicontinuous structure.</td>
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<tr>
<td>3</td>
<td>Droplet diameter: 1 – 20 mm</td>
<td>Droplet diameter: 10-100 nm</td>
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<td>4</td>
<td>Most emulsions are opaque (white) because bulk of their droplets is greater than wavelength of light and most oils have higher refractive indices than water.</td>
<td>Microemulsions are transparent or translucent as their droplet diameter are less than ¼ of the wavelength of light, they scatter little light.</td>
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<tr>
<td>5</td>
<td>Ordinary emulsion droplets, however small exist as individual entities until coalescence or Ostwald ripening occurs.</td>
<td>Microemulsion droplet may disappear within a fraction of a second whilst another droplet forms spontaneously elsewhere in the system.</td>
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<tr>
<td>6</td>
<td>They may remain stable for long periods of time, will ultimately undergo phase separation on standing to attain a minimum in free energy. They are kinetically stable thermodynamically unstable.</td>
<td>More thermodynamically stable than macro emulsions and can have essentially infinite lifetime assuming no change in composition, temperature and pressure, and do not tend to separate.</td>
</tr>
<tr>
<td>7</td>
<td>They are lyophobic.</td>
<td>They are on the borderline between lyophobic and lyophilic colloids.</td>
</tr>
<tr>
<td>8</td>
<td>Require intense agitation for their formation.</td>
<td>Generally obtained by gentle mixing of ingredients.</td>
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Figure 4: Some formulation approaches to improve bioavailability of poorly water soluble drugs
Glipizide is an oral drug that can be used in the treatment of type 2 diabetes in humans and pet animals i.e. cats. The FDA approved glipizide in May 1984. Diabetes mellitus is a most common disease in cats similar as humans. Oral hypoglycemic drugs can be a potential treatment option for affected cats, especially when cats or owners do not tolerate administration of injectable insulin. Glipizide is especially helpful in cats with type II diabetes. It is not effective in insulin dependent diabetics (type I diabetes) or in insulin resistant animals. Glipizide has not been shown effective in dogs.\textsuperscript{54,57}

Glipizide belongs to the sulfonylurea class of drugs. Other examples of this class are Glimepride, Glyburide, Tolbutamide etc. Their strongest method of action is to stimulate the beta cells of the pancreas to produce insulin. They also increase the sensitivity of other tissues to insulin, either by causing insulin to bind to the insulin receptor more easily, or by causing the cell to respond more strongly to the insulin. These results into the fall of blood glucose level by increasing the glucose metabolism. Literature data shows that, Glipizide may have other effects producing by various mechanism of actions and which also contributes to the lowering of blood glucose level, however the mechanism of actions are still unclear.\textsuperscript{53,55,56}

Glipizide is a weak acidic drug (pKa = 5.9), practically insoluble in water and acidic condition. It is absorbed rapidly in the small intestine and has a rapid onset of action. The absorption mechanism in the intestine is primarily passive diffusion and the driving force is the concentration gradient of the unionized species in accordance with the pH partition hypothesis. Furthermore, the PK of Glipizide in humans is characterized with high peak blood concentrations within 1–3 h after administration, and short elimination half lives ranging from 2 to 4 hours. Therefore, it is routinely administered two to three times daily. Careful adjustment of the dose is necessary to avoid hypoglycaemic symptoms.\textsuperscript{54,55,56,57}