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A REVIEW ON COMPARATIVE STUDY BETWEEN EMULSION, MICROEMULSION AND NANOEMULSION

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ABSTRACT

Emulsion is a biphasic liquid dosage form. These are of two type oil in water and water in oil, it is a conventional method now days novel dosage forms are used like microemulsion and nanoemulsion. These are prepared by using different process and provide better bioavilability and response. There size are also differ and provide good result as comparison of emulsion. Novel drug delivery system is commonly used having better approach towards other dosage form. Emulsion is one of the most important system of dosage form. Applications of emulsions increased especially after micro and nano-emulsion emergence. This paper is an attempt to summarise comparative aspects like definition, theories, types, methods of preparations, advantages, disadvantages and methods of analysis of emulsion, micro-emulsion and nano-emulsion.

KEYWORDS

Emulsion, Microemulsion, Nanoemulsion, Dry gum method and Shear force.

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INTRODUCTION

Emulsion

An emulsion is a dynamically ambiguous system subsisting of partially two non- miscible liquidstate, upon which is diffuse as drop (the dispersed phase) in the other liquid state (the continuous phase), preserved by the existence of an emulsifying agent. The molecule diameter of the diffuse states usually develop from about 0.1 to 10 µm, despite particle diameters as slight as 0.01 µm and as extensive as 100 µm are not infrequent in some formations[1].

Type of Emulsion[2]

Oil in water (o/w) in the departed system the oil (or internal) phase is disappearing as droplets over the extrinsic aqueous phase.

Water in oil (w/o) inversely, in w/o emulsions, the intrinsic phase is prepared of water drop and the external phase is non-aqueous.

Oil in water in oil (w/o/w) In extension to the emulsion type variety expressed raised there are further more structurally complex types, termed multiple emulsions However, the pharmaceutical usage of these are acutely narrow due to their achievable inversion to the architect primary emulsion. For example, an o/w/o emulsion can degenerate to a w/o emulsion. Emulsions and creams, are essentially erratic systems, which, in the nonappearance of emulsifying agents, will disassociated into the two parted phases.

Water in oil in water (o/w/o) the emulsifying agent advantage is basically surface-active agents. o/w emulsions may be executed topically or orally although the advantage of w/o creams is basically (but not entirely) narrow to composition arrange for topical appliance.

PREPARATION OF EMULSION[3]

Emulsion containing natural gum

(a) Gum acacia accommodate emulsion- Acacia in fine powder form is used as an emulsifying agent. The following methods are generally advantage for the formation of emulsion on a small scale. There are two methods of formation a primary emulsion:

Dry gum method

Emulsifier is blended with oil previously water addition.

The amount of oil, water and gum for chief emulsion are determined. The acacia and the oil are located in a dry porcelain mortar. When the acacia is comprehensively distributed through the oil, Water is combined, all at once. The mixture is crushed frequently but slightly in one order until the mixture swell bottom the pestle.

The chief emulsion is crushed for at least 5 minutes. Completely, the emulsion is conveyed to an accredited cylinder and delivers to volume with water.

Wet gum method

Emulsifier is enumerate to water to design a mucilage then oil is gradually enumerate to emulsion.

The amount of oil, water and gum for chief emulsion are determined. Acacia and water are crushed of or mucilage in porcelain in mortar. The oil is also combined. A limited quantity with consistant, acclerated and slight crushed. When all the oil has been added, the mixture is crushed actively for a few minutes. Completely, the emulsion is conveyed to accredited cylinder and delivers to volume with water.

Emulsions accommodated more than one oily liquid: When two or more oily liquids are present, the amount of acacia needed for each is determination, and the total of these total is beneficial for the emulsion. Secondly each oil may be emulsified individually previously mixing.

Micro-emulsion[4-6]

IUPAC defines micro-emulsion as dispersion made of water, oil, and surfactant(s) that is an isotropic and thermodynamically stable system with dispersed domain diameter varying approximately from 1 to 100 nm, usually 10 to 50 nm.

Theories

Interfacial theory

This is also known as mixed film or dual film theory. Surfactant and co-surfactant together forms complex film at the oil water interface and thus creates generation of micro emulsion droplets.

Solubilization theory

This theory tells that swollen miceller system forms in the form of micro emulsion. Oil is solubiliseddue to normal micelle formation and water solubilised by reverse micelle formation. Phase diagram is generally useful to understand this theory assumption[7-10].

Thermodynamic theory

When interfacial tension between two immiscible phases reduces zero it cause spontaneous formation of micro emulsions and formed negative free energy helps to make emulsion thermodynamically stable. Microemulsions are also known as transparent emulsion, swollen micelle and micellar solution.

Self-microemulsifying drug delivery system (SMEDDS) is also one of the popular term for microemulsion mediated delivery of drugs[11].

Preparation methods

Phase titration method

Micro emulsion was prepared by dispersing required quantity of drug in appropriate quantity of oil which is required for the solubilisation of drug[12]. The mixture was homogenized and accurately weighed quantity of surfactant: co surfactant blends was added in small portion with stirring to it[13-16]. The blends were mixed thoroughly using magnetic stirrer and drop wise double distilled water added to it with continuous stirring around 10 minute and rate of stirring was optimized as per requirement of particle size[17].

Phase inversion temperature method (PIT)

Phase inversion of micro emulsions means conversion of O/W to W/O system by adding excess of the dispersed phase or by rising temperature when non-ionic surfactant are used to change spontaneous curvature of the surfactant which brings system near to minimal surface tension and to form fine dispersed oil droplets[18-20]. This method shows extreme changes in particle size which further leads to changes in in-vivo and in-vitro drug release pattern[21-22.]

Advantages[23-25]

- It is very easy process to prepare and due to spontaneous formation ability.
- It is very good system to raise rate of absorption as well as bio avaibility by eliminating interfering variations
- This formulation is able to improve solubility of lipophilic drugs
- This is thermodynamically more stable system as compared to conventional system and so suitable for long term purpose.
- This would be preferred to develop sustained and controlled releases drug system
- This is best system to minimise first pass metabolism.

Disadvantages[26-27]

- Use of excess amount of surfactant and co-surfactant increases cost.
- Excess amount of surfactants can improve to mucosal toxicity.

The major components of micro emulsion system are[28]

- Oil phase
- Surfactant (Primary surfactant)
- Co-surfactant (Secondary surfactant)
- Co-Solvent

Nanoemulsions

A nanoemulsion can be considered to be a conventional emulsion that contains very small particles[30]. Nanoemulsions may be of the oil-in-water (O/W) or water-in-oil (W/O) types depending on whether the oil dispersed as droplets in water, or vice versa. As mentioned previously, we are primarily concerned with colloidal dispersions suitable for encapsulating lipophilic components in aqueous environments, and so we focus on oil-in-water nanoemulsions that consists of small particles of oil and surfactant molecules dispersed within an aqueous medium. The following definition is proposed to describe oil-in-water nanoemulsions: An oil-in-water nanoemulsion is defined as a thermodynamically unstable colloidal dispersion consisting of two immiscible liquids, with one of the other liquids being dispersed as small spherical droplets ($r < 100$ nm) in the other liquid. So a nanoemulsion could be formed from oil and water without using a surfactant. In practice, this system would be highly unstable to droplet coalescence and a surfactant is needed to facilitate the formation of the nanoemulsion and to ensure its kinetic stability during storage[31]. Sometimes a combination of surfactants other than a single surfactant are used to form and stabilize nanoemulsions. A nanoemulsion is therefore usually prepared using the same components as a microemulsion: oil, water, surfactant and possibly a co-surfactant. The structure of the particles in a nanoemulsion are also very similar to those found in a microemulsion: the non-polar tails of the surfactant molecules poke into the hydrophobic form formed by the oil phase, while the polar head groups of the surfactant molecules protrude into the surrounding aqueous phase (Figure No.1). The major distinction between a nanoemulsion and a microemulsion is therefore their thermodynamic stability: nanoemulsions are thermodynamically unstable, whereas microemulsions are thermodynamically stable.

Types of nanoemulsion[32-33]

1. Oil-in-water (o/w)
2. Water-in-oil (w/o)
3. Oil-in-water-in-oil (o/w/o)
4. Water-in-oil-in-water (w/o/w)

Preparation methods of nanoemulsion

High energy emulsification method: this include ultra-sonication and high pressure homogenization.

Low energy emulsification

In this phase inversion temperature method, solvent displacement method and phase inversion composition method are involved.

High-Pressure Homogenization

This method is specially designed high- pressure homogenization instrument is used to produce nano sized particles. At high pressure (500 to 5000 psi), oil phase and water phase are allowed to force through small inlet orifice[34].

So extremely small size particles are created due to strong turbulence and hydraulic shear. But this method requires high temperature and energy. Pressure, homogenization cycles are directly responsible for particle size. Higher the pressure and higher the homogenization cycles, smallest is particle size. This method is easy to scale up[35].

Microfluidization

In this method also specially designed device called as micro fluidizer is used to create high-pressure (500 to 20000psi). Coarse emulsion is prepared initially by mixing oil and water phase. This device consists of interaction of small micro channels through which coarse emulsion is forced to an impingement area to form nano size fine particles followed by filteration to obtain uniform particles[36-37].

Ultrasonication

This method is based on principle that when coarse emulsion is put in ultrasonic field and external pressure is increased, cavitations threshold also increases to limit where fine nano size particles are formed[38].

Phase inversion method

This method is based on principle of phase inversion temperature which is the temperature at which phase transition occurs. Low temperature involves O/W emulsions and high temperature involves W/O emulsion. Rapid cooling and heating cycles produces fine particles. Non-ionic surfactant like polyoxyethylene becomes lipophilic at high temperature and hydrophilic at low temperature due to dehydration of the polymer chain.

Spontaneous Emulsification

This method is very simple and uses volatile organic solvent composition of oil, water, lipophilic and hydrophilic surfactant. This composition is used to mix homogenously by magnetic stirring then evaporate the water-miscible solvent under vaccum to obtained nano-emulsion[39].

Solvent Evaporation Technique

Initially drug mix with organic solvent using suitable surfactant and prepare O/W emulsion by mixing continuous phase. Then organic solvent was evaporated under vacuum or heating or at atmospheric conditions to obtain microspheres loaded with drug followed by centrifugation or filtration[40].

Hydrogel Method

This method is similar with solvent evaporation method. Higher shear force are used to form nano-emulsion of drug- solvent which is miscible with the drug anti-solvent.

Advantages[41-42]

- Nano emulsion is helpful to improve water solubility and bioavailability of lipophilic drugs.
- It is preferred to incorporate GIT irritation causing active drugs.
- It is dosage form to incorporate first pass metabolism mediated degradation prone drugs.

- Stability issues like creaming, flocculation, coalescence, and sedimentation are rarely observed in nano-emulsion.

Dis-advantages[43-44]

- The major disadvantage of nanoemulsion is cost of fabrication which is expensive.

Table No.1: Different components used in formation of Microemulsion

S.No	COMPONENTS	EXAMPLES[28-29]
1	Oils	Saturated fatty acid-lauric acid, myristic acid, capric acid Unsaturated fatty acid like oleic acid, linoleic acid, and linolenic acid, Fatty acid ester-ethyl or methyl esters of lauric, myristic and oleic acid.
2	Surfactants	Polyoxyethylene, Polysorbate,Tween 20, 40, 60, 80 or SorbitanMonolaurate (Span), Soybean lecithin, egg lecithin, lyso lecithin, Sodium dodecyl sulphate (SDS),
3	Co-Surfactants	Ethanol, propanol, Isopropanol, butanol, pentanol, hexanol, sorbitol, n–pentanoic acid, n–hexanoic acid, n–butylamine, 1, 2-butanediol, Propylene glycol.

Table No.2: Difference between emulsion, microemulsion and nano emulsion

Parameters	Emulsion[32-35]	Microemulsion[4-16]	Nano emulsion[36-41]
Appearance	Turbid	Clear	Clear
Particle Size	1-20mm	1-100micro meter	1-100nm
Formation	Mechanical Shear	Phase inversion	Ultrasonication
Stability	Thermodynamically unstable Kinetically stable	Thermodynamically stable Long shelf life	Thermodynamically unstable Kinetically stable
Phases	Biphasic	Monophasic	Monophasic
Viscosity	High	Low	Low
Interfacial Tension	High	Low	Ultra low

Figure No.1: Appearance of different emulsion[29]

CONCLUSION

This article has highlighted the most important differences and similarities between two types of colloidal dispersions widely used to encapsulate lipophilic components: oil-in-water nanoemulsions and microemulsions. Microemulsion, nanoemulsion are similar in the composition, dimensions, structures, and fabrication methods for these two systems, which has led to considerable confusion in the literature about the precise nature of the colloidal dispersion being studied. Following definition are proposed to show similarities and differences microemulsions and nanoemulsions:

Microemulsion. An oil-in-water microemulsion is defined as a thermodynamically stable colloidal dispersion consisting of small spheroid particles (comprised of oil, surfactant, and possibly co-surfactant) dispersed within an aqueous medium.

Nanoemulsion. An oil-in-water nanoemulsion is defined as a thermodynamically unstable colloidal dispersion consisting of two immiscible liquids, with one of the liquids being dispersed as small spherical droplets ($r < 100$ nm) in the other liquid.

It is necessary to accurately make the distinction between microemulsions and nanoemulsions since this determines the methods used to prepare them, their long term stability, and their functional performances. We also propose a number of practical methods that might be useful for determining whether a given colloidal dispersion is a microemulsion or a nanoemulsion, such as long-term storage, shelf life, altering sample history, particle size distribution measurements, or particle shape measurements.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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