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NANO EMULSION: A BOON TO HYDROPHOBIC DRUGS TO AUGMENT THEIR SOLUBILITY AND BIO-AVAILABILITY .

Chemistry

Reema Nagda Department of Chemistry Maharaj Vinayak Global University. Jaipur. Rajasthan.

ABSTRACT

Solubility has been an essential element when conferred in terms of dissolution and absorption of drug. Poor water-soluble drugs have a major setback since these drugs fail to show greater efficacy, moderated industrial application and the formulation thus formed is challenge to the pharma companies and marketers. Nevertheless, these drugs show good pharmacological activity the estimated clinical effectiveness has not been acknowledged. Nano emulsion technology can be used a carrier to enhance the solubility and oral bioavailability. This is possible because the drug in its dissolved state is kept in the nanodroplet form throughout its entire passage via the GI tract. The reduction of the drug particles to the nanodroplet level also aids in dose reduction because of enhanced absorption of drug through GI tract. Clarity, high stability, and ease of preparation are some of the advantages of Nano emulsion.

KEYWORDS

Nano Emulsion, Oral Bioavailability, Solubility, Dissolution

INTRODUCTION:

The drug delivery often signifies the right kind of approaches, perfect formulations and appropriate techniques and well-designed transport system to deliver the drug at the desired target site. There are number of routes through which the drugs can be delivered to the anticipated site, For example non-invasive per oral (through the mouth), topical (skin),(nasal, buccal/sublingual, vaginal, ocular and rectal) and inhalation routes .The orally administration of the drug is the most convenient and generally preferred by population because of ease in consumption, patient compliance and hassle free. But this is often hindered by the drugs that are insoluble in water. This has become a major concern for the Pharma companies and manufacturers since 40 % of the New molecular entities showcases less affinity towards water. Poorly aqueous soluble drugs are usually characterized by low bioavailability due to less absorption.

Because of the poor water solubility, the dissolution in the gastro-intestinal tract is remarkable hampered. Since solubility is directly proportional to bioavailability, the oral bioavailability and the drug efficacy is hindered as well. This complication has hampered the permeation as well as the quantity of the drug absorbed, which further leads to low and unpredictable oral bioavailability. Techniques such solid dispersion, complexation, and aggregates of compounds, pH adjustment, co-solvency, micellar solubilization and hydro-trophy has been established to overcome the solubility issue, however, these approaches suffer from low bioavailability and insignificant pharmacokinetics. Since drug solubility, dissolution and gastrointestinal penetrability are the keys to control the rate and extent of drug absorption and bioavailability, it very important to develop a technique that does not compromise the pharmacokinetics of the drug and enhances its solubility as well as bioavailability. Nano emulsion drug delivery is one such promising technique and boon to the hydrophobics.

Importance Of Solubility

Lately, the pharma companies are tending to produce orally ingested drugs due to its ease of administration, high patient compliance, cost-effectiveness, minimum sterility constraints, and suppleness in the design of dosage form. But orally administrated drugs are often found to have poor bioavailability due its hydrophobicity and low permeability. Poorly water-soluble drugs are often consumed at a higher dose owing to the high doses required to reach therapeutic plasma concentrations after oral administration. For a drug to be absorbed at the target site, it must be in the form of an aqueous solution. Water serves as an excellent liquid for pharmaceutical formulations.

The prime reason for deficient bioavailability of hydrophobic drugs is the poor solubility and dissolution rate. In Biopharmaceutics Classification System for class II (low solubility and high permeability) the bioavailability can be elevated by increasing the solubility and dissolution rate of the drug in the gastro-intestinal fluids.

Biopharmaceutics Classification System

It is a system to differentiate the drugs on the basis of their solubility and permeability. The drugs are classified on the basis of solubility, permeability and dissolution:

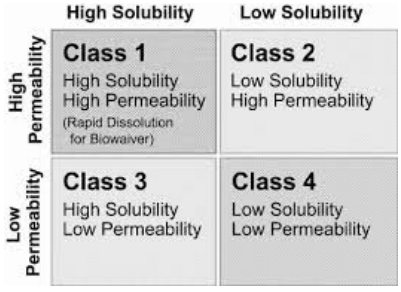

Figure 1 :BCS classification chart

NANOEMULSION

Nano emulsions shows immense potential for efficient delivery of hydrophobic drugs. The term "Nano-emulsion" are thermodynamically stable isotropic clear dispersion of two immiscible liquid such as oil and water. They are usually stabilized by interfacial film of surfactant molecules. The surfactant as well as co-surfactant used are approved for human consumption and common food substances and are "Generally Recognized as Safe" (GRAS) by the FDA. The droplet diameter ranges from 50nm to 1000nm. Usually the average droplet size is between 100nm to 500nm. A Nano-emulsion is considered to be a thermodynamically or kinetically stable liquid dispersion of an oil phase and a water phase in combination with a surfactant. The fine droplets of the Nano emulsion helps to keep the drug in the dissolved form providing a large surface for drug absorption which in turn leads to increased bioavailability. Nano emulsions do not form spontaneously; an external shear must be applied to rupture larger droplets into smaller ones.

Nano-emulsion are transparent or translucent dispersions having very low interfacial tension and has prolonged and sustainable stability.

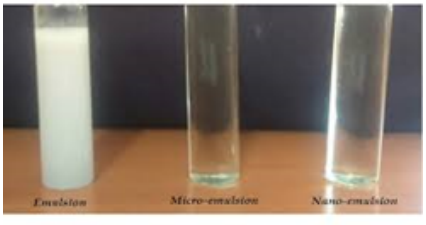

Figure 2: Physical appearance of Emulsion, Microemulsion and Nano-emulsion

Gears Of Nano Emulsion:

1. OIL:

The type of oil selected has a major influence on the formation of Nano-emulsion also the selected oil becomes the deciding factor for other ingredients as well. The oil having the maximum capacity to solubilize the oil is selected. Triglycerides are often selected as the oily phase. Triglycerides are of three types: short chain (<5 carbons),

medium (6-12 carbons), or long chain (>12 carbons). Sometimes the selection of oil can either compromise the ability of oil to solubilise the drug or can compromise facilitation of formation of Nano emulsion. To overcome this a mixture of oil and medium chain Triglyceride (6-12 carbons) is used.

Other suitable oil phases are modified vegetable oils, olive oil, palm oil, corn oil, oleic acid, sesame oil, soybean oil, hydrogenated soybean oil, peanut oil and beeswax

2. SURFACTANT:

The use of Nano-emulsion might get restricted due to the toxicity caused by addition of surfactants in large quantity. Overuse of surfactants may lead to problems related to GI tract and irritation of the skin. Thus, it is of immense importance to select and use the surfactant cautiously. Surfactants with an HLB value <10 are hydrophobic (such as sorbitan monoesters) and form w/o Nano emulsion where as high HLB (>10) surfactants such as polysorbate 80 are hydrophilic and form o/w Nano emulsion. The use of non-ionic surfactants in preparation of Nano emulsion is snowballing due to its reduced toxicity as compared to that of ionic surfactants. Non-ionic surfactants used for oral or parental nano-emuslion dosage shows enhanced in vivo stability.

3. Co-surfactant:

A chemical added to the process of emulsification to enhance the effectiveness of a surfactant is called Co-surfactant. Cosurfactants are often used to increase the oil-solubilizing capacity of nano- emulsion surfactant systems. Short- to medium-chain-length alcohols (C3–C8) are commonly added as cosurfactants. Co-surfactant helps the Nano emulsion to achieve ultralow interfacial tension. Characteristically, the use of very low HLB cosurfactant along with a high HLB surfactant is done to transform the overall HLB of the system.

4.Co-solvents:

Organic solvents such as ethanol, glycerol, propylene glycol (PG), polyethylene glycol(PEG) are used as co-solvents suitable for oral delivery.

Three types of Nano emulsion are most likely to be formed depending on the composition.

- Oil in water Nanoemulsion
- Water in oil Nanoemulsion
- Bi-continuous Nanoemulsion

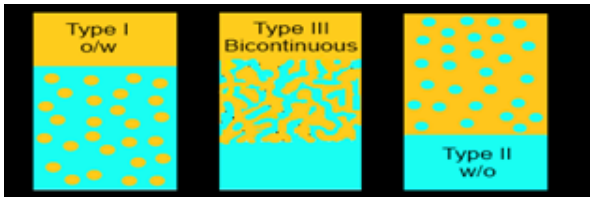

Figure 3: types of Nano emulsion

Characterization Of Nanoemulsions

Characterization of Nano emulsion will be subject to its particle size, viscosity, density, phase inversion, turbidity, refractive index etc. The techniques are as follows:

- Thermal Conductivity Technique
- Dynamic Light Scattering Spectrophotometer
- Zeta Potential
- Transmission Electron Microscopy
- Drug Content
- Viscosity Measurement
- Phase Analysis Technique

Advantages Of Nanoemulsion As A Drug Delivery System:

- It enhances the bioavailability of drug.
- It is non-toxic and non-irritant in nature.
- physical stability is well developed
- The nano-sized particles renders greater surface area and greater absorption.
- It can be framed in variety of blends such as foams, creams, liquids, and sprays.
- It provides better uptake of oil-soluble supplements in cell culture technology.
- It helps in solubilizing lipophilic drug.
- Helpful in taste masking.
- Less amount of energy is required

Nano Emulsion Fabrication Method

Table 1: Methods to prepare Nano emulsion

High Energy	Low energy
High pressure homogenisation	Spontaneous
Ultra-sonification	Solvent displacement
Micro fluidisation	Phase inversion temperature /Point

Limitations Of Nano Emulsion

- The involves a lot of finance in preparation of nanoemulsion since the procedure to reduce the drop size like Micro fluidization and ultrasonication are specialised techniques and expensive .
- Stability of Nano emulsion creates a big problem during storage and formulation for longer time.
- Less availability of surfactant and co-surfactant used to prepare Nano emulsion.

Mecahnimism Of Nanoemulsion Instability

Physical instability of Nano emulsion can be classified into

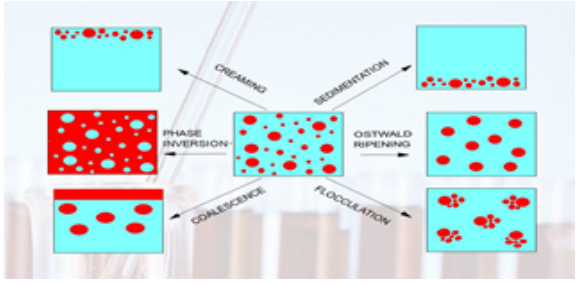

Figure 4: Factors responsible for Nano emulsion instability

CONCLUSION

Nanoemuslsion has acquired a lot of popularity and utility in diversified industries namely pharmaceutical, food, cosmetic, and chemical industries mainly because of its nanosized particle and its properties to overcome instability factors such as flocculation, creaming, coalescence and sedimentation. Oswald ripening is the only restricting factor that hinders the stability which can be over ruled by The drug delivery system seems to have acquired a lot of benefit from Nano emulsion since they dissolve large amount of hydrophobics and substantially enhance the bioavailability. Moreover, the dosage and the frequency of injections can be reduced during the course of drug therapy. This is possible because Nano emulsion help the drugs to be released in sustainable and controlled manner. Larger interfacial area of nanoemulsion aids drug transport and delivery at the targeted site.

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