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NANOEMULSION : AN EMERGING TECHNOLOGY IN MEDICINAL CHEMISTRY

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ABSTRACT Emulsions are liquid–liquid dispersions with one liquid phase dispersed in the other liquid phase as small droplets. Nanoemulsions are nano-sized emulsions with sizes ranging from tens to hundreds of nanometers, and have great potential applications in pharmaceutics, medicine and health due to their attractive properties, such as small sizes, high surface area per unit volume, improved dispersion of active hydrophobic components and enhanced absorption. This review paper provides an overview of nanoemulsions for drug delivery, starting with an introduction of emulsion types, components of nanoemulsion, nanoemulsion preparation and nanoemulsion stability. Then the applications of nanoemulsions as nanomedicine in drug delivery are presented. Finally, applications of nanoemulsions in vaccine and cancer treatment are discussed.

KEYWORDS : Nanotechnology, Nanoemulsion, Drug delivery , Nanomedicine

INTRODUCTION : About 60 percent of drugs on the market have hydrophobic molecules as their active ingredients. These drugs, which are not soluble in water, can be difficult to formulate into tablets because they need to be broken down into very small crystals in order to be absorbed by the human body. Nanoemulsion drug delivery systems are a promising tool for delivering and improving the bioavailability of hydrophobic drugs and bioactive food components in the blood. This is very important because if we can achieve high drug loading, it means that we can make smaller dosages that still achieve the same therapeutic effect. This can greatly improve patient compliance because they just need to take a very small drug and it's still very effective. Nanoemulsion drug delivery systems are lipid-based formulation system which improve the solubility and bioavailability of hydrophobic drugs and bioactive food components. [1,2] Flavonoids (flavanols, flavones, flavanones, and isoflavones), nonflavonoids (hydroxybenzoic acids, stilbenes, and curcuminoids), and carotenoids (carotenes and xanthophylls) are food bioactive compounds that have been encapsulated successfully in nanoemulsions formulations. [3]

NANOEMULSION TECHNIQUE : Nanoemulsion is defined as a colloidal dispersion of two immiscible liquids that is thermodynamically unstable. In nanoemulsion, one of the liquids forms the dispersed phase and other liquid forms the dispersing medium. Nanoemulsion comprises droplets with diameters ranging from 10 -200 nm and each droplet has a protective coating of emulsifier molecules. [4]

TYPES OF NANOEMULSION :
1. Water in oil (W/O) Nanoemulsion: During which droplet of Water was dispersed in continuous phase oil.
2. Oil in water (O/W) Nanoemulsion: During which Oil droplet was dispersed in continuous phase Water.
3. Bi-continuous Nanoemulsion: During which Surfactant was soluble in both oil as well as water Phase, and droplet was dispersed in both oil also as water phase.

COMPONENTS OF NANOEMULSION :
1. OIL - In the formulation of nanoemulsions, the oil phase may include triglycerides like tri-, di-, or mono-acylglycerols, vegetable oils, mineral oils, free fatty acids etc. Oil selection is generally based on the drug solubility. Triglycerides are highly lipophilic oily molecules and thus the solvent capacity of medicine is common function of effective concentration in ester groups, the medium chain triglycerides (MCT). molecules having higher solvent capacity and skill for resistance to oxidation as compare to long chain triglycerides molecules.

2. SURFACTANTS - Common surfactants used in the nanoemulsion systems for drug delivery and food ingredients are spans (sorbitan fatty acid esters), tweens [polyoxyethylene (POE) derivatives of sorbitan fatty acid ester], Cremophor® EL (polyoxyl-35 castor oil), lauroyl macro-golglycerides (Gelucire® 44/14), polysaccharides (gum and starch derivatives), phospholipids (egg, soy, or dairy lecithin), and amphiphilic proteins (whey protein isolate and caseinate) [5]. Optimum amount of surfactant unit is employed for preparation nanoemulsion but great quantity of surfactant can chemical toxicity. Hence the security is major considerable parameter for selection of Surfactant molecule. The molecule of surfactant is obtained in natural also as synthetic origin. Surfactant having limited capacity of Self Emulsification. [6]

3. CO SURFACTANT - Ultra-low negative interfacial tension is required for nanoemulsion formation. For this purpose, co-surfactants or co-solvents are used along with a surfactant. Co-surfactants or co-solvents that are generally used in formulation of nanoemulsion systems are polyethylene glycol, propylene glycol, ethanol, transcutol-P (diethylene glycol monoethyl ether), ethylene glycol, glycerin, and propanol. The co-surfactant molecule is inheriting contact with surfactant, oil and water it can separated by Monomolecular Layer of surfactant molecule. The Monomolecular Layer of Surfactant molecule is understood as Liquid Crystal formation layer. The foremost important application of co-surfactant in self Nanoemulsifying Drug Delivery system (SNEDDS) is to stop interfacial natural phenomenon between oil and water interface.

METHOD OF PREPARATIONS: Various methods for preparation of nanoemulsion including the high-energy and low-energy emulsification methods and therefore the combined methods are reviewed. Among the high-energy methods, the stress is placed on high-energy stirring, ultrasonic emulsification, high homogenization including micro fluidics and membrane emulsification. Among the low- energy emulsification methods, the phase inversion temperature method, the emulsion inversion point method and therefore the spontaneous emulsification. Employing a combined method, which incorporates the high-energy and low energy emulsification, it's possible to organize reverse nanoemulsions in highly viscous systems. Main advantages and limitations off different methods of nanoemulsion preparation are discussed and therefore the potential fields of nanoemulsion applications are considered.

The techniques employed in formulation of nanoemulsion drug delivery systems are diverse and show a large degree of overlapping. We have classified different methods for preparation of nanoemulsion drug delivery systems by energy requirements, nature of phase inversion and self-emulsification

HIGH ENERGY METHODS
1. High-pressure homogenization
2. Microfluidization
3. Ultrasonication

LOW ENERGY METHODS
1. Phase inversion emulsification method
2. The self-nano emulsification method

STABILITY OF NANOEMULSION SYSTEM

During storage, nanoemulsion may become turbid or phases of nanoemulsion may separate due to mechanisms of instability such as flocculation, sedimentation, coalescence, and Ostwald ripening. Nanoemulsion system destabilization kinetics are very slow (several months), therefore nanoemulsion systems are kinetically stable. Nanoemulsion systems produce smaller droplets sizes than conventional macro emulsions; thus, Brownian motion effects are much more dominate then gravitational forces and have greater gravitational separation stability. Flocculation and coalescence occur due to the attractive forces between the droplets, which are generally very low in nano-sized emulsion systems. Thus, nanoemulsion also shows much better stability towards the flocculation and coalescence .[7]

NANOEMULSION APPLICATIONS

1. IN MORE EFFECTIVE DRUG - Once the nanocrystal-loaded particles are formed, they can be crushed into powder and then compressed into tablets, using standard drug manufacturing techniques. This can enable us to make more effective and smaller drugs that are easier to swallow, and that can be very beneficial for many people who have difficulty swallowing drugs. It is estimated that about 90 percent of the drugs now in development are hydrophobic, so this approach could potentially be used to develop formulations for those drugs, as well as hydrophobic drugs that are already in use.

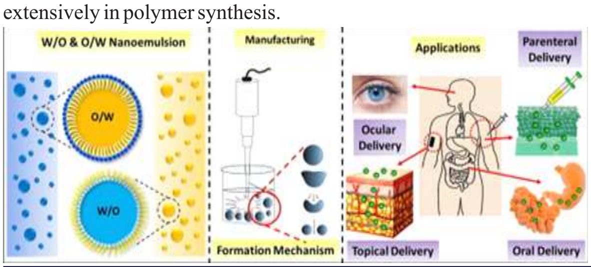
Nanoemulsions are more advantageous than the conventional emulsions and other systems since their droplet sizes are below the micrometers range, and thus they easily pass the stringency of intravenous administration of drugs. The parenteral administration of nanoemulsions employed in nutrition of vitamins and other bioactive substances, attest to the merits they possess over other systems as their transit time, absorption, and efficacy are highly improved, while drug toxicity is reduced. Therefore, they are perfect drug delivery systems for antimicrobials, diuretics, steroids, and hormones.[8]

2. IN VACCINES - Of equal importance is the delivery of vaccines by nanoemulsion. Nanoemulsions are used in this case as adjuvants to deliver proteins onto the mucosal surface in order to instigate rapid absorption of antigen presenting cells. Physical adsorption, encapsulation (with or without coating and targeting), and conjugation (with chemical or targeting) mechanisms are often used to load antigens into nanocarriers.

3. IN CANCER TREATMENT- Poor solubility and hydrophobicity of most anticancer drugs connote their inability to reach or effect their action on cancer cells [9]. This is where nanoemulsions are essential, as they proffer solubility to hydrophobic drugs and their stability. The resultant effect is that cancerous cells are selectively targeted earlier, leading to a high rate of successful cancer treatment.

4. NANOEMULSIONS AS BUILDING BLOCKS-
Nanoemulsions can be used as building blocks for the preparation of more complex materials through exploitation of their small size and high surface area which enable easy decoration of a liquid–liquid surface with functional moieties such as designer macromolecules.

Emulsion polymerization is perhaps the best-known example in polymer synthesis where hydrophobic monomers contained in droplets are polymerized to create polymeric particles. Nanoemulsions (also known as miniemulsions) have been utilized extensively in polymer synthesis.



CONCLUSION : Nanoemulsion is colloidal dispersion of two or more immiscible phase i.e., oil and water. They need more recently received increasing attention as colloidal carriers for targeted delivery of various anticancer drugs, photosensitizers, neutron capture therapy agents, or diagnostic agents. Nanoemulsion drug delivery systems effectively overcome the low bioavailability drawback related to drugs and food components which are hydrophobic, and having high first pass metabolism. High energy methods for nanoemulsion drug delivery system formulation have greater control over dispersion of particle sizes and are more flexible for the choice of composition. High energy methods have been used by researchers to improve delivery of drugs and bioactive food components.

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