Nanoemulsion as strategy to improve oral bioavailability of poorly water soluble drugs

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Abstract

Combinatorial chemistry has played a vital role in design and synthesis of new drug molecules in recent years resulting a significant low water solubility hence creating a challenge for scientists to formulate drugs with appropriate bioavailability. The bioavailability of low solubility drugs may be related, in part, to drug particle size. Reducing particle size increases the surface area of the compound and can improve the dissolution properties of the drug to allow a wider range of formulation approaches and delivery technologies.

Nano-emulsions are one of the most promising strategies to improve the oral bioavailability of poorly water soluble drugs.By reducing drug particle size to the absolute minimum ,bioavailability may be significantly improved. They are usually obtained by different methods, for example, high-energy methods, the low-energy spontaneous emulsification method, and the low-energy phase inversion temperature (PIT) method.In this review, it is intended to discuss the recent advances related on the area of nano-emulsions and bioavailability.

Introduction

One of the major obstacles to the development of highly potent pharmaceutics is the poor water solubility of many drugs. Approximately 40% of potential new drugs identified by pharmaceutical companies are poorly soluble in water, which greatly hinders their clinical translations . Low water solubility limits the bioavailability and absorption of these agents . Several strategies and formulations have been employed to overcome these limitations. Although existing strategies such as complexing drugs with cyclodextrins , conjugation to dendrimers , salt formation of ionizable drugs and the use of co-solvents have been shown to improve drug solubility, universal solubilization methods that can improve the drugs' bioavailability significantly are still highly desirable.

Recently, various nanonization strategies have emerged to increase the dissolution rates and bioavailability of numerous drugs that are poorly soluble in water. These strategies include increasing the surface area to volume ratios of drug powders, changing the crystalline forms and designing novel nanomaterials that can act as carriers for controlled release .

Nanonization can result in improved drug solubility and pharmacokinetics, and it might also decrease systemic side-effects .Nanonization of hydrophobic drugs generally involves the production of drug nanocrystals through either chemical precipitation or disintegration . Alternatively, nanotechnology-based drug delivery systems such as nanoemulsions and polymeric micelles can be used .

During the past decade, several drug nanoformulations have been clinically approved or are under clinical investigation . Major research efforts have been focused on the development of enabling nanoformulation technologies, new pharmaceutical materials and quality control to improve product properties while reducing production costs.

Nanoemulsion

The use of nano technology in pharmaceuticals and medicine has grown over the last few years. The various nanopharmaceuticals currently being used or in the process of development are Nanoemulsions (NE) (submicron sized emulsions), nanosuspensions (submicron sized suspensions), nanospheres (drug nanoparticles in polymer matrix), nanotubes (sequence of nanoscale C60 atoms arranged in a long thin cylindrical structure), nanoshells (concentric sphere nanoparticles consisting of a dielectric core and a metal shell), nanocapsules (encapsulated drug nanoparticles), lipid nanoparticles (lipid monolayer enclosing a solid lipid core) and dendrimers (nanoscale three-dimensional macromolecules of polymer).

NEs are a group of dispersed particles used for pharmaceutical and biomedical aids and vehicles that show great promise for the future of cosmetics, diagnostics, drug therapies, and biotechnologies. NEs can be defined as oil-in-water (o/w) emulsions with mean droplet diameters ranging from 50 to 1000 nm. Usually, the average droplet size is between 100 and 500 nm. The particles can exist as water-in-oil and oil- in water forms, where the core of the particle is either water or oil, respectively.

NEs are made from surfactants approved for human consumption and common food substances that are Generally Recognized as Safe by the FDA. These emulsions are easily produced in large quantities by mixing a water-immiscible oil phase into an aqueous phase with a high-stress, a mechanical extrusion process that is available worldwide·

NEs posses various advantages such as:

NEs have a much higher surface area and free energy than macro emulsions that make them an effective transport system.
NEs do not show the problems of inherent creaming, flocculation, coalescence, and sedimentation, which are commonly associated with macroemulsions.
NEs can be formulated in variety of formulations such as foams, creams, liquids, and sprays.
NEs are non-toxic and non-irritant, hence can be easily applied to skin and mucous membranes.
NEs do not damage healthy human and animal cells, hence are suitable for human and veterinary therapeutic purposes.
NEs increase drug loading and enhance bioavailability.

Applications of Nanoemulsions	*Methods of Preparation of Nanoemulsions*
Use of nanoemulsions in cosmetics ***Nanoemulsion as a mucosal vaccines*** ***Antimicrobial nanoemulsions*** ***Prophylactic in bio-terrorism attack*** ***Nanoemulsion as non-toxic disinfectant cleaner*** ***Nanoemulsions in cell culture technology*** ***Nanoemulsion in cancer therapy and in targeted drug delivery*** ***Nanoemulsion in the treatment of various other disease conditions*** ***Nanoemulsion formulations for improved oral delivery of poorly soluble drugs*** ***Nanoemulsions as a vehicle for transdermal delivery*** ***Self-nanoemulsifying drug delivery systems*** **Solid self-nanoemulsifying delivery systems as a platform technology for formulation of poorly soluble drugs**	***High -pressure homogenization*** ***Microfluidization*** **Ultrasonication** **Spontaneous emulsification** **Phase inversion temperature technique**

Lipid based drug delivery systems(Nanoemulsion)

One of the most popular approaches to overcome barriers and to improve the oral bioavailability of poorly water soluble drugs is the utilization of oral lipid-based drug delivery systems. The ability of lipid vehicles (either in the pharmaceutical delivery system or in food) to enhance the absorption of lipophilic drugs has been well known for many years.

The additional mechanisms by which lipid-based drug delivery systems (LBDDS) enhance the absorption of lipophilic drugs are:

1. Enhanced dissolution/solubilization
2. Prolongation of gastric residence time
3. Stimulation of lymphatic transport
4. Affecting intestinal permeability
5. Reduced metabolism and efflux activity.

Concluding remarks

In summary, numerous studies have demonstrated the feasibility of nanonization strategy to improve solubility, dissolution kinetics and bioavailability of hydrophobic drugs. Multiple nanoformulations have recently been approved for clinical use, and several products are still in the pipelines of preclinical and clinical trials such as Saquinavir,primaquine,ezetimibe,cefopdoxime,ramiprill,Q10,Vit E,cyclosporin ,etc. Commercial products that are nanoemulsions include Estrasorb® and Flexogan® . The diverse nanonization strategies provide flexible options to develop tailor-made nanotherapeutics for different drugs and administration routes. These techniques can also be used to revive the clinical efficacy of toxic drugs or facilitate the clinical translation of drug candidates that are deemed failures simply because of lack of solubility. With rapid scientific and technological advancements, nanonization of hydrophobic drugs can potentially be vital for clinical applications of highly potent drugs.

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