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Review Article

Current Update on Nanoemulsion: A Review

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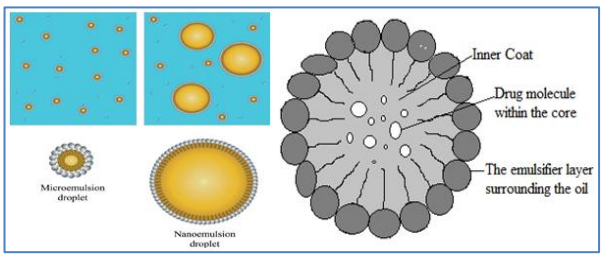
Abstract

In this review, the formation, characterization, properties and applications of nano-emulsions are reviewed and summarized. Nanoemulsions are submicron sized emulsions that are under extensive investigation as drug carriers for improving the delivery of therapeutic agents. Nanoemulsions are the thermodynamically stable isotropic system in which two immiscible liquid (water and oil) are mixed to form a single phase by means of an appropriate surfactants. Due to their small droplet size nano-emulsions possess stability against sedimentation or creaming with Ostwald ripening forming the main mechanism of nanoemulsion breakdown. Nanoemulsion droplet sizes fall typically in the range of 20-200nm. Diameter and surface properties of droplets of nanoemulsion plays an important role in the biological behavior of the formulation. Nanoemulsion show great promise for the future of cosmetics, diagnostics, drug therapies, and biotechnologies. The main application of nanoemulsions is the preparation of nanoparticles using a polymerizable monomer as the disperse phase (the so-called miniemulsion polymerization method) where nanoemulsion droplets act as nanoreactors. Another interesting application which is experiencing an active development is the use of nanoemulsions as formulations, namely for controlled drug delivery and targeting.

Key words: Nanoemulsion, Microfluidization, microchannels, nanospheres.

INTRODUCTION

Nanoemulsions 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. Nanoemulsions 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. The terms sub-micron emulsion (SME) and mini-emulsion are used as synonyms. Usually, SMEs contain 10 to 20 per cent oil stabilized with 0.5 to 2 per cent egg or soybean lecithin [1]. Phase into an aqueous phase with a high-stress, mechanical extrusion process that is Nanoemulsions are made from surfactants approved for human consumption and common food substances that are 'Generally Recognized as Safe' (GRAS) by the FDA. These emulsions are easily produced in large quantities by mixing water immiscible oil available worldwide [2]. The Nanoemulsions are also referred as miniemulsions, ultrafine emulsions and submicron emulsions. Phase behavior studies have shown that the size of the droplets is governed by the surfactant phase structure (bicontinuous microemulsion or lamellar) at the inversion point induced by either temperature or composition. Studies on Nanoemulsions formation by the phase inversion temperature method have shown a relationship between minimum droplet size and complete solubilization of the oil in a microemulsion bicontinuous phase independently of whether the initial phase equilibrium is single or multiphase [3].



Structure of Nanoemulsion

Nanoemulsions possess various advantages such as [4]

- Nanoemulsions have a much higher surface area and free energy than macroemulsions that make them an effective transport system.

- Nanoemulsions do not show the problems of inherent creaming, flocculation, coalescence and sedimentation, which are commonly associated with macroemulsions.
- Nanoemulsions can be formulated in variety of formulations such as foams, creams, liquids and sprays.
- Nanoemulsions are non-toxic, non-irritant hence can be easily applied to skin and mucous membranes.
- Nanoemulsions do not damage healthy human and animal cells hence are suitable for human and veterinary therapeutic purposes.

FORMULATION ASPECTS FOR NANOEMULSIONS

Since nanoemulsions have very small particle size range, they can be most effectively produced using high-pressure equipment [5].

High-Pressure Homogenisation

This technique makes use of high-pressure homogenizer/piston homogenizer to produce nanoemulsions of extremely low particle size (up to 1nm). In a high-pressure homogenizer, the dispersion of two liquids (oily phase and aqueous phase) is achieved by forcing their mixture through a small inlet orifice at very high pressure (500 to 5000 psi), which subjects the product to intense turbulence and hydraulic shear resulting in extremely fine particles of emulsion. Homogenizers of varying design are available for lab scale and industrial scale production of nanoemulsions. This technique has great efficiency, the only disadvantage being high energy consumption and increase in temperature of emulsion during processing [6, 7].

Microfluidization

Microfluidization is a patented mixing technology, which makes use of a device called microfluidizer. This device uses a high-pressure positive displacement pump (500-20000 psi), which forces the product through the interaction chamber, which consists of small channels called "microchannels." The product flows through the microchannels on to an impingement area resulting in very fine particles of submicron range. The two solutions (aqueous phase and oily phase) are combined together and processed in an inline homogenizer to yield a coarse emulsion. The coarse emulsion is into a microfluidizer where it is further processed to obtain a stable nanoemulsion. The coarse emulsion is passed through the interaction chamber of the microfluidizer repeatedly until desired particle size is obtained. The bulk emulsion is then filtered through a filter under nitrogen to remove large droplets resulting in uniform nanoemulsions. Other method used for nanoemulsions preparation is the phase inversion temperature technique [8].

Characterization of Nanoemulsions

Different characterization parameters for nanoemulsion include transmission electron microscopy, nanoemulsion droplet size analysis, viscosity determination, refractive index, in vitro skin permeation studies, skin irritation test, in vivo efficacy study, thermodynamic stability studies, and surface characteristics. The surface charge of the nanoemulsion droplets has a marked effect on the stability of the emulsion system and the droplet in vivo disposition and clearance [9].

Application of Nanoemulsions in Cosmetics

Nanoemulsions have recently become increasingly important as potential vehicles for the controlled delivery of cosmetics and for the optimized dispersion of active ingredients in particular skin layers. Due to their lipophilic interior, nanoemulsions are more suitable for the transport of lipophilic compounds than liposomes. Nanoemulsions are acceptable in cosmetics because there is no inherent creaming, sedimentation, flocculation, or coalescence that is observed with macro emulsions. The incorporation of potentially irritating surfactants can often be avoided by using high-energy equipment during manufacturing [10].

Nanoemulsions have attracted considerable attention in recent years for application in personal care products as potential vehicles for the controlled delivery of cosmetics and the optimized dispersion of active ingredients in particular skin layers [11].

Antimicrobial Nanoemulsions

Antimicrobial nanoemulsions are oil-in-water droplets that range from 200 to 600 nm. They are composed of oil and water and are stabilized by surfactants and alcohol. The against bacteria (e.g. E. coil, Salmonella s, S. aureus), enveloped viruses (e.g. HIV, Herpes simplex), fungi (e.g. Candida, Dermatophytes), and spores (e.g. anthrax). The nanoemulsion particles are thermodynamically driven to fuse with lipid-containing organisms.

This fusion is enhanced by the electrostatic attraction between the cationic charge of the emulsion and the anionic charge on the pathogen. When enough nanoparticles fuse with the pathogens, they release part of the energy trapped within the emulsion. Both the active ingredient and the energy released destabilize the pathogen lipid membrane, resulting in cell lysis and death. In the case of spores, additional germination enhancers are incorporated into the emulsion. Once initiation of germination takes place, the germinating spores become susceptible to the antimicrobial action of the nanoemulsion. As a result, the nanoemulsion can

achieve a level of topical antimicrobial activity that has only been previously achieved by systemic antibiotics [12-13].

As A Mucosal Vaccine

Nanoemulsions are being used to deliver either recombinant proteins or inactivated organisms to a mucosal surface to produce an immune response. The first applications, an influenza vaccine and an HIV vaccine, can proceed to clinical trials. The nanoemulsion causes proteins applied to the mucosal surface to be adjuvant and it facilitates uptake by antigen-presenting cells. Additional research is ongoing to complete the proof of concept in animal trials for other vaccines including Hepatitis B and anthrax [14]. Mice and guinea pigs intranasally immunized by the application of recombinant HIV gp120 antigen mixed in nanoemulsion demonstrated robust serum anti-gp120 IgG, as well as bronchial, vaginal, and serum anti-gp120 IgA in mice.

The serum of these animals demonstrated antibodies that cross-reacted with heterologous serotypes of gp120 and had significant neutralizing activity against two clade-B laboratory strains of HIV (HIVBaL and HIVSF162) and five primary HIV-1 isolates. The analysis of gp120-specific CTL proliferation, INF-g induction, and prevalence of anti-gp120 IgG2 subclass antibodies indicated that nasal vaccination in nanoemulsion also induced systemic, Th1-polarized cellular immune responses. This study suggests that nanoemulsion should be evaluated as a mucosal adjuvant for multivalent HIV vaccines [15]. Hepatitis B virus infection remains an important global health concern despite the availability of safe and effective prophylactic vaccines. Limitations to these vaccines include requirement for refrigeration and three immunizations thereby restricting use in the developing world. A new nasal hepatitis B vaccine composed of recombinant hepatitis B surface antigen (HBsAg) in a novel nanoemulsion adjuvant (HBsAg- nanoemulsion) could be effective with fewer administrations. Comprehensive pre-clinical toxicology evaluation demonstrated that HBsAg- nanoemulsion vaccine is safe and well tolerated in multiple animal models. Our results suggest that needle-free nasal immunization with HBsAg-NE could be a safe and effective hepatitis B vaccine, or provide an alternative booster administration for the parenteral hepatitis B vaccines. This vaccine induces a Th1 associated cellular immunity and also may provide therapeutic benefit to patients with chronic hepatitis B infection who lack cellular immune responses to adequately control viral replication. Long-term stability of this vaccine formulation at elevated temperatures suggests a direct advantage in the field, since potential excursions from cold chain maintenance could be tolerated without a loss in therapeutic efficacy [16].

A novel technique for vaccinating against a variety of infectious diseases-using an oil-based emulsion placed in the nose, rather than needles-has proved able to produce a strong immune response against smallpox and HIV in two new studies. Developing mucosal immunity may be very important for protection against HIV. In the study, the nanoemulsion HIV vaccine showed that it was able to induce mucosal immunity, cellular immunity, and neutralizing antibody to various isolates of HIV virus. A protein used by the team, gp120, is one of the major binding proteins under study in other HIV vaccine approaches [17].

Nanoemulsion as Non-Toxic Disinfectant Cleaner

A breakthrough nontoxic disinfectant cleaner for use in commercial markets that include healthcare, hospitality, travel, food processing, and military applications has been developed by EnviroSystems, Inc. that kills tuberculosis and a wide spectrum of viruses, bacteria and fungi in 5-10 min without any of the hazards posed by other categories of disinfectants. The product needs no warning labels. It does not irritate eyes and can be absorbed through the skin, inhaled, or swallowed without harmful effects. The disinfectant formulation is made up of nanospheres of oil droplets #106 mm that are suspended in water to create a NE requiring only miniscule amounts of the active ingredient, PCMX (parachlorometaxylenol). The nanospheres carry surface charges that efficiently penetrate the surface charges on microorganisms' membranes-much like breaking through an electric fence. Rather than "drowning" cells, the formulation allows PCMX to target and penetrate cell walls. As a result, PCMX is effective at concentration levels 1-2 orders of magnitude lower than those of other disinfectants; hence, there are no toxic effects on people, animals, or the environment. Other microbial disinfectants require large doses of their respective active ingredients to surround pathogen cell walls, which cause them to disintegrate, fundamentally "drowning" them in the disinfectant solution. The formulation is a broad-spectrum disinfectant cleaner that can be applied to any hard surface, including equipment, counters, walls, fixtures, and floors. One product can now take the place of many reducing product inventories and saving valuable storage space [18, 19].

Nanoemulsions in Cell Culture Technology

Cell cultures are used for in vitro assays or to produce biological compounds, such as antibodies or recombinant proteins. To optimize cell growth, the culture medium can be supplemented with a number of defined molecules or with blood serum. The advantages of using nanoemulsions in cell culture technology are better uptake of oil-soluble supplements in cell cultures; improve growth and vitality of cultured cells, and

allowance of toxicity studies of oil-soluble drugs in cell cultures [20, 21].

Nanoemulsion in Cancer Therapy and Targeted Drug Delivery

The effects of the formulation and particle composition of gadolinium (Gd)-containing lipid nanoemulsion (Gd-nanoLE) on the biodistribution of Gd after its intravenous (IV) injection in D1-179 melanoma-bearing hamsters were evaluated for its application in cancer neutron-capture therapy. Biodistribution data revealed that Brij 700 and HCO-60 prolonged the retention of Gd in the blood and enhanced its accumulation in tumors. Upon dermal application, the drug was predominantly localized in deeper skin layers, with minimal systemic escape. This has amounted to an absolute bioavailability of 70.62%. Inhibition of P-glycoprotein efflux by D-tocopheryl polyethyleneglycol 1000 succinate and labrasol would have contributed to the enhanced peroral bioavailability of PCL. This investigation provides direct evidence on the localization of high-molecular-weight, lipophilic drug, PCL, in dermis. Further, the nanoemulsion formulation has enhanced the peroral bioavailability significantly to more than 70%. The developed nanoemulsion formulation was safe and effective for both peroral and dermal delivery of PCL [22]. Camptothecin is a topoisomerase-I inhibitor that acts against a broad spectrum of cancers. However, its clinical application is limited by its insolubility, instability, and toxicity. The aim of the present study was to develop acoustically active nanoemulsions for camptothecin encapsulation to circumvent these delivery problems. The nanoemulsions were prepared using liquid perfluorocarbons and coconut oil as the cores of the inner phase. These nanoemulsions were stabilized by phospholipids and/or Pluronic F68 (PF68). The nanoemulsions were prepared at high drug loading of approximately 100% with a mean droplet diameter of 220-420 nm. Camptothecin in these systems showed retarded drug release. Camptothecin in nanoemulsions with a lower oil concentration exhibited cytotoxicity against melanomas and ovarian cancer cells. Confocal laser scanning microscopy confirmed nanoemulsion uptake into cells. Using a 1 MHz ultrasound, an increased release of camptothecin from the system with lower oil concentration could be established, illustrating a drug-targeting effect [23]. The scientists have investigated the nanoemulsion containing risperidone (RSP) to accomplish the delivery of drug to the brain via nose. Risperidone nanoemulsion (RNE) and mucoadhesive nanoemulsion (RMNE) were characterized for drug content, pH, percentage transmittance, globule size, and zeta potential. Biodistribution of RNE, RMNE, and risperidone solution (RS) in the brain and blood of Swiss albino rats following intranasal (i.n.) and intravenous (i.v.) administration was examined using optimized technetium-labeled [(99 m) Tc-labeled] RSP formulations. Gamma scintigraphy imaging of rat brain following i.v. and i.n. administrations were performed to ascertain the localization of drug in brain. Higher drug transport efficiency (DTE%) and direct nose to brain drug transport (direct transport percentage, DTP%) for mucoadhesive nanoemulsions indicated more effective and best brain targeting of RSP amongst the prepared nanoemulsions. Studies conclusively demonstrated rapid and larger extent of transport of RSP by RMNE (i.n.) when compared to RS (i.n.), RNE (i.n.), and RNE (i.v.) into the rat brain [24]. Another study reported the formulation of filter sterilizable emulsion formulation of paclitaxel using á-tocopherol as the oil phase and á-tocopherylpolyethyleneglycol-1000 succinate (TGPS) and poloxamer 407 as emulsifiers. The formulation exhibited better efficacy and was more tolerable when studied in B16 melanoma tumor model in mice [25].

Emulsion formulations also show promise in cancer chemotherapy as vehicles for prolonging the drug release after intramuscular and intratumoral injection (W/O systems) and as a means of enhancing the transport of anti-cancer drugs via the lymphatic system [26]. Positively charged nanoemulsions systems are expected to interact with negatively charged cell surfaces more efficiently, and this aspect of the positively charged nanoemulsions has been explored for possibility of oligonucleotide delivery to cancer cells [27-30]. Photodynamic therapy (PDT) of cancer is based on the concept that certain photosensitizers can be localized in the neoplastic tissue, and subsequently, these photosensitizers can be activated with the appropriate wavelength (energy) of light to generate active molecular species such as free radicals and singlet oxygen (1O2) that are toxic to cells and tissues [31-33]. Various PDT therapies have reported two different vehicles for photosensitizers, a cremophor oil emulsion and DPPC (dipalmitoylphosphatidylcholine) liposomal vesicles. The reported pharmacokinetic studies clearly indicate that the former vehicle yields a significantly larger selectivity of tumor targeting, mainly as a consequence of an enhanced accumulation in the malignant lesion. Neutron Capture Therapy (NCT) is a binary radiation therapy modality that brings together two components that when kept separate had only minor effects on the cells. The first component is a stable isotope of boron or gadolinium (Gd) that can be concentrated in tumor cells by a suitable delivery vehicle. The second is a beam of low-energy neutrons. Boron or Gd in or adjacent to the tumor cells disintegrates after capturing a neutron, and the high energy heavy charged particles produced through this interaction destroy only the cancer cells in close proximity to it, leaving adjacent normal cells largely unaffected [34]. The success of NCT relies on the targeting of boron and Gd-based compounds to the

tumor mass and to achieve desirable intracellular concentrations of these agents. At the present time, there are two targets with NCT, namely glioblastoma (malignant brain tumor) and malignant melanoma. The perfluorochemical nanoemulsions (PFCE) have opened interesting opportunities in cancer therapy. It is suggested that fluorocarbon emulsions might find a role in photodynamic therapy, both as carriers for sensitizing dyes and to maintain tissue oxygenation in hypoxic regions of solid tumors. The high solubility of oxygen in fluorocarbon emulsions maintains solution oxygen tension, optimizing photo-oxidative damage. The hydrophobic anti-cancer drugs can be delivered to the tumor mass by dissolving them in a hydrophobic core of the emulsion. Furthermore, PFCE can be used as an adjuvant to radiation therapy and/or chemotherapy in the treatment of solid tumors [36, 37]. The preclinical studies have shown very positive effects with single dose and fractionated radiation in several rodent solid tumor models. Many widely used anticancer drugs, including anti-tumor alkylating agents and doxorubicin, have shown improved response by PFCE coadministration [38]. Also, local application of toxic doses of PFCEs resulted in the necrosis of cancer cells. This is especially promising in the treatment of cancers of the head and neck regions that are currently difficult to treat [39].

Nanoemulsion in the Treatment of Various Other Disease Conditions

Pharmos' (US-based Company) has developed the nanoemulsion topical diclofenac cream as a potential treatment for osteoarthritis (OA) pain. OA is a painful condition affecting more than 30 million people in the USA and is the most frequent cause of physical disability among adults, mainly elderly. Topical diclofenac is also being considered as treatment for soft tissue injuries, sprains, and strains. It is estimated that 20% of OA patients are not receiving treatment, mainly due to gastrointestinal side effects of oral NSAIDs and cardiovascular risk of COX-2 inhibitors. A topical NSAID offering adequate pain relief targeted to the site of injury with an improved safety profile could become a treatment alternative for these patients. In the USA, there are no approved topical NSAIDs for the treatment of OA. Pharmos' NE technology consists of an efficient solvent-free topical vehicle based and drug entrapment in stable, submicron particles of oil-in-water emulsions with a mean droplet size between 100 and 200 nm that are uniformly dispersed in an aqueous phase. One of the unique characteristics of the nanoemulsion technology is the relatively high percentage of total particle volume occupied by the internal hydrophobic oil core of the droplets. This provides high solubilization capacity for lipophilic compounds compared to other lipoidal vehicles such as liposomes. Viscosity-imparting agents are used for nanoemulsion thickening to produce creams with the desired semisolid consistency for application to the skin. The skin penetrative properties of the solvent-free nanoemulsion delivery technology and its low irritancy make this novel topical nanovehicle a promising candidate for effective transcutaneous delivery of lipophilic drugs. Primaquine (PQ) is one of the most widely used antimalarial and is the only available drug till date to combat relapsing form of malaria especially in case of Plasmodium vivax and Plasmodium ovale. Primaquine acts specifically on the pre-erythrocytic schizonts that are concentrated predominantly in the liver and causes relapse after multiplication. However, application of PQ in higher doses is limited by severe tissue toxicity including hematological and GI-related side effects that are needed to be minimized. Lipid nanoemulsion has been widely explored for parenteral delivery of drugs. Primaquine when incorporated into oral lipid nanoemulsion having a particle size in the range of 10-200 nm showed effective antimalarial activity against Plasmodium bergheii infection in Swiss albino mice at a 25% lower dose level as compared to conventional oral dose. Lipid nanoemulsion of primaquine exhibited improved oral bioavailability and was taken up preferentially by the liver with drug concentration higher at least by 45% as compared to the plain drug [40].

Nanoemulsion Formulations for Improved Oral Delivery of Poorly Soluble Drugs

Nanoemulsion formulations were developed to enhance oral bioavailability of hydrophobic drugs. Paclitaxel was selected as a model hydrophobic drug. The oil-in-water (o/w) nanoemulsions were made with pine nut oil as the internal oil phase, egg lecithin as the primary emulsifier, and water as the external phase. Stearylamine and deoxycholic acid were used to impart positive and negative charge to the emulsions, respectively. The formulated nanoemulsions had a particle size range of 90-120 nm and zeta potential ranging from +34 mV to 245 mV. Following oral administration, a significantly higher concentration of paclitaxel was observed in the systemic circulation when administered in the nanoemulsion relative to control aqueous solution. The results of this study suggest that nanoemulsions are promising novel formulations that can enhance the oral bioavailability of hydrophobic drugs. [41]. Coenzyme Q10 (CoQ10), also known as ubiquinone, is used for energy production within cells and acts as an anti-oxidant. Since CoQ10 is highly lipophilic, the topical and oral bioavailability is very low. Several attempts have been made to improve absorption. Latest technical developments reveal that encapsulation of CoQ10 in nanoemulsion s results in a significantly enhanced bioavailability. The application of CoQ10 has been further improved by the development of novel CoQ10 double nanoemulsions containing tocopherol and CoQ10 in individual nanodroplets. In addition, the CoQ10 concentration in

these nanoemulsions could be increased by the development of a supersaturated CoQ10 nanoemulsion [42].

Nanoemulsions as a Vehicle

From in vitro and in vivo data, it was concluded that the developed nanoemulsion s have great potential for transdermal drug delivery of aceclofenac [43]. The nanoemulsion of the system containing ketoprofen evidenced a high degree of stability. Ketoprofen-loaded nanoemulsions enhanced the in vitro permeation rate through mouse skins as compared to the control [44].

The study was developed to evaluate the potential of nanoemulsions for increasing the solubility and the in vitro transdermal delivery of carvedilol. The prepared nanoemulsion s were subjected to physical stability tests. Transdermal permeation of carvedilol through rat abdominal skin was determined with the Keshary-Chien diffusion cell. Significant increase ($P < 0.05$) in the steady state flux (Jss) and permeability coefficient (Kp) was observed in nanoemulsion formulations as compared to control or drug-loaded neat components. The irritation studies suggested that the optimized nanoemulsion was a non-irritant transdermal delivery system [45]. Celecoxib, a selective cyclo-oxygenase-2 inhibitor, has been recommended orally for the treatment of arthritis and osteoarthritis. Long-term oral administration of celecoxib produces serious gastrointestinal side effects. Skin permeation mechanism of celecoxib from nanoemulsion was evaluated by FTIR spectral analysis, DSC thermogram, activation energy measurement, and histopathological examination. The optimized nanoemulsion was subjected to pharmacokinetic (bioavailability) studies on Wistar male rats. Photomicrograph of a skin sample showed the disruption of lipid bilayers as distinct voids and empty spaces were visible in the epidermal region. The absorption of celecoxib through transdermally applied nanoemulsion and nanoemulsion gel resulted in 3.30- and 2.97-fold increase in bioavailability as compared to oral capsule formulation. Results of skin permeation mechanism and pharmacokinetic studies indicated that the nanoemulsions can be successfully used as potential vehicles for enhancement of skin permeation and bioavailability of poorly soluble drugs [46].

Self-Nanoemulsifying Drug Delivery Systems

Self-nanoemulsifying drug delivery systems for oral delivery of protein drugs: Formulation development, in vitro transport study and in vivo oral absorption study [47]. The research project was done to develop a self-nanoemulsifying drug delivery system (SNEDDS) for non-invasive delivery of protein drugs. An experimental design was adopted to develop SNEDDS. Fluorescent-labeled beta-lactamase (FITC-BLM), a model protein, was loaded into SNEDDS through the solid dispersion technique. The experimental design provided 720 compositions of different oil, surfactant, and co-surfactant at various ratios, of which 33 SNEDDS prototypes were obtained. A SNEDDS was developed to load FITC- BLM into the oil phase that can spontaneously form O/W NE upon the addition of water. Fluorescently labeled BLM (FITC-BLM), a model protein, formulated into 16 SNEDDS preparations through a solid dispersion technique were studied for transport across monolayer. All the SNEDDS NEs resulted in higher transport rate than the free solution. The transport rate by SNEDDS depends on the SNEDDS composition. The SNEDDS significantly increased the transport of FITC-BLM across MDCK monolayer in vitro. SNEDDS may be a potential effective delivery system for non-invasive protein drug delivery. The oral absorption of BLM in rats when delivered by such a SNEDDS was investigated and showed significantly enhance in the oral bioavailability of BLM. So the SNEDDS has a great potential for oral protein delivery [48-50].

CONCLUSION

Nanoemulsion formulations offer several advantages for the delivery of drugs, biological, or diagnostic agents. Traditionally, nanoemulsions have been used in clinics for more than four decades as total parenteral nutrition fluids. Although nanoemulsions are chiefly seen as vehicles for administering aqueous insoluble drugs, they have more recently received increasing attention as colloidal carriers for targeted delivery of various anticancer drugs, photo sensitizers, neutron capture therapy agents, or diagnostic agents. Because of their submicron size, they can be easily targeted to the tumor area. It is expected that further research and development work will be carried out in the near future for clinical realization of these targeted delivery vehicles.

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