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Review Article

A REVIEW ON DEVELOPMENT AND IMPORTANCE OF NANOEMULSIONS

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ABSTRACT

Nanoemulsions are novel drug delivery systems consisting of emulsified oil and water systems with mean droplet diameters ranging from 50 to 1000 nm. Usually, the average droplet size is between 100 and 500 nm and can exist as oil-in-water (o/w) or water-in-oil (w/o) form, where the core of the particle is either oil or water, respectively. Nanoemulsions are made from pharmaceutical surfactants that are generally regarded as safe (GRAS). The surfactant type and concentration in the aqueous phase are chosen to provide good stability against coalescence. The capacity of nanoemulsions to dissolve large quantities of low soluble drugs along with their mutual compatibility and ability to protect the drugs from hydrolysis and enzymatic degradation make them ideal drug delivery vectors. This review provides brief information about method of preparation and evaluation of nanoemulsion as drug carriers for improving the delivery of therapeutic agents [1].

Keywords: *Nanoemulsions, Oil-in-water, Coalescence, surfactant.*

INTRODUCTION

An emulsion is generally described as a heterogonous system composed of two immiscible liquids. Emulsions like other disperse systems are thermodynamically unstable as a result of excess free energy associated with the surface of the internal phase. Nanoemulsion is a type of emulsion sized between 20-200 nm with narrow distributions. They are transparent or translucent with a bluish coloration. So, the definition is different from that of sub-micron emulsions.

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It is worth saying that, while the distinction between a nanoemulsion and an emulsion, in terms of their size, is rather arbitrary, nanoemulsions because of their small droplet size, cause a large reduction in gravity force; therefore, Brownian motion may be sufficient to possess a higher stability against sedimentation or creaming than an emulsion [1]. Nanoemulsions are formed when the interfacial tension at the oil/water interface is brought to a very low level and the interfacial layer is kept highly flexible and fluid. These two conditions are usually met by a careful and precise choice of the components and of their respective proportions and by the use of a "co-surfactant" which brings flexibility to the oil/water interface [2]. Besides, nanoemulsions are two-phase systems where the dispersed phase droplet size has been made in the nanometer size range, the microemulsions, and micellar systems are single-phase systems. As a consequence, many of the nanoemulsions

reported in the literature do not possess long-term stability. They may experience Ostwald ripening or coalescence instabilities that could be controlled by modifying oily phase solubility, surfactant quantity and molecular weight [1, 3]. Some nanoemulsions have, however, exhibited sufficiently high levels of stability to be proposed as vehicles for drug delivery. One supposed advantage of a nanoemulsion over a microemulsion is that it requires a lower surfactant concentration for its formation. When comparing this surfactant concentration with the 20% surfactant typically needed to prepare a microemulsion containing a comparable amount of oil, one should realize that the droplet size of a microemulsion thus produced would typically be ~10 nm. Consequently, in order to produce nanoemulsion droplets of the comparable size, the amount of surfactant required would increase (the surface area of the droplet varies with the square of the droplet radius) to a comparable value. Moreover unlike microemulsions, they can be diluted with water without changing the droplet size distribution [4]. Nanoemulsions contain oil phase, surfactants or emulsifiers, active pharmaceutical ingredients (drugs or diagnostic agents), and additives. The oil phases are mainly natural or synthetic lipids, fatty acids, oils such as medium or long chain triglycerides, or perflurochemicals. The most commonly used emulsifiers and coemulsifiers include either natural or modified lecithins, poly (ethylene oxide) (PEO)-containing block copolymers, PEG-conjugated castor oil derivatives (Cremophore EL), glycerides, and positively charged lipids. Other pharmaceutical additives such as pH adjustment agents, antioxidants, flavors, and preservatives may also be included in the final formulation, if requested [7].

METHODS OF PREPARATION OF NANOEMULSIONS

As nanoemulsions are non-equilibrated systems [8-10] and so their preparation involves the input of a large amount of either energy or surfactants and in some cases a combination of both. As a result, high energy or low energy methods can be used in their formulation. Although high energy emulsification method is traditionally used for the preparation of nanoemulsion formulation but low emulsion emulsification method now create an attraction due to their wide application and advantages as a formulation and stability aspects. Generally, energy is usually required in emulsion formulation because the process may be non-spontaneous. The production of nanoemulsions costs more energy than that required to produce macroemulsions. Presence of surfactants help lower the surface tensions between oil and water. Small molecules such as non-ionic surfactants lower surface tension more than polymeric surfactants such as poly (vinyl alcohol). Another important role of the surfactant is its effect on the interfacial dilatational modulus. During emulsification an increase in the interfacial area takes place and this causes a reduction in surface excess [11].

LOW ENERGY METHODS

As the name suggests, low-energy emulsification methods require low energy for the fabrication of nanoemulsions. These methods are mainly dependent on modulation of interfacial phenomenon/phase transitions and intrinsic physicochemical properties of the surfactants, coemulsifiers/co-surfactants and oil to yield nano-sized emulsion droplets. The lower energy method, also called the condensation method, is based on the phase transitions taking place during the emulsification process [12, 13]. These phase transitions result from changes in the spontaneous curvature of the surfactant and can be achieved (i) at constant composition by changing the spontaneous curvature of non-ionic surfactants with temperature, the well known Phase Inversion Temperature, PIT, widely used in industry or (ii) at constant temperature by varying the composition of the system by the Emulsion Inversion Point (EIP) method [14, 15].

In other words, low-energy emulsification method was developed according to the phase behavior and properties of the constituents, to promote the formation of ultra small droplets. These low-energy techniques include self-emulsification, phase transition and phase

inversion temperature methods [82]. The low energy method is interesting because it utilizes the stored energy of the system to form small droplets. This emulsification can be brought about by changing the parameters which would affect the hydrophilic lipophilic balance (HLB) of the system like temperature, composition, etc. [19, 20]. The most commheonly used low-energy emulsification methods include:

Phase inversion temperature (PIT) method

This method employs temperature-dependent solubility of non-ionic surfactants, such as polyethoxylated surfactants, to modify their affinities for water and oil as a function of the temperature. It has been observed that polyethoxylated surfactants tend to become lipophilic on heating owing to dehydration of polyoxyethylene groups. This phenomenon forms a basis of nanoemulsion fabrication using the PIT method. In the PIT method, oil, water and nonionic surfactants are mixed together at room temperature. This mixture typically comprises o/w microemulsions coexisting with excess oil, and the surfactant monolayer exhibits positive curvature. When this macroemulsion is heated gradually, the polyethoxylated surfactant becomes lipophilic and at higher temperatures, the surfactant gets completely solubilized in the oily phase and the initial o/w emulsion undergoes phase inversion to w/o emulsion. The surfactant monolayer has negative curvature at this stage. The ternary system at this stage typically consists of a D-phase bicontinuous microemulsion or a mixture of a Dphase bicontinuous microemulsion and lamellar liquid crystalline phases. It has been observed that nanoemulsions with very small droplet size and polydispersity index can be generated by rapid cooling of the single-phase or multiphase bicontinuous microemulsions maintained at either PIT or a temperature above PIT (transitional-phase inversion) [17].

Solvent displacement method

The solvent displacement method for spontaneous fabrication of nanoemulsion has been adopted from the nano-precipitation method used for polymeric nanoparticles. In this method, oily phase is dissolved in water-miscible organic solvents, such as acetone, ethanol and ethyl methyl ketone. The organic phase is poured into an aqueous phase containing surfactant to yield spontaneous nanoemulsion by rapid diffusion of organic solvent. The organic solvent is removed from the nanoemulsion by a suitable means, such as vacuum evaporation [21, 23].

Phase inversion composition method (self-nanoemulsification method)

This method generates nanoemulsions at room temperature without use of any organic solvent and heat. Forgirani et al.observed that kinetically stable nanoemulsions with small droplet size (~50 nm) can be generated by the stepwise addition of water into solution of surfactant in oil, with gentle stirring and at constant temperature. Although the components used in the aforementioned investigation were not of pharmaceutical grade, the investigation opened doors to design pharmaceutically acceptable nanoemulsions using a similar approach. The spontaneous nano-emulsification has been related to the phase transitions during the emulsification process and involves lamellar liquid crystalline phases or D-type bicontinuous microemulsion during the process [29].

HIGH ENERGY METHODS

High-energy emulsification methods make use of devices that use very high mechanical energy to create nanoemulsions with high kinetic energy. The high-energy method utilizes mechanical devices to create intensely disruptive forces which break up the oil and water phases to form nano-sized droplets. This can be achieved with ultrasonicators, microfluidiser and high pressure homogenisers. Particle size here will depend on the type of instruments employed and their operating conditions like time and temperature along with sample properties and composition [27].

High-pressure homogenization

This is the most common method used for the fabrication of nanoemulsions. During high-

pressure homogenization, the coarse macroemulsion is passed through a small orifice at an operating pressure in the range of 500 to 5000 psi. During this process, several forces, such as hydraulic shear, intense turbulence and cavitation, act together to yield nanoemulsions with extremely small droplet size.The resultant product can be re-subjected to high-pressure homogenization until nanoemulsion with desired droplet size and polydispersity index is obtained. Micro-fluidization employs a high-pressure positive displacement pump operating at very high pressures, up to 20,000 psi. This pump forces macroemulsion droplets through the interaction chamber consisting of a series of micro-channels. The macroemulsion flowing through the micro channels collides with high velocity on to an impingement area resulting in very fine nanoemulsions. The nanoemulsions with desired size range and dispersity can be obtained by varying the operating pressure and the number of passes through interaction chambers like high pressure homogenization [21]

Microfluidization

Microfluidization is a mixing technique, which makes use of a device called microfluidizer. This device uses a high-pressure positive displacement pump (500 to 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 sub- micron 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 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 a uniform nanoemulsion [16].

Ultrasonication

The preparation of nanoemulsion is reported in various research papers which aim to use the ultrasonic sound frequency for the reduction of the droplet size. Another approach is the use of a constant amplitude sonotrode at system pressures in excess of the ambient value. It is well known that increasing the external pressure increases the cavitations threshold within an ultrasonic field and thus fewer bubbles form. However, increasing the external pressure also increases the collapse pressure of cavitations bubbles. This means that the collapse of the bubbles when cavitation occurs becomes stronger and more violent than when the pressure is at atmospheric conditions. As cavitation is the most important mechanism of power dissipation in a low frequency ultrasonic system, these changes in navigational intensity can be related directly to changes in the power density. The system also uses a water jacket to control the temperature to optimum level.

CHARACTERIZATION OF NANOEMULSIONS

Dynamic light scattering

DLS also known as photon correlation spectroscopy or quasi-elastic light scattering is a technique used for rapid determination of the size distribution profile of small particles in suspensions or polymers in solution. DLS measures Brownian motion and relates this to the size of the particles through Stokes–Einstein equation. Through the illumination of the particles with a laser and analyzing the intensity fluctuations in the scattered light, DLS allows calculating the size of the particles. DLS provides a fast and adequate evaluation of the size of nanoemulsions and is often used to evaluate the size distribution of nanoemulsions.

Zeta potential

Zeta potential is a scientific term for electrokinetic potential in colloidal systems. In colloidal chemistry literature, zeta potential is the potential difference between the dispersion medium and the stationary layer of

fluid attached to the dispersed particle. A value of 30 mV (positive or negative) can be taken as the arbitrary value that separates low-charged surfaces from highly charged surfaces. Zeta potential value can be related to the stability of colloidal dispersions, indicating the degree of repulsion between adjacent, similarly charged particles in dispersion. For molecules and particles that are small enough, a high zeta potential will confer stability, i.e., the solution or dispersion will resist to aggregation. When the potential is low, attraction exceeds repulsion and the dispersion will break and flocculate. So, colloids with high zeta potential (negative or positive) are electrically stabilized while colloids with low zeta potentials tend to coagulate or flocculate. Briefly, zeta potentials from 0 to ±30 mV indicate instability, while zeta potentials higher than ±30 mV indicate stability. The zeta potential of nano-scaled particles is influenced by many factors, such as the source of particles and the treatment with different surfactants, electrolyte concentration (ionic strength), particle morphology and size, pH of the solution and state of hydration. For instance, Preetz et al., evaluated the zeta potential of nanoemulsions: the information given by the zeta potential allows stating that the nanoemulsions with highly charged surfaces are stable and will resist to droplet aggregation [24].

Differential scanning calorimetry

DSC is a thermo-analytical technique in which the difference in the amount of heat required to increase the temperature of a sample and reference is measured as a function of temperature. Both the sample and reference are maintained at nearly the same temperature throughout the experiment. Generally, the temperature program for a DSC analysis is designed such that the sample holder temperature increases linearly as a function of time. The reference sample should have a well-defined heat capacity over the range of temperatures to be scanned. DSC can be used to detect phase transitions including the melting of crystalline regions, and to analyse the proportion of solid fat or the proportion of ice crystals in emulsions. Thanasukarn et al. shows that fat crystallization affects the emulsion stability depending on the emulsifier used. They showed that the thermal decomposition follows the melting of the drug encapsulated have shown that DSC can be used to determine the crystallization temperature of a mixture of surfactants too [17, 16]

Transmission electron microscopy (TEM)

TEM is a technique capable of a resolution on the order of the 0.2 nm. It is widely used in the study of materials for science/metallurgy and biological sciences; in both cases the samples must be very thin and able to withstand the high vacuum present inside the instrument. Nevertheless, this technique has some drawbacks. Some materials require extensive sample preparation to produce a sample thin enough to be electron transparent, which makes TEM analysis a relatively time-consuming process with a low throughput of samples. The structure of the sample may be changed during the preparation process; the field of view is relatively small and the sample may be damaged by the electron beam. Bouchemal et al. studied the morphology and structure of the nanoemulsions using TEM. the combination of bright field imaging at increasing magnification and of diffraction modes were used to reveal the form and size of the emulsions and to determine the amorphous or crystalline character of the components. They direct observation enabled the possibility to perform selected area electron diffraction in order to check the crystallinity of the emulsion core components. The microstructure and the particle-size distribution in their nanoemulsions, concluding that β-carotene particles exhibited spherical morphology with a mean diameter of 20 nm, confirming the results obtained by DLS [26, 28].

Viscosity

This is carried out using a viscometer. The viscosity of nanoemulsions is a function of the surfactant, water and oil components and their

concentrations. Increasing the water content lowers the viscosity, while decreasing the amount of surfactant and cosurfactant increases interfacial tension between water and oil resulting in increased viscosity. Viscosity is very important for stability and efficient drug release. Nanoemulsion carrier formulations are basically oil-in-water and so in addition to being less greasy than water-in-oil formulations, often possess lower apparent viscosities. They are therefore expected to exhibit faster release of active ingredients and wash out easily after application on the skin surface. Various equipment and methods are available for assessment of rheological properties of nanoemulsion carriers. Monitoring of viscosity change is a method of assessing stability of liquid and semi-solid preparations including nanoemulsion formulations [28].

In-vitro skin permeation

Franz diffusion cell is used to obtain the drug release profile of the nanoemulsion formulation in the case of formulations for transdermal application. The extent or depth of skin penetration by the released content can be visualized by confocal scanning laser microscopy. *In vitro* drug release can be determined by dispersing an amount of the preparation in the donor compartment of a Franz cell having a membrane as barrier and monitoring the appearance of the encapsulated drug in the receptor compartment, usually containing phosphate buffer saline (PBS, pH 7.4) and stirring on a magnetic stirrer at 100 rpm at 37 ± 1 °C. Samples (1 ml) of the dispersion are withdrawn from the receptor medium and replaced with an equivalent amount of the medium at definite intervals. The withdrawn sample is then filtered using a 0.22-50 µm filter (e.g., Millipore, USA) and the drug released then analyzed using HPLC or UV-Vis spectroscopy at wavelength of peak absorption of the drug. An alternative and popular method of *ex-vivo* release study is performed using diffusion cell. The skin is cut from the ear or abdomen and underlying cartilage and fats carefully removed. Appropriate size of skin is cut and placed on the diffusion cell which had earlier been filled with receptor solution. Samples of the vesicular preparation are then applied on the dorsal surface of the skin and the instrument started. At intervals, up to 24 h, samples are withdrawn from the receptor medium and replaced with equal amounts of the medium and the withdrawn samples analyzed for the drug permeated using HPLC or UV spectroscopy. Semipermeable membrane such as regenerated cellulose could be used in place of skin for in vitro release studies [16, 18]. The flux J, of the drug across the skin or membrane is calculated from the formula:

$$J=Ddc/dx$$

Where D is the diffusion coefficient and is a function of the size, shape and flexibility of the diffusing molecule as well as the membrane resistance, c is the concentration of the diffusing species, x is the spatial coordinate [18].

APPLICATIONS OF NANOEMULSIONS IN DRUG DELIVERY

Nanoemulsions could be and have been applied in various aspects of drug delivery including: cosmetics and transdermal delivery of drug, cancer therapy, vaccine delivery, non-toxic disinfectant cleaner, cell culture technology, formulations for improved oral delivery of poorly soluble drug, ocular and otic drug delivery, intranasal drug delivery, parenteral drug delivery and pulmonary delivery of drugs.

Applications in cosmetics

Recently importance of nanoemulsions have become increasing as good vehicles for the controlled delivery of cosmetics and for the optimized dispersion of active ingredients inparticular skin layers. Due to their lipophilic interior, nanoemulsions are more suitable for the transport of lipophilic drug than liposomes Similar to liposomes, nanoemulsions supports the skin penetration of active ingredients and thus increases their concentration in the skin. Another advantage is the small-sized droplet with its high surface area permit effective delivery of the active to the skin. Morever, nanoemulsions gain increasing interest due to

their own bioactive effects. This may reduce the trans-epidermal water loss (TEWL), suggesting that the barrier function of the skin is strengthened. Nanoemulsions are acceptable in cosmetics because there is no chance of creaming, sedimentation, flocculation or coalescence, which is observed within microemulsions. The incorporation of potentially irritating surfactants can be avoided by using high-energy equipment during manufacturing process. PEG free nanoemulsions for cosmetics has also been developed and formulations exhibited good stability [30, 31].

Antimicrobial nanoemulsions

Antimicrobial nanoemulsions are o/w droplets that range from 200-600 nm. They are made of oil and water and are stabilized by surfactants and alcohol. The nanoemulsions has a broad spectrum of activity against bacteria like E. coli, salmonella, S. aureus; enveloped viruses like HIV, herpes simplex; fungi like candida, dermatophytes, and spores like anthrax. The nanoemulsions 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 celllysis and death. In the case of spores, additional germination enhancers are added into the emulsion. Once starting of germination takes place, the germinating spores become susceptible to the antimicrobial action of the nanoemulsions. An aspect of the nanoemulsions is their highly selective toxicity to microbes at concentration range that are non-irritating to skin or mucous membrane. The safety range of nanoemulsions is because of the low amount of detergent in each droplet, yet when acting in concert, these droplets have enough energy and surfactant to destabilize targeted microbes without affecting healthy cells. Nanoemulsions can get a level of topical antimicrobial activity, which can only be previously achieved by systemic antibiotics [30].

Nanoemulsions in vaccines delivery

This medication delivery system uses nanotechnology to vaccinate against human immune deficiency virus (HIV). There is recent evidence that HIV can infect the mucosal immune system. Therefore, developing mucosal immunity through the use of nanoemulsions may become very important in the future fight against HIV [32]. The oil-based emulsion is administered in the nose, as opposed to traditional vaccine routes. Recent research results indicate that genital mucosa immunity may be attained with vaccines that are administered into the nasal mucosa. Nanoemulsions are being used to transport inactivated organisms to a mucosal surface to produce an immune response. The first applications as vaccine, 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 help uptake by antigen presenting cells. This results in the significant systemic and mucosal immune response due to that the production of specific IgG and IgA antibody as well as cellular immunity. Work in influenza has shown that animals can be prevented against influenza after a single mucosal exposure to the virus mixed with thenanoemulsions. Research has also show that animals exposed to recombinant gp120 in nanoemulsions on their nasal mucosa create significant responses to HIV, thus giving a basis to use of this material as an HIV vaccine. Additional research has been ongoing to complete the proof of concept in animal trials for other vaccines including Anthrax and Hepatitis B [29, 30].

Nanoemulsions as non-toxic disinfectant cleaner

Nanemulsions have been employed as a disinfectant cleaner. A nontoxic disinfectant cleaner for use in routine markets that include healthcare, travel, food processing and military applications has been developed by EnviroSystems. They have been found to kill tuberculosis and a large spectrum of

viruses, bacteria and fungi within 5 to 10 min without any of the hazards posed by other categories of disinfectants. The product requires no warning labels. It does not irritate eyes and can be absorbed through the skin, inhaled or swallowed with harmless effects. The disinfectant formulation is made up of nanospheres of oil droplets less than 100 µm which are suspended in water to produce a nanoemulsions requiring only small amounts of the active ingredient, parachlorometaxylenol. The nanospheres have surface charges that efficiently penetrate the surface charges on microorganisms membranes like breaking through an electric fence. Rather than 'drowning' cells, the formulation allows parachlorometaxylenol to target and penetrate cell walls. So parachlorometaxylenol is applicable at concentration ranges 1-2 times lower than those of other disinfectants, so there are no toxic effects on human, animals or the environment [30].

Nanoemulsions in cell culture technology

Cell cultures are used for *in-vitro* assays or to produce biological compounds like an antibodies or recombinant proteins. For optimization of cell growth, the culture medium can be supplemented with a large number of molecules or with blood serum. It has been very difficult to provide the media with oil-soluble substances that are available to the cells, and only few amounts of the lipophilic compounds could be absorbed by the cells. Nanoemulsions are a new method for the delivery of oil-soluble substances to human cell cultures. The system is based on a nanoemulsions that is stabilized by phospholipids. This nanoemulsions is transparent and can be passed through 0.1 mm filters for sterilization. Nanoemulsions oil droplets are very easily taken up by the cells. The encapsulated oil-soluble substances therefore have a high bioavailability to cells in culture [33].

Improved oral delivery of poorly soluble drugs

Nanoemulsions formulation was developed to increase oral bioavailability of hydrophobic drugs. Paclitaxel was selected as a model hydrophobic drug. The o/w nanoemulsions were made with pine nut oil as the internal oil phase, water as the external phase and egg lecithin as the primary emulsifier. Stearylamine and deoxycholic acid were used to give positive and negative charge to the emulsions, respectively. The formulated nanoemulsions had a particle size range of 100-120 nm and zeta potential ranging from 34 mV to 245 mV. After oral administration of nanoemulsions, a significantly higher concentration of paclitaxel was observed in the systemic circulation compare to control aqueous solution. The results of this study suggest that nanoemulsions are promising novel formulations which can promote the oral bioavailability of hydrophobic drugs [30].

Nanoemulsions in ocular and otic drug delivery

Ophthalmic drug delivery is one of the most interesting and challenging endeavors facing the pharmaceutical scientist. It is a common knowledge that the application of eye drops as conventional ophthalmic delivery systems results in poor bioavailability and therapeutic response because of lacrimal secretion and nasolacrimal drainage in the eye. Most of the drug is drained away from the precorneal area in few minutes. As a result, frequent instillation of concentrated solutions is needed to achieve the desired therapeutic effects. But, by the tear drainage, the main part of the administered drug is transported via the nasolacrimal duct to the gastric intestinal tract where it may be absorbed, sometimes causing side effects. In order to increase the effectiveness of the drug, a dosage form should be chosen which increases the contact time of the drug in the eye [34-36].

Nanoemulsion in cancer therapy and in targeted drug delivery

Another interesting application, which is experiencing an active development, is the use of nanoemulsion formulations, for controlled

drug delivery and targeting. Because of their submicron size, they can easily be targeted to the tumor area. 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, photosensitizers, neutron capture therapy agents, or diagnostic agents. The development of magnetic nanoemulsions is an innovative approach for cancer therapy. This methodology can be used for the treatment of cancer in the form of photodynamic therapy [29].

Nanoemulsions and parenteral drug delivery

This is one of the most common and effective routes of drug administration usually adopted for actives with low bioavailability and narrow therapeutic index. Their capacity to dissolve large quantities of hydrophobics, together with their mutual compatibility and ability to protect the drugs from hydrolysis and enzymatic degradation make nanoemulsions ideal vehicles for the purpose of parenteral transport. Further, the frequency and dosage of injections can be reduced throughout the drug therapy period as these emulsions guarantee the release of drugs in a sustained and controlled mode over long periods of time. Additionally, the lack of locculation, sedimentation and creaming, combined with a large surface area and free energy, offer obvious advantages over emulsions of larger particle size, for this route of administration [31].

FUTURE PERSPECTIVES

Nanoemulsions are proposed for numerous applications in pharmacy as drug delivery systems because of their capacity to solubilize non-polar active compounds. Future perspectives of nanoemulsion are very promising in different fields of therapeutics or application in development of cosmetics for hair or skin. One of the versatile applications of nanoemulsions is in the area of drug delivery where they act as efficient carriers for bioactives, facilitating administration by various routes. The advantages and applications of nanoemulsions for oral drug delivery are numerous, where the droplet size is related to their absorption in the gastrointestinal tract. Due to the renewed interest in herbal drug formulation, nanoemulsion may be the ideal delivery platform for these difficult-to-formulate phytopharmaceuticals. The prospects of nanoemulsions lie in the ingenuity of formulation experts to utilize the advantages of nanoemulsion carriers in overcoming peculiar problems of drug delivery such as absorption, permeation and stability of both orthodox and herbal drugs [25, 22]

CONCLUSION

Nanoemulsions are submicron (range of 5-200 nm) sized emulsion that is under extensive investigation as drug carriers for improving the delivery of therapeutic agents. These are by far the most advanced nanoparticle systems for the systemic delivery of active pharmaceutical for controlled drug delivery and targeting. Nanoemulsions constitute one of the most promising systems to improve solubility, bioavailability, and functionality of hydrophobic compounds. Food industry seeks to use these systems for the incorporation

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