RETINOID BASED NANOEMULSIONS: PREPARATION TO THERAPEUTIC APPLICATIONS

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Submitted 27th June 2019, Accepted 17th January 2020

ABSTRACT
Modern mode of drug delivery system has been constructed to defeat the main issues linked with the traditional drug delivery system. This particular review will give an idea about the retinoid based nanoemulsion system. The main focus is to briefly explain the different aspects of nanoemulsion formulations, procedure of preparation, portrayal procedures with special focus on different utilizations of nanoemulsion in various area. Nanoemulsions are colloidal dispersion system that are composed of two non-miscible mixtures mixed along with surfactants and co-surfactants emulsifier to develop a single phase which is thermodynamically balanced. Nanoemulsion droplet sizes commonly fall in the range of 20-200 nm and show thin size distributions. Nanoscale dispersions of droplets of one liquid in another insoluble liquid can be achieved by using extreme emulsification procedures. Retinoid, better known as vitamin A are lipophillic in nature. They are vastly used for therapeutic purpose in skin disorders. Retinoid are among one of the fundamental compound found in cosmeceuticals. They are the most investigated compound with sufficient information supporting them. Retinoid include natural or synthetic derivatives that decrease hyper pigmentation and limit collagen breaking enzymes. Nanoemulsions comprise of tiny oil-in-water globules, having less than 100 nm diameter. They are delicate frameworks by nature. Traditional formulations are restricted because of irritation, poor aqueous solubility and high instability of retinoid. But administration of retinoid in aqueous media is enabled due to nanoemulsion based formulation, decreasing degradation, controlled release, high stability, improve targeting and enhance efficacy. Nanoemulsion show incredible guarantee for the future of beauty care products, diagnostics, treatments, and biotechnologies. The unique properties of nanoemulsions such as high stability, translucent appearance and efficient drug delivery attribute has attracted researchers interest which is one of the reason why the usage of nanoemulsion has grown rapidly during the recent decades. Nanoemulsion formulation might be considered as viable, safe and with enhanced bioavailability. Comparing to the conventional topical formulation, nanoemulsion possess advance transdermal permeation of various drugs such as gels and emulsions. Nanoemulsion is significantly important in modern pharmaceutical industry and provide many benefits in drug delivery systems. This review is focused on the most recent literature on developments of retinoid based nanoemulsions.

Keywords: Retinoid, Vitamin A, Controlled release, Nanoscale, Surfactant.

INTRODUCTION
Modern mode of drug delivery system has been constructed to defeat the main issues linked with the traditional drug delivery system. This particular article will give an idea about the retinoid based nanoemulsion system [1]. Nano-Emulsions are colloidal dispersion system that are composed of two non-miscible mixtures mixed along with surfactants and co-surfactants emulsifier to develop a single phase which is thermodynamically balanced. A variety of ionic and non-ionic surfactants with various distinctiveness had been utilized with such nanoemulsions. Most broadly used among them were nonionic surfactants (sorbitan esters, polysorbates), anionic surfactants (potassium laurate, sodium lauryl sulfate), cationic surfactants (quaternary ammonium halide) and zwitterions surfactants (quaternary ammonium halide). Nano emulsions have widely been explored as drug delivery system [2]. Nanoemulsion bead sizes commonly fall in the range of 20-200 nm and show thin size distributions.
Nanoemulsion show incredible guarantee for the future of beauty care products, diagnostics, tranquilize treatments, and biotechnologies. In this review the main focus is to briefly explain the different aspects of nanoemulsion formulations, procedure of preparation, portrayal procedures with special focus on different utilisations of nanoemulsion in various area for example treatment of cancer, as a mucosal vaccine, lipophilic drug, as a self-nanoemulsifying and solid self-nanoemulsifying drug delivery system and as a transport for transdermal drug delivery [3].

Nanoemulsions are broadly used in pharmaceutical framework. The most significant utilization of nanoemulsions for masking the disagreeable taste of oily fluids. Nanoemulsion formulation provide various benefits such as delivery of drugs, diagnostic or biological agents, plus these days its used in targeting drug delivery of different anticancer drugs, therapeutic agents and photo sensitizers. Nanoemulsion also helps to guard the drugs, which are vulnerable to oxidation and hydrolysis. Nanoemulsion can likewise provide extended action of the medicaments. Nanoemulsion formulation might be considered as viable, safe and with enhanced bioavailability [4]. As mentioned earlier, the expression emulsion carries with it no size implication. In the past efforts have been made to outline the tiniest end of the size range, normally less than 1 mm, with distinctive nomenclature such as ultrafine emulsion, submicron emulsions and miniemulsions. In the recent times the term nanoemulsion has been used extensively, however it has not been utilized with steady importance. There have been three different ways the term has been utilized [5].

It is estimated that around 40% of the newly discovered Chemical Entities (NCEs) by the researchers and even many of the existing entities are water-immiscible and existence of the lipophilic compounds leads to low oral bioavailability, high Intra- and Intersubject Inconsistency in oral drug absorption and low-dose proportionality. In order to overcome the problem in existing drugs which are having low water solubility, numerous formulation techniques are listed in the pharmaceutical literature which includes the use of permeation enhancers, surfactants, nanoparticles, micronization, lipids and cyclodextrins [6].

In the coming years, the ability to deliver drugs which are poorly soluble will increase significantly as many pharma industry researchers are depending upon NCEs for a bigger stake of revenues in the market. Lipophilic compounds are having significant importance in current pharmaceutical industry. The main focus is on the biotransformation of these immiscible component in order to improve the oral bioavailability of poorly water soluble drug substances. The integration of the active lipophilic components into inert lipid vehicles is the most famous technique such as surfactant dispersions, nano and micro emulsions, liposomes and emulsions as well as self-emulsifying formulations. Thermo dynamical stability of nanoemulsion makes it one of the favorable biotechnology to increase the oral bioavailability of the poorly miscible drugs. An interfacial film of surfactant molecules which are having droplet size lesser then 100 nm stabilized thermodynamically, transparent dispersions of oil to develop nanoemulsions and provides large O/w interfacial areas and ultra-low interfacial tensions. Nanoemulsions have greater solubilization capacity as compared to simple micellar fluids and not only that , its thermo dynamical stability offers an edge over unstable dispersions such as suspensions and emulsions and they are energy efficient because they require little energy input to heat or mix and have extended shelf life. Nanoemulsion plays a vital role in sustained and targeted delivery of the drugs. Due to its nano sized droplets it creates vast interfacial area linked with NE to impact carrying properties of the drug and plays a vital role in targeted and persistent delivery of the drug [7].

Various studies have revealed that the formulation of nanoemulsion contains enhanced transdermal and dermal transport properties in vitro.8-16 and in vivo.17-19. Comparing to the conventional topical formulation, nanoemulsion possess advance transdermal permeation of various drugs such as gels and emulsions [8]. Nanoscale dispersions of droplets of one liquid in another insoluble liquid can be achieved by using extreme emulsification procedures. These ultrasonic and microfluidic techniques split bigger micro scale droplets into nonoscale droplets are giving interesting and helpful nonequilibrium systems of structured fluids. The existence of a stabilizing surfactant that restrain the coalescence of the droplets helps the nanoemulsion to continue to exist over many months or years regardless of their metastability. The physical properties of the nanoemulsions can be a lot different as compared to their microscale counterparts [9].

RETINOID
Barrier function of skin allows low permeability to foreign substances to permeate to the skin thus protecting it from environmental threats like microorganisms, harmful chemicals and toxins. Stratum corneum is the most substantial barrier and studies reveals that SC do not allow molecules to diffuse through the skin estimated around 70% of drug products cannot cross the skin barrier. Good skin permeation can be achieved using nanoparticles
of size range less than 40 nm. Shape of nanoparticles also play significant role in skin permeation ellipsoidal particles have less permeation than spherical particles. Absorption of topically applied products varies due to some factors including structural characteristics of skin, physicochemical properties of the product, skin age and anatomical site, contact time, the degree of hydration, skin temperature and peripheral circulation [10].

Synthetic Vitamin A derivatives are termed as retinoid. Vitamins are essential for regulation of body functions. Functions of Vitamin A includes differentiation of epithelial tissues, visual function, reproduction and it is essential for general growth. Need of tissues for Vitamin A is regulated by the system designed in the body to utilize nutrients according to its requirements. Liver is the storage of retinol ester that is vitamin A. Toxicity of liver may develop due to high pharmacological doses of vitamin A that is commonly used in skin diseases treatment. Toxicity may also occur at low doses when used for longer period of time [11].

A group compounds derived from all trans retinol, including retinal, retinol and retinoic acid, are termed as retinoid, better known as Vitamin A derivatives. These naturally occurring or synthetic derivatives of Vitamin A are essential in cellular proliferation, differentiation, vision and regulating morphogenesis [12]. Retinoid, better known as vitamin A are lipophilic in nature. They are vastly used for therapeutic purpose in skin disorders. Traditional formulations are restricted because of irritation, poor aqueous solubility and high instability of retinoid. But administration of retinoid in aqueous media is enabled due to nanoemulsion based formulation, decreasing degradation, controlled release, high stability, improve targeting and enhance efficacy [13].

Retinoid are among one of the fundamental compounds found in cosmeceuticals. They are the most investigated compound with sufficient information supporting them. Retinoid include natural or synthetic derivatives that decrease hyper pigmentation and limit collagen breaking enzymes. Nanoemulsions comprise of tiny oil-in-water globules, having less than 100nm diameter. They are delicate frameworks by nature [14].

ADVANTAGES OF NANOEMULSION OVER OTHER DOSAGE FORMS

- Rate of absorption Augmented.
- Variability in absorption decreased.
- Assist lipophilic drug to solubilize.
- Enhanced bioavailability of active drug.
- Requirement of less energy.
- Enhance patient compliance.
- Proficient and rapid absorption of drug.

- Prevent hydrolysis and degradation of drug as in O/W nanoemulsion drug stays in oily phase and do not interact with water.
- Being thermodynamically stable, the stability allows self-emulsification of the system whose properties are not subject to the procedure pursued.
- Minimized side effects as the dose is reduced due to improved efficacy [15].

DISADVANTAGES OF NANOEMULSION BASED SYSTEMS

- Use of a large concentration of surfactant and co-surfactant necessary for stabilizing the nanodroplets.
- Limited solubilizing capacity for high-melting substances.
- The surfactant must be nontoxic for using pharmaceutical applications.
- Nanoemulsion stability is influenced by environmental parameters such as temperature and pH. These parameters change upon Nanoemulsion delivery to patients [15].

APPLICATIONS OF NANOEMULSIONS IN TOPICAL DELIVERY SYSTEMS

Nanoemulsion possess distinctive properties such as tiny size of droplet, excellent stability, translucent appearance and so on. These unique properties make nanoemulsion striking applicant in the various fields such as cosmetics, food, pharmaceutical industry and in controlled drug delivery system.

Nanoemulsions in Drug Delivery

Nanoemulsion is significantly important in modern pharmaceutical industry and provide many benefits in drug delivery systems. Enhancing potency of the active ingredients, controlling drug release system and increasing the biological life-time as well as transporting multiple agents in a single preparation are some of the advantages when nanoemulsion is engaged. Recent studies have shown use of different nanoparticles for deliverance of drug in acne treatment. These nano transporters are transparent and offer various other advantages such as low viscosity, larger surface area which helps them to become efficient transdermal and topical system of drug delivery. Ease of preparation and their thermodynamically stable nature gives them an advantage over conventional drug delivery system. If we compare these with other nanoparticles, they give some considerable advantages which includes high permeation and high drug loading ability for topical treatment as well as low skin irritation. Nanoemulsions are formulated in various topical dosage types such as creams, gels, fluids, sprays and foams [16].
Nanoemulsions as Building Blocks

Nanoemulsions are exploited for their small size and high surface area and serve as building blocks for preparation of complex materials. Polymeric particles are synthesized through polymerization of hydrophobic monomers confined in the form of droplets. Nanoemulsions also termed as miniemulsions have been extensively utilized for the synthesis of polymers [17].

Nanoemulsions in Food Industry

Food industry have taken a huge advantage using nanoemulsion to design smart foods with ingredients that are difficult to integrate because of poor water solubility. Its example includes β-carotene, in vegetables like carrot is an important pigment having pH and temperature by preparing its nanoemulsion. Various studies on nanoemulsions application in food industry have discovered the permanence and preparation of flavored nanoemulsions using energy efficient procedures. Number of review articles have covered broadly the use of nanoemulsions in food industry [18].

DROplet SIZE and STABILITY

The diameter of the nanoemulsions droplet is roughly 100 nm, or some have defined it as below 100 nm. Its even smaller than the wavelength of visible light. The usual transparent look of nonemulsions can be modified by controlling the size of the droplets. It can be turned from transparent to milky white appearance. Nanoemulsions can have firm stability and their shelf life ranges from months to years plus the additional benefit of being rather less sensitive towards temperature [19, 20].

CONCLUSION

In recent years, the pharmaceutical industry has grown rapidly and due the extensive and constant increase in consumer demand, the industry is compelled to develop more advanced formulations, targeting at higher performance, efficiency, striking appearance and sensorial advantages and wellbeing. However in spite of increasing petition, the researchers are facing certain limitations with respect to the optimum dosage. The unique properties of nanoemulsions such as high stability, translucent appearance and efficient drug delivery attribute has attracted researchers interest which is one of the reason why the usage of nanoscale emulsion has grown rapidly during the recent decades. Therefore, lipid base nanocarrier ensures the improvement in performance. There are various methods to produce Nanoemulsions such as High-Energy and Low-Energy Procedures.

REFERENCES


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