WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 10, Issue 6, 299-313. Review Article ISSN 2277– 7105

NANOEMULSIONS: A SHORT REVIEW

Deepak Yadav*

M. Pharmaceutics Scholar, University Institute of Pharma Sciences, Chandigarh University, Gharaun, Punjab, India.

Article Received on
24 March 2021,

Revised on 13 April 2021,
Accepted on 04 May 2021

DOI: 10.20959/wjpr20216-20479

***Corresponding Author**
Deepak Yadav
M. Pharmaceutics Scholar, University Institute of Pharma Sciences, Chandigarh University, Gharaun, Punjab, India.

ABSTRACT

The Nano emulsion is quite possibly the most proficient scattered Nano systems of drop size running to submicron size. Nano emulsions/Sub-micron emulsions (SMEs)/Mini-emulsions are thermodynamically steady straightforward or clear scatterings of oil and water balanced out by an interfacial film of surfactant and co surfactant particles having a drop size of under 100 nm. The fundamental distinction among emulsion and Nano emulsion lies in the size and state of particles scattered in the persistent stage. In this survey, the consideration is engaged to give a fundamental thought regarding its detailing, strategy for arrangement, portrayal strategies, assessment boundaries, assessment of nanoemulsion as medication transporters for improving the conveyance of helpful specialists and different uses of Nano emulsion. A few strategies are to be utilized for readiness of nanoemulsions like microfluidization, high pressing factor homogenization, low energy emulsification and dissolvable vanishing strategy and boundary that are to be utilized for its portrayal like drop size investigation, thickness assurance, drug content, refractive record, pH, zeta potential.

KEYWORDS: Nano emulsion, Thermodynamically stable, emulsion, Characterization, Evaluation.

INTRODUCTION

Nanoemulsions are a colloidal particulate framework in the submicron size range going about as transporters of medication particles. Their size shifts from 10 to 1,000 nm. These transporters are strong circles and their surface is indistinct and lipophilic with a negative charge. Attractive nanoparticles can be utilized to upgrade site particularity. As a medication conveyance framework they improve the restorative viability of the medication and limit

unfavorable impact and harmful responses. Significant application incorporates therapy of contamination of the reticuloendothelial framework (RES), compound substitution treatment in the liver, therapy of malignancy, and inoculation. An emulsion is a biphasic framework in which one stage is personally scattered in the other stage as moment drops going in breadth from 0.1 to 100 μm. It is a thermodynamically temperamental framework, which can be settled by the presence of an emulsifying specialist (emulgent or emulsifier). The scattered stage is otherwise called inside stage or the intermittent stage while the external stage is called scattering medium, outside stage or nonstop stage. The emulsifying specialist is otherwise called transitional or interphase. The term 'nanoemulsion' likewise alludes to a miniemulsion which is fine oil/water or water/oil scattering balanced out by an interfacial film of surfactant atom having bead size range 20–600 nm. Due to little estimate, nanoemulsions are straightforward.[1-5]

Three Types of Nanoemulsions are well on the way to be formed depending upon the composition.

- Oil in water Nanoemulsions wherein oil drops are scattered in the continuos aqueous stage;
- Water in oil Nanoemulsions wherein water droplets are scattered in the continous oil stage;
- Bi-continous Nanoemulsions wherein microdomains of oil and water are interdispersed inside the system.

In every one of the three Types of Nanoemulsions, the interface is stabilized by an appropriate blend of surfactants and additionally co-surfactants.

Advantages Of Nanoemulsion[6-8]

1. It could be utilized an alternative for liposomes and vesicles.
2. It improves the bioavailability of medication.
3. It is non-poisonous and non-aggravation in nature.
4. It has improved actual dependability.
5. Nanoemulsions have little measured drops having more noteworthy surface area giving greater absorption.
6. It gives better take-up of oil-dissolvable enhancements in cell culture innovation.
7. It serves to solubilize lipophilic medication.

8. Supportive in taste covering.
9. Less measure of energy is required.

Disadvantages Of Nanoemulsion[6-8]

1. Utilization of an enormous convergence of surfactant and co-surfactant essential for balancing out the nanodroplets.
2. Restricted solubilizing limit with regards to high-softening substances.
3. The surfactant should be nontoxic for utilizing drug applications.
4. Nanoemulsion solidness is affected by ecological boundaries like temperature and pH. These boundaries change upon Nanoemulsion conveyance to patients.

Types of nanoemulsion systems

Nanoemulsions, are basically categorized into O/W emulsions and W/O emulsions.[9]

Water in oil (W/O)

Water in oil nanoemulsion (W/O) is a class of emulsion that has nano-sized water drops scattered in natural media through the activity of surfactants.[10] Planning of some random sort of emulsion should consider hydrophile-lipophile balance (HLB). HLB is a semi-observational scale that guides formulators to choose surfactants.[11] It shows the proportion of the hydrophilic segment of the non-ionic surfactant to the lipophilic bit[12], to yield the 'best emulsion' and, not go through flocculation or blend.[13] Above all, surfactants of a last HLB worth of 4–6 are ideal for planning of W/O nanoemulsions. W/O nanoemulsions are modernly valuable in miniature reactors to control nanoparticles development[14], for example, CdS nanoparticles[15] and titania–silica nanoparticles.[16] Artistic nanoparticles[17] are delivered utilizing different W/O emulsions as the response media. In the drug field, W/O emulsions are significant as adjuvants for antibodies with strange antigens, for example manufactured peptides, recombinant proteins or DNA.[18]

Oil-in-water (O/W)

Oil-in-water, or water-based, nanoemulsions are contained little lipid drops scattered inside a watery stage, with ordinary mean bead breadth of <200 nm.[19] While nanoemulsions and traditional O/W emulsions are thermodynamically shaky frameworks, the homogenisation strategy utilized in their creation directs their drop sizes.[20] As indicated by Winsor, there are four sorts of emulsion stages existing in balance, alluded to as Winsor stages. An O/W type is delegated Winsor[21], a two stage framework whereby the upper oil layer exists in harmony

with the lower (O/W) emulsion stage.[22] The schematic outline of W/O and O/W nanoemulsions comprising of surfactant micelles.

Components of nanoemulsion

Main three components of Nanoemulsions are as follows.[23,24]

1. Oil
2. Surfactant/Cosurfactant
3. Aqueous phase

Oils can be of any sort like castor oil, corn oil, coconut oil, evening primrose oil, linseed oil, mineral oil, olive oil, nut oil, and so forth A combination of oil and water may yield a rough transitory emulsion, which after standing, will isolate in two unmistakable stages because of the blend of the scattered globules. Emulgents or emulsifying specialists can give steadiness to such frameworks. Emulgents are extensively named surfactants like ranges and tweens, hydrophilic colloids like acacia and finely partitioned solids, e.g., bentonite and veegum. An emulgent, notwithstanding its emulsifying properties, ought to be nontoxic and its taste, smell and substance solidness ought to be viable with the item.

A portion of the alluring properties of an emulgent are: (1) it ought to have the option to decrease the surface pressure to under 10 dynes/cm, (2) it ought to be adsorbed quickly around scattered stage globule to shape a total and rational film to forestall blend, (3) it should help in developing a satisfactory zeta potential and consistency in the framework to bestow ideal security, and (4) it ought to be viable in a genuinely low fixation. Emulgents structure monomolecular, multimolecular or particulate movies around the scattered globules.[25]

Monomolecular films

Surfactant kind of emulgents settles a nanoemulsion by shaping a monolayer of adsorbed atoms or particles at the interface diminishing interfacial strain. In advanced practice, blend of emulgents is liked over single emulgent. The blend comprises of a transcendently hydrophilic emulgent in the watery stage and a hydrophobic specialist in the slick stage to frame a mind boggling film at the interface.

Multimolecular films

Hydrated lyophilic colloids structure multimolecular films around globules of scattered oil. Hydrated colloids don't cause any calculable bringing down of surface pressure and their capacity to shape solid, sound multimolecular films. Their inclination to expand the thickness of the ceaseless stage upgrades the steadiness of emulsion.

Strong particulate films

The emulgents framing particulate movies are little strong particles that are wetted somewhat by both watery and non-fluid stages. They are amassed at the interface where they produce a film around the scattered globules in this way forestalling blend.

Formulation aspects and method of preparation of nanoemulsion

Definition of nanoemulsion incorporates dynamic medication, added substance and emulsifier. The different strategies for the planning of nanoemulsion incorporate two techniques: (a) high-energy emulsification and (b) low-energy emulsification. The high-energy emulsification strategy incorporates high-energy blending, ultrasonic emulsification, high-pressure homogenization, microfluidization, and film emulsification.[26,27] The low-energy emulsification technique incorporates stage reversal temperature, emulsion reversal point, and unconstrained emulsification.[28] Utilizing a consolidated strategy, which incorporates the high-energy and low-energy emulsification, it is feasible to plan invert nanoemulsion in a profoundly gooey framework.

Ultrasonic emulsification

Ultrasonic emulsification is exceptionally effective in decreasing drop size. In ultrasonic emulsification, the energy is given through sonotrodes called as sonicator test. It contains piezoelectric quartz gem which can extend and contract in light of exchanging electric voltage. As the tip of sonicator contacts the fluid, it produces mechanical vibration and cavitation happens. Cavitation is the development and breakdown of fume pits in fluid. Hence, ultrasound can be straightforwardly used to create emulsion; it is basically utilized in research centers where emulsion bead size really low acquired.[29]

High-pressure homogenization

The arrangement of nanoemulsion requires high-pressure homogenization. This method utilizes high-pressure homogenizer/cylinder homogenizer to deliver nanoemulsion of amazingly low molecule size (up to 1 nm).[30]

Microfluidization

Microfluidization is a licensed blending innovation, which utilizes a gadget called microfluidizer. This gadget utilizes high pressing factor which powers the medication item through the association chamber bringing about an exceptionally fine molecule of submicron range. The interaction is rehashed a few times to acquire an ideal molecule size to deliver uniform nanoemulsion.[31]

Phase inversion temperature

This strategy includes change in stage by applying a higher temperature to a microemulsion.[32]

Spontaneous emulsification

It includes three stages: (a) planning of homogeneous natural arrangement comprising of oil and lipophilic surfactant in water miscible dissolvable and hydrophilic surfactant, (b) the natural stage is infused in fluid stage under persistent attractive blending, o/w emulsion is framed, and (c) the watery stage is eliminated by dissipation under decreased pressing factor.[33]

Factors to be considered during preparation of nanoemulsion[20]

1. Surfactant should be chosen cautiously with the end goal that an ultralow interfacial pressure might be accomplished which is an essential necessity to create nanoemulsion.
2. Convergence of surfactant should be sufficiently high to settle the microdroplets to create nanoemulsion.
3. The surfactant should be adaptable or liquid enough to advance the development of nanoemulsion.

Characterization of nanoemulsion

A steady nanoemulsion is described by the shortfall of the inside stage, nonattendance of creaming, nonappearance of crumbling by microorganisms, and support of polish in regard of appearance, shading, smell and consistency.[25] Henceforth the precariousness of emulsion can be named follows.

Flocculation and creaming

Flocculation comprises of the association of globules to shape enormous clusters or floccules, which rise or get comfortable the emulsion more quickly than the individual globules. The

ascending or settling down of scattered globules to give a concentrated layer is known as creaming. Along these lines flocculation prompts creaming.

Cracking

Cracking of an emulsion alludes to partition of the scattered stage as a layer. While a creamed emulsion might be reconstituted by shaking or unsettling, a cracked emulsion can't be adjusted. Breaking addresses lasting precariousness. Breaking of the emulsion might be because of: (1) expansion of an emulgent of inverse nature, (2) deterioration or precipitation of emulgent, (3) expansion of a typical dissolvable in which both slick and watery stages are miscible, (4) limits of temperature, (5) microorganisms, (6) creaming.

Miscellaneous instability

Emulsions may decay whenever put away under very high or low temperature or within the sight of light. Thus emulsions are normally stuffed in impenetrable, shaded holders and put away at moderate temperature.

Phase inversion

It is the adjustment of the sort of emulsion from o/w to w/o and the other way around. It is the actual interaction. Stage reversal might be achieved by fluctuating the stage volume proportion, expansion of electrolytes, and temperature changes.

Evaluation parameters of nanoemulsion

Droplet size analysis

Droplet size examination of nanoemulsion is estimated by a dispersion technique utilizing a light-dissipating, molecule size-analyzer counter, LS 230. It is likewise estimated by relationship spectroscopy that breaks down the variance in dispersing of light because of Brownian movement. Bead size investigation of nanoemulsion can likewise be performed by transmission electron microscopy (TEM).[6,34]

Viscosity determination

The viscosity of nanoemulsion is estimated by utilizing Brookfield-type rotational viscometer at various shear rates at various temperatures.

Dilution test

Dilution of a nanoemulsion either with oil or with water can uncover this sort. The test depends on the way that a greater amount of the consistent stage can be added into a

nanoemulsion without causing the issue of its steadiness. In this manner, an o/w nanoemulsion can be weakened with water and a w/o nanoemulsion can be weakened with oil.

Drug content

Preweighed nanoemulsion is removed by dissolving in a reasonable dissolvable, extricate is broke down by spectrophotometer or HPLC against standard arrangement of medication.[35]

Polydispersity

It demonstrates the consistency of drop size in nanoemulsion. The higher the worth of polydispersity, lower will be consistency of bead size of nanoemulsion. It tends to be characterized as the proportion of standard deviation to mean drop size. It is estimated by a spectrophotometer.

Dye test

In the event that a water-dissolvable color is included an o/w nanoemulsion the nanoemulsion takes up the shading consistently. Alternately, if the emulsion is w/o type and the color being solvent in water, the emulsion takes up the shading just in the scattered stage and the emulsion isn't consistently hued. This can be uncovered quickly by tiny assessment of the emulsion.

Refractive index

Refractive index of nanoemulsion is estimated by Abbes refractometer.

pH

The pH of nanoemulsion can be estimated by pH meter.

Zeta potential

Zeta potential is estimated by an instrument known as Zeta PALS. It is utilized to gauge the charge on the outside of bead in nanoemulsion.[36]

Fluorescence test

Numerous oils display fluorescence when presented to UV light. At the point when a w/o nanoemulsion is presented to a fluorescence light under a magnifying lens, the whole field fluoresces. In the event that the fluorescence is inconsistent, the nanoemulsion of o/w type.

Percentage transmittance

Percentage transmittance of nanoemulsion is estimated by an UV-apparent spectrophotometer.

Conductance measurement

The conductance of nanoemulsion is estimated by a conductometer. In this test a couple of anodes associated with a light and an electric source is plunged into an emulsion. On the off chance that the emulsion is o/w type, water directs the ebb and flow and light gets lit because of entry of momentum between the anodes. The light doesn't sparkle when the emulsion is w/o: oil being in outer stage doesn't direct the current.

Filter paper test

This test depends on the way that an o/w nanoemulsion will fan out quickly when dropped onto filter paper. Conversely, a w/o nanoemulsion will relocate just gradually. This strategy ought not be utilized for exceptionally thick creams.[25]

Applications of Nanoemulsions

1. Parenteral Delivery: Nanoemulsion are benefits for intravenous organization, because of the exacting prerequisite of this course of organization, especially the need for the plan bead size lower than 1 micrometer. Parenteral (or Injectable) organization of nanoemulsion is utilized for an assortment of purposes, to be specific sustenance eg. Fats, Carbohydrates, Vitamins and so on.[37,38]

Nanoemulsions of characteristic oils (soyabean, sesame and olive) with the nonpoisonous surfactant Pluronic F-68 by means of ultrasound for parentral feeding. Lipid nanoemulsion has been generally investigated for parentral conveyance of medications. Nanoemulsion details have unmistakable benefits over macroemulsion frameworks when conveyed parenterally as a result of the fine molecule Nanoemulsion is cleared more gradually than the coarse molecule emulsion and, hence, have a more extended home time in the body. Both O/W and W/O Nanoemulsion can be utilized for parenteral conveyance.[39]

2. Oral Delivery: Nanoemulsion plans offer the few advantages over traditional oral definition for oral organization including expanded retention, improved clinical strength and diminished medication poisonousness. Accordingly, Nanoemulsion have been accounted for to be ideal conveyance of medications like steroids, chemicals, diuretic and anti-toxins. Drug

medications of peptides and proteins are profoundly strong and explicit in their physiological capacities.[40]

Primaquine when fused into oral lipid nanoemulsion showed compelling antimalarial action against Plasmodium bergheii contamination in mice at a 25% lower portion level when contrasted with traditional oral dose.Lipid nanoemulsion of primaquine improved oral bioavailability by the liver with drug fixation higher at any rate by 45% as contrasted and the plain medication.[41]

3. Topical Delivery: Topical organization of medications can have benefits over different techniques for a few reasons, one of which is the evasion of hepatic first pass digestion of the medication and related harmfulness impacts. Another is the immediate conveyance and targetability of the medication to influenced space of the skin or eyes. The nanoemulsion can accomplish a degree of effective antimicrobial movement that has just been recently accomplished by foundational anti-microbials. The nanoemulsion has expansive range action against microbes (for example E. coli, S. aureus) parasites (for example Candida, Dermatophytes).[42]

4. Ocular Delivery: For the treatment of eye illnesses, drugs are basically conveyed topically. O/W Nanoemulsions have been researched for visual organization, to break up ineffectively solvent medications, to build retention and to achieve draw out discharge profile.[43]

5. In Cosmetic: The stylish properties, for example low consistency and straightforward visual parts of nanoemulsion with bead sizes beneath 200nm, its high surface territory permitting successful vehicle of the dynamic fixing to the skin make them particularly alluring for their application in beautifying agents.[44] Nanoemulsions are satisfactory in makeup on the grounds that there is no characteristic creaming, sedimentation, flocculation or combination that are seen with full scale emulsion. The joining of conceivably aggravating surfactants can be kept away from by utilizing high energy hardware during assembling. Nanogel innovation to make miniemulsion from oil-in water concentrate fit to limiting transepidermal water misfortune, improved skin insurance and infiltration of dynamic fixing. It would be valuable for sun care items, moisturing and antiageing creams. It assists with giving healthy skin definitions a decent skin feels.[45]

6. Transdermal: Indomethacin a powerful NSAID, the calming impacts of genuine improved nanoemulsion detailing were contrasted and showcased gel in carragenan actuated paw edema in rodents. The %inhibition esteem was huge for created Nanoemulsion, so extraordinary potential for transdermal utilization of indomethacin. Nanoemulsions for transdermal conveyance of celecoxib. Plan which comprised of 2% celecoxib 10% oil stage (Sefsol 218 and Triacetin) half surfactant combination (Tween 80 and Transcutol – P) and 40% water.

The calming impact and percentrestraint esteem after 24h organization was discovered to be high for nanoemulsion definition (81.2%) when contrasted with celecoxib gel (43.7%) and nanoemulsion gel (64.5%). The in vitro-in vivo examines uncovered a huge expansion in the counterfiery impacts of aceclofenac nanoemulsion(82.2%) when contrasted with nanoemulsion geldetailing (71.4%) and traditional gel (41.8%).[46,47]

7. In Biotechnology: Many enzymatic and biocatalytic responses are led in unadulterated natural or water natural media. Biphasic media are likewise utilized for these kinds of responses. The utilization of unadulterated apolar media causes the denaturation of biocatalysts. The utilization of water-confirmation media is generally worthwhile.[48]

Catalysts in low water content show and have.

1. Increased solvency in non-polar reactants.
2. Possibility of moving thermodynamic equilibria for buildups.
3. Improvement of warm security of the compounds, empowering responses to be done at higher temperatures.[49,50]

CONCLUSION

Nanoemulsions are broadly utilized in drug frameworks. Nanoemulsion definition offers a few benefits like conveyance of medications, natural or symptomatic specialists. The main use of nanoemulsion is for covering the obnoxious taste of slick fluids. Nanoemulsion may likewise ensure the medications, which are defenseless to hydrolysis and oxidation. These days, nanoemulsions are utilized for focused medication conveyance of different anticancer medications, photograph sensitizers or helpful specialists. Nanoemulsion can likewise give delayed activity of the medicaments. Generally all nanoemulsion detailing might be considered as successful, safe and with expanded bioavailability. It is normal that further innovative work will be completed later on in regards to nanoemulsion.

REFERENCES

1. Royer M, Prado M, García-Pérez ME, Diouf PN, Stevanovic TJP. Study of nutraceutical, nutricosmetics and cosmeceutical potentials of polyphenolic bark extracts from Canadian forest species, 2013; 1(4): 158-67.
2. Katz LM, Dewan K, Bronaugh RLJF, Toxicology C. Nanotechnology in cosmetics, 2015; 85: 127-37.
3. Singh R, Lillard Jr JWJE, pathology m. Nanoparticle-based targeted drug delivery, 2009; 86(3): 215-23.
4. Tadros T, Izquierdo P, Esquena J, Solans CJAic, science i. Formation and stability of nano-emulsions, 2004; 108: 303-18.
5. Mason TG, Wilking JN, Meleson K, Chang CB, Graves SMJJoPcm. Nanoemulsions: formation, structure, and physical properties, 2006; 18(41): R635.
6. Bouchemal K, Briançon S, Perrier E, Fessi HJIjop. Nano-emulsion formulation using spontaneous emulsification: solvent, oil and surfactant optimisation, 2004; 280(1-2): 241-51.
7. Wagner JG, Gerard ES, Kaiser DGJCP, Therapeutics. The effect of the dosage form on serum levels of indoxole, 1966; 7(5): 610-9.
8. Kim C-K, Cho Y-J, Gao Z-GJJocr. Preparation and evaluation of biphenyl dimethyl dicarboxylate microemulsions for oral delivery, 2001; 70(1-2): 149-55.
9. Costa R, Santos LJPt. Delivery systems for cosmetics-From manufacturing to the skin of natural antioxidants, 2017; 322: 402-16.
10. Peng L-C, Liu C-H, Kwan C-C, Huang K-FJC, Physicochemical SA, Aspects E. Optimization of water-in-oil nanoemulsions by mixed surfactants, 2010; 370(1-3): 136-42.
11. Kubitschek-KM ARJ, Zero JMJLAJP. Development of jojoba oil (Simmondsia chinensis (Link) CK Schneid.) based nanoemulsions, 2014; 33(3): 459-63.
12. Gursoy RN, Benita SJB, pharmacotherapy. Self-emulsifying drug delivery systems (SEDDS) for improved oral delivery of lipophilic drugs, 2004; 58(3): 173-82.
13. Americas I. The HLB system: a time-saving guide to emulsifier selection: ICI Americas, Incorporated, 1984.
14. Uskoković V, Drofenik MJSR, Letters. Synthesis of materials within reverse micelles, 2005; 12(02): 239-77.

15. Tata M, Banerjee S, John VT, Waguespack Y, McPherson GLJC, Physicochemical SA, et al. Fluorescence quenching of CdS nanocrystallites in AOT water-in-oil microemulsions, 1997; 127(1-3): 39-46.
16. Liu M, Gan L, Pang Y, Xu Z, Hao Z, Chen LJC, et al. Synthesis of titania–silica aerogel-like microspheres by a water-in-oil emulsion method via ambient pressure drying and their photocatalytic properties, 2008; 317(1-3): 490-5.
17. Porras M, Martínez A, Solans C, González C, Gutiérrez JMJC, Physicochemical SA, et al. Ceramic particles obtained using W/O nano-emulsions as reaction media, 2005; 270: 189-94.
18. Aucouturier J, Dupuis L, Deville S, Ascarateil S, Ganne VJErov. Montanide ISA 720 and 51: a new generation of water in oil emulsions as adjuvants for human vaccines, 2002; 1(1): 111-8.
19. McClements DJJSm. Nanoemulsions versus microemulsions: terminology, differences, and similarities, 2012; 8(6): 1719-29.
20. Solans C, Izquierdo P, Nolla J, Azemar N, Garcia-Celma MJJCoic, science i. Nano-emulsions, 2005; 10(3-4): 102-10.
21. Winsor P. Hydrotropy, solubilisation and related emulsification processes. Trans Faraday Soc, 1948; 44: 376–398.
22. Kale SN, Deore SL. Emulsion micro emulsion and nano emulsion: a review. Syst Rev Pharm, 2016; 8: 39–47.
23. Gasco MR, Gallarate M, Pattarino F. In vitro permeation of azelaic acid from viscosized microemulsions. *Int J Pharm*, 1991; 69: 193–196. doi: 10.1016/0378-5173(91)90361.
24. Trotta M. Influence of phase transformation on indomethacin release from microemulsions. *J Control Release*, 1999; 60: 399–405. doi: 10.1016/S0168-3659(99)00094-2.
25. Sharma SN, Jain NK (1985) A text book of professional pharmacy. Vallabh Prakashan, 1st edn, p 201.
26. Tiwari SB, Amiji MM (2006) Nanoemulsion formulations for tumor-targeted delivery. Nanotech Cancer Therapy. Taylor and Francis Group Editors, pp 723–739.
27. Banker GS, Lieberman HA, Rieger MM. Pharmaceutical dosage forms. *Disperse Syst Marcel Dekker*, 2002; 2(3): 339–340.
28. Ahuja A, Ali J, Baboota S, Faisal MS, Shakeell F, Shafiq S. Stability evaluation of Celecoxib nanoemulsion containing Tween 80. *Thai J Pharm Sci*, 2008; 32: 4–9.

29. Asua JM. Miniemulsion polymerization. *Prog Polym Sci*, 2002; 27: 1283–1346. doi: 10.1016/S0079-6700(02)00010-2.
30. Anton N, Benoit JP, Saulnier P. Design and production of nanoparticles formulated from nano-emulsion templates-a review. *J Control Release*, 2008; 128: 185–199. doi: 10.1016/j.jconrel.2008.02.007.
31. El-Aasser MS, Lack CD, Vanderhoff JW, Fowkes FM. Miniemulsification process-different form of spontaneous emulsification. *Coll Surf*, 1986; 29: 103–118. doi: 10.1016/0166-6622(88)80174-4.
32. Pouton CW. Formulation of selfemulsifying drug delivery systems. *Adv Drug Deliv Rev*, 1997; 25: 47–58. doi: 10.1016/S0169-409X(96)00490-5.
33. Tadros T, Izquierdo P, Esquena J, Solans C. Formation and stability of nano-emulsions. *Adv Coll Interface Sci*, 2004; 108: 303–318. doi:10.1016/j.cis.2003.10.023.
34. Alka AJA, Baboota S, Shakeel F, Shafiq S. Design development and evaluation of novel nanoemulsion formulations for transdermal potential of Celecoxib. *Acta Pharm*, 2007; 57: 315–317.
35. Chen H, Du D, Mao CMD, Wan J, Xu H, Yang X. Hydrogel-thickened nanoemulsion system for topical delivery of lipophilic drugs. *Int J Pharm*, 2008; 353: 272.
36. Erol Y, Hans-Hubert B. Design of a phytosphingosine-containing, positively-charged nanoemulsion as a colloidal carrier system for dermal application of ceramides. *Eur J Pharm Biopharm*, 2005; 60: 93.
37. Hussan R: Nanoemulsion as a Novel Transdermal Drug Delivery System. International Journal of Pharmaceutical Sciences and Research, 2011; 2(8): 1938-1946.
38. Simonnet *et al*.: Nanoemulsion based on ethoxylated fatty ethers or on ethoxylated fatty esters and its uses in the cosmetics, dermatological and/or ophthalmological fields, 2002.
39. Hadgraft J: Skin, the final frontier. Int. J. Pharm, 2001; 224: 1–18.
40. Fang J Y, Yu S Y, Wu P C, Huang Y B, Tsai Y H: *In-vitro* skin permeation of estradiol from various proniosome formulations. Int. J. Pharm, 2001; 215: 91–99.
41. Kumar M, Mishra A, Pathak K et.al: Intranasal nanoemulsion based brain targeting drug delivery system of resperidone Int J Pharm, 2008; 358: 285-291.
42. Ruktanonchai U, Sakulku U, Nuchuchua o, et.al: Characterization and mosquito repellent activity of citronella oil nanoemulsion Int. J Pharm, 2009; 112: 256-282.
43. Tajima K, Imai Y, Ujiie N et.al.: Three phase structure of hexadecane nanoemulsion formed with Phospholipid-surfactant mixtures and its novel Phase transition temperature TE colloids and surfaces. Pharm. Res, 2006; 276: 134-142.

44. Basphinar Y, Keck M.C, Borchert H.H: Development of a positively charged prednicarbate nanoemulsion Int. J. Pharm, 2010; 383: 201-208.
45. Junyaprasert B.V, Muller H.R, Souto B.E *et al*.: Q10 loaded NLC versus nanoemulsions; stability, rheology and in vitro skin permeation. Int. J Pharm, 2009; 377: 207-214.
46. Constantinides P.P, Chaubal V.M, Shorr R, Advances in Lipid nanodispersions for parental drug delivery and targeting. Adv. Drug Del. Rev, 2008; 60: 757-767.
47. Vyas T.K, Amiji M.M, Shahiwala A: Improved oral bioavailability and brain transport of saquinavir upon administration in novel nanoemulsion formulations Int. J. Pharm, 2008; 347: 93-101.
48. Leong T.S.H, Kentish S.E, Wooster T.J, et.al.: Minimizing oil droplet size using ultrasonic emulsification Ultra Sonochem, 2009; 16: 721-727.
49. Aubrun O.S, Simonnet J.T, Alloret F.L: Nanoemulsions: a new for skincare products Ad. Collo. Inter Sci, 2004; 108-109: 145-149.
50. Nicolosi J.R, Kuo F, Kotyla T, *et al*.: Nanoemulsion of an anti-oxidant synergy formulation containing gamma tocopherol have enhanced bioavailability and anti-inflammatory properties. Int J. Pharm, 2008; 363: 206-213.