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Microemulsion a Novel Approach for cardiovascular Drug Delivery

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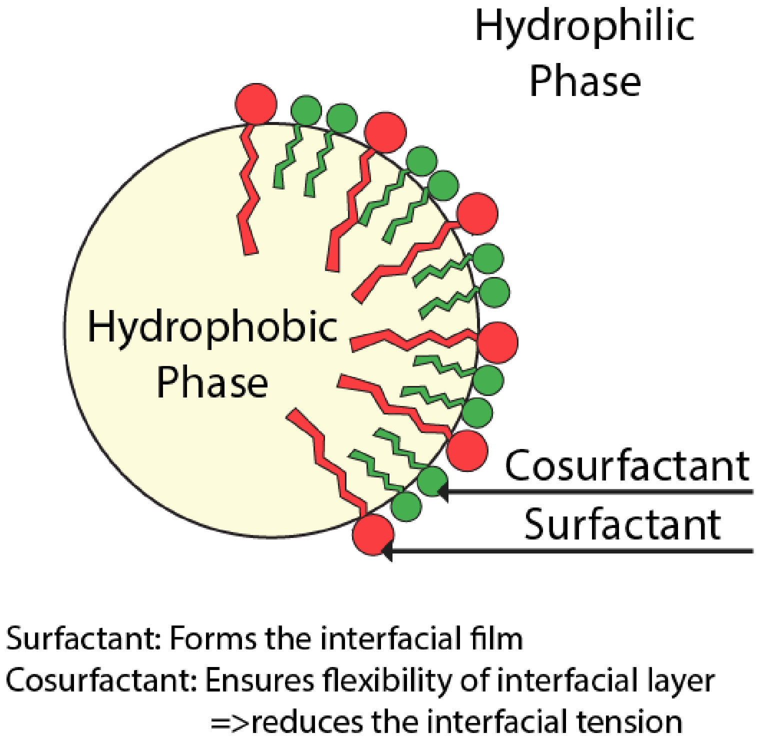
ABSTRACT: The time period "microemulsion" refers to a thermodynamically stable isotropically clear dispersion of two immiscible liquids, such as oil and water, stabilized by way of an interfacial film of surfactant molecule. Now a day Microemulsion is an rising alternate and having global significance in a variety of technological applications. These applications include more advantageous oil recovery, combustion, cosmetics, pharmaceuticals, agriculture, metal cutting, lubrication, food, enzymatic catalysis, organic and bio-organic reactions, chemical synthesis of nanoparticles etc. This evaluation article deals with feature and application of microemulsion. a quick introduction and definition, structure, type, formation characteristics, stability, section behavior and the effect of additives, pressure, temperature on the phase behavior of microemulsion.

I. INTRODUCTION

Micro emulsion is Dispersion made of water, oil, and surfactant(s) that is anisotropic and thermodynamically steady device with dispersed domain diameter various approximately from 1 to a hundred nm, usually 10 to 50 nm.[1]Micro emulsions are clear, thermodynamically stable, isotropic liquid combos of oil, water and surfactant, frequently in mixture with a co surfactant. The aqueous segment may additionally contain salt(s) and/or different ingredients, and the "oil" may additionally honestly be a complex mixture of distinct hydrocarbons and olefins.[2] The term of micro emulsion applies to a combination with at least three components; an oily phase, an aqueous segment and a surface active species, so known as surfactants. Sometimes the forth thing i.e., co-surfactant can/must be present. Depending on the ratios between the components, in the two extremes the microstructure of the micro emulsions differ from a very tiny water droplets dispersed in oil section (w/o micro emulsion) to a oil droplets dispersed in water section (o/w micro emulsion). The microstructure of the mixture changes continuously from one to every other extreme, namely, from a spherical to cylindrical, tubular and interconnected continuous oil and water phases separated with a very skinny layer of surfactant molecules, in the middle, which is described as discontinues micro emulsion. The micro emulsions of every variety are thermodynamically stable and transparent solutions. There are important variations between emulsions and micro emulsions in phrases of structure and stability. In distinction to the micro emulsions, the emulsions are unstable systems and except agitation, phase separation will manifest in them. The different distinction is that the size of droplets in emulsions are in the range of micrometers, while in micro emulsions the size of micelles are in the range of 5-100 nm, depending on the some parameters such as surfactant type and concentration, the extent of dispersed . Hence, on occasion the micro emulsion term is misleading, due to the fact it doesn’t mirror the measurement of dispersed segment droplets in the device which, are in the nanometer range. Depending on the kind of the surfactants employed in the coaching of the micro emulsion, some other vital parameter that influences the most important traits of a micro emulsion is the presence of electrolytes in the aqueous phase.[2]

Structure of Micro Emulsion

Small scale emulsions or Micellar emulsion are energetic system in which the interface is persistently and spontaneously fluctuating.[29] Structurally, they are isolated in to oil in water (o/w), water in oil (w/o) and bi-continuous micro emulsions. In w/o smaller scale emulsions, water beads are dispersed within the ceaseless oil stage whereas o/w micro emulsions are shaped when oil beads are scattered in the nonstop watery stage. In framework where the amounts of water and oil are comparative, the bi-continuous micro emulsions may result.[30] The blend oil water and surfactants are able to make a wide assortment of structure and stage depending upon the extents of component



Advantages of Microemulsion Based Systems [3]

Microemulsions exhibits several advantages as a drug delivery system:

1. Microemulsions square measure thermodynamically stable system and also the stability permits self-emulsification of the system.
2. Microemulsions act as supersolvents for drug. they will solubilize each deliquescent and lipotropic medicine together with medicine that square measure comparatively insoluble in each binary compound and hydrophobic solvents.
3. The dispersed particles, lipotropic or deliquescent (oilin-water, O/W, or water-in-oil, W/O microemulsions) will act as a possible reservoir of lipotropic or deliquescent medicine, severally. Drug unharness with pseudo-zero-order dynamics are often obtained, counting on the quantity of the dispersed particles, the partition of the drug and also the transport rate of the drug.
4. The mean diameter of droplets in microemulsion is below zero.22 mm. the tiny size of driblet in microemulsions e.g. below a hundred nm, yields terribly giant surface space, from that the drug is free quickly into external section once absorption (in vitro or in vivo) takes place, maintaining the concentration within the external section on the brink of initial levels.
5. Same microemulsions have the flexibility to hold each oleophilic and hydrophilic medicine.
6. as a result of physics stability of microemulsions, they're straightforward to organize and need no important energy contribution throughout preparation. Microemulsions have low consistency compared to primary and multiple emulsions.
7. the employment of microemulsion as delivery systems will improve the efficaciousness of a drug, permitting the entire dose to be reduced and so minimizing aspect effects.
8. The formation of microemulsion is reversible. they'll become unstable at low or warm temperature however once the temperature returns to the soundness vary, the microemulsion reforms

Disadvantages of Microemulsion Based Systems [4]

1. Use of an oversized concentration of wetting agent and cosurfactant is critical for helpful the droplets of microemulsion.
2. restricted solubilizing capability for high-melting substances utilized in the system.
3. The wetting agent ought to be nontoxic to be used in pharmaceutical applications.
4. Microemulsion stability is influenced by environmental parameters like temperature and pH. These parameters amendment as microemulsion delivered to patients.

Characteristics

If a chemical agent possessing balanced deliquescent and oleophilic properties is employed within the right concentration, a distinct oil and water system are going to be created. The system remains Associate in Nursing emulsion, however exhibits some characteristics that square measure completely different from the whitish emulsions mentioned earlier. These new systems square measure “micro emulsions”. The interfacial surface tension between phases, quantity of energy needed for formation, drop sizes, and visual look square measure solely many of the variations seen once scrutiny emulsions to small emulsions. Water-in-oil small emulsions also are referred to as reverse micelles. These systems have the flexibility to solubilise each deliquescent and hydrophobic substances. small emulsions typically exhibit low viscosities and Newtonian flow characteristics. Their flow remains constant once subjected to a spread of shear rates.

Discontinuous formulations might show some non-Newtonian flow and plasticity. small emulsion consistence is near to that of water, even at high drop concentrations. The microstructure perpetually changes, creating them very dynamic systems with reversible drop coalescency. a range of techniques ar used to characterize completely different properties of small emulsions. lightweight scattering, X-ray diffraction, centrifugation, electrical conduction, and consistence measurements are wide used.

TYPES OF MICROEMULSIONS [15-18]

Microemulsions ar thermodynamically stable, however ar solely found below carefully outlined conditions. in line with Winsor, there ar four sorts of microemulsion phases exists in equilibria, these phases also are referred as Winsor phases. They are,

1. Oil- in- water microemulsion or winsor I
2. Water – in oil microemulsion or winsor II
3. Bicontinuousmicroemulsion or winsor III
4. Single phase homogeneous mixture or winsor IV

Oil- in- water microemulsion or winsor I

In Oil-in-water form of microemulsions droplets of oil is encircled by a wetter (and is also cosurfactant) film that forms the inner part distributed in water, that is that the continuous part. this kind of microemulsion typically incorporates a larger interaction volume than the w/o microemulsions.

Water - in - oil microemulsion or winsor II

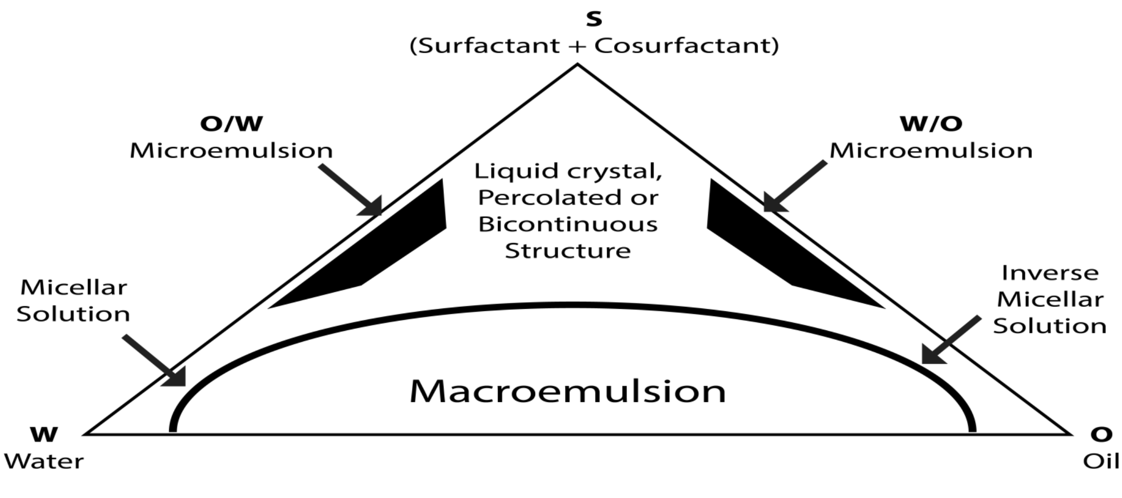
In Water-in-oil sort of microemulsions droplets of water encircled by an eternal oil section. These area unit recognized as “reversemicelles”, wherever the polar headgroups of the wetting agent face into the droplets of water, with the carboxylic acid tails facing into the oil section. A w/o microemulsion used orally or parenterally is also destabilized by the binary compound biological system

Bicontinuousmicroemulsion or winsor III.

In bicontinuousmicroemulsion system the quantity of water and oil present ar similar, during this case, each water and oil exist as an eternal part. associate degree irregular channel of oil and water ar combined, and appears sort of a “sponge-phase”. Transitions from o/w to w/o microemulsions could undergo this bicontinuous state. Bicontinuous microemulsion, could show non-Newtonian flow and physical property. These properties build them particularly helpful for topical delivery of medication or for blood vessel administration

HYPOTHETICAL PHASE DIAGRAM[69]

Figure 4: Hypothetical Phase region of Microemulsion system



It is clear from the above figure that •

If the concentration of oil is high then reverse misclles square measure formed by the surface-active agent which might solubilize relatively large no. of water molecules in their deliquescent interior. • If during this system water is extra continuously then, it should cause the formation of w/o microemulsions within which the water exists as droplets encircled and stable by the surface layer of the surfactant/ co-surfactant mixture. • The isotropic clear region changes into a bifringent, cloudy one at a restricted water content. • The liquid crystalline region with water sandwiched between the surface-active agent double layers is also formed, on more dilution with water. • Finally, this lamellar structure can break down and therefore the water can kind a continous section containing the droplets of oil stable by a surfactant/co-surfactant (o/w microemulsion), because the quantity of water is accumulated.

METHOD OF FORMULATION [24, 25]

Microemulsions square measure ready once surface tension at the oil/water is unbroken at terribly low level. surface layer is unbroken greatly versatile and fluid concentration of wetting agents ought to be high enough to convey surfactant molecules to be stabilised the microemulsion at a very low surface tension.

Two main method are reported for the formulation of microemulsion, these are

1. Phase Inversion Method
2. Phase Titration Method

Phase Inversion Method [26]

In the section inversion technique section inversion of microemulsions happens by addition of excess quantity of the phase. throughout section inversion fast physical changes occur as well as changes in particle size that may have an effect on drug unharness each in vivo and in vitro. For non-ionic surfactants, this will be completed by dynamical the temperature, forcing a transition from oil in water microemulsion at low temperatures to water in oil microemulsion at higher temperatures (transitional section inversion). throughout cooling, the system crosses some extent of zero spontaneous curvature and smallest physical phenomenon, promoting the formation of finely distributed oil droplets. This technique is additionally referred to as section inversion temperature (PIT) technique. apart from temperature, different parameters like hydrogen ion concentration price or salt concentration could also be thought-about additional effectively rather than the temperature alone.

. in addition, a transition within the spontaneous radius of curvature will be obtained by dynamic the water volume fraction. By in turn adding water into oil, at the start water droplets square measure fashioned in an exceedingly continuous oil section. By increasing the water volume fraction changes the spontaneous curvature of the wetter from at the start helpful a w/o microemulsion to associate degree o/w microemulsion at the inversion purpose

Phase Titration Method [27]

Microemulsions area unit developed by the spontaneous emulsification methodology (phase volumetric analysis method) and might be shown with the assistance of part diagrams. a mix of carboxylic acid and oil is adscititious to a caustic resolution to arrange a microemulsion, then once it's titrated with a cosurfactant, an alcohol, till the system turned clear. Microemulsions area unit shaped in conjunction with varied association structures (including emulsion, micelles, lamellar, hexagonal, cubic, and varied gels and oily dispersion) looking on the chemical composition and concentration of every element. it's found that because the chain length of the chemical agent raised, microemulsions with important transmittances by spectrum is shaped with oils of longer chain lengths. it's conjointly found that totally different alcohols have an effect on the formation of microemulsions in numerous ways that. the most effective results, in terms of the best % transmission let alone the widest vary of oil (dispersed in water) concentration, area unit obtained from short or branched alcohols.

INGREDIENTS OF MICROEMULSION [18-20]

Various ingredients area unit utilized in the formulation and development of microemulsions. primarily oil and surfactants area unit utilized in microemulsion they must be biocompatible, non-toxic and clinically acceptable. Main parts of microemulsion area unit

1. Oil phase
2. Aqueous phase
3. Surfactant
4. cosolvent

Oil phase [21]

Oil is one in all the most necessary elements of microemulsion as a result of it will solubilise the desired dose of the lipophilic drug and it will increase the fraction of lipophilic drug transported via the enteral lymphatic system. Oil is outlined as any liquid having low polarity and low miscibility with water. The samples of such section area unit cyclohexane, oil, toulene, etc.

Aqueous phase

Generally the binary compound section contains hydrophilic active ingredients and preservatives. typically Buffer solutions area unit used as binary compound section.

Surfactant [22]

The term wetter (surface-active-agent) denotes a substance that exhibits some superficial or surface activity lower the surface or interface tension. it's affinity for polar solvents. Surfactants square measure the molecules that contain a polar head cluster and a polar tail. wetter molecules self-associate thanks to numerous inter- and intra-molecular forces furthermore as entropy concerns. for instance, once wetter is mixed with oil and water, they accumulate at the oil/water interface, as a result of it's thermodynamically favorable. The wetter molecules will organize themselves during a type of shapes. they'll kind spherical micelles, a polygon section, lamellar (sheet) phases, rodshaped micelles, reverse micelles, or polygon reverse micelles. At low concentrations of spread (internal) section, spherical, isolated droplets square measure gift within the microemulsions. the varied forms of surfactants that facilitate within the progressive development of microemulsion system square measure

1. Cationic
2. Anionic
3. Non-ionic
4. Zwitterionic surfactants.

Cationic surfactant

Cationic Surfactants once are available in contact with water they are available into amphiphiliccation and ion kind, most frequently of group sort. a really great quantity of this category corresponds to element compounds like quaternary ammoniums and fatty paraffin salts, with one or many long chain of the alkyl radical sort, typically returning from natural fatty acids. the foremost well-known examples from the cationic wetter category ar hexadecyl trimethylammonium bromide and didodcecyl ammonium ion bromide. These surfactants ar generally costlier than anionics.

Anionic surfactant

When associate degreeionic Surfactants ar unconnected in water in an amphiphilic ion, and a ion, that is normally associate degree metallic element (Na, K) or a quaternary ammonia. These ar the foremost normally used surfactants. The anionic charge in these surfactants comes from the ionised chemical group. Anionic surfactants account for about fifty you look after the world production. Alkalialkanoates, additionally called soaps, ar the foremost common anionic surfactants. this can be the foremost well-known sort of wetter once it involves their form and performance. The 3 most vital anionic teams altogether of those surfactants ar treat, salt and salt teams.

Non-ionic surfactant

Non-ionic surface-active agent is stabilised by dipole and bond interactions with the association layer of water on its hydrophilic surface. they are doing not ionize in solution, as a result of their deliquescent cluster is of non-dissociable sort, like phenol, alcohol, ester, or amide. an outsized proportion of those nonionic surfactants ar created hydrophilic by the presence of a synthetic resin glycol chain.

Zwitterionic chemical agent Zwitterionic surfactants contain each positively and charged teams and kind microemulsions by addition of co-surfactants. Phospholipids, like phospholipid, obtained naturally from soybean or egg square measure common zwitterionic surfactants. unlike different ionic surfactants, that square measure somewhat noxious, lecithin that contains diacyl phosphatidylcholine because the major constituent show excellent biocompatibility. different vital category of zwitterionic surfactants is that the betaines, like alkylbetaines, and heterocyclic betaines .

Cosolvent [23]

It has been discovered that single-chain surfactants ar unable to scale back the o/w surface tension sufficiently to create a microemulsion. The addition of co-surfactants permits the surface film to be versatile to require up totally different curvatures needed to create microemulsion over a good vary of excipients. If one wetter film is desired, the lipotropic chains of the wetter ought to be sufficiently short, or contain fluidizing teams (e.g. unsaturated bonds). Basic co-surfactants ar short chain alcohols (ethanol to butanol), glycols like humectant, medium chain alcohols, amines or acids. the utilization of co-surfactant is to destroy liquid crystalline or gel structures that are available place of a microemulsion part

FACTOR AFFECTING FORMULATION OF MICROEMULSION SYSTEM [31-33]

Property of surfactant

Surfactant contains 2 cluster oleophilic and hydrophilic teams. hydrophilic single chain surfactants like cetylethyl ammonia bromide dissociate fully in dilute answer and have a bent to create o/w microemulsion. once the wetter is in presence of salt or once high concentration of wetter is employed, degree of dissociation of polar teams becomes lesser and ensuing system could also be w/o sort.

Property of Oil Phase

Oil part additionally influence curvature by its ability to penetrate & Swell the tail cluster region of the chemical agent monolayer, swelling of tail results into an raised negative curvature to w/o microemulsion.

Packing Ratio [34]

HLB of chemical agent determines the kind of microemulsion through its influence on packing and film curvature. The analysis of film curvature for chemical agent association`s resulting in the formation of microemulsion.

Temperature [35]

. Temperature is very necessary in decisive the effective head cluster size of nonionic surfactants. At coldness, they're hydrophilic and kind traditional o/w system. At higher temperature, they're oleophilic and kind w/o systems. At an intermediate temperature, microemulsion coexists with excess water and oil phases and forms bicontinuous structure.

II. EVALUATION OF THE MICRO-EMULSIONS

Visual Inspection

By the visual inspection we are able to check the properties like fluidity, homo-genicity and optical clarity.

Percent Transmittance Test (Limpidity Test)

The percent transmission take a look at of the micro emulsion may be measured spectrophotometrically using spectrophotometer. 32

Measurements of Droplet Size

Size examination of micro-emulsion may be obtained by Dynamic-Light-Scattering experiments or microscopy. The polydispersity may be done by the similar Instrument. 33, 34

Zeta-Potential Dimensions and Globule-Size

Zeta-Potential and Globule-Size of the micro-emulsion will be resolute by Dynamic-Light-Scattering, via a ZETASIZERHAS3000. 35

Examination Under cross-polarizing Microscope

The nonappearance of fringence on the way to eliminate LiquidCrystalline-Systems, the micro-emulsion should be examined below cross polarizing microscope. 36-37

Constancy studies (Stability studies)

Physical stability of the micro-emulsion ought to be resolute to a lower place altogether completely different storing surroundings (four, twenty 5 and forty °C) throughout twelve months. Recent preparations equally by suggests that of these that are reserved to a lower place many strain things supposed for prolonged amount of your time were imperiled to drop Dimensions Delivery Examination. Conclusion of surface-active-agent& their attention on size of drop is additionally to be calculated. 38

pH of the Micro-emulsion

Different samples of the micro-emulsions area unit taken within the sample tubes. Then a small pH-meter is used to see the Ph-scale of the assorted samples. Since the pH-scale of the preparation is that the difficulty upon that the micro-emulsion Bioavailability and also the constancy of the drug over micro-emulsion by the permeation spot depends upon. 39-41

Scattering Methods

The Scattering strategies is like very little angle of nucleon scattering, very little angle of X-Ray-Scattering and Light-Scattering have produce submissions in revisions of micro-emulsion assembly, considerably simply just in case of diluted mono-disperse spheres, once poly-disperse or targeted systems like as those typically seen in micro-emulsions. 42

Transmittance Examination

Constancy of the adjusted micro-emulsion preparation with relevance dilution was check by measure transmission at a selected wavelength with a immoderate Violet photometer.43

In-Vitro drug release

The diffusion study is usually disbursed on a modified FranzDiffusion cell, among capability of 20mL. The Receptor section was occupied with of Buffer. The donor section was secure with wrap membrane, holding the micro-emulsion preparation and additionally the fundamental drug resolution, distinctly. At planned time intermission trials were reserved from the receptor section and examined for drug content, using a immoderate Violet photometer at definite wavelength. 44, 45

Theory of microemulsion formulation:

Microemulsion formation and stability may be explained on the premise of a simplified natural philosophy rationalization. The free energy of microemulsion formation may be thought of to rely on the extent to that wetting agent lowers the physical phenomenon of the oil–water interface and therefore the amendment in entropy of the system such thirty four,

$DG\ f = \gamma DA - T\ DS$

Where, DG f =free energy of formation, γ = Surface tension of the oil–water interface, DA =Change in interfacial area on microemulsification, DS = Change in entropy of the system which is effectively the dispersion entropy, and T = Temperature.
It should be noted that once a microemulsion is created, the modification in DA is extremely large thanks to the big range of nanodroplets area unit formed. it's seen that whereas the worth of γ is positive in any respect times, it's very tiny (of the order of fractions of mN/m), and is offset by the entropic element. The dominant favorable entropic contribution is that the terribly giant dispersion entropy arising from the blending of 1 introduce the opposite within the variety of giant numbers of nanodroplets. However, favorable entropic contributions additionally arise from different dynamic processes like surface-active agent diffusion within the surface layer and monomer-micelle surface-active agent exchange.
Thus, a negative free energy of formation is achieved once massive reductions in physical phenomenon area unit accompanied by important favorable entropic modification. In such cases, microemulsification is spontaneous and therefore the ensuing dispersion is thermodynamically stable
Though, it's been understand that many factors verify whether or not a w/o or o/w microemulsion system are shaped however generally it can be summarized that the most possible microemulsion would be that during which the section with the smaller volume fraction forms.
Application of Microemulsion
The application of micro-emulsion is given as follows
- Oral delivery system
- Parental delivery system
- Ophthalmic delivery system
- micro-emulsion in detergency
- micro-emulsion in cosmetics
- micro-emulsion in food

III. CONCLUSION

Microemulsions are having a vast and significant potential in drug delivery as well as in the industrial process. Researchers are working in this field for drug release, coatings, dyes, agrochemicals and in enzyme reaction. In the future prospects, microemulsions will be used in synthesis of nanoparticles and as a industrial chemical sensors. The role of microemulsion in providing novel solutions to overcome the problems of poor aqueous solubility of highly lipophilic drug compounds and provide high, more consistent and reproducible bioavailability. Furthermore, these formulations can be easily manufactured in term of the relative cost of commercial production. Topical products are now employing the microemulsion technology are likely to emerge.Microemulsions can also be used to achieve drug however challenges remain, primarily because of the layers of barriers that these systems need to overcome to reach to the target. Recent research work is focused on the production of safe, efficient and more compatible microemulsion constituents which will further enhance the utility of these novel vehicles. Microemulsion in today's world can be accepted as full of potential in a novel drug delivery systems.

REFERENCE

[1]. B Prince, Leon M, Micro emulsions in Theory and Practice, Academic Press, New York, 1197.
[2]. Henri L, Clausse, Marc, Micro emulsion Systems, Marcel Dekker, 1987, 6.
[3]. Ghosh, P.K., Murthy, R.S.R: Microemulsions: A Potential Drug Delivery System, C. Drug. Del., 2006, 3; 167-180
[4]. Vyas, S.P., Khar, R.K: Submicron emulsions in targeted and controlled drug delivery, Novel Carrier Systems; CBS Publishers and Distributors, New Delhi, 2002; 282 – 302
[5]. Kumar. K. Senthil, Dhachinamoorthi. D, Saravanan. R; Microemulsions as Carrier for Novel Drug Delivery: A Review; International Journal of Pharmaceutical Sciences Review and Research, 2011; 10: 37-45.
[6]. Patel R. Mrunali, Microemulsions: As Novel Drug Delivery Vehicle, 2007; 5.
[7]. Madhav. S, Gupta. D, A review on microemulsion based system, IJPSR, 2011; 2(8): 1888-1899
[8]. Maqsood A.M,Mohammad Y.W,Microemulsion method: A novel route to synthesize organic and inorganic nanomaterials,Arebian Journal of chemistry, 5(4), 2012, 397417
[9]. Kunieda H. et al. The Journal of Physical Chemistry 1988; 92: 185.
[10]. Mukherjee K. et al. Journal of Colloid and Interface Science 1997; 187: 327.
[11]. Aboofazeli R and Lawrence M.J. Investigations into the formation and characterization of phospholipid microemulsions. I. Pseudoternary phase diagrams of systems containing water- lecithin-alcohol-isopropyl myristate. International Journal of Pharmaceutics 1993; 93: 161-175.

[12]. JhaSajal Kumar et al. Microemulsions- Potential Carrier for Improved Drug Delivery. Internationale Pharmaceutica Sciencia 2011; 1(2): 25-31.
[13]. Shaji. J, Reddy M. S.; Microemulsions as drug delivery systems; Pharma Times., 2004; 36(7): 17–24
[14]. Shaji J. and Reddy M.S. Microemulsions as drug delivery systems. Pharma Times 2004; 36 (7): 17 – 24.
[15]. Kayes F.B. Disperse systems In Pharmaceutics: The Science of Dosage Form Design. International Student Edition Ed: Aulton. M.E.; Churchill Livingstone 1999; p110.
[16]. JhaSajal Kumar et al. Microemulsions- Potential Carrier for Improved Drug Delivery. Internationale Pharmaceutica Sciencia 2011; 1(2): 25-31.
[17]. Vyas S P. Theory and practice in novel drug delivery system. CBS Publishers New delhi. 2009; p115.
[18]. Prince L. M. A theory of aqueous emulsions I. Negative interfacial tension at the oil/water interface. Journal of Colloid and Interface Science 1976; 23: 165173.
[19]. Constantinides PP. Water-in-oil microemulsions containing medium-chain fatty acids/salts: formulation and intestinal absorption enhancement evaluation. Pharmaceutical Research. (1996) 13(2); 205-105.
[20]. JhaSK, Dey S, Karki R. Microemulsions- Potential Carrier for Improved Drug Delivery, Asian Journal of Biomedical and Pharmaceutical Sciences. (2011) 1(1); 5-9.
[21]. Patel P,Monpara MA, Mandal SN, Patel N, Rajesh KS. Formulation and Evaluation of Microemulsion Based Gel of Itraconazole. Pharmagene. (2009) 1(2); 32-36.
[22]. Brime B. Amphotericin B in oil-water lecithin-based microemulsions: formulation and toxicity evaluation. Journal Pharmaceutical Sciences. (2002) 91(4); 1178–85.
[23]. Malcolmson C, Lawrence M. Three-component non-ionic oil-in-water microemulsions using polyoxyethylene ether surfactants, Colloids Surf, B Biointerfaces. (1995)4; 97– 109
[24]. Constantinides PP, Scalart JP, Lancaster C, Marcello J, Marks GH. Formulation and intestinal absorption enhancement evaluation of water-in-oil microemulsions incorporating medium-chain glycerides. Pharm Res. (1994) 11; 1385–90.
[25]. Patel MR, Patel RB, Parikh JR, Solanki AB, Patel BG. Effect of formulation components on the in-vitro permeation of the Microemulsion of drug delievery system of Fluconazole. AAPS Pharm. Sci. Tech. (2009) 10; 917-923.
[26]. Bajpai M, Sharma PK, Mittal A. A study of oleic acid oily base for the tropical delivery of dexamethasone microemulsion formulation. Asian J Pharm. (2009) 3; 208214.
[27]. Nour SA, Shalaby SH, Afify NN, Abd EAS, Mekhael MK. Formulation and evaluation of econazole nitrate emulgels. Journal Drug Res Egypt. (2002) 24(1); 63-71.
[28]. Lucero MJ, Vigo J, Leon MJ. A study of shear and compression deformations on hydrophilic gels of tretinoin. Int J Pharm. (1994) 106; 125–33.
[29]. Constantinides PP. et al. Formulation and intestinal absorption enhancement evaluation of water-in-oil
[30]. Lam AC, Schechter R S, The theory of diffusion in micro emulsions, J Colloid Interface Sci., 120, 1987, 56-63.
[31]. Hellweg T, Phase structure of micro emulsions, Curr opin colloid interface sci., 7, 2002, 50-56.

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