International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 4 July-Aug 2022, pp: 934-945 www.ijprajournal.com ISSN: 2456-4494

Microemulsion –A Multidimensional Formulation

Ashish Srivastava[1]*, Dr Vijay Singh [2], Dr Naresh Kalra[3]
1,2 &3- Lords college of pharmacy, Lords university, Chikani, Alwar Rajasthan-301028 India

Submitted: 15-07-2022 Accepted: 30-07-2022

ABSTRACT
The trend of developing new formulation for drug delivery is growing worldwide due to introduction of new drugs as well as to solve problems of existing drugs. However, the formulation for lipophilic drugs needs much concern due to low aqueous solubility and bioavailability issues in oral route . Microemulsion plays an important role in drug delivery due to its ability to reduce interfacial tension between oil and water to a large extent as well its high solubilization ability. This paper reviews the structure of microemulsion and their components like oil, surfactant, cosurfactant and water. HLB value was considered for the selection criteria of surfactant that is the essential component of microemulsion. The method os preparation as well as characterization parameters were also discussed This review also discussed the multiple importance of micromulsion. The microemulsion formulation can be used for the different route of drug administration like parenetaral, oral etc.. This paper also described the application of microemulsion in cosmetic as well as washing applications.

Keywords- Microemulsion, Interfacial tension, HLB, Solubilization934

I. INTRODUCTION

In the newly developed drugs, 40-50% drugs are water insoluble in nature due to which oral bioavailability is dependent upon dissolution rate and due to different dissolution rate they show variable absorption. Besides this rapid metabolism, unsteady drug level in plasma, and interindividual variability through oral route is also observed [1]. The inherent water solubility of drug can be improved by various ways like reduction in particle size as well as by salt formation to enhance the bioavailability. However all drug molecules can not follow this because salt formation is not possible in neutral drug molecules and the efficacy of the drug in salt form is also poor due to conversion into acid or base in physiological acidic or basic system as per Handerson Hasselbalch equation. The second approach milling or Particle size reduction is also associated with poor wet ability and low stability of fine powders. So it is better to formulate lipid soluble drugs into lipid formulations to overcome the above mentioned problems. The lipid based formulations like liposomes, solid lipid nanoparticles (SLNs), self-dispersing tablets, and microemulsions are getting more focus by formulation scientists due to their advantageous like their bioavailability, stability,ease of preparation, and scale-up. [2,3].
Microemulsion is isotropic, homogeneous, optically transparent (or translucent), thermodynamically stable, low viscous dispersions of oil and water stabilized by a surfactant, generally in association with a cosurfactant. The microemulsion globule size diameter exist in the range of 10-100 nm. The oil and water when mixed try to separate due to their opposite polarity and to avoid this, surfactant molecules are added . Surfactant molecules are amphiphilic molecule containing both polar as well as nonpolar group. So they come to the interface of oil and water , where they show dual affinity with hydrophilic groups attached to water phase and hydrophobic groups to oil .[4-5] The microemulsion systems, can be developed over a vast range of surfactant concentration as well different oil to water ratio. The microemulsion as drug delivery vehicle represent favorable properties like long shelf-life, easy preperation (spontaneous formation due to ultra low interfacial tension).It can also be sterilized by filtration process and due to very fine globule size and high surface area having high solubilization capacity. The small globules also provide better adherence to membranes of absorption site and release drug molecules in a controlled fashion [6-9].

Components of Microemulsion System
1-Oil/lipid phase
2. Aqueous phase
3. Surfactant
4. Co surfactant
the components of microemulsion should be non-toxic, biocompatible and clinically acceptable. The

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 4 July-Aug 2022, pp: 934-945 www.ijprajournal.com ISSN: 2456-4494

component should be under "generally regarded as safe"(GRAS)[10] category.

1. **Lipid (Oils).** Oils are the first and most important component of microemulsion, because the absorption of drug depends upon their solubility in oil and solubility of drug depends upon the variety and concentration of oil used for formulation. The oils may be digestive lipids like fatty acids, phospholipids, cholesterol tri and diglycerides [11],or it may be synthetic origin because they offer better bioavailability of the drug opposite to the indigestible lipids. The bioavailability may be poor in indigestible lpids because drug remains in undigested fraction of lipid in git. The other category of oils, natural edible oils are better in bioavailability but they are not able to solubilize high dose of lipophilic drugs [12].It was proved that the mixture of lipids (fatty acids) of mono, di or triglyceride in similar ratio generated higher microemulsion zone [13]. Some Oils have enhanced the bioavailability of hydrophobic drugs by initiation of lymphatic transport of drugs through oral route[14-15].

2. **Surfactants.** The primary use of surfactant is to lower the interfacial tension to the very small value during the preparation of the microemulsion, to provide a flexible film that can readily deform around the droplets and to provide the correct curvature at the interfacial region. Surfactants may be non-ionic, zwitterionic, cationic, anionic types. In the formation of microemulsion the surfactant may be ionic or non-ionic, depending upon the interaction ability of the hydrophilic portion of the surfactant with the water phase. Non-ionic surfactant works by dipole and hydrogen bond interactions with the water, but in ionic surfactant electrical double layer works additionally to stabilize the layer. So the salt concentration have more profound effect in the case of ionic surfactant than non-ionic surfactants. However toxicological concerns of ionic surfactants are high so are not preferred for pharmaceutical applications, [16-17]. The low toxicity produced by nonionic surfactants like polysorbates, polyoxyls and oleates, are generally considered to be acceptable for oral ingestion in the formulation of microemulsion [18] The toxicity of natural surfactants are less, but the emulsification efficiency is also limited [19] because surfactants must achieve very low interfacial tension as well as spontaneous emulsification in microemulsion formation[20]. HLB value is the selection criteria for surfactant. If the surfactants HLB value is (>10) then it will form O/W microemulsion [21]. Those surfactants which have HLB value (> 12) and at high concentration, should be mixed with cosurfactants to generate very fine droplets (<100 nm) for nonpolar drugs[22]. For stable microemulsion the surfactant concentration range is about 30–60%. The surfactant concentration should be minimized as possible as because it causes GI irritation, tissue damage [23] as well as low emulsification ability due to the generation of liquid crystalline phase [24]. Although surfactant concentration has indirect relationship with droplet size because it stabilizes oil droplets up to certain limits by its adsorption at oil/water interface. If the surfactant concentration becomes high above the limit , disruption of water oil interface occurs by entry of water into oil droplets [25]

3. **Co-surfactants** are added during microemulsion formation because generally surfactants alone are inefficient to reduce the o/w interfacial tension upto ultralow level required for microemulsion formation. The addition of cosurfactant provides flexibility to the oil water interface resulting free movement of the hydrophobic part of surfactant at interface which gives flexibility or dynamic behavior of microemulsion. Commonly used courfactants are short to medium chain length alcohols (C3- C8) like ethanol, n propanol,n-butanol, propylene glycol, polyethylene glycol and amines or acids [26-28]. Surfactant and cosurfactant are selected on the basis of their efficiency, irritancy, change in efficiency during repeated administration, their interaction potential with body proteins and lipids [29]. The co-surfactant also maintains the fluidity by destroying liquid crystalline or gel structures during formation of microemulsion phase [30]

Method of preparation[31-32]
1.-Phase Titration Method- also called as spontaneous emulsification method In this method, the oils, surfactants, co-surfactants and water are mixed in fixed weight ratios. All these mixtures will be stirred at room temperature for some time and kept for standing , than after the visual inspection, monophasic/biphasic system will be confirmed. Turbidity appears in biphasic system and the monophasic system appears as clear and transparent mixtures. The result of monophasic and biphasic phase are marked in phase diagram and due to four component system, pseudo ternary phase diagram is prepared in which different zones

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 4 July-Aug 2022, pp: 934-945 www.ijprajournal.com ISSN: 2456-4494

and O/W , W/O and bicontinous microemulsion zones are shown figure-1 .

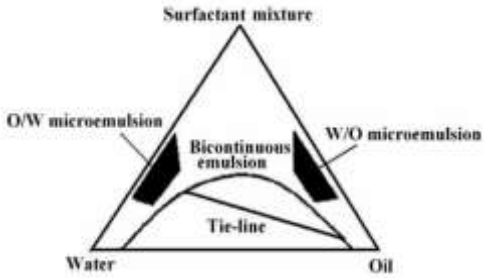

Figure-1 phase diagram showing microemulsion zones

2. Phase inversion method- can be used to prepare microemulsion in which phases (internal and external) are inverted by generally on addition of excess of the dispersed phase or in response to temperature. In the process, physical changes may also occur, like changes in particle size, viscosity, conductivity etc. For non-ionic surfactants system it can be facilitated by temperature change in this an o/w microemulsion exist at low temperature but changes to w/o microemulsion at higher temperature. This is called as transitional phase inversion method. Apart from temperature, salt concentration and pH value can also do the phase inversion. Figure-2

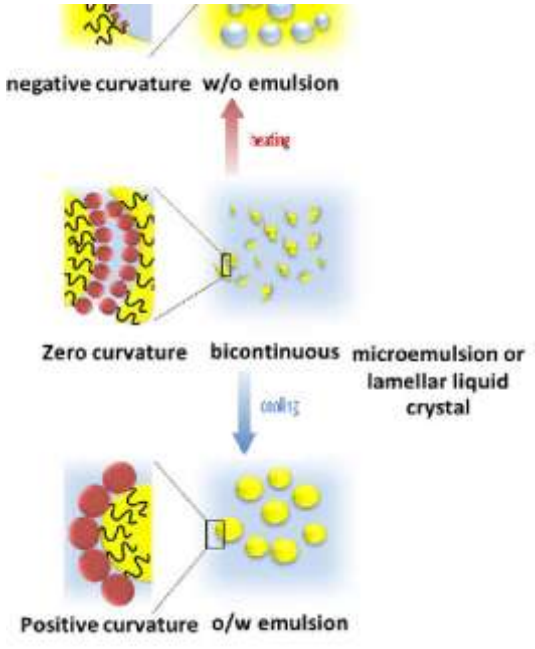

Figure-2 phase inversion method

Importance of microemulsion

(i) Generally the solid drug come into the contact of GIT wall and causes Irritation which can be removed by the microemulsion because drug remains in solubilized state and distribute easily into whole GIT and the drugs are transferred quickly from the stomach [33].

(ii) Fine sized globules of microemulsion, gives very high interfacial area which facilitates in the partitioning of the drug very easily from oil medium to the aqueous medium resulting better drug release which cannot be obtained in case of simple oily formulations of lipophilic drugs[10].

(iii) Microemulsions are better thermodynamic stable than emulsions because of the ease of manufacturing process as well as low energy and time requirement in comparison to emulsion. Only Simple mixing equipment and no critical steps are required to formulate microemulsion [34-35].

(iv) The absorption of water insoluble drugs (lipophilic drugs) due to variable dissolution rate can be efficiently improved by the formulation of microemulsion which results in stable Plasma drug concentration-time profile [3]. This was due to dissolved state of the water insoluble drug in microemulsion that bypass the most important step of drug absorption i.e. dissolution of solid drug [36].

(v)Literature studies shows that nonionic surfactants like Tweens, Spans, Cremophors, and Pluronics bind and also inhibit the action of efflux transporters like P-glycoprotein [37]present on git membrane. The drugs bioavailability becomes low when the drugs are substrates to the efflux transporters but bioavailability can be improved by using the microemulsion formulation with above given surfactants [38-40]. Tween 80 improved the bioavailability of drug paclitaxel by inhibiting efflux transporter [41].

(vi)In GIT certain Drugs which are unstable due to the chemical and enzymatic reactions can be protected by the microemulsion as the drug remains in oil droplets [42].

(ix) Surfactants used in microemulsion formulation improve the permeability of the drug by loosening of n tight junctions [43].

Characterization of microemulsion

1. Visual inspection. The evaluation of microemulsion is possible by visual assessment. The systems should show homogeneity, optical clarity and fluidity After dilution of continuous phase it must maintain the transparency till certain limit and the formulation stability is confirmed

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 4 July-Aug 2022, pp: 934-945 www.ijprajournal.com ISSN: 2456-4494

when there is no drug precipitation. Precipitation is common due to use of water soluble cosurfactants and can be minimized by using high concentration of surfactant [44].

2. Droplet Size Analysis. The globule shape and size of microemulsion is highly affected by the nature and amount of surfactant [12]. When microemulsion forms on dilution with water,it generates globules of very fine size and size distribution which is highly effective in drug release, stability as well as in vivo absorption. Spectroscopic techniques like Dynamic Light-Scattering (DLS) acronym (photon correlation spectroscopy) or, in the past, QELS (Quasielastic Light-Scattering) .and microscopic techniques can be applied for globule size analysis [31-32,45].In DLS techniques Zetasizer can be employed for globule size analysis [46]. The polydispersity index (PDI) should be determination to get appropriate information regarding size distribution.The PDI value should be low because it describes the similar and narrow size distribution [47].

3. Zeta Potential determination :-to evaluate the stability of any emulsion zeta potential value can be used. The instrument zeta potential analyzer or zetameter is generally used for measurement [48-49]. Zeta potential value is directly related to stability so higher zeta potential means the better stability of formulation [49]. Zeta potential value may be negative or positive due to the presence of free fatty acids [32] or cationic lipid respectively [3]. The positively charge globules have better interaction ability with the membrane of the GIT and due to these strong electrostatic interactions, enhanced absorption can be expected [10].

4. Cloud Point Determination. Cloud point is the temperature value above that transparency of microemulsion decreases and the system becomes cloudy. It is determined by increasing the temperature of formulation gradually using water bath as a heating medium and transparency is measured by UV vis spectrophotometer. Cloud point is affected by drug lipophilicity as well as other formulation variables [33, 50]. At higher temperature, microemulsion can observe phase separation and low drug solubility due to the dehydration of surfactant [50].

5. Viscosity Measurements. Viscosity of microemulsion is determined to evaluate the Newtonian behavior of the system in which shear stress is directly related to shear rate and the Newtonian behavior shows small and spherical globules[51]. Viscosity can be measured by cone and plate rheometer and Brookfield viscometer [52]. Viscosity value changes during titration by water, initially W/O microemulsion, intermediate bicontinuous and final O/W microemulsion with the increase in water[53].

6. Refractive Index measurement. Isotropic nature of microemulsion can be visualised by refractive index measurement . If there is no significant difference in refractive index value of optimized formulation stored at 4^{o}C and 25^{o}C up to 6hrs at different time intervals then it indicates the same microemulsion structure [49]. Refractive index can be measured by Refractometers.[53]. Cosurfactant concentration and globule size can affect the refractive index value because refractive index value becomes less as cosurfactant concentration increases it may due to loss of the close structure of microemulsion and its value becomes high as the size of globule increases[55].

7. Percentage Transmittance. This test evaluates the transparency of microemulsion. It is determined spectrophotometrically at visible wavelength after dilution with water, using water as blank. Higher the value of percentage transmittance higher will be the clarity or transparency of formulation. The value close to 100% confirms the clear, homogenous and transparent microemulsion formation [56].

8. Transmission Electron Microscopy (TEM) Study. can be used to study the shape, structure or morphology of microemulsions [57]. It can also be used for determination of uniformity of the globule size [58]. In this combination of bright field images at high magnification and diffraction modes are used [59]. Staining of the samples are required before TEM study. The sample is stained with suitable staining agent like uranyl acetate then the sample was dried after placing on copper grid and then the globules were visualized for the size and shape of the globules. phosphotungstic acid solution as well as methylamine vanadate are also used for the staining purpose. [46].

9. Differential Scanning Colorimetry. can be applied for the characterization of microemulsions by using water peaks. The peaks become different during free or bound state of water [52].The pure

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 4 July-Aug 2022, pp: 934-945 www.ijprajournal.com ISSN: 2456-4494

water act as reference material which gives large, sharp peak nearly at −17°C that is the freezing point. Podlogar et al. performed DSC experiments on IPM Tween 40/Imwitor 308 water microemulsion and found peaks of water at very low temperature (−45°C at 15%w/w) than the pure water , due to bound state of water with surfactants, and as you increase the water content, water becomes free and the peak comes a higher temperature . On seeing result of DSC, it was concluded that O/W microemulsion was formed with high concentration of water (>35%W/W) [60].

10. NMR Techniques. As you dilute the microemulsion W/O microemulsion becomes bicontinuous and and on further dilution bicontinuous becomes O/W type and it can be determined by self diffusion NMR studies. The microemulsion diffusive behavior can be determined by Fourier transforms pulsed gradient spin-echo (PGSE) method because self diffusion coefficient value of microemulsion components may be lower or in same magnitude to the pure components and if values are lower it shows the presence of globules either O/W or W/O and if value is similar to pure components then it shows bicontinuous structure of microemuslion. PGSE-NMR method is used for the study of transformations between microemulsion to bicontinuous phase or vice versa .The globule size of the microemulsion can also be determined by using 129xe NMR, it can be visualized by the shifting of signal from lower field to higher field as the size of the globules increases[61].

11. Neutron Scattering and Small Angle X-Ray Methods. The transitions in microemulsion structure, due to dilution can be determined by neutron scattering methods and it can also be used to evaluate the size and shape of the globules [32, 61]. Small angle Xray scattering studies can be used to study structure of microemulsion with respect to different amount of water. The structure may show periodic, lamellar and hexagonal structure at 10% w/w, 20% w/w and 40% w/w water concentration respectively. [62]

12. Thermodynamic Stability Study-.this study was used to evaluate the effect of temperature change on formulation stability. Firstly microemulsion is centrifuged either at 15,000 rpm for 15 min [56] or at 3500 rpm for 30min [57].if the phase separation is observed the it confirms the thermodynamic unstability and if the sample is able to withstand centrifugation cycle then microemulsion is subjected to freeze thaw cycles (−20°C and 40°C temperature, resp.) and observed visually. There will be no change in visual appearance in the thermodynamically stable microemulsion formulation[56, 57].

13.Stability Assessment. The ICH guidelines are used to perform stability studies of microemulsion formulation. The samples are collected at predefined time and tested for visual appearance, colour, phase separation, drug content and pH of formulation. If the properties remains same during different storage conditions, the formulation is stable in nature. [49, 56, 63, 64].

Applications of microemulsions

A. Pharmaceutical applications

Parenteral Delivery- the preparation of parenteral dosage form of lipophilic and hydrophilic drugs is quite difficult. Sparingly soluble drugs can be formulated in w/o microemulsions for parenteral delivery when the dosage form suspensions is not required. Microemulsion provide better physical stability of drug in plasma in comparison to liposomes or other lipid vehicle as well as it resist the leaching of drug from internal phase so it provides high concentration in plasma. The o/w microemulsions can also be used for several water insoluble drugs for parenteral delivery. Von Corsewant et.al used parenterally acceptable cosurfactants, poly ethylene glycol (400)/ poly ethanol glycol (600) in place of C3- C4 alcohols to maintain flexible surfactant film for the microemulsion formulation.[65]

Oral Delivery- In oral delivery systems poor solubility or instability of the drug in gastrointestinal system is main hurdle for absorption. Microemulsion can enhance the solubility of water insoluble drugs like BCS class II/class IV drugs) and due to solubilized state of drug in microemulsion it can obviate the dissolution related absorption problems. In microemulsion polar, non-polar and interfacial domains are present and drugs are generally in encapsulated form which protect the drugs aganist oxidation, enzymatic degradation etc and that enhances better drug absorption and membrane permeability. Following drugs are Commercially formulated in microemulsions like Cyclosporine A (Sandimmune Neoral®), Saquinavir (Fortovase®), Ritonavir (Norvir®)for oral delivery to enhance the oral bioavailability [66- 68].

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 4 July-Aug 2022, pp: 934-945 www.ijprajournal.com ISSN: 2456-4494

Topical Delivery- Topical administration have multiple advantages like direct drug delivery and targetting of the drug to the skin and eyes and avoid first-pass metabolism and gastrointestinal side effects of oral drug delivery. Microemulsion can incorporate both hydrophilic (5-fluroracil, , diphenhydramine hcl, tetracaine hydrochloride, methotrexate etc) as well as lipophilic drugs (meloxicam, finasteride, ketoprofen, oestradiol , felodipine,etc.) and enhance their permeation. In the preparation of microemulsion high surfactant concentration is required so selection of surfactant should be nonirritating, nontoxic and should be GRAS category [69].

Nasal drug Delivery- now the nasal route is becoming a preferred route for some drugs because of its rapid absorption through nasal mucosa. Mucoadhesive polymers present in microemulsion provides better adhesion to the nasal mucosa. Lianly et al. investigated the drug diazepam in microemulsion through nasal route for the emergency treatment of status epilepticus. The result showed very rapid absorption of diazepam at 2mg/kg dose reaching maximum drug plasma concentration within 2-3 min [70-71].

B. Cosmetic applications

Cleanser- for efficient cleanser formulations interfacial tension should be very low and microemulsion fulfill this requirement so microemulsion may be the good alternative for cleansing applications. Watanabe et al. developed the microemulsion system having the non-ionic surfactant polyoxyethylene glyceryl monoisostearate (PGMI), the silicone oil decamethyl cyclopentasiloxane (DC) and cosurfactanat ethanol for make-up cleanser applications [72].The formulation showed better cleansing effects than normal methods without any irritation and toxic effects. Due to daily environment effect the skin becomes dirty due to presence of dirt and skin secreted sebum and to remove dirt and sebum skin cleanser products are used. For the development of efficient formulations, the phase behaviour of microemulsions with artificial sebum must be studied with non-ionic and anionic surfactants, ester oil, salt and water. The presence of salt improve the cleansing ability of formulation. A mixture of a tri-block polypropylenoxide–polyethyleneoxide ether surfactant with a block copolymer of polybutadiene and polyethylenoxide improved the performance significantly on sebum[73]. The flow properties are also very important for topical cleanser product because it must be easily spreadable on the skin without running. Ayannidis et al. studied the flow properties of microemulsion based on span60, IPM, glycerol and water [74]. The flow behaviour can be adjusted by varying glycerol to water ratio. The increase in glycerol content decreases the viscosity [75]. So the resulting microemulsion flow performance is mostly better to non-microemulsion products. Aftershave gels are also formulated with Microemulsions due to its transparent nature and very good sensorical properties. A mixture of a cross-linking polymer with an o/w microemulsion can be used for that[76].

Bath oils - are scented oils that are added to the water for cleaning and relaxing atmosphere of a bath. Chemically, they have surfactants and oils, surfactants for good foaming as well as cleaning properties, and oil for refattening the skin. Miller et al. studied the phase behavior of bath oil microemulsion having non-ionic surfactants, oil, peg and water forming three-phase microemulsions with an upper oil and a lower water phase [77]. On shaking, it forms a macroemulsion which will again separate into three visible phases on standing. The three phase microemulsion are better and unique aesthetics properties than one-phase microemulsions for bath oils [78].

Sunscreen - Modern sunscreen formulations are used to protect skin from sunrays. It should be non-sticky, waterproof and easily spreadable. Generally milks or macroemulsions are available in the market. Carlotti et al. evaluated microemulsion-based sunscreen formulations due to its transparent aesthetics with good sensorial and water-repellant properties [79]. The microemulsion consisted of mixture of three different surfactants, cosolvents, oils, sunscreen actives and water. The most effective microemulsion with the lowest amount of surfactants was screened with the help of phase diagram like the combination of alkylbenzoate, lecithin, decylpolyglucose mixture with hexanediol and water[80]. High transparency and good stability was found in the prepared sunscreen products. A another surfactant like Polyglycol ester sulphates can also be used for the microemulsion-based sunscreens formulation [81]. For eye applications two-phase sunscreen microemulsions can be created [82]. The O/w microemulsions used for first layer made up of non-ionic surfactants and organic oils and second

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 4 July-Aug 2022, pp: 934-945 www.ijprajournal.com ISSN: 2456-4494

layer is formed by silicon oil added with sunscreen actives.

Permanent wave products- are products to produce curls or to modify existing curls. In cosmetic science, it is also known as curl reformation. Microemulsions based on non-ionic surfactants are better compatible to the skin than macroemulsions which are generally irritating. Holloran et.al prepared microemulsion product using silicone oils and cationic surfactants. This product showed better stability, high transparency and exhibited excellent performance on the compatibility of treated hair [83]. Hair conditioners can also be prepared from microemulsions, which maintain their transparency on dilution as well as they are highly freeze stable, [84].

Hair styling waxes- based on microemulsions, shows high viscosity, better spreadability, and visible Transparency[85]. These products can be prepared using oil upto 10% and non-ionic surfactants more than 30%. The resultant product showed a better styling product. Cross-linking polymers addition can reduce the required quantity of surfactants without altering much viscosity value[86].

Fragrances- The quality of a fragrance is related to the evaporation rate of a product and microemulsion becomes a attractive choice for perfumes due to its long term stability as well as aesthetics. Rybinski et al. prepared the microemulsion with 20% perfume oil, 20% emulsifier mixture of alkyl polyglycosides and glyceryl monooleate, an oil content of less than 1% (dicapryl ether and octyldodecanol) and water [87]. Fragrance compounds are also prone to autooxidation, so fragnance should be protected from autoxidation. Carlotti et al. analysed the stability of linalool, citral and limonene in three different formulations [88]. (A) a micellar solution of citral with decyl polyglucoside, (B) a micellar solution of citral with polyoxyethylene sorbitane monolaurate and (C) a microemulsion with citral, decyl polyglucoside, propyleneglycol and dodecanol. On evaluating all three formulations, microemulsion formulation was found significantly better against oxidation than other two formulations.

C. Washing applications

Detergents -The washing and cleaning of any surfaces is generally required due to adsorption of dirt or soil on that surfaces. It is very complex process influenced by various parameters [89, 90]. surfaces may be from fabrics to metal surfaces to ceramics. Therefore, the mechanism of the cleaning process may vary, although the basic effects are similar. Cleaning process is highly dependent on the surface properties of the substrates. Polarity, specific surface area, surface charge and porosity are Important surface properties. Besides the surface properties, interaction between the surface with the cleaning agent also affect the cleaning process. For example, surface that have a high concentration of bivalent cations like calcium etc. behave differently from surfaces that have low concentration of these ions. Due to which the different washing results were obtained for cotton (high adsorption) to the synthetic fibres (low adsorption). The dirt or soils may be very different either solid pigments or a liquid phase like oils or fats, pigments like carbon black or inorganic oxides, waxes or denatured proteins and certain dyes generally they occur in mixtures [91]). Microemulsions are highly efficient in removing oily dirt or soils due to their ultralow interfacial tension and their microstructure. The interfacial tension is one of the decisive parameters for cleaning process [92] and can be very different dependant on the surfactant structure and the type of the oily soil [93]. On adding some electrolytes like sodium triphosphate and sodium citrate works as builders and used in very small quantity in microemulsion, the dirt or Soil removal efficiency was increased by 20–25%. The microemulsions was found superior to the liquid detergent, because they don't lose cleaning effectiveness till used by seven times.[94]

Dry cleaning -for dry cleaning, degreasing and hard surface cleaning organic solvents are generally used but microemulsions may be the alternative for that because organic solvents residue and waste after washing is highly toxic for environment so biocompatible microemulsions was prepared by using biocompatible surfactant and linker molecule like lecithin as main surfactant and linker molecules (hexyl polyglucoside (hydrophilic linker) and sorbitan monooleate (lipophilic linker)[95]. Formulation parameters were evaluated using isopropylmyristate as the model oil. The alcohol-free microemulsion with linkers-achieved higher solubilisation capacity than similar systems available in the literature. The mixtures of anionic–cationic surfactant can also work

synergistically to form middle-phase alcohol free microemulsions [96,97].

Conclusion- Research into microemulsions shows that Microemulsion becoming a great pharmaceutical alternative formulations for the delivery of drugs either hydrophilic or hydrophobic having ingredients of varying physicochemical properties by different routes, but the mechanism is not fully clear. This review has provided information regarding the considerations of microemulsion in cosmetics because of its superiority over various different cosmetic products that are available in market but not fulfilling the requirement. The washing products are also considering the microemulsion as alternative due to multiple advantages and superior performance. Although progress is growing at slow rate because it requires proper understanding of the surfactants, preparation of microemulsion system etc. The surfactants are one of the essential ingredient for the preparation of all microemulsion systems, so there is requirement of a predictive selection process of surfactants for the development of microemulsion.

Acknowledgment
The authors wish to thank the Lords university, Rajasthan for providing technical as well as guidance support for completion of this work.

REFERENCES

[1]. Chakraborty S., Shukla D., Mishra B., and Singh S., Lipid— an emerging platform for oral delivery of drugs with poor bioavailability, European Journal of Pharmaceutics and Biopharmaceutics, vol. 73, no. 1, pp. 1–15, 2009
[2]. Lawrence J, Rees G. Microemulsion-based media as novel drug delivery systems. Adv Drug Deliv Rev 2000; 45:89-121.
[3]. Sharma, N., Jain, S.. Microemulsion: A Review. Asian Journal of Pharmaceutical Research and Development, (2013);1(2), 23-36.
[4]. Tartaro G, Mateos H, Schirone D, Angelico R, Palazzo G. Microemulsion Microstructure(s): A Tutorial Review. Nanomaterials (Basel). 2020 Aug 24;10(9):1657
[5]. Heuschkel S, Goebel A, Neubert RH. Microemulsion – modern colloidal carrier for dermal and transdermal drug delivery. J Pharm Sci 2008; 97:603-631.
[6]. Kang BK, Lee JS, Chon SK. Development of microemulsion drug delivery system for oral bioavailability enhancement of simvastatin in beagle dogs. Int J Pharm 2004; 274:65-73.
[7]. Patel D, Sawant KK. Oral bioavailability enhancement of acyclovir by self microemulsifying drug delivery systems. Drug Dev Ind Pharm 2007; 33:1318-1326.
[8]. Abbofazeli R, Lawrence MJ. Investigation into the formation and characterization of phospholipids ME II: pseudoternary phase diagram of system containing waterlecithin-isopropyl myristate and alcohol: influence of purity of lecithin. Int J Pham 1994; 106:51-61.
[9]. Sarkhejiya Naimish A, Nakum Mayur A, Patel Vipul P, Atara Samir A, Desai Thusarbindu R. Emerging trend of the microemulsion in formulation and research. Int Bull Drug Res 2010;1:54-83.
[10]. Jha Sajal Kumar, Dey Sanjay, Karki Roopa, Microemulsions- Potential Carrier for Improved Drug Delivery, Internationale Pharmaceutica Sciencia.,2011 1(2) 25-31.
[11]. Dahan A. andHoffman A., Rationalizing the selection of oral lipid based drug delivery systems by an in vitro dynamic lipolysismodel for improved oral bioavailability of poorly water soluble drugs, Journal of Controlled Release,2008; 129, 1,1–10.
[12]. Djekic L. and Primorac M., The influence of cosurfactants and oils on the formation of pharmaceutical microemulsions based on PEG-8 caprylic/capric glycerides, International Journal of Pharmaceutics, 2008;352, 1-2, 231–239..
[13]. Prajapati H. N., Dalrymple D. M., and Serajuddin A. T. M., A comparative evaluation of mono-, di- and triglyceride of medium chain fatty acids by lipid/surfactant/water phase diagram, solubility determination and dispersion testing for application in pharmaceutical dosage formdevelopment, Pharmaceutical Research, ; 29; 1;285–305, 2012.
[14]. V. Jannin, J. Musakhanian, and D. Marchaud, Approaches for the development of solid and semi-solid lipid-based formulations, Advanced Drug Delivery Reviews; 60; 6;734– 746, 2008.
[15]. R. Nankervis, S. S. Davis, N. H. Day, and P. N. Shaw, Effect of lipid vehicle on the

ntestinal lymphatic transport of isotretinoin in the rat, International Journal of Pharmaceutics; 119; 2;173–181, 1995.
[16]. Narang AS, Delmarre D and Gao D; Stable Drug Encapsulation in Micelles and Microemulsions; Int. J. Pharm., 345 (2007) 9– 25.
[17]. Strickley RG; Solubilizing Excipients in Oral and Injectable Formulations; Pharm. Res., 21 (2004) 201-230.
[18]. Hauss D. J., Oral lipid-based formulations, Advanced Drug Delivery Reviews; 59; 7;667–676, 2007.
[19]. Sourav De,a Susanta Malik,a Aniruddha Ghosh,a Rumpa Sahab and Bidyut Saha; A review on natural surfactants RSC Adv., 2015, 5, 65757–65767..
[20]. Lawrence MJ, Rees GD. Microemulsion-based media as novel drug delivery systems. Adv Drug Deliv Rev. 2000 Dec 6;45(1):89-121.
[21]. Kohli K., Chopra S., Dhar D., Arora S., and Khar R. K., Selfemulsifying drug delivery systems: an approach to enhance oral bioavailability, Drug Discovery Today;2010 15; 21-22;958–965.
[22]. Pouton C. W., "Lipid formulations for oral administration of drugs: non-emulsifying, self-emulsifying drug delivery systems,European Journal of Pharmaceutical Sciences; 2000, 11; 2;S93–S98.
[23]. Constantinides P. P., Lipid microemulsions for improving drug dissolution oral absorption: physical and biopharmaceutical aspects, Pharmaceutical Research; 1995,12; 11;1561– 1572.
[24]. Sarciaux J.M., Acar L., Sado P.A., Using microemulsion formulations for oral drug delivery of therapeutic peptides, International Journal of Pharmaceutics, 1995;120, 127-136.
[25]. Bagwe R. PKanicky ., J. R., Palla B. J., Patanjali P. K., and Shah D. O., "Improved drug delivery using microemulsions: rationale, recent progress, and new horizons," Critical Reviews in Therapeutic Drug Carrier Systems; 2001 18; 1;77–140.
[26]. Szumała, P. Structure of Microemulsion Formulated with Monoacylglycerols in the Presence of Polyols and Ethanol. J Surfact Deterg;2015; 18, 97–106.
[27]. Sarkhejiya Naimish A, Nakum Mayur A, Patel Vipul P, Atara Samir A, Desai Thusarbindu R; Emerging Trend Of Microemulsion In Formulation And Reserach; International Bulletin of Drug Research.,2013;1(1) 54-83.
[28]. Roux D and Coulon C; Modelling Interactions in Microemulsion Phases; J. Physique., 47 (1986) 1257- 1264.
[29]. Gershanik T. and Benita S., Self-dispersing lipid formulations for improving oral absorption of lipophilic drugs, European Journal of Pharmaceutics and Biopharmaceutics; 2000 50; 1;179–188.
[30]. Durmaz H, Mehmet ˙C Influence of hexylamine and alcohols as cosurfactants on microemulsion phase behavior and solubilization, Nanosystems: Physics, Chemistry, Mathematics, 2019, 10 (2) ; 176–183.
[31]. Mrunali R Patel B. Patel Rashmin, Parikh R Jolly, Bhatt K Kashyap,; Investigating the effect of vehicle on in vitro skin permeation of ketoconazole applied in O/W Microemulsions; Acta Pharmaceutica Sciencia., 2010; 52 ; 65-77.
[32]. Sushama Talegaonkar, Adnan Azeem, Farhan Ahmad J, Roop Khar K, Shadab Pathan A, Zeenat Khan I; Microemulsions:A Novel approach to enhanced drug delivery; Recent patents on drug delivery and formulation; 2008; 2,;238-257.
[33]. Tang J.-L., Sun J., and He Z.-G., "Self-emulsifying drug deliverysystems: strategy for improving oral delivery of poorly soluble drugs," Current DrugTherapy, 2007; 2, 1, 85–93.
[34]. Kogan Anna, Garti Nissim, Microemulsions as transdermal drug delivery vehicles, Advances in Colloid and Interface Science, 2006; 123–126;369-385.
[35]. Shannon P. Callender, Jessica A. Mathews, Katherine Kobernyk, Shawn D. Wettig, Microemulsion utility in pharmaceuticals: Implications for multi-drug delivery, International Journal of Pharmaceutics, 2017,526,1–2, 425-442.
[36]. Narang S., Delmarre D, and Gao D., "Stable drug encapsulation in micelles and microemulsions," International Journal of Pharmaceutics,2007; 345,1-2, 9–25.
[37]. Ke W.T., Lin S.-Y., Ho H.-O., and Sheu M.-T., "Physical characterizations of microemulsion systems using tocopheryl polyethylene glycol 1000 succinate (TPGS) as a surfactant for the oral delivery of

protein drugs," Journal of Controlled Release, 2005 102, 2, 489–507,.

[38]. Gohel M. C., Parikh R. K., Modi S. C., Vyas K. G., and Sheth K. M., "Novel drug delivery approaches to bypass Pglycoprotein efflux pump," Pharmainfo.net, vol. 9, no. 1, 2011,http://www.pharmainfo.net/reviews/novel-drug-delivery-approaches- bypass-p-glycoprotein-efflux-pump.

[39]. Bansal T., Akhtar N., Jaggi M., Khar R. K., and Talegaonkar S., "Novel formulation approaches for optimising delivery of anticancer drugs based on P-glycoprotein modulation, Drug Discovery Today,2009;14, 21-22, 1067–1074.

[40]. Dwibhashyam V. S. N. M. and Vijayaralna J., "The permeability glycoprotein (P-GP)—a threat to effective drug therapy?" Indian Drugs;2006, 43, 8, 609–615.

[41]. Nornoo A. O., Zheng H., Lopes L. B., Johnson B. Kannan Restrepo,K., and Reed R., Oral microemulsions of paclitaxel: in situ and pharmacokinetic studies, European Journal of Pharmaceutics and Biopharmaceutics,2009; 71, 2, 310–317.

[42]. Gursoy R. N. and Benita S., Self-emulsifying drug delivery systems (SEDDS) for improved oral delivery of lipophilic drugs, Biomedicine and Pharmacotherapy,2004; 58, 3; 173–182.

[43]. Buyukozturk F., Benneyan J. C., and Carrier R. L., Impact of emulsion-based drug delivery systems on intestinal permeability and drug release kinetics, Journal of Controlled Release,2010;142,1, 22–30.

[44]. Patel A. R. and Vavia P. R., Preparation and in vivo evaluation of SMEDDS (self-microemulsifying drug delivery system) containing fenofibrate, The AAPS Journal; 2007; 9; 3;E344– E352,.

[45]. Goddeeris C, Cuppo F, Reynaers H, Bouwman WG, Van den Mooter G. Light scattering measurements on microemulsions: estimation of droplet sizes. Int J Pharm. 2006 7;312(1-2):187-95.

[46]. Sharma G.,.Wilson K, van derWalle C. F., N. Sattar, Petrie J. R., and. Kumar M. N. V. R, "Microemulsions for oral delivery of insulin: design, development and evaluation in streptozotocin induced diabetic rats," European Journal of Pharmaceutics and Biopharmaceutics;2010; 76; 2;159–169.

[47]. Bali V., Ali M., and Ali J., Nanocarrier for the enhanced bioavailability of a cardiovascular agent: in vitro, pharmacodynamic, pharmacokinetic and stability assessment, International Journal of Pharmaceutics;2011; 403; 1-2;45–56.

[48]. Balakrishnan P., Lee B.-J., Oh D. H. , Enhanced oral bioavailability of Coenzyme Q10 by self-emulsifying drug delivery systems, International Journal of Pharmaceutics; 2009;374; 1-2;66–72.

[49]. Atef E. and Belmonte A. A., Formulation and in vitro and in vivo characterization of a phenytoin self-emulsifying drug delivery system (SEDDS), European Journal of Pharmaceutical Sciences;2008; 35; 4;257–263.

[50]. Elnaggar Y. S. R., Massik M. A. El, and Abdallah O. Y., Selfnanoemulsifying drug delivery systems of tamoxifen citrate: design and optimization, International Journal of Pharmaceutics; 2009;380; 1-2;133–141.

[51]. Karamustafa F. and Celebi N. , Development of an oral microemulsion formulation of alendronate: Effects of oil & cosurfactant type on phase behaviour, Journal of Microencapsulation; 2008; 25; 5;315–323.

[52]. Boonme P., Krauel K., Graf A., Rades T., and Junyaprasert V. B., Characterization of microemulsion structures in the pseudoternary phase diagramof isopropyl palmitate /water/Brij 97:1- butanol, AAPS PharmSciTech;2006;7; 2, p. E45.

[53]. Araujo L. M. P. de Campos, Thomazine J. A., and Lopez R. F. V., Development of microemulsions to topically deliver 5-aminolevulinic acid in photodynamic therapy, European Journal of Pharmaceutics and Biopharmaceutics; 2010;75; 1;48–55.

[54]. Karamustafa F. and Celebi N. , Development of an oral microemulsion formulation of alendronate: Effects of oil & cosurfactant type on phase behaviour, Journal of Microencapsulation; 2008;25; 5;315–323.

[55]. Parveen R., Baboota S., Ali J., Ahuja A., Vasudev S., and Ahmad S., Oil based nanocarrier for improved oral delivery of silymarin: In vitro & In vivo studies, International Journal of Pharmaceutics; 2011;413; 1-2;245–253.

[56]. Singh A. K., Chaurasiya A., Awasthi A., Oral bioavailability enhancement of exemestane from self-microemulsifying

drug delivery system (SMEDDS), AAPS Pharm Sci Tech; 2009;10; 3;906–916.

[57]. Shafiq S., Shakeel F., Talegaonkar S., Ahmad F. J., Khar R. K., and Ali M., Development and bioavailability assessment of ramipril nanoemulsion formulation, European Journal of Pharmaceutics and Biopharmaceutics; 2007;66; 2;227–243.

[58]. Basalious E. B., Shawky N., and Badr-Eldin S. M., SNEDDS containing bioenhancers for improvement of dissolution and oral absorption of lacidipine. I.Development and optimization, International Journal of Pharmaceutics;2010; 391; 1-2,;203– 211.

[59]. Shafiq-un-Nabi S., Shakeel F., Talegaonkar S..,Formulation development and optimization using nanoemulsion technique: a technical note, AAPS PharmSciTech;2007; 8; 2;E12–E17.

[60]. Podlogar F., Gasperlin M., Tomsic M., Jamnik A., and Roga, M. B. Structural characterisation of water-Tween 40/Imwitor 308-isopropyl myristate microemulsions using different experimental methods," International Journal of Pharmaceutics; 2004;276; 1-2;115–128.

[61]. Gradzielski M., Recent developments in the characterization of microemulsions, Current Opinion in Colloid and Interface Science; 2008;13; 4;263–269.

[62]. Goddeeris C., Goderis B., and Mooter G. van den, Lyotropic, liquid crystalline nanostructures of aqueous dilutions of SMEDDS revealed by small-angle X-ray scattering: impact on International Scholarly Research Notices 11 solubility and drug release, European Journal of Pharmaceutical Sciences;2010; 40; 2;110–117.

[63]. Borhade V., Nair H., and Hegde D., Design and evaluation of self-microemulsifying drug delivery system (SMEDDS) of tacrolimus, AAPS PharmSciTech; 2008; 9; 1;13–2 .

[64]. Kale A. A. and Patravale V. B., Design and evaluation of selfemulsifying drug delivery systems (SEDDS) of nimodipine, AAPS PharmSciTech;2008; 9; 1;191–196.

[65]. Corswant C, Thoren P, Engstrom S, Triglyceride-based microemulsion for intravenous administration of sparingly soluble substances. J. pharm. Sci. 1998; 17;200-208.

[66]. Hsiu-O Ho, Chih-Chuan Hsiao, Ming-Thau Sheu, preparation of microemulsions using polyglycerol fatty acid esters as surfactant for the delivery of protein drugs. J. pharm. Sci. 1996; 58: 138-143.

[67]. Dreher F, Walde P, Walther P, Wehrli E, Interaction of a lecithin microemulsion gel with human stratum corneum and its effect on transdermal transport. J. Control. Rel.1997; 45:131-140.

[68]. Zheng Lv FF. , Tung CH, Studies on the stability of the chloramphenicol in the microemulsion free of alcohols. Eur J Pharm Biopharm.2006; 62:288-294.

[69]. Fialho SL, da Silva-Cunha A. New vehicle based on a microemulsion for topical ocular administration of dexamethasone. Cl i n Ex p e r Op h t h a lmo l., 2004; 32(6):626-632

[70]. Gupta Syamasri, Moulik S.P., Biocompatible microemulsions and their prospective uses in drug delivery. Journal of Pharmaceutical Sciences. 2008; 97:22-45.

[71]. Paul, B.K., Moulik, S.P: Uses and Applications of Microemulsions, Current Science, 2001, 80 (8); 990 – 1001.

[72]. Watanabe, K., Noda, A., Masuda, M. and Nakamura, K. Bicontinuous microemulsion type cleansing containing silicon oil. J. Oleo Sci., 2004; 53, 537-548.

[73]. Komesvarakul, N., Sanders, M.D., Szekeres, E., Acosta, E.J., Faller, J.F.,Mentlik, T., Fisher, L.B., Nicoll, G., Sabatini, D.A. and Scamehorn, J.F, Microemulsions of triglyceride-based oils: The effect of co-oil and salinity on phase diagrams. J. Cosmet. Sci., 2006;57, 309-318.

[74]. Ayannides, C.A. and Ktistis, G. A rheological study on microemulsion gels of isopropyl myristate, polysorbate 80, glycerol and water. J. Cosmet. Sci., 1999; 50, 1-9.

[75]. Hua, X.Y., Van, G.L., Aronson, M.P. and Zhu, Z. (to Unilever). (2004) EP Patent 1397108.

[76]. Diec, K.H., Meier,W. and Schreiber, J. (to Beiersdorf). (1999) EP Patent 934053.

[77]. Miller, D.J. and Henning, T. Three phase bath oils – an attractive application for microemulsions. SO¨FW J., (2003) 129, 22-41.

[78]. Kahre, J., Engels, T.,Hensen, H., B¨ottcher, A., Gutsche, B. and Jackwerth, B. (toHenkel). (1999) EP Patent 927553.

[79]. Carlotti, M.E., Gallarate, M. and Rossatto, V. O/W microemulsion as a vehicle for sunscreens. J. Cosmet. Sci., 2003; 54, 451-462.

[80]. F¨orster, T., Class, M., Guckenbiehl, B. and Ansmann, A. (to Henkel). 2003; EP Patent 813861.
[81]. Ansmann, A., Fabry, B. and Hensen, H. (to Henkel). 2000 EP Patent 1007508.
[82]. Schulz, J. and Goppel, A. (to Beiersdorf). 2004 EP Patent 1478326.
[83]. Halloran, D.J. and Hoag, C. Organofunctional silicone microemulsions for hair formulations. J. Cosmet. Sci., 1998;113, 61.
[84]. Dalrymple, D.M. and Manning, M. (to Goldschmidt). 200) EP Patent 12518250.
[85]. Maillefer, S., Chambettaz, D. and Franzke, M. (toWella). 200) EP Patent 1559395.
[86]. Barreleiro, P., Hloucha, M., Dorn, K., Hentrich, D., Knappe, T. and Scheffler, R. (to Henkel). 2006, WO Patent 2006136331.
[87]. Von Rybinski, W., Guckenbiehl, B. and Tesmann, H. Influence of cosurfactants on microemulsions with alkyl polyglycosides. Colloid Surf. A, 1998; 142, 333-346.
[88]. Carlotti M.E., Gallarate M., Morel S. andUgazio E. Micellar solutions and microemulsions of odorous molecules. J. Cosmet. Sci., 1999; 50, 281-293.
[89]. Smulders, E. Laundry Detergents, in Ullmann's Encyclopedia of Industrial Chemistry. Wiley,Weinheim, Germany ;2002.
[90]. Von Rybinski, W. Physical aspects of cleaning processes. In I. Johansson and P. Somasundaran (eds), Handbook for Cleaning Decontamination; 1. Elsevier, Amsterdam, The Netherlands, 2007.
[91]. Lange, R. Detergents and Cleaners. Hanser, Munich 1994.
[92]. Kling, C. Rolling-up process as basis for detergency. Kolloid-Z, 1949; 115, 37-51.
[93]. Nickel, D., Speckmann, H.D. and von Rybinski, W. Interfacial tension and wetting – parameters for the characterization of products. Tenside Surfactants Det., 1995;32, 470-451.
[94]. Jakobi, G. and L¨ohr, A. Detergents and Textile Washing. VCH,Weinheim, 1986.
[95]. Acosta, E.J., Nguyen, T.,Witthayapanyanon, A., Harwell, J.H. and Sabatini, D.A. Linkerbased bio-compatible microemulsions. Environ. Sci. Technol., 2005; 39, 1275-1296.
[96]. Upadhyaya, A., Acosta, E.J., Scamehorn, J.F. and Sabatini, D.A. Microemulsion phase behavior of anionic–cationic surfactant mixtures: Effect of tail-branching. J. Surfactants Det., 2006; 9, 169-182.
[97]. Doan, T., Acosta, E., Scamehorn, J.F. and Sabatini, D.A. Formulating middle-phase microemulsions using mixed anionic and cationic surfactant systems. J. Surfactants Det., 2003; 6, 215-225.