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REVIEW ON: MICROEMULSION

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ABSTRACT

Microemulsions are clear, thermodynamically stable isotropic liquid mixtures of oil, water and surfactant, frequently in combination with a co-surfactant. They can be classified as oil-in-water (o/w), water-in-oil (w/o) or bi-continuous systems depending on their structure and are characterized by ultra-low interfacial tension between oil and water phases. Microemulsions are point of interest to the pharmaceutical scientists because of their molecules. The purpose of study was to enhance the dissolution rate and the effect of microemulsion on the oral and other administration means. These versatile and adaptable delivery systems provide protection against various stages like oxidation, enzymatic hydrolysis and improve the solublization of liphophilic drugs and hence their bioavailability. In addition to the oral and intravenous delivery they are amenable for sustained and targeted delivery through ophthalmic, dental, pulmonary, vaginal and topical routes.

Keywords: Microemulsion, components, phase behaviour, delivery system.

INTRODUCTION

The first Commercial microemulsion was used by Radawald in 1928. Then microemulsion was recognized as special kind of colloidal dispersion before the work of Schulman in 1943.[1]

Emulsions are pharmaceutical preparations consisting of a minimum of two immiscible liquids; typically, oil and water. A microemulsion is defined as a dispersion consisting of oil, surfactant, co surfactant and an aqueous phase. it's one optically isotropic and thermodynamically stable liquid solution with a droplet diameter usually within the range of 10– 100 nm. Microemulsions have variety of special properties like enhanced drug solubility, good thermodynamic stability, easy manufacturing and permeation enhancement ability over conventional formulations, which are exploited in drug delivery systems, pharmaceutics, and food industries.[2]

Emulsion and microemulsion have difference in structure and stability. Unlike the microemulsions, emulsions are unstable systems and phase separation occurs without agitation. The further distinction is that the droplets in emulsions are within the range of micrometers where as in micro-emulsions the droplets are between 5 and 100 nm, reckoning on the degree of their distribution, betting on certain factors like surfactants type and concentration.[3]

Microemulsion systems consisting of at least 30% of oil,1 to 30% of non-ionic surfactant system having a hydrophilic lipophillic balance, HLB, comprised between 9 and 18, 20% of co-solvent and at least 30% of water**.** [4]

Microemulsion are currently the topic of the many investigations thanks to their wide selection of potential and actual utilization. The high capacity of microemulsions for drugs makes them attractive formulations for pharmaceuticals[5]

Microemulsions have been used to improve the solubility and bioavailability of various drugs such as elacridar, paclitaxel, cyclosporine, acyclovir tetramethylpyrazine, fexofenadine and simvastatin.[6]

microemulsions are intensively studied during the last decades by many scientists and technologists due to their great potential in many food and pharmaceutical applications.[7] Microemulsions are widely studied to boost the bioavailability of the poorly soluble drugs. The delivery of microemulsion-loaded drugs is achieved through oral and intravenous delivery, transdermal delivery or sustained and targeted delivery.[8]

TYPES OF MICROEMULSION

According to Winsor, there are four types of micro emulsion phases exists in equilibrium, these phases ar e referred as Winsor phases. they are:

Winsor I (two phase system)

Upper oil layer exists in equilibrium with lower (o/w) micro emulsion phase.[2] Oil in-water type of microemulsions droplets of oil is surrounded by a surfactant (and may be cosurfactant) film that forms the internal phase distributed in water, which is the continuous phase. This type of microemulsion generally has a larger interaction volume than the w/o microemulsions.[5]

Winsor II (two phase system)

The upper(w/o) microemulsion exists in equilibrium with lower excess water.[2] Water-in-oil type of microemulsions droplets of water surrounded by a continuous oil phase. These are recognized "reversemicelles", where the polar headgroups of the surfactant are facing into the droplets of water, with the fatty acid tails facing into the oil phase. A w/o microemulsion used orally or parenterally may be destabilized by the aqueous biological system.[5]

Winsor III (three phase system)

Middle bi-continuous phase of o/w and w/o called) exists in equilibria with upper phase oil and lower phase water[2] bi-continuous microemulsion system the amount of water and oil present are similar, In this case, both water and oil exist as a continuous phase. An irregular channel of oil and water are combined, and looks like a "sponge-phase". Transitions from o/w to w/o microemulsions may pass through this bi-continuous state. Bi-continuous microemulsion, may show non-Newtonian flow and plasticity. These properties make them especially useful for topical delivery of drugs or for intravenously administration. [9]

Winsor IV (single phase system)

it forms homogenous mixture of oil, water and surfactant. [2]

The R-ratio is one of the characterisation concepts which were first proposed by Winsor to explain the influence of amphiphiles and solvents on interfacial curvature. R-ratio compares the affinity for an amphiphile to disperse into oil, to its affinity to dissolve in water. If one phase is favoured, the interfacial region forms a definite curvature. Thus, if R > 1, the interface increases its area of contact with oil while decreasing its area of contact with water. Thus oil becomes the continuous phase and the corresponding characteristic system is type II (Winsor II). Similarly, a balanced interfacial layer is represented by R = 1.[10]

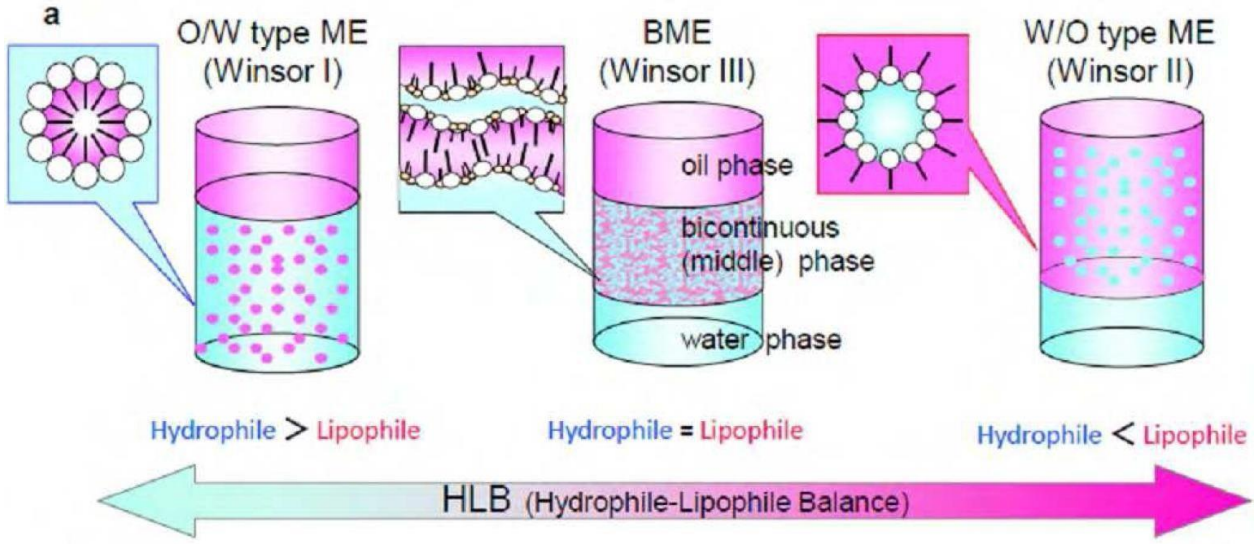

Fig.1 Classification of microemulsion

COMPONENTS

The formulation and development of microemulsions, several substances are employed. In microemulsion, most oils and surfactants should be biocompatible, not poisonous and therapeutically acceptable. Main microemulsion components

1. Oil Phase
2 .Aqueous phase
3. Surfactant
4. Co. Surfactant[10]

1.Oil phase

The oil is an important part of microemulsion because the dose required of a lipophilic medicinal product can be solubilized and the fraction of lipophilic medicinal product carried by a lymphatic intestinal system rises. Oil is a liquid with low polarity and low water miscibility.[9]

2.Aqueous phase

The hydrophilic active components and preservatives usually form within the aqueous phase. Buffer solutions are sometimes employed as an aqueous phase.

3.Surfactant (surface-active-agent)

Is a word want to describe a chemical that has some superficial or interfacial activity and is employed to scale back surface or interface tension. it's interested in both polar and nonpolar liquids. The molecules that have a polar head and a polar tail are surfactants. Surfactant molecules are independent due to different inter- and intramolecular forces and entropy concerns. the various surfactants that contribute to the gradual microemulsion development system are 1. Cationic 2. Anionic 3. Non-ionic 4. Zwitterionic surfactants.[11]

4.co surfactant

In most cases, single-chain surfactants alone are unable to reduce the o/w interfacial tension sufficiently to enable a micro emulsion to form. The presence of cosurfactants allows the interfacial film sufficient flexibility to take up different curvatures required to form micro emulsion over a wide range of composition. If a single surfactant film is desired, the lipophilic chains of the surfactant should be sufficiently short, or contain fluidizing groups (eg. unsaturated bonds).[12]

Table 1. Component of Microemulsion System: [10]

Component	Example
1.Oil	1-saturated fatty acid – lauric acid, carpic acid. 2-unsaturated fatty acid – oleic acid. Linolic acid. 3-fatty acid - ester-ethyl or methyl ester of lauric, oleic acid myristic acid.
2.surfactant	1-Polyoxyethylene/polysorbate/tween 20,40,60,80 2-sorbitan monolaurate, eggs lecithin 3-sodium dodecyl sulphate
3.Co-surfactant	1-ethanol, propanol, butanol isopropanol, pentanol, hexanol 2-polyoxyethylene -10-oelyl ether 3- sodium monohexyl phosphate 4- cinnamic alcohol.

STRUCTURE OF MICROEMULSIONS

Microemulsions or Micellar emulsion are dynamic system in which the interface is continuously and spontaneously fluctuating. Structurally, they are divided in to oil in water (o/w), water in oil (w/o) and bi-continuous microemulsion. w/o micro emulsions, water droplets are dispersed in the continuous oil phase while o/w micro emulsions are formed when oil droplets are dispersed in the continuous aqueous phase.[13] In system where the amounts of water and oil are similar, the bi-continuous microemulsions may result .The mixture oil water and surfactants are able to form a wide variety of structure and phase depending upon the proportions of component. [14]

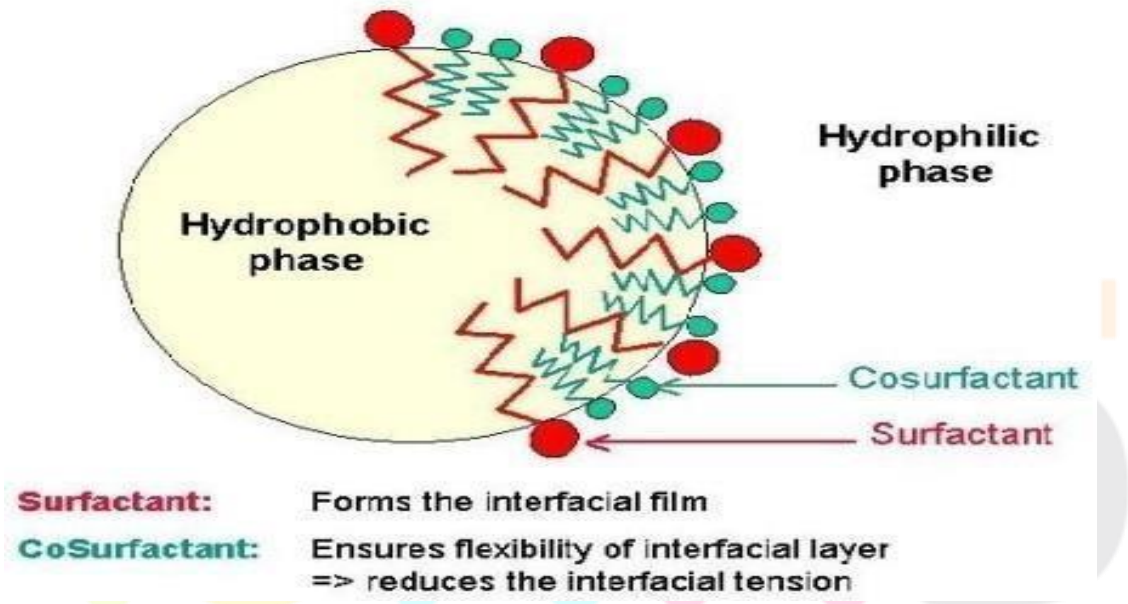

Fig.2.Structure of microemulsion

CHARACTERISTICS:

If a surfactant possessing balanced hydrophilic and lipophilic properties is used in the right concentration a different oil and water system will be produced. The system remains an emulsion, but exhibits some characteristics that are different from the milky emulsions discussed earlier. These new systems are "micro emulsions".[3] The interfacial tension between phases, amount of energy required for formation, droplet sizes, and visual appearance are only a few of the differences seen when comparing emulsions to micro emulsions. Water-in oil micro emulsions are also known as reverse micelles. These systems have the ability to solubilise both hydrophilic and hydrophobic substances. Micro emulsions usually exhibit low viscosities and Newtonian flow characteristics. Their flow remains constant when subjected to a variety of shear rates. Discontinuous formulations may show some non Newtonian flow and plasticity .Micro emulsion viscosity is close to that of water, even at high droplet concentrations.[10]The microstructure constantly changes, making them very dynamic systems with reversible droplet coalescence. A variety of techniques are employed to characterize different properties of micro emulsion. [15]

ADVANTAGES[1,13]

1.Various routes like tropical, oral and intravenous can be used to deliver the product.
2.Provides a aqueous dosage form for water insoluble drugs.
3.These are thermodynamically stable and require minimum energy for formation.
4.Ease of manufacturing and scale-up .
5.Improved drug solubilisation and bioavailability.
6.This system is reckoned advantageous because of its wide applications in colloidal drug delivery systems for the purpose of drug targeting and controlled release.
7.Liquid dosage form increases patient compliance.
8.Provides protection from hydrolysis and oxidation as drug in oil phase in O/W microemulsion is not exposed to attack by water and air.
9.Less amount of energy requirement.
10.Increase the rate of absorption.

DISADVANTAGE[1, 3]

1. Having limited solubilizing capacity for high- melting substances.
2.Require large amount of Surfactants for stabilizing droplets.
3.The surfactant must be nontoxic for using pharmaceutical applications
4.Micro emulsion stability is influenced by environmental parameters such as temperature and pH These parameters change upon micro emulsion delivery to patients.
5.High cost of surfactant .
6.Narrow range of surfactant, co-surfactant, solvents
7.Formulation containing several components become more challenging to validate
8.The precipitate tendency of the drug on dilution may be higher due to the dilution effect of the hydrophilic solvent
9.The tolerability of formulations with high levels of synthetic surfactants may be poor in cases where long term chronic administration is intended.

METHOD OF PREPARATION

Phase titration method

Microemulsions are prepared by the spontaneous emulsification method (phase titration method) and can be depicted with the help of phase diagrams. Construction of phase diagram is a useful approach to study the complex series of interactions that can occur when different components are mixed. Microemulsions are formed along with various association structures (including emulsion, micelles, lamellar, hexagonal, cubic, and various gels and oily dispersion) depending on the chemical composition and concentration of each component. The understanding of their phase equilibria and demarcation of the phase boundaries are essential aspects of the study.[12]

As quaternary phase diagram (four component system) is time consuming and difficult to interpret, pseudo ternary phase diagram is often constructed to find the different zones including microemulsion zone, in which each corner of the diagram represents 100% of the particular component. The region can be separated into w/o or o/w microemulsion by simply considering the composition that is whether it is oil rich or water rich. Observations should be made carefully so that the metastable systems are not included.[2]

Phase Inversion Method

In the phase inversion method phase inversion of microemulsions occurs by addition of excess amount of the dispersed phase. During phase inversion quick physical changes occur including changes in particle size that can affect drug release both in vivo and in vitro. For non-ionic surfactants ,this can be completed by changing the temperature, forcing a transition from oil in water microemulsion at low temperatures to water in oil microemulsion at higher temperatures (transitional phase inversion).[11]

During cooling, the system crosses a point of zero spontaneous curvature and minimal surface tension, promoting the formation of finely dispersed oil droplets. This method is also known as phase inversion temperature (PIT) method Instead of the temperature, other parameters such as salt concentration or pH value may be considered as well instead of the temperature alone[16] Additionally, a transition in the spontaneous radius of curvature can be obtained by changing the water volume fraction. By successively adding water into oil initially water droplets are formed in a continuous oil phase. Increasing the water volume fraction changes the spontaneous curvature of the surfactant from initially stabilizing a w/o microemulsion to an o/w microemulsion at the inversion locus. Short-chain surfactants form flexible monolayers at the o/w interface resulting in a bi-continuous microemulsion at the inversion point.[17]

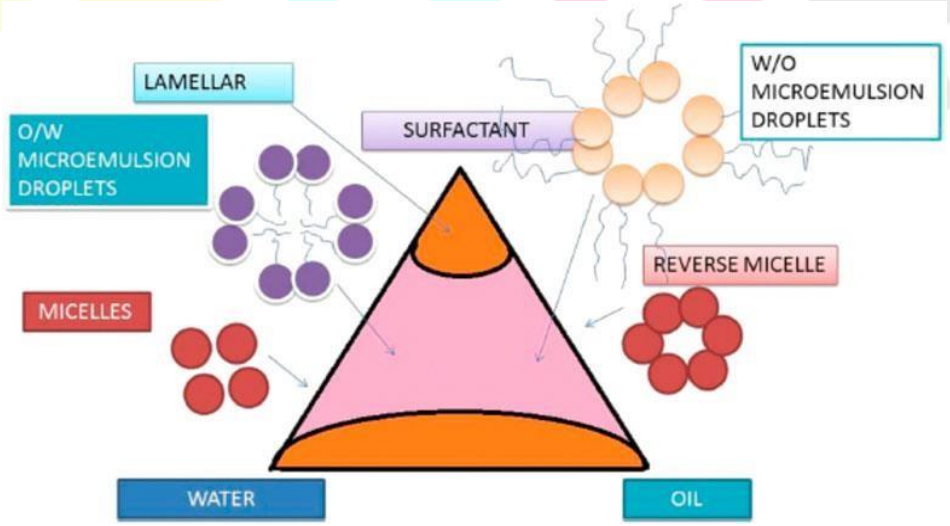

Fig 3 Ternary phase diagram

FACTOR AFFECTING THE MICROEMULSION ARE AS FOLLOWS

Packing ratio: HLB of surfactant influences the type of microemulsion by affecting the packaging and therefore the curvature of the film.

Property of surfactant: Two lipophilic group and hydrophilic group include surfactants. Hydropyl single chain surfactants, such cetyl ammonium bromide, are totally dissociated into a diluted solution and have a tendency to provide o/w microemulsion.[3]

Property of oil phase: By its capacity to enter and swell the tail group area of a surfactant monolayer, the oil phase influences a curvature swelling the tail resulting in an enhanced negative curvature to W/O microemulsion.[5]

Temperature: The efficient head group size of non-ionic surfactants is very essential to determine the temperature. The hydrophilic and the typical O/W system are formed at low temperatures. They are lipophilic and w/o systems at higher temperatures.[9]

APPLICATIONS

Parenteral Delivery: Both O/W and W/O microemulsion can be used for parenteral delivery. The literature contains the details of the many microemulsion systems, few of these can be used for the parenteral delivery be because of toxicity of surfactant and parental use.

Oral Delivery: Microemulsion formulations offer the several benefits over conventional oral formulation including increased absorption, improved clinical potency, and decreased drug toxicity. Therefore, microemulsion have been reported to be ideal delivery of drugs such as steroids, hormones, diuretic and antibiotics.[17]

Topical Delivery: Topical administration of drugs have advantages like avoidance of hepatic first pass metabolism of the drug and targetability of the drug to affected area of the skin or eyes.The use of lecithin/IPP/water microemulsion for the transdermal transport of indomethacin and diclofenac has also been reported.

Ocular and Pulmonary Delivery: For the treatment of eye diseases, drugs are essentially delivered topically.O/W microemulsions have been investigated for ocular administration, to dissolve poorly soluble drugs, to increase absorption and to attain prolong release[2]

Microemulsions in cosmetics: It is believed that microemulsion formulation will result in a faster uptake into the skin. Cost, safety, appropriate selection of ingredients are key factors in the formulation of micro emulsions. Unique microemulsions as hair care products contain an amino-functional polyorganosiloxane and an acid and/or a metal salt.

Microemulsions in agrochemicals: Microemulsions have a variety of applications in agrochemical industry, of which pesticide containing systems are relatively old. The ease of handling and lower requirement of smelly solvents go in favour of the use of micro emulsions. Microemulsions formulated with a hydrotope solubilizing the herbicide can be promising. The much finer droplet size of the microemulsion leads to higher penetrability, much larger contact area of the active substance to the treated surface and a much more even distribution during application[1]

Nasal delivery: Microemulsions are now being studied as a delivery system to enhance uptake across nasal mucosa. Addition of a mucoadhesive polymer helps in prolonging the residence time on the mucosa.

Tumor targeting: The utility of microemulsions as vehicles for the delivery of chemotherapeutic or diagnostic agents to neoplastic cells while avoiding normal cells. A method for treating neoplasms, wherein neoplasms cells have an increased number of LDL (low density, lipoprotein) receptors compared to normal cells. The micro emulsion comprised of a nucleus of cholesterol esters and not more than 20% triglycerides surrounded by a core of phospholipids and free cholesterol and contained a chemotherapeutic drug. The microemulsions could then be incorporated into cells via receptors for LDL and delivered the incorporated molecules. Thus, higher concentration of anticancer drugs could be achieved in the neoplastic cells that have an increased expression of the receptors. In this way toxic effects of these drugs on the normal tissues and organs could be avoid.[18]

EVALUTION OF MICROEMULSION

The microemulsions are evaluated by the subsequent techniques. They

1.Visual Inspection: For visual inspection microemulsion is inspect visually for homogeneity, optical clarity, and fluidity.

2.Examination under Cross-polarizing Microscope: The microemulsion systems are subjected to examination under cross polarizing. microscope for the absence of birefringence to exclude liquid crystalline systems.[11]

3.Limpidity Test (Percent Transmittance): The limpidity of the microemulsion is measured spectrophotometrically using spectrophotometer.

4.Globule size and zeta potential measurements

The globule size and zeta potential of the micro emulsion may be determined by dynamic light scattering, employing a Zetasizer HSA 3000.[16]

5.Viscosity measurements Rheological behaviour of the formulation is observed by employing a Brookfield LVDV III+ cone and plate (CP) viscometer using rheocal software at a temperature.[12]

6. Electrical conductivity The water phase was added drop wise a mix of oil, surfactant and co-surfactant and also the electrical conductivity of formulated samples are often measured employing a conductometer (CM 180 conductivity meter, Elico, India) at ambient temperature and at a continuing frequency of 1 Hz.

7.Drug stability The optimized microemulsion was kept under cold condition o (48 C), temperature and at elevated temperature (50 ± 2 o C). After every 2 months the microemulsion are often analyzed for phase separation, % transmittance, globule size and zippers assay.[16]

CONCLUSION

Microemulsions are thermodynamically stable, posses excellent solublisation properties. These properties can be incorporate in different liphophilicity. They can be used to optimize drug targeting devoid of concomitant increase in systemic absorption. In recent years microemulsions came as attention making novel drug delivery system because of their importance in various application. During the last two decades lots of research work has been carried out on microemulsions systems for providing novel solutions.

REFERENCES

[1] Sharma, N., Antil, V. and Jain, S., 2013. Microemulsion: A review. Asian Journal of Pharmaceutical Research and Development, pp.23-36.
[2] Pavankumar K. M., and Parthbans S., 2020.Microemulsion: A promising drug delivery strategy: A Review. European journal of pharmaceutical and medical research, 7(10), pp. 346-353.
[3] Mane, V. D., Patil, V. M., Mane, M. V., Patil, S. V., 2021.A Review on microemulsion -A recent approach for topical drug delivery system. International journal of creative research Thought, vol(9), p.p 62-71.

[4] Yadav, S., Kawtikwar, P.S., Sakarkar, D.M., Gholse, Y.N. and Ghajbhiye, S.D., 2009. Microemulsion: A Review. Research Journal of Pharmacy and Technology, 2(3), pp.441-448.

[5] Singh, P.K., Iqubal, M.K., Shukla, V.K. and Shuaib, M., 2014. Microemulsions: current trends in novel drug delivery systems. J Pharm Chem Biol Sci, 1(1), pp.3951.
[6] Subongkot T. and Ngawhirunpat T., 2017. Development of a novel microemulsion for oral absorption enhancement of all-trans retinoic acid. International Journal of Nanomedicine, 12, p.5585.

[7] Kumar, K.J.R., Muralidharan, S. and Dhanaraj, S.A., 2012. Anti-fungal activity of microemulsion based fluconazole gel for onychomycosis against Aspergillus Niger.

[8] International Journal of Pharmacy and Pharmaceutical Sciences, 5(1), pp.96-102. 8.Onah chinweM., Mbah chuka J., 2019.Pharmaceutical Microemulsion Gel :Functioning as a Drug delivery system. Journal of Chemical and Pharmaceutical Reaserch, 11(10), p.p 48- 55.

[9] Sk, A., Sk, N.M., Konda, R.K. and Naik, V., 2020. Micro Emulsions: An Overview And Pharmaceutical Applications. World Journal of Current Medical and Pharmaceutical Research, pp.201-205.

[10] Jadhav, A., Daundkar, A., Morale, D., Bhujbal, N. and Kshirsagar, S., 2018.
Review On: Microemulsion a Novel Approach for Drug Delivery. Int J. Pharm Sci.
Rev. Res, 52(2), pp.60-65.

[11] .Muzaffar, F.A.I.Z.I., Singh, U.K. and Chauhan, L., 2013. Review on microemulsion as futuristic drug delivery. Int J Pharm Pharm Sci, 5(3), pp.39-53.
[12] Shinde, S., Panchal, K., Dhondwad, M., 2020.Review article -Microemulsion :Novel drug delivery system. International journal of scientific Development and research, vol (5), p.p 94- 101.
[13] Sarkhejiya Naimish, A., Nakum Mayur, A., Patel Vipul, P., Atara Samir, A. and Desai Thusarbindu, R., 2000. Emerging trend of microemulsion in formulation and research. International bulletin of drug research, 1(1), pp.54-83.

[14] Kumar, K. S., Dhachinmoorthi. D., Saravanan. R., Udaykumar. G., Shanmugam. V., 2011.Microemulsion as carrier for Novel drug delivery : A Review.
International journal of pharmaceutical science review and research., vol (10), p.p 37-45.

[15] Tanzeem., Shukla, P., 2021.Preparation of microemulsion for transdermal drug delivery system. International journal of science and research Vol (10) , p. p 798- 801

[16] Singh, V., Bushettii, S.S., Raju, A.S., Ahmad, R., Singh, M. and Bisht, A., 2011. Microemulsions as promising delivery systems: a review. Ind J Pharm Edu Res, 4, p.54.
[17] Lalage, M.B., Kakade, S. and Bhosale, A., 2019. Review on Microemulsion a Novel Approach for Antifungal Drug Delivery.international journal of trend scientific research and development.vol(4), p.p 917- 923.

[18] Sahu, G.K., Sharma, H., Gupta, A. and Kaur, C.D., 2015. Advancements in microemulsion based drug delivery systems for better therapeutic effects. International journal of pharmaceutical sciences and developmental research, 1(1), pp.008-015.