International Journal of Pharmacy and Herbal Technology

e-ISSN: 2583-8962 Vol. 2, Issue 4 (October – December, 2024) pp: (2521-2532)

Review on a Microemulsion

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Received Date: November 27, 2024; Published Date: 17 December,2024

Abstract

There have been significant advancements once utilizing small emulsion technologies to numerous scientific and industrial activities since Jack H. Shulman's discovery of microemulsions. Water, oil, and surfactant; commonly utilized together with an its co-surfactant combine to form transparent, stable, isotropic microemulsions. Aqueous solutions of optically isotropic in nature and thermodynamically inert amphiphile, water, and oil are called microemulsions. Thus far, research has demonstrated that microemulsions can guard sensitive medications, control the dispensing of medicines, acceptance, enhance bioavailability, and lessen variations in participants. It has moreover shown to be feasible to create preparations appropriate for the majority of administrative routes. Since microemulsions were discovered, their importance has grown in both basic and applied research. Microemulsions offer a number of uses additionally applications due to their special characteristics, which include enormous ultralow surface tension, a thermally stable surface area, and a capacity to absorb liquids than would otherwise be impermeable. The main characteristics that set microemulsions apart from regular their emulsions low slickness, transparency, most especially, with thermodynamic stability. For a number active compounds used in pharmaceutical and cosmetic applications, microemulsions have been demonstrated to be an efficient dermal delivery system. Because of their substantial internal phase surface area and components that lower the stratum corneum's barrier property, topical microemulsions facilitate the fast entry of active compounds. Because microemulsions have the ability to deliver drugs transdermal, they improve skin absorption when compared to conventional formulations. This makes them a promising carrier.

Keywords - Microemulsion, Surfactant, thermodynamically stable

INTRODUCTION

Pharmaceutical research is always designing and developing novel techniques for delivering drug store raise the effectiveness of previously-approved drugs. One particular type of "dispersion" that can seem either translucent or transparently. However, prior to Schulman's study in 1943, microemulsion was acknowledged as a unique type of colloidal dispersion. Hoar and Schulman (1943) made the initial discovery of them In their day of trial investigation the medium-/short-chain alcohol measurement of long-chain fats (soapy milky emulsions) of, resulting a transparent, translucent Emulsion system. In pharmaceutical research, the proposed creation of new drug delivery methods aimed at enhancing the efficacy of currently available medications is a continuous endeavour. Considering that a wide variety of drug delivery devices have been created. Hoar and Schulman's 1940s introduction of the principle of microemulsion involved triturating a

solvent hex with a milky mixture to create a clear one phase solution.[1] Emulsions are medicinal treatments made up of at least combining two immiscible liquids, for example water and oil. A small emulsion is a combination with oil, surfactant used, co surfactant agents, and the water phase. It is a one physically isotropic, that thermodynamically unchangeable liquid solution with a spray thickness that is generally about 10 and 100 nm. Drug delivery systems, pharmaceutics, and the food sectors use microemulsions because of their many unique qualities, which include improved chemical solubility, constant the laws of thermodynamic and simplification of manufacture, the capacity to boost permeation over standard formulations.[2]The stability and structure of emulsion and microemulsion differ. The alternative difference is which, subject to the degree of diffusion and more variables such stabilizer type and quantity, particles in small emulsion may range from 5 to 100 nm, and particles from formulations fall within a variety of microns.[3]A mix of liquids of water, oil, and amphiphile that is chemically inert and mechanically non-isotropic can be referred to as a microemulsion. Microemulsion has a few benefits within coarse a fluid, including increased loading of drugs and contact within biologic membranes, raised the bioavailability decreased between- and intra-individual variations in drug absorption, clear and graceful look, thermodynamic stability, spontaneous production, and a lot more. In recent times, a number of uses, particularly timely, orally, intravenously, and cosmetically ones both have been study for microemulsions. Applying drugs as the additive, they initially produced a small emulsion by spreading oil in a water-based surfactant solution in order to develop a translucent permanent product. Microemulsion is defined as an oil and water dispersion that is clear, transparent, and thermodynamically stable. A substance called a contact covering maintains it, usually combined with the additive.[4]

Definition and History

Danielsson and Lindeman's definition of a microemulsion, this characterizes a microemulsion as a structure consists of water, oil, and an amphiphile, which is a single solution of fluid that can be both thermodynamically unchanging and mechanically isotropic in character It represents one of the most effective.[5] the search with Hoar and Schulman in 1943 of a spontaneously combination of water and oil resulting from the addition of a powerful surface-active element. Marked the beginning of the true recognition of microemulsions. It was not until much later that Schulman et al. used the word "microemulsion.[6] The discovery of microemulsions predates Schulman's studies by a significant margin. Australian housewives have been washing wool with mixtures of water, eucalyptus oil, soap flake, and white spirit since the turn of the 20th century. Rodawald's 1928 discovery of liquid waxes is likely the first commercial microemulsion. The late 1970s and early 1980s saw a significant increase in interest in microemulsions as tertiary recovery technologies became profitable and it became apparent that these systems may enhance oil recovery. Hoar and Schulman introduce microemulsions.[7]

Advantages of Microemulsion

Micro emulsion is quick to create and use no resources as a result their better temperature stability. Compared to main and multiple emulsions, microemulsions are less viscous.

By reducing the overall dosage and hence lowering adverse effects, the adoption of micro-emulsion delivery devices can increase a drug's effectiveness.

The microemulsion method effortless to prepare and doesn't need a lot of energy improved thermodynamic stability, which was a factor in the preparation.

It is possible for the distributed period, which includes lipophilic or hydrophobic micro emulsion medicines, to serve as a potential reserve wire.

Disadvantages of Microemulsion

The system can be emulsified because microemulsions are thermodynamically stable.
Need a lot of surfactants to keep droplets stable.
Need a significant quantity of S/Cs to stabilize droplets.
The surfactant ought to be safe to use in medicinal settings.
Having a low ability to solubilize compounds with high melting points.

Limitations of Microemulsion

The following factors restrict the use of micro-emulsion technologies in pharmaceutical submissions:
The instance of micro-emulsions frequently presents the issue of phase separation.
Low amounts of both the two types of detergent are necessary because of worries about toxicology.
The surfactants that will be employed in the micro-emulsion systems must be a part of the "Generally-Regarded-as-Safe" class in order to lessen their toxicity.

Properties of Emulsion [8]

Emulsion	Droplet Size	Thermodynamic Stability	Appearance
Microemulsion	5-100um	Stable	Transparent
Macroemulsion	0.1-100um	Unstable	Turbid
Nano emulsion	5-200um	Unstable	Transparent

Table 1*: *Properties of microemulsion

Components of Microemulsion

The creation and formulation of microemulsions include the usage of several ingredients. Microemulsions mostly contain oil and surfactants; these ingredients should be safe, biocompatible, and acceptable in clinical settings.[9]
The essential ingredients on a micro-emulsion are:

1. Oil Phase

A single the many essential components in a micro-emulsion is oil, that improves the level of a lipophilic medicine's absorption within the intestinal lymph node or may breakdown the right amount of the medication. Oil is the word utilized to denote any liquid experiencing little polarity and weak mixing with liquid.
Examples: toluene, vegetable Grease, mineral oil, cyclohexane, among others.

2. Aqueous Phase

The hydrophilic active ingredients and antioxidants typically appear inside the water stage. Sometimes buffering solutions are used using a water-based component.[10]

3. Surfactant

"A surfactant, or surface-active agent, is a chemical compound that reduces the surface tension between two liquids, a liquid and a gas, or a liquid and a solid. It is attracted to both polar and non-polar liquid". Surfactant particles have two different advantages: a polar cap groups as well as a magnetic end Surfactant molecule a person -assemble as a result of entropy factors, as well as a variety of intra- and intermolecular forces. For instance, because the oil/water interface is thermodynamically favoured, surfactants tend to gather there when combined with oil and water. [11]

Example: Egg lecithin, soyabean lecithin.

4. Co solvent

Studies have suggested indicated single-chain surfactant can insufficient in their ability to lower the tension that exists between each o/w and create a microemulsion. The interfacial film becomes

flexible when co-surfactants are added, allowing it to absorb various curves required for a variety of emulsifier that create a micro. The liquid compounds that compose the surfactants need to be appropriately short or comprise lubricating groups, like conjugated bonds, in order to form one single agent films.[12]

Example: ethanol, propanol, isopropanol.

Types of Microemulsion

Winsor was observed four separate kinds of stable macro dispersion phases, which are collectively referred to as Winsor had stages.

They are provided under-

Victory 1

There is balance between on the lower (o/w) micro particle phases and the greater fluid phase. In Microemulsion Types: seawater with oil in it Oil particles are surround by a continuously layer of detergent (or maybe co surfactant), that produces the inside portion spread in fluid. Typically talking, this type of the microemulsion has a higher interacting region than w/o micro-emulsion

Victory 2

The highest (w/o) the microemulsion and the part with water surplus remain in balance. Drops of water are enveloped by a constant layer of oil in small emulsion called waters-in-oil. Known as "reverse micelles," Them feature the tails of fatty acids pointed into the oil stage and the two polar head groups pointing the detergent into the liquid particles. The aqueous biological system has the potential to destabilize a w/o microemulsion employed parenterally or orally.[13]

Victory 3

The early bi-continuous phase containing o/w and w/o, having higher stage oily and bottom portion fluid, is known as stabilization. The percentages of fat and fluid in a bi-continuous microemulsion technology are equal. In this particular instance, the mixture's two phases are consistent. Combining oil and water creates an uneven channel that resembles a "sponge-phase." These bi-continuous Transfers of o/w to w/o small emulsion can meet these criteria. Bi-continuous small emulsion can be elastic and travel non-Newton. These characteristics are extremely useful for distributing medication physically or systemically.[14]

Victory 4

It generates a uniform combination of water, oils, and agent. The R-ratio represents one of several definition elements which the article originally suggested to clarify how fluids and aphids impact contact tension. The R-ratio can be utilized to compare the amphiphile's sensitivities for spreading in oils and absorbing in fluid.[15]

Methods Preparations of Microemulsion

1. Phase Titration Method

The phase diagram is commonly utilized to show the creation of micro-emulsion these are generated via the procedure of measurement procedure, additionally referred to as spontaneous emulsification. Creating a diagram of phases is a useful instrument for understanding the complicated structure of relationships what can take place when various elements connect. With in addition to micro emulsion various relationship structure such as a solution, micelles, which are laminated, rectangular, square, and others Gelatin and also grease diffusion may arise with respect to the concentration and chemical breakdown each component. Identifying the stage boundary and recognizing their phase balancing represent crucial components of this research.

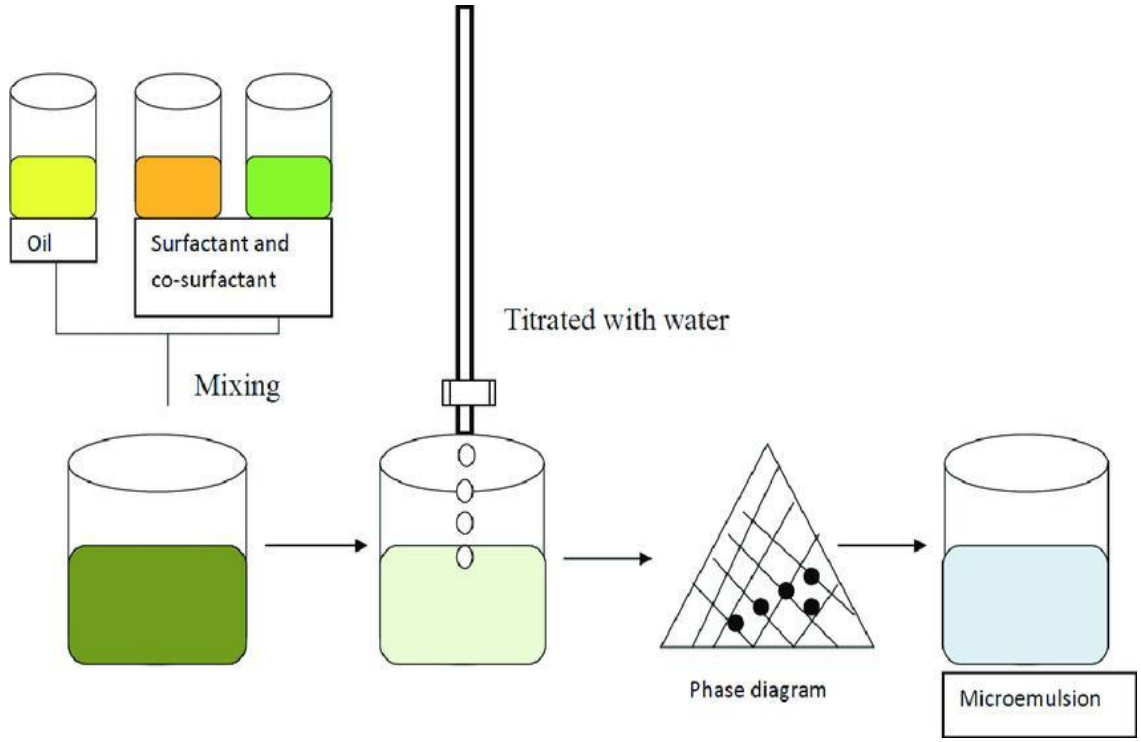

Figure 1*: *Phase titration diagram

2. Phase Inversion Method

The phase inversion occurs when the micro emulsion's heating increases as well as after a large quantity of the dispersed stage is added. Rapid physical modifications, like variations in size of particles, are indications of an inverted phase and may alter inside in vitro and in vivo release of medicines. The above techniques perform by changing the organic bending of the detergent. It can take place for non-ionic surfactants respond in this way by generating a change (transitional phase inversion) between an o/w microemulsion at lower temperatures to a w/o micro-emulsion at higher temperatures. After temperature, the entire structure passes an area of low spontaneously bending and little contact tension, facilitating the development of distributed oil particles. The stage inverting thermal (PIT) technique is the name that utilized for this kind of technique. Additional factors, which include quantity of salt or pH value, can also be taken to heart in along with temperatures. Additionally, an adjustment in the natural diameter of bending can be accomplished by adjusting the amount of water ratio.[16]

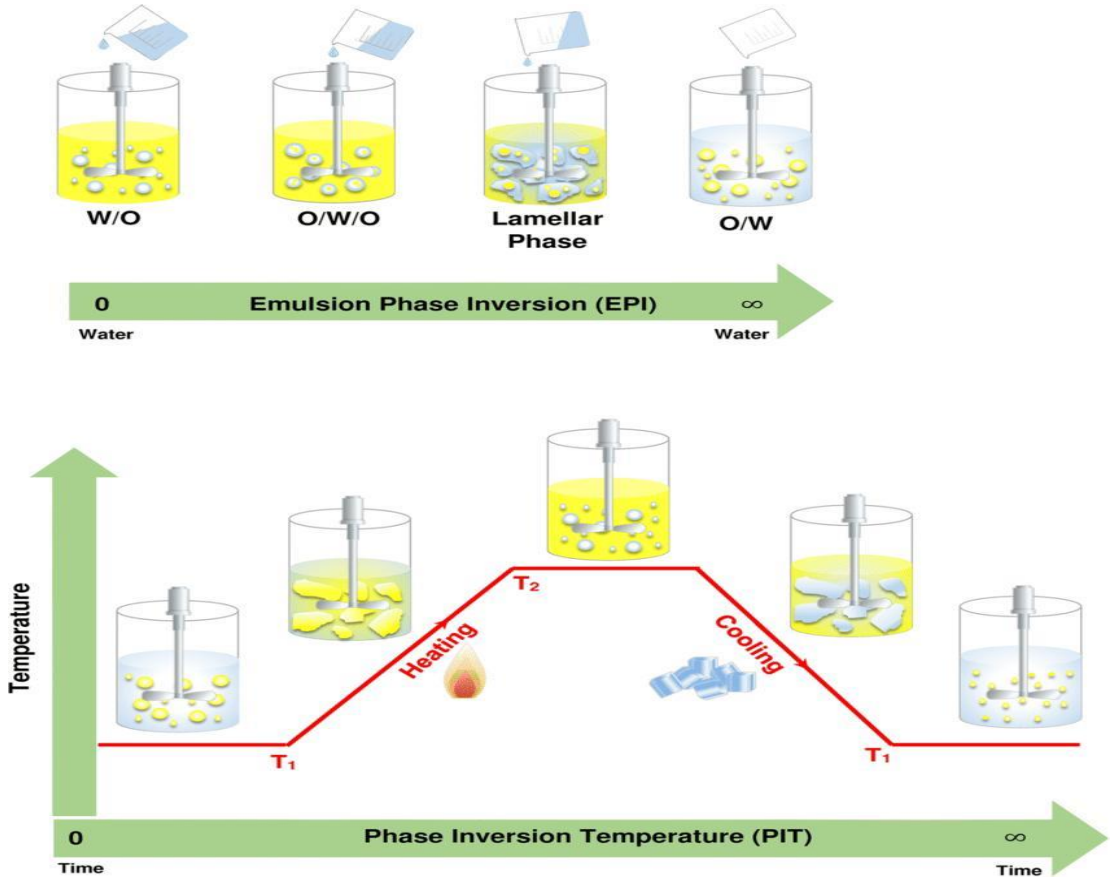

***Figure 2*:** *Phase inversion method*

Characterization of Microemulsion

If surfactant containing balancing hydrophobic and lipophilic qualities gets used at the proper quantity, an original oil-water mixture can be generated. The method changes with the before article on white oil emulsion in multiple ways, but it is still a mixture. These novel systems are called "smaller the emulsion".[17] There are also some differences separating the emulsion and small the emulsion that must be detected while studying them as well, such as particles shapes and sizes, their physical characteristics, and the interfacial tension between phases. Reverse micelles are a different term for oil-in-water micro-emulsion. Both water-loving and water-hating compounds dissolves by these systems. Micro emulsions typically have Newtonian flow properties and low viscosities. When sheared at different rates, their flow doesn't change. Non-Newtonian flow and plasticity may be observed in discontinuous formulations. Even at high droplet concentrations, the thickness in a microscopic particle is identical to that of normal liquid. These systems are exceedingly dynamic with reversible droplet coalescence due to the continual changes in the microstructure. To characterize the various features of the micro emulsion, several approaches are used. [18]

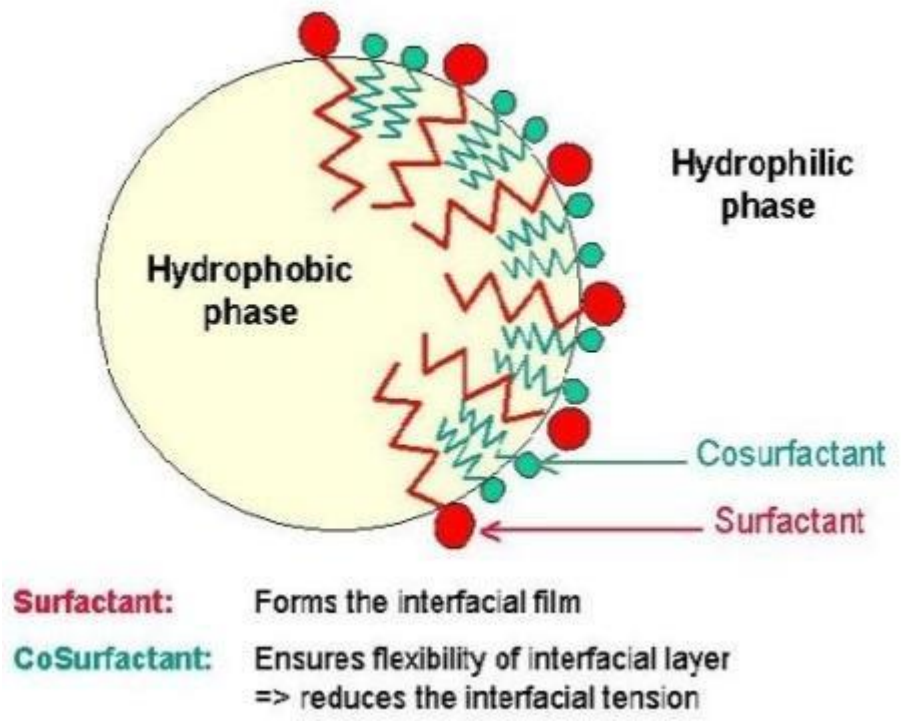

Figure 3*: *Microemulsions Structure

Evaluation of System

1. Visual inspection

The homogeneity, optical clarity, and fluidity of a microemulsion can be examined visually.

2. Examination under cross polarizing microscope

A cross polarizing microscope is used to examine the microemulsion systems To remove water crystallization formations by looking for the lack of birefringence.[19]

3. Limpidity test

Equipped with a spectrophotometer, using spectrometers the micro emulsion's limpidity can be calculated.[20]

4. Assessment of the rheological properties

A key factor in stability is the rheological characteristics. It may prove determined with an electronic instrument designed by Lakeside.[21]

5. Accelerated stability test

Centrifugation stress testing Accelerated stability tests are recommended since stability studies are a time-consuming process. To evaluate the mechanical abnormalities in the Products including separate phases, phase inversion, grouping, mixing, as well as breaking down, microemulsions were centrifuged at 5000 and 10,000 rpm for 30 minutes. Centrifugation sampling containers, that are placed inside the centrifugal the container, are stocked containing formerly previously verified mixtures in order to achieve a balanced position of equilibrium at the room temperature.

Freeze thaw cycles They are kept for 24 hours at 25°C and then for another 24 hours at -5°C to see if the micro emulsion's stability changes. This cycle is performed three times, and any changes are recorded.[22]

6. Determination of the globule size

US Instrument' measuring the globule thickness for the microemulsion mixture is possible performed with the JDS Construction Double Flexible the Light Reflection, Uniphase

methodology. The amount of light scattering method is quite easy when compared with photomicroscope methods used for size measurement.[23]

7. Determination of thermal stability

A 25 ml clear borosil volumetric container containing 20 millilitres of drug-loaded microemulsions is kept in BOD at three different temperatures-4°, 25°, and 40°C-for a month.

8. Specific gravity testing at 28°C

The particular gravity is measured employing the capillary tension bottles technology. The force of gravity bottle has to be managed care after drying and cleaning that a single drop of humidity can result in mistakes regarding the gravity measurement information.[24]

9. pH of microemulsion

With using of a pH indicator, one various microemulsion samples is measured after the samples are placed into sample tubes. It is important to note that stability of the microemulsions affects. The drug's bioavailability at the site of permeation, so it's not just the formulation's pH that matters.

10. Study of microstructure of microemulsion

Because it can capture micro structural changes and co-existing structures and directly produce high-resolution pictures, The most significant instrument when investigating the microscopic properties of small emulsion is the transmission electron microscope.[25]

Marketed Preparation

Drug	Product Name	Company	Therapeutic Area
Cyclosporine	Sand immune oral	Novartis	Immunosuppressant
Cyclosporine	Neoral	Novartis	Immunosuppressant
Ritonovir	Norvir	Abbott	AIDS
Lopanavir	Kaletra	Abbott	AIDS
Isotretinoin	Accutane	Roche	Acne

Table 2*: *Marketed preparation

Use of Micro-Emulsion in The Delivery Medical Care

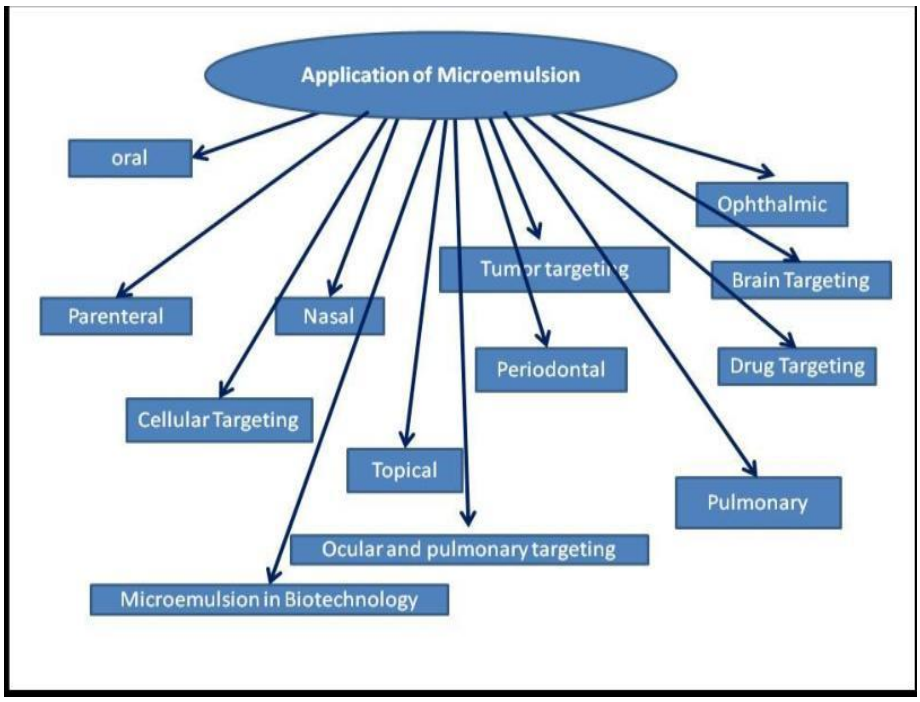

Figure 4*: *Application of Microemulsion

Oral delivery

Specialists have historically challenged to develop successful oral methods for administration when poor solubility or instabilities in digestive fluid can limit effectiveness for therapy. Micro-emulsion having the possibility for solving absorption complications connected with disintegrating and to improve the dissolving of drugs with poor solubility (BCS of class II or class IV in particular). When aqueous medications have polar substances non-polar even intermediate regions, they may be packed with a variety of the solubility of including molecules. These developments increase permeability of Membrane by preventing the included drugs avoiding oxidizing and enzyme breakdown. Microemulsion formulation such sand immune Neoral (R) (Cyclosporine A), Fort vase (R) (Saquinavir), Norvir (R) (Ritonavir), etc. are presently provided for sale. Microemulsion manufacturing composition may be effective to increase the oral absorption of weakly water- soluble drugs through making them more easily soluble in stomach liquid.[26]

Parenteral delivery

Developing intravenous medicinal products dose formulations with hydrophobic as well as lipophilic substances proved to be hard. O/w small emulsion can be used for the parenteral distribution of small amounts of drugs when it is unnecessary to use the treatment. They supply a means to acquire these medications at a respectably high concentration, that's frequently requires repeated administration.

Topical delivery

The advantages of cosmetic delivery of medications over alternative techniques involve avoiding metabolic metabolism in its initial phase, drug the breakdown in the salivary and digestion, and related negative effects. Additional benefit is that the medicine will be specifically targeted and applied to the harmed skin or cornea. In recent times, a lot of studies has been carried out regarding this topic of drug transmission via skin. Drugs such as testosterone, finasteride and ketoprofen to, meloxicam to felodipine to, and the triptolide, products can be both aqueous and lipophilic in nature may be added and its absorption improved. Such these drugs are this medicine, apomorphine hydrochloride, 5-flurouracil, diphenhydramine hydrochloride, and tetracaine hydrochloride. As the emulsion requires an elevated level of surfactant that skin irritation must be taken into your head, particularly if it can be applied over a long amount of contact.[27]

Ophthalmic delivery

Water-soluble drugs are given as aqueous solutions in conventional ocular dosage forms, whereas water-insoluble drugs are prepared as suspensions or ointments. These techniques have numerous serious problems, such as inefficiency in the posterior region of the ocular tissue and limited corneal bioavailability. Recent research has focused on developing new and better distribution strategies. Microemulsions are a possible effective dosage form for ocular use. Common eye drops, which are used to treat keratitis and trachoma, easily hydrolyse the antibiotic chloramphenicol.[28]

Nasal delivery

Recently, research has focused on using microemulsions as a drug delivery mechanism to improve medication absorption through the nasal mucosa. Longer residence time on the mucosa is another benefit of using mucoadhesive polymer. Lianly and others looked at the implications of benzodiazepine on seizures that required medical treatment. At a dosage for 2 mg kg-1, they noticed that benzodiazepines could be absorbed by the respiratory tract very quickly, without the greatest drug level in the blood attained in two or three minutes.

Drug targeting

As the ideal objective of drug delivery now seems to be drug targeting to distinct tissues. One can obtain greater drug efficacy with a corresponding decrease in adverse impacts include changing the way that medications are transported especially absorbed, and by reducing the extent of activity within the targeted tissue. Clainomycin a (ACM), a lipophilic antibiotic that targets tumors, has a new microemulsion formulation that was reported by Shiokawa et al. There is a possibility to distribute ACM tailored to tumors by a folate-linked microemulsion. They also mentioned that emulsions modified with folate and a long enough PEG chain can be effectively targeted to tumor cells.[29]

Periodontal delivery

A group of degenerative inflammatory conditions related to the oral transmission, including inflammation and disintegration of the oral tissues, periodontal tendons and ligaments cementum, and the bone supporting it, collectively are referred to as "periodontia". It correlates substantially to losing teeth. Brodin and associates, developed a new pharmaceutical formulation that included water, surfactant, a regional anaesthesia using oil, and maybe a taste-masking agent.[30]

Cellular targeting

Nucleic acids have significant medicinal value after they are transported to neurons. Monahan was et al. inserted the nucleic acid into opposing particles for encouraging cell motion. They identified them as reversing micelles-free microemulsions. The opposing micelle's capacity to reduce the nucleic acid made its delivery easier. To keep improving delivery, further molecules, such as a polyion or a solvent with disulphide bonds, may be supplied inside the genetic acid-micelle combinations.

Brain targeting

A simple, practical, inexpensive, easy, and transparent way of providing medications consists of intramuscular administration, resulting in a fast delivery of the medical school to the nervous system. It promotes the directly transport of drugs to neurons through removing the cerebral boundaries. Vyas and others created a the adhesive microemulsion that of the antiepileptic medicine a medication called. The aim was rapid delivery to the animal brain.[31]

Ocular and pulmonary delivery

Drugs are typically used topically to manage complications connected to one’s vision. The use of O/W microemulsions for optical delivery, dissolving drugs (in particular for little-soluble treatments), absorbed additions, and prolonged absorption structure are currently investigated.[32]

CONCLUSION

Microemulsions are new, easy-to-use, and inexpensive drug delivery systems that can improve medication absorption while minimizing systemic side effects. Without increasing systemic absorption, they may be applied to the procedure for maximum targeting drugs. While creating microemulsions, it is essential to choose the right excipients and assess their safety, particularly with regard to co surfactants. They could be used as possible drug delivery devices to administer multiple medications at once. Research has demonstrated that microemulsions can effectively safeguard drugs that are labile, decrease patient variation promote treatment the solubility of promote accessibility, and manage release of drugs. It is also believed that it truly can be achieved to develop arrangement acceptable for most administration methods. With a number of recent investigations focused on enhancing delivery of drugs, more research needed to be carried out on the characteristics of the pharmaceuticals, specifically experimental assessment. But toxicological

examination of the ready the microemulsion is not available, possibly opening up a wide research avenue in the future.

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