IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Review Article
May 2022 Vol.:24, Issue:2

Overview of Micro-Emulsion for Wound Healing Activity

IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Madhuri Manikrao Landge

Latur college of pharmacy, Latur, Maharashtra, India.

Submitted: 24 April 2022
Accepted: 29 April 2022
Published: 30 May 2022

Keywords: Spontaneous emulsification, Interfacial theory, Solubilisation theory, Thermodynamic theory, Skin, Body, Micro-emulsion.

ABSTRACT

Microemulsions refer to the thermodynamically stable substance which is made up of oil and water and it is a clear dispersion of these two elements. Here, the report has reflected the characteristics and preparation methods of the microemulsion. This study highlights the efficiency and effectiveness of topical medications. The entire skin of the human body is nourished and penetrated by topical medications. The study has discussed the multiple formation types of the microemulsion. Several theoretical explanations are given to clarify the efficacy of the microemulsion for wound healing. The study has reflected on its methodology and has analyzed the data in a disciplinary manner. It can be said that the study may help in the future to observe the theory of micro-emulsion from different aspects.

1. INTRODUCTION

Microemulsions are the thermodynamically stable liquid substance of oil and water and it is a clear dispersion of these two elements. The microemulsion is produced when a mixture of the surfactants and the co-surfactants lowers the interfacial tension of the oil and water which allows the thermal motions to disperse two immiscible phases. However, it is not like the conventional emulsion and its domains fluctuate in size and shape. Microemulsion undergoes spontaneous coalescence and the breakup. Microemulsion exhibits the water-continuous or the discontinuous structures with equilibrium domain and the size can be from 100 to 1000 A. Low surfactant produce the micro-emulsion in the equilibrium with dispersed phase. Micro-emulsion systems are discussed in a broad range of the technological applications here, in this study the multiple factors regarding Micro-emulsion are investigated in a broad range and the influencing factors for wound healing.

2. ANATOMY AND PHYSIOLOGY OF SKIN

The skin of human beings is formed with three layers such as the epidermis, the dermis, and subcutaneous tissue. According to the statement of Bani (2021, p. 105), the outer layer is known as the epidermis, and then comes the second layer which is known as the dermis. The inner layer is considered the subcutaneous tissue. Various aspects of human health are circulated and controlled by the skin of human beings. From the perspective of Reddy *et al.* (2021, p. 1961), one of the instances of these aspects is that the temperature of the human body is regulated through hair and sweat. Some changes are also controlled by the skin and peripheral circulation is one of these changes. Vitamin D is also synthesized by the skin and this vitamin is absorbed from the sun. There are a total of seventy hair follicles on the surface of the human skin. As per the opinion of Lawton (2019, p. 30), per square meter of the skin consists of approximately three thousand sweat ducts. The skin works as a protector of the human body. It protects the body of human beings from changes in temperature, several mechanical pressures and mechanical impacts, harmful chemicals, and different radiation.

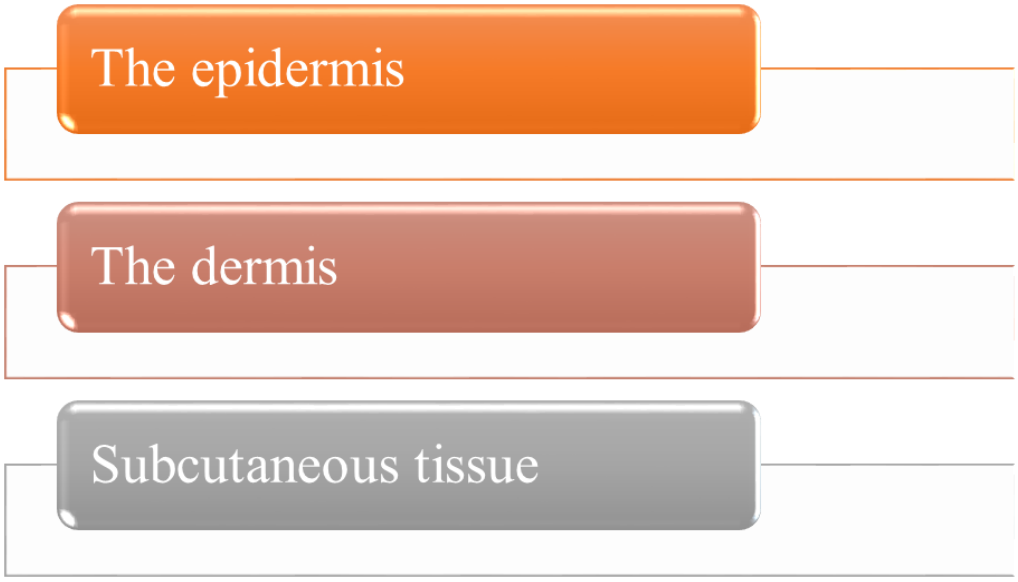

Figure No. 1: Anatomy of human skin

(Source: Learner)

The skin of human beings plays an indispensable role in acquiring senses. There is an unfathomable connection between the nerve cells and the skin. Skin works as the network of nerve cells. Several receptors are there in nerve cells and these receptors are pain, touch, cold, and heat. Skin performs multiple functions in the human body water loss is controlled by the skin, the sensation is created by the skin, and water resistance is also provided by the skin.

3. Topical drug delivery system

A topical drug delivery system refers to a specific method through which medication is delivered. According to Menditto *et al.* (2020, p. 12), the application of this kind of medication happens on the skin and these medicines are applied in the field of treating several skin diseases. Topical medicines consist of several forms like gels, lotions, powders, and patches. As per the viewpoint of Yousuf *et al.* (2020, v. 16), these medicines are generally composed in the form of ointments. Products related to topical drug delivery have two kinds such as internal topical and external topical. The application of internal topical products occurs on the mucous membrane and external topical products are utilized on the diseased portion. Some issues that are created by topical medications are allergies and irritation on the skin. A limitation is drawn by topical drugs in the case of hydrophobic medications. Solubility works as an obstacle in the way the mixing of hydrophobic drugs into a gel. In this case, this problem is solved by the emulgel because there is a possibility of

creating a mixture of gel base and emulgel. There are some benefits of the topical drug and these benefits have been discussed below:

- ***Decrease the risk:***

Issues related to drug abuse are prevented with the aid of topical medications. Patients get addicted to drug abuse while these people continue to take pain medications. Topical medications help these patients to protect themselves from drug abuse.

- ***Decrease the congestion in hospitals:***

Topical medications help patients to save money. Patients are also able to manage their time with the aid of topical medications.

- ***Reduction of the fear of people:***

In the opinion of Kale (2017, p. 39), many people are afraid of tablets and injections. In this case, topical medications have reduced the fear of these patients.

The popularity of topical drug delivery systems has escalated for the affordability and convenience of this kind of medication. Topical drugs have concentrated upon the minimization of side consequences. In recent days, the topical drug delivery system has been popularized because it brings safety and this kind of medication has also shown its efficiency. “Topical administration” is considered the most acceptable way in the field of local delivery. There are some drawbacks to topical drug delivery systems like low bio-accessibility and “poor retention”. Topical drug delivery methods are too easy to be utilized and hence, patients who have various skin issues, focus on topical medications. There are generally two ways through which topical medication is applied in the human body. These two ways are mucous membranes and skin; the skin is nourished with the aid of topical medication. According to the statement of Rivera-Rangel *et al.* (2018, p. 60), it brings a strange and outstanding refreshment to the skin of the human body. Topical medication protects the skin from damage. In the viewpoint of Jiang *et al.* (2020, p. 5437), this type of medicine is absorbed under the skin by the middle layer, the dermis. This kind of medication gets mixed within the bloodstream. The skin is protected by the topical medication and in this case, sunshine, air, and moisture are prevented by this type of medicine. The skin of the human body is penetrated by topical medication. Topical medication consists of excessive low cost

and it prevents the metabolism of the skin. This kind of medicine can be dispersed throughout the skin of human beings.

4. IMPORTANCE OF MICRO-EMULSION

Biological membranes can absorb drugs with the aid of micro-emulsions. Micro-emulsion has been capable of achieving significant attention from scientists since it has been discovered for its excellent properties which are related to solubility, stability, simplicity, or formulation aspects. Application of the micro-emulsion is not confined to the drug delivery through the 'ocular' and 'oral' routes but it is also seen in immunology, in sensor devices, coating, and also in the textile and analytical chemistry or the spermicidal. Finally, it can be said that the rationale of this study is to briefly discuss the various applications of the 'micro-emulsions' and their advancement in the drug delivery system. In today's globe as explained by Attwood can be discussed as the micro-emulsion is the mixture of the water, oil, or the 'amphiphilic' compounds- the surfactant or the co-surfactant compounds that are visually isotropic, 'thermodynamically liquid' and transparent.

The size of the droplet may revolve around 10 to 200 nm and broadly it is divided into 3 major types- O/W micro-emulsions, 'W/O micro-emulsion, and the 'bicontinuousmicro-emulsion' which contains huge solubilizing power. The rationale of this study is to study the significant power of micro-emulsions in wound healing. The mechanism of its action of it on the skin is very unique since it tends to react with the lipids of the skin. As a result of the penetration, the intercellular part is transformed and here the drug is transported. According to Golwala *et al.* (2020), the prime distinguishing feature of the emulsion and the micro-emulsion depends on the size of the droplet in the dispersed phase. The rationale of this research is to analyze the major differences between the applications of 'emulsion' and 'micro-emulsion'. Micro-emulsions are considered as promising tools or ingredients as the delivery system and it allows both types of drug releases for multiple administration routes.

The reason for the research on micro-emulsion is to identify how the micro-emulsion penetrates for wound healing and its broad spectrum of applications targeting drugs and controlling the drug revelation. Micro-emulsions consist of multiple distinguishing features like it is less toxic, facilitate the enhanced absorption of the drugs, and also regulate the scale of drug release varies significantly. From viewpoint of Bonfanti *et al*. (2018, p. 103), micro-emulsion contains unique characteristics like it enhances the bioavailability for their

capability of solubilizing the lipophilic drugs. The rationale of this research is to focus on these capabilities to get a view of its actions. Another purpose of the research is to discuss the different thermodynamic properties of the 'micro-emulsion', such as free energy, the surface tension, or the interfacial area which are independent in terms of unique algebraic equations. It can bear the water-soluble drugs into the aqueous phase.

The study has focused on the wheel-defined linkage between different properties and on the interfacial area of the micro-emulsion. It differs from the conventional emulsion. The preparation procedure of micro-emulsion is very straightforward and contains a lipophilic surfactant. This paper has concentrated on the wheel-defined linkage between different properties and the interfacial area of the micro-emulsion. It differs from the conventional emulsion. According to Kumar *et al.* (2020), in today's world, it can be very useful for wound healing and the research can be helpful in this context. The inquiry through this research has reflected on the different advantages and disadvantages of micro-emulsion with its unique features. Micro-emulsion aids the lipophilic drug to be solubilized. The study related to micro-emulsions is considered as the systems related to drug delivery. Effective penetration of topical medication to the skin is explicitly shown in this paper. One of the disadvantages of topical medications is the sticky nature of this kind of medicine.

5. Formulation

5.1 Formulation of microemulsion

The notion of the micro emulsion was at first advocated by ***Hoar*** and ***Schulman*** in the year of 1940. Micro-emulsions are formed with water, oil, and surfactant and these are considered isotropic. There is also the presence of co-surfactant in the micro-emulsions. The mixture of microemulsions has stability and clarity. There are several ingredients in the mixture of microemulsions like ethanol, plurololeique, isopropyl alcohol, aceclofenac, itraconazole, cottonseed oil, soybean oil, oleic acid, nimesulide, and olive oil.

5.2 Formulation of emulgel

Emulgel refers to the amalgamation of gel and emulsion. Several components are utilized at the time of the formulation of the emulgel. These ingredients are gel-like sodium carboxymethyl cellulose, oils like maize or cottonseed oil, alcohol, water, emulsifiers like stearic acid, and an agent of pH adjustment like sodium hydroxide. As per the perspective of

Rivera-Rangel *et al.* (2018, p. 60), emulgel helps people to reduce the pain in joints and muscles. It also provides relief from sports wounds and strains.

6. Types and the process of preparation of the micro-emulsion

Types

Given Windsor, four types of the micro-emulsion phases are in existence in the equilibrium and these phases are mainly referred to as the Winsor phases. The four types of Winsor phase are-

Windsor I- It is a two-phase system, the upper layer of it consists of the oil and it exists in the equilibrium in the lower micro-emulsion phase.

Windsor II- It is also a two-stage formation, the O/W or upper 'micro emulsion' exists in the equilibrium in the lower with excessive water.

Windsor III- It is a three-phase system, the middle bi-continuous stage exists in the equilibrium and the upper phase of it consists of oil while the lower phase of water.

Windsor IV- It is the only single-phase system among the four and it forms a homogeneous mixture of oil, water, and surfactant.

The R-ratio- The r-ratio is the feature concept and it was proposed by renowned Winsor too to describe the significance of the amphiphiles and the solvents on the interfacial curvature. The r-ratio mainly compares affinity for dissolving in the water. If one of these phases is significantly favored, the interfacial region prepares definite curvature (Richard *et al.* 2017).

Preparation method

Microemulsion refers to a colloidal system that is cloudy and there are few droplets in microemulsion. According to the statement of Jiang *et al.* (2020, p. 5437), one of the instances of the microemulsion is the mixture of oil and water. Co-surfactant and surfactant are also present in microemulsion. Microemulsion refers to the integration of surfactant, co-surfactant, and oil. In this mixture, water is also included with the aid of magnetic stirring at 37 degrees C temperature. Some steps are followed at the time of the preparation of the microemulsion method. At first co-surfactant, surfactants and oil are brought. Several oils and surfactants are utilized to examine the solubility of the drug. In case there is an excessive

amount of drug, then this is added to oil which is mixed with co-surfactant and surfactant and the amount of this drug is 5 mL. As per the opinion of Bonfanti *et al.* (2018, p. 103), excessive solubility helps the drug to be dissolved in the oil. After that surfactant and cosurfactant are included in a specific zone where the solubility of the drug is excessive. In this way, the microemulsion is prepared with the help of surfactant and co-surfactant. The preparation methods of the micro-emulsion include-

- High energy emulsification method- The ultrasonication is prepared at high pressure.

- Low energy emulsification method- It is the phase inversion method where the solvent displacement or phase inversion method appears in the formation of micro-emulsion.

- High-pressure Homogenization- It is designed especially with high-pressure instruments to form nano-sized particles. At a very high pressure which is almost 500-5000 psi, the oil phase, and the water phase are placed to force through the small inlet. Hence, the extremely small-sized particles are formed due to the very strong turbulence and the hydraulic shear. But this procedure requires a high temperature and the energy to form those particles. According to Sharma *et al*. (2017), high pressure in the homogenization is mainly responsible for the nano-sized particles (Sharma *et al.* 2016).

- Microfluidization- In this particular method device is specially designed which is named a microfluidizer. It is mainly used to create the high pressure which varies from 500-20000psi. Initially, it forms a coarse emulsion mixing the oil and the water phase. The device is made up of the interaction chamber of many small channels by which the coarse emulsion is mistaken for forced impingement to form very small-sized and fine particles which are followed by the filtration to gain the small uniform particles.

- Ultrasonication- This preparation method depends on the principle that when the coarse emulsion appears in the ultrasonic field the external pressure is increased and the cavitations thresholds are also increased to form those fine and small particles.

- Phase inversion- This method follows the principle of the inversion temperature where the phrase transition appears. The low temperature nurtures the O/W emulsion whereas the very high temperature affects the W/O emulsion. According to Tagavifar *et al.* (2018), the cycles of rapid cooling or heating help in producing fine particles. The non-ionic surfactant,

such as polyoxyethylene appears as lipophilic at the high temperature and the hydrophilic at the low temperature respectively due to the dehydration of the polymer cycle.

- Spontaneous emulsification- It is a very simple method and it is used as a volatile organic solvent of oil, the water, the lipophilic, and the. Hydrophilic surfactant. The composition is permitted to make the mixture homogeneously through magnetic stirring. After that, the evaporation of the water-miscible solvent leads to the nano-emulsion.

- Solvent evaporation- Initially this technique mixes the drug with the organic solvent by using a suitable surfactant and it prepares the O/W emulsion in the continuous phase. After that, the evaporation of the organic solvent under the vacuum or heating to gain the microspheres loaded with the drug is followed by centrifugation.

- Hydrogel Method- It is similar to solvent evaporation where high shear is forced to prepare the nano-emulsion of the drug solvent (Shukla *et al.* 2017).

The types and the concentration of the initiator, the surfactant, and the temperature are considered very crucial factors which affect the micro-emulsion very significantly. Several interesting characteristics of the micro-emulsion consist of enhancing the drug solubilization, effective thermodynamic stability, the ease of the preparation, and the fine and nanodroplet size. These vibrant and crucial characteristics are very unique and they develop the very core of the microemulsion formation. Today the effectiveness of the micro-emulsion is seen in many areas of drugs used to produce the effective medicine for the wound and it is widely accepted by today's scientists.

7. CHARACTERIZATION

7.1 Characterization of microemulsion

There are some basic traits of microemulsion like the comfort of processing, little size of droplets, well “thermodynamic stability”, the ability of high drug loading, conductivity, and centrifugation. Measurement of different characteristics of microemulsion has been discussed below:

- ***Measurement of conductivity:***

There is a particular measurement process of the conductivity of microemulsion and this measurement is taken with the aid of a digital conductometer. The conductivity of microemulsion is measured at the temperature of the surrounding area.

- ***Measurement of pH***

A digital pH meter helps to measure the pH of the microemulsion. According to the statement of Kale (2017, p. 39), in this particular case of measurement average consequence is considered. There is a huge requirement of checking the pH of micro-emulsion because a little bit of change can affect the stability and quality of the product.

- ***Measurement of viscosity***

Viscosity helps to apprehend the basic properties and traits of the mixture of the microemulsion. Viscometer Brookfield Rotational is applied in the field of measuring viscosity.

- ***Centrifugation***

Centrifugation is utilized in the case of measuring the physical capability of the micro-emulsion and this measurement also helps to assess the physical stability of the mixture.

- ***Measurement of drug***

Method related to UV visible spectroscopy is utilized in the case of measuring the drug content.

- ***"Zeta potential"***

In the perspective of Jiang *et al.* (2020, p. 5437), the "dynamic light scattering technique" is utilized to measure the "zeta potential" of the micro-emulsion.

7.2 Characterization of microemulgel

Characterization of microemulgel has been discussed below:

- ***Measurement of the main viscosity***

Viscosity is measured with the aid of a Brookfield viscometer and this measurement is taken at the temperature of 37 degrees C.

- ***Measurement of drug content***

In this case, VIS and UV spectrophotometer is utilized at the time of measuring drug content.

- ***Study of skin irritation***

In this case, the skin of rabbits is utilized and the mixture which is utilized on the skin of rabbits is 0.5 g. The skin of rabbits is generally hair free and this mixture is spread on a $4cm^2$ area of the skin of rabbits. Then, the skin is noticed carefully to check the skin irritation.

8. MICRO-EMULSION

Emulsions are the dispersions that are prepared with two basic liquid stages and they are blended using the 'mechanical shear' and the surfactant. The 'amphiphilic surface' based particles are identified as the 'surfactants'; it reduces natural attractive forces as 'surface tension'. The surfactant is based on HLB ('hydrophilic-lipophilic balance') or on the CPP ('critical packing parameter') to develop the desired emulsion. Micro-emulsions are the transparent, 'thermodynamically stable' and 'isotropic liquid' which is prepared by mixing oil, water, and the surfactant. Micro-emulsion incorporates small particles, nano-size particles in comparison with the traditional emulsion. According to IUPAC, it is the dispersion that is made of these things. It is isotropic with a domain diameter that varies from 1-100 nm approximately, usually 10-50 nm. It is easy to produce or scale up for the spontaneous ability of formation and it is also considered a very good system that increases the absorption rate as well as the bioavailability by eliminating the interfacing variations.

The prime ingredient of the microemulsion consists of the 'oil-phase', the 'surfactant' (the 'primary surfactant'), 'co-surfactant' ('secondary surfactant'), and the 'co-solvent'. Usually, saturated fatty acid, lauric acid linoleic acid, ester ethyl, myristic, and oleic acid are used as oil components in micro-emulsion. According to Nastuiti *et al.* (2017), the surfactants are polyoxyethylene, the 'polysorbate', 'Tween 20, 40, 60, 80', the 'sorbitan monolaurate', sodium deciding sulfate, sodium deoxycholate, the labrasol or the dioctyl sodium sulfosuccinate which are used in micro-emulsion preparation while the co-surfactants are

ethanol, isopropanol, butanol, propanol, hexanol, sorbitol, hexanoic acid, butanediol, cinnamyl alcohol, cinnamic aldehyde or many more.

The oil phase of the micro-emulsion is the second most necessary component vehicle after the water which is important for its properties and it helps to solubilize the 'lipophilic drug particles' and it improves the absorption by the lipid layer which is present in the human body. Given Okur *et al.* (2020), it has the unique property to penetrate the cell wall. Hence, the oil component is very useful for the lipophilic active delivery of the drugs. The swelling of the tail group region of surfactant micro-emulsion is influenced by the oil phase. The surfactants must be capable of decreasing interfacial tension during the preparation of the microemulsion. The surfactants can be 'non-ionic', 'anionic', 'cationic', or 'zwitter ionic'. The nature of these surfactants helps to decide the stability in micro-emulsion formation.

'Dipole' and the 'hydrogen bond' stabilize the 'non-ionic surfactant' and the electrical part mainly stabilize the 'ionic surfactants. The ionic surfactants are affected by the salt present there. Hence, it is sensitive regarding the sensibility issues and the toxicity concern. But the non-ionic surfactants produce the non-toxic pharmaceutical dosage; hence it is more popular than the rest. The surfactants in terms of HLB are important in 'W/O micro-emulsion. The surfactants with more than '20 HLB values' are important in the preparation of 'O/W emulsion'. It is observed that a high concentration of the single-chain surfactants is necessary to decrease the O/W tensions to enable the spontaneous formation of the 'micro-emulsion'. However, with the co-surfactants, minimum concentrations of different curvatures can be produced to generate a stable micro-emulsion composition. Given Patel *et al.* (2014), the co-surfactants mainly affect fluidity due to the presence of the 'fluidizing groups', such as 'unsaturated bonds', and then it affects the 'liquid crystalline' or the 'gel structure' and replaces 'HLB value' to gold the spontaneous formation of the microemulsion.

While discussing the micro-emulsion., it is also necessary to focus on the co-solvent which are the organic solvents like the ethanol, PG, or PEG that help in resolving high concentrations of the surfactants or the drugs which are lipid-soluble. Here, the co-solvents are also identified as co-surfactants.

Advantages and disadvantages

The advantages of the micro-emulsion are the following-

- It can be prepared very easily and can be scaled up for its spontaneous formation capability.

- It is considered a very unique and useful system to enhance the rate of absorption like the bioavailability by cutting the inferring variations very easily.

- Micro-emulsion can enhance the solubility of the 'lipophilic drugs'.

- Thermodynamically it is more stable compared with the traditional one and for this, it is more effective for long-term usage (Qin *et al.* 2017).

- It may be preferred more to develop the sustained releases of the drug system.

- It is one of the best systems to minimize the first metabolism very easily.

- Micro-emulsion increases the bio-accessibility and in this way, it brings a dose reduction.

- According to the statement of Bonfanti *et al.* (2018, p. 103), it brings betterment in the storage stability, and in this case, lymphatic transport is escalated for the lipids.

- There are several fields in which micro-emulsion is utilized and these areas are sensor devices, cosmetics, analytical chemistry, textiles, spermicide, and immunology.

Besides these unique and effective advantages of micro-emulsion, there are several disadvantages of it too. The disadvantages of the micro-emulsion are-

- The additional use of the excessive surfactant and the co-surfactants can increase the cost.

- Excessive concentration of the surfactants can cause mucosal toxicity (Golwala *et al.* 2020).

9. THEORIES

9.1 Interfacial theory

The other name for 'Interfacial theory' is 'mixed film' or the 'dual film theory'. The 'surfactant' and the 'co surfactant' actually form the crucial and complex film in collaboration at the oil-water surface and thus the generation of the 'micro emulsion'.

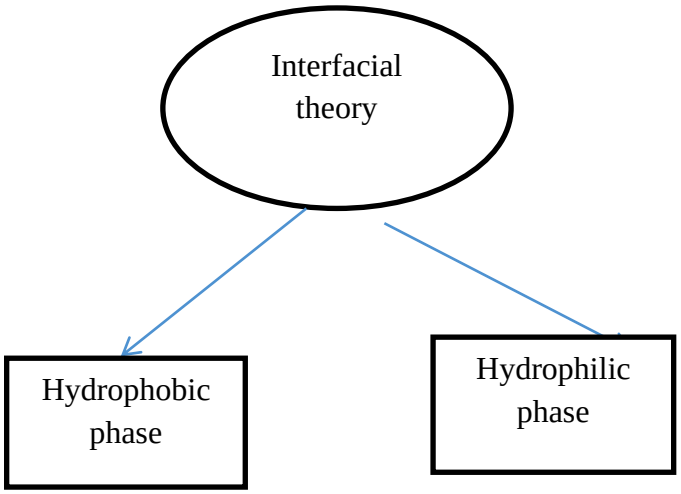

Figure No. 2: Interfacial theory

(Source: Learner)

9.2 Solubilisation theory

Solubilization theory describes that the micellar system forms as the 'micro-emulsion'. The oil was solubilized due to the general 'micelle formation and the water was solubilized by the 'reverse micelle preparation'.

9.3 Thermodynamic theory

When the interfacial tension among the two phases decreases to '0', it results in natural formation and forms the negative free energy which helps to make the emulsion stable 'thermodynamically' (Richard *et al.* 2017). Micro-emulsion is also referred to as the transparent emulsion, the swollen micelle, or the micellar solution. The shelf micro emulsifying delivery system of the drugs is also popular for the mediated delivery of the drugs. 'Micro-emulsion', the biological term was coined by 'Hoar and Shulman' describing the multiphase system which consists of oil, water, alcohol, and the surfactant. All of these components prepared a transparent solution in the year 1953. The discovery of this micro-emulsion has been confirmed using the inj form of the white spirit or the liquid waxes (Qin *et al*. 2017).

10. APPLICATION ON DRUG DELIVERY

The use of microemulsion is beneficial in the administration of oral formulation, as they offer a variety of advantages such as improved clinical potency, absorption factor, and use of fewer drugs. Therefore the use of microemulsion has been regarded as the most convenient carrier of drugs such as steroids, hormones, diuretics, and antibodies. According to Callender *et al*. (2017), the application of microemulsion is useful in various drug usage such as in tropical delivery, as microemulsion can deliver a large portion of water. The tropical agents into the skin more than any other traditional carrier such as lotion or cream into the skin because microemulsion has the property to act as a reservoir for certain drugs that are poor insoluble. The developments of antifungal lotion along with the microemulsion have been made successfully like miconazole nitrate.

The creation of clotrimazole and fluconazole which is a micro emulsion-based made for the vaginal delivery was developed and rather made compared with the market-based gel clotrimazole through the process of *vitro* method. The creation of microemulsion has significantly increased the absorption factor in both lipophilic and hydrophilic medication as compared to the other carriers like oil, cream, or any kind of aqueous solution. As per Tagavifar *et al*. (2017), due to its improved mechanism and behavior microemulsion has received great importance in transdermal drug delivery. Along with its tropical usage microemulsion is also applicable in the ocular drug delivery application, such as in the treatment of eye disease microemulsion is used to dissolve the drugs to improve and enhance the absorption capacity. Microemulsion possesses a wide range of advantages as the ocular delivery carrier.

Thereby offering low surface tension, stability in thermodynamics, creation of liquid crystal state and small size of the droplet that can improve the retention capacity of the ocular and improve the permeation of loaded drugs is necessary. Despite possessing various advantages the ocular route also curtails some disadvantages as the eye drop is the most common route for ocular dosage but it can also be treated as low biodiversity and increased pulsed release apart from that it also offers stability and specific structure that are beneficial in use. According to Volpe *et al*. (2018), another use of microemulsion is in the application of cosmetics, microemulsion provides enhanced stability, and solubility power and also eases penetration which intern enhances the skin with loaded substances thereby reducing the toxicity from the skin. The cosmetics and substances that are used in the microemulsion tend

to be absorbed by the skin and improve the condition of the skin. The use of microemulsion in cosmetics is highly concerned with safety and cost as most people are not suitable for certain products hence the use of lecithin, and sodium alkaline sulfate are used in the microemulsion formula to reduce the change inflammability. The main topic of the article deals with the concept of microemulsion and its related facts. However there have been several types of research done and relevant information has also been found about the use of microemulsion in the wound healing process along with its various applications, its characteristics, and also the advantages and the disadvantages of the microemulsion. However, after considerable research, there have been some facts that have not been found in the research and that is the future scope of the microemulsion, different innovations, and development in the field of microemulsion with its limitations?

11. ANALYSIS OF THE TOPIC

After the discussion of the various methods required for conducting the research, it is now required to evaluate all the objectives individually using a theme. It has been found that the topic consisted of objectives that discuss the analysis of the microemulsion process in wound healing, along with the advantages and disadvantages, characteristics of the microemulsion, and lastly find out how microemulsion works for wound healing. However, the themes mentioned below have been formulated to derive a clear overview of the topic and its significance in the current scenario.

11.1 Evolution in the wound healing process

The cause of any damage to the skin can be from various reasons it can be caused by a burn or any other chemical reactions. The problems arising from a burn can act as a critical factor and the microorganism that causes infection in the wound has also evolved over some time. Hence to initiate the result it is important to start the wound healing process right from the moment of injury. Most antimicrobial agents have been designed to use prophylactically to prevent the infection, while some others have been designed to kill the microorganism and its ability to cause infection. Over some time the treatment procedure has evolved thus creating more convenient and effective ways in the wound healing process such as the inclusion of microemulsion. It is regarded as a thermodynamically stable liquid solution consisting of oil surfactant and aqueous solution.

It is the homogeneous dispersion of water in oil or oil in the water droplet, they are considered useful and inexpensive. As per Pal *et al*. (2019), the implication of microemulsion onto the skin can be challenging due to its property of low viscosity. Hence to optimize the microemulsion as the dermal formula different agents of hydrogels like chitosan, carbomer, and xanthan gum have been studied and applied in the microemulsion process to improve its viscosity. To minimize its effect the thickening agent can be used in the system to transform it into a semi solid-state from the liquid state. This will lead to the creation of micro emulsion-based hydrogels that are comparatively easier to apply to the skin as compared to the other runny liquid formulation. Along with that, the gel-based micro-emulsion allows for a permeable ability to restrain and also suitable viscosity for the topical delivery that provides longer resistance to the skin.

11.2 Positive and negative impact of microemulsion

The microemulsion as a drug delivery system improves the therapeutic efficiency of the drug along with reducing the volume of the drug delivery system by reducing the toxic level. The use of microemulsion is considered to be beneficial for those children and adults that face difficulty in swallowing tablets along with oral administration that includes improved clinical potency and decreased toxicity level. According to Mico *et al*. (2017), the microemulsion is considered ideal for the delivery of drugs taken orally such as steroids, hormones, diuretics, and antibiotics. The use of microemulsion as a drug delivery system offers excellent potential and additional benefits because of its high thermodynamics stability, transparency, high dissolution, and absorption rate.

However, the use of microemulsion required certain environmental parameters such as temperature, and PH level. Along with it, acceptance of its ingredient by the pharmaceutical industry and the concentration of surfactants and co-surfactants needs to be kept low to reduce the toxicity level and it requires high solubility capacity for the lipophilic and hydrophilic drugs in the microemulsion process.

11.3 Recent development in technologies

The rationale behind the exploration of water into the oil is to protect the water-soluble drugs, mainly protein and peptides from metabolism and also to overcome the physical barrier. These are in hand considered to be useful as these drug molecules are sensitive to heat and do not require high temperature for their formulation. As per Maeda *et al*. (2019), the addition of

microemulsion with the encapsulated active pharmaceutical ingredient is likely to convert the oil into the water after the addition of the aqueous solution into the microemulsion leading to the release of the API in the required location. The microemulsion used in the form of oral drug delivery comes with a self-emulsifying ability; these are known as self-micro emulsifying drug delivery systems due to their ability to deliver hydrophobic drugs.

Despite having several usages and the increased dissolution and the bioavailability of the API in the oral form of drugs as well as the SMEDD are necessary to be observed. It has not been commercially exploited and used in the industry widely due to several factors such as a lack of knowledge on how to manage and operate the drug molecules in the system between the oil and the aqueous solution. Hence further research has been conducted to understand and establish the drug's relation with those of its related molecules along with its exploiting different aspects and related advantages of the microemulsion in the drug delivery system.

12. CONCLUSION

It is clear from this discussion that topical medicine heals many skin diseases effectively. The main finding of the topic consisted of the conversion of microemulsion in the drug delivery system. However, there were several findings related to the concept of microemulsion indicating various theories related to the microemulsion and its development over different stages. After considerable research on the topic, the conclusion that can be drawn from the analysis is that introduction of microemulsion in the drug delivery system has improved the overall system of drug delivery and opened wide different ranges of development associated with it that can improve the medication facility all over the structure.

REFERENCES

1. Abrar, I., & Bhaskarwar, A. N. (2019). Micro-emulsion fuels for compression ignition engines: A review on engine performance and emission characteristics. *Fuel*, *257*, 115944.
2. Bani, K. S., & Bhardwaj, K. (2021). Topical Drug Delivery Therapeutics, Drug Absorption, and Penetration Enhancement Techniques. *Journal of Drug Delivery and Therapeutics*, *11*(4), 105-110.
3. Bonfanti, P., Saibene, M., Bacchetta, R., Mantecca, P., & Colombo, A. (2018). A glyphosate micro-emulsion formulation displays teratogenicity in Xenopus laevis. *Aquatic Toxicology*, *195*,103-113.
4. Callender, S. P., Mathews, J. A., Kobernyk, K., &Wettig, S. D. (2017). Micro-emulsion utility in pharmaceuticals: Implications for multi-drug delivery. *International journal of pharmaceutics*, *526*(1-2), 425-442.
5. De Assis, K. M. A., da Silva Leite, J. M., de Melo, D. F., Borges, J. C., Santana, L. M. B., Dos Reis, M. M. L., ... & de Lima Damasceno, B. P. G. (2020). Bicontinuous microemulsions containing *Melaleuca alternifolia* essential oil as a therapeutic agent for cutaneous wound healing. *Drug Delivery and Translational Research*, *10*(6), 1748-1763.

6. Froiio, F., Lammari, N., Tarhini, M., Alomari, M., Louaer, W., Meniai, A. H., &Elaissari, A. (2020). Polymer-based nanocontainers for drug delivery. In *Smart Nanocontainers* (pp. 271-285) Elsevier.
7. Golwala, P., Rathod, S., Patil, R., Joshi, A., Ray, D., Aswal, V. K., ... & Tiwari, S. (2020). Effect of cosurfactant addition on phase behavior and microstructure of a water-dilutable micro-emulsion. *Colloids and Surfaces B: Biointerfaces*, *186*, 110736.
8. Jiang, B., Wang, X., Wang, L., Wu, S., Li, D., Liu, C., & Feng, Z. (2020). Fabrication and characterization of a microemulsion stabilized by integrated phosvitin and gallic acid. *Journal of agricultural and food chemistry*, *68*(19), 5437-5447.
9. Kale, S. N., & Deore, S. L. (2017). Emulsion microemulsion and nanoemulsion: a review. *Systematic Reviews in Pharmacy*, *8*(1), 39.
10. Kumar, H., Sarma, A. K., & Kumar, P. (2020). A comprehensive review of preparation, characterization, and combustion characteristics of micro-emulsion-based hybrid biofuels. *Renewable and Sustainable Energy Reviews*, *117*, 109498.
11. Lawton, S. (2019). Skin 1: The structure and functions of the skin. *Nurs. Times*, *115*, 30-33.
12. Maeda, R., Ito, T., Tagami, T., Takii, T., & Ozeki, T. (2019). Development of Dried Emulsion/Mannitol Composite Microparticles through a Unique Spray Nozzle for Efficient Delivery of Hydrophilic Anti-tuberculosis Drug against Alveolar Macrophages. *Biological and Pharmaceutical Bulletin*, *42*(11), 1846-1853.
13. Menditto, E., Orlando, V., De Rosa, G., Minghetti, P., Musazzi, U. M., Cahir, C., ... & Almeida, I. F. (2020). Patient-centric pharmaceutical drug product design—The impact on medication adherence. *Pharmaceutics*, *12*(1), 44.
14. Mico, V., Charalambous, A., Peyman, S. A., Abou-Saleh, R. H., Markham, A. F., Coletta, P. L., & Evans, S. D. (2017). Evaluation of lipid-stabilized tripropionin nanodroplets as a delivery route for combretastatin A4. *International journal of pharmaceutics*, *526*(1-2), 547-555.
15. Nastiti, C. M., Ponto, T., Abd, E., Grice, J. E., Benson, H. A., & Roberts, M. S. (2017). Topical nano and micro-emulsions for skin delivery. *Pharmaceutics*, *9*(4), 37.
16. Okur, M. E., Ayla, Ş., Yozgatlı, V., Aksu, N. B., Yoltaş, A., Orak, D., ... & Okur, N. Ü. (2020). Evaluation of burn wound healing activity of novel fusidic acid loaded microemulsion based gel in male Wistar albino rats. *Saudi Pharmaceutical Journal*, *28*(3), 338-348.
17. Pal, N., Kumar, S., Bera, A., & Mandal, A. (2019). Phase behavior and characterization of micro-emulsion stabilized by a novel synthesized surfactant: Implications for enhanced oil recovery. *Fuel*, *235*, 995-1009.
18. Patel, R. R., Patel, Z. K., Patel, K. R., & Patel, M. R. (2014). Micro emulsion-based gel: recent expansions for topical drug delivery system. *J Med Pharm Allied Sci*, *1*, 1-15.
19. Qin, T., Javanbakht, G., Goual, L., Piri, M., & Towler, B. (2017). Micro-emulsion-enhanced displacement of oil in porous media containing carbonate cement. *Colloids and Surfaces A: Physicochemical and Engineering Aspects*, *530*, 60-71.
20. Reddy, R., Priya, S., Akula, G., Santhosh, S., &Jaswanth, A. (2021). Formulation and evaluation of Naproxen Emulgel for topical delivery. *Research Journal of Pharmacy and Technology*, *14*(4), 1961-1965.
21. Richard, B., Lemyre, J. L., & Ritcey, A. M. (2017). Nanoparticle size control in micro-emulsion synthesis. *Langmuir*, *33*(19), 4748-4757.
22. Rivera-Rangel, R. D., González-Muñoz, M. P., Avila-Rodriguez, M., Razo-Lazcano, T. A., & Solans, C. (2018). Green synthesis of silver nanoparticles in oil-in-water microemulsion and nano-emulsion using geranium leaf aqueous extract as a reducing agent. *Colloids and Surfaces A: Physicochemical and Engineering Aspects*, *536*, 60-67.
23. Singh/post/Can_anyone_suggest_methods_to_synthesis_nanoparticle_from_oil/attachment/5b64266db53d2f89289d1c52/AS%3A655480313638918%401533290093108/download/1-s2.0-S0927775717307008-main.pdf.
24. Sharma, A. K., Garg, T., Goyal, A. K., & Rath, G. (2016). Role of microemulsions in advanced drug delivery. *Artificial cells, nanomedicine, and biotechnology*, *44*(4), 1177-1185.
25. Shukla, T., Upmanyu, N., Agrawal, M., Saraf, S., Saraf, S., & Alexander, A. (2018). Biomedical applications of micro-emulsion through dermal and transdermal routes. *Biomedicine & Pharmacotherapy*, *108*, 1477-1494.

26. Tagavifar, M., Herath, S., Weerasooriya, U. P., Sepehrnoori, K., & Pope, G. (2018). Measurement of micro-emulsion viscosity and its implications for chemical enhanced oil recovery. *SPE Journal*, *23*(01), 66-83.
27. Volpe, V., Nascimento, D. S., Insausti, M., & Grünhut, M. (2018). Octyl p-methoxycinnamate loaded micro-emulsion based on *Ocimum basilicum* essential oil. Characterization and analytical studies for potential cosmetic applications. *Colloids and Surfaces A: Physicochemical and Engineering Aspects*, *546*, 285-292.
28. Yousuf, M. A., Jabeen, S., Shahi, M. N., Khan, M. A., Shakir, I., & Warsi, M. F. (2020). Magnetic and electrical properties of yttrium substituted manganese ferrite nanoparticles prepared via microemulsion route. *Results in Physics*, *16*, 102973.

Author -1

Author Name: Ms.Madhuri Manikrao Landge

– Corresponding Author

Author Affiliation: Assistant professor

Author Address/Institute Address:

Latur college of pharmacy, Latur.413512