



## A comprehensive review on microemulsions

Aysha Aslam\*, Saad bin zulfiqar, Javeid Iqbal, Rushda Bedar

*Faculty of Pharmacy, University of Lahore, Lahore, Pakistan*

**Key words:** Microemulsions, Surfactant, Pharmaceuticals, Oil, Cosmetics.

<http://dx.doi.org/10.12692/ijb/18.2.163-173>

Article published on February 26, 2021

### Abstract

Microemulsions are thermodynamically stable, transparent and isotropic liquid mixtures which are consisted of oil, water and surfactant. The particle size of the microemulsions may range from 10 to 300 nanometers. In this review, properties, structure, types, theories, characterization and applications of the microemulsions are discussed in detail. They can be prepared simply by mixing the different components without specific equipment and conditions. In w/o type, oil is the continuous phase and water as droplets are dispersed in it, whereas in o/w type microemulsion there is an aqueous continuous phase and oil droplets are dispersed in it. Microemulsions are widely used in pharmaceutical industries, cosmetics and analytical techniques. Microemulsions permit self-emulsification owing to the thermodynamically stable system and are utilized for the palatability of unpleasant drugs. The characterization of the microemulsions can be done by various methods, including microscopy, nuclear magnetic resonance and light scattering methods. Comprehensive knowledge of microemulsions will guide their physicochemical and biopharmaceutical properties that could be beneficial in designing the drug formulations and cosmetics.

\* **Corresponding Author:** Aysha Aslam ✉ [Ayesha.aslam@pharm.uol.edu.pk](mailto:Ayesha.aslam@pharm.uol.edu.pk)

## Introduction

Schulman upon imaging by electron microscopy in 1959 coined the term “microemulsion”. In order to define such systems, there has been much discussion around the word “microemulsion”. Though not methodically used nowadays, some favor the terms “swollen micelles” or “micellar emulsion”. Microemulsions were perhaps exposed well already before Schulman studies (Talegaonkar *et al.*, 2008). Rodawald in 1928 probably discovered the 1<sup>st</sup> commercial microemulsion and they were the liquid waxes. Danielsson gives the best description of Microemulsions as “a microemulsion is a system of water, oil and an amphiphile (surfactant + cosurfactant) which is a single optically isotropic and thermodynamically stable liquid solution” (Danielsson, 1981). In distinction with ordinary emulsions which are stable kinetically, unstable thermodynamically and phase separation occurs, the microemulsions are stable thermodynamically and no shear conditions and high energy inputs are required for their development (Lee, 2011; Sharma *et al.*, 2013; Hejazifar *et al.*, 2020). Microemulsion system forms while a surfactant or a blend of surfactants and co-surfactants, lowers the water/oil interfacial tension to extreme-low values (often  $< 0.001$  dynes/cm), and allow the dispersion of two immiscible phases spontaneously through thermal motions. Surfactant is a blend of lipophilic and hydrophilic groups in a single molecule and the percentage weight of these groups in surfactant is a signal of its performance. The act of a surfactant is projected by the HLB value, for example  $HLB > 10$  means O/W emulsion while  $HLB < 10$  would be good for W/O emulsion. If relative area of the head group is denoted by  $a_o$  and the tail area of surfactant is denoted by  $v/l_c$ , then (Gadhve and Waghmare, 2014).

If  $a_o < v/l_c$ , then W/O microemulsion

If  $a_o > v/l_c$ , then O/W microemulsion

Molecules of surfactant contain both non-polar and polar groups. Strange behavior is shown by them; initially, adsorption occurs at the interface, wherever they can accomplish their double duty with hydrophobic groups in air or oil and hydrophilic

groups positioned in aqueous part. Furthermore, the Micellization process diminishes mismatching with solvent (Saini *et al.*, 2014). The formation of the microemulsion is hooked on surfactant structure and type. Microemulsions are only designed if the surfactant is ionic and comprises a single hydrocarbon chain (e.g., SDS, sodium dodecylsulphate) plus a co-surfactant (e.g., a medium-size aliphatic alcohol) or electrolytes (e.g., 0.2M NaCl) are also present. A co-surfactant is not needed when consuming double chain ionic (e.g., Aerosol-OT) and certain non-ionic surfactants (Danielsson 1981; Chen *et al.*, 2018). Low viscosity, homogeneity and transparency are definite physical and chemical properties of microemulsions. Microemulsions stand transparent as the size of the droplet is less than the wavelength of visible light up to 25%. Microemulsion droplet size varies from 3-50 nm (Gadhve and Waghmare, 2014; Saini *et al.*, 2014; Roohinejad *et al.*, 2018). Microemulsion constituents are categorized into oils, co-surfactant and surfactants. Oils are modest to large alkyl hydrocarbons ranging 140-900 Da that might hold carboxylic acid or ester moieties. Surfactants are a composite blend of phospholipids categorized with 500-700 Da molecular weight range and two primarily distinctive parts of contrasting hydrophilicity/ lipophilicity properties are minor 60-190 Da, carboxylic acids, or mono or multi-hydroxy alcohols that might have ether linkages. The co-surfactant is similarly amphiphilic and stabilize microemulsion, with an attraction mutually for aqueous and oil partitions and phases to a relevant extent into the surfactant interface. A wide range of non-ionic surfactants can perform the role of co-surfactant containing alkanoids, alkylamines, and alcohol and alkanolic acids (Agrawal and Agrawal, 2012). For industrial procedures especially, it is significant to characterize microemulsions accurately, despite their easiness of formation. Both microenvironment techniques and macroscopic measurements are involved for the characterization of microemulsions. The macroscopic studies consist of viscosity measurement which specifies the existence

(or lack) of certain surfactants, conductivity measurement which can define the dispersed and continuous phase and dielectric measurements which give the perception to the dynamics and structure of the specific microemulsion. On the other side, microenvironment techniques can comprise scattering methods such as X-ray, light and neutron scattering and pulsed-field NMR (Lee, 2011; Cadogan *et al.*, 2017). Concerning the release of solubilized material microemulsion shows a rich behavior. Similarly, if the interactions between surfactant and drug and partitioning of the drug between water and oil phase strongly affect the drug release, one can grasp sustained-release (Agrawal and Agrawal, 2012; Hejazifar *et al.*, 2020). To boost the bioavailability of poor water-soluble drugs, microemulsions have been extensively studied. For drugs the extraordinary capability of microemulsions makes them striking preparations for pharmaceuticals. For oral administration, these structures also propose numerous benefits containing improved absorption, enhanced clinical potency and reduced toxicity. The worth and potential that investigators award to microemulsions is in no small part owing to their distinctive properties that are capable to dissolve immiscible liquids, great thermodynamic stability, high interfacial area and small interfacial tension. It has been assessed that when given through oral route, almost half of the permitted drugs are lipophilic and have reduced absorption characteristics (Callender *et al.*, 2017; Paliwal *et al.*, 2019).

#### *Types of Microemulsions*

Four common types of phase equilibria have been recognized by Winsor. On that base, microemulsion can be categorized into four varieties (Winsor 1948).

Type I: In this kind of microemulsions, O/W (oil in water) microemulsion is preferably made by solubilizing surfactant in the water part. The type is named as “Winsor I” microemulsion.

Type II: In this type, W/O (water in oil) microemulsion is preferably made by solubilizing

surfactant in the oil part. The surfactant-loaded oil part associates with the surfactant-poor aqueous part. This type is “Winsor II” microemulsion.

Type III: Surfactant-rich medium part pools equally with oil as well as water segments and formation of 3 phase microemulsion takes place. Now this microemulsion has both the oil and water as surfactant-insufficient phases. This is moreover termed as “Winsor III”.

Type IV: A single micellar (isotropic) solution is formed by adding an ample quantity of alcohol and surfactant (amphiphile). This is titled “Winsor IV”. At greater surfactant concentrations this type of microemulsion is an extension lead of Winsor III type, as the intermediate phase outspreads and becomes a single phase.

#### *Advantages*

Due to enhanced thermodynamic stability microemulsions are prepared simply and need no energy involvement during preparation. It offers prompt and effective permeation of the drug moiety. The microemulsion is not vulnerable to attack by air and water due to the presence of the drug in the oil phase in O/W also delivers protection from oxidation and hydrolysis. For water-insoluble drugs, microemulsion offers an aqueous dosage form. Microemulsion established system has extended shelf-life. They entertain as super solvents and the presence of microdomains of dissimilar polarities within the similar single-phase solution supports to solubilize of both lipophilic and hydrophilic drugs that are comparatively insoluble in both lipophilic and aqueous solvents. Microemulsions permit self-emulsification owing to a thermodynamically stable system. They are utilized for the palatability of unpleasant drugs, and to be used to taste masking of nutrient oils. The microemulsion average droplet diameter is under 0.22  $\mu\text{m}$ . When absorption (in vivo or in vitro) occurs drug is rapidly released into the external phase due to large interfacial area thus preserving the concentration to initial stages in the external phase. They can transport both hydrophilic

and lipophilic drugs, and having less viscosity in comparison to multiple and primary emulsions. (Hou and Xu, 2016; Cespi *et al.*, 2017; Sujatha *et al.*, 2020).

#### *Disadvantages*

The droplets of the microemulsion delivery systems become stable, a huge concentration of co-surfactant and surfactant is desired. For pharmaceutical applications, the surfactant must be inert. Environmental factors such as pH and temperature influence microemulsion stability. These factors alter microemulsion supply to patients. High melting substances used in the system have restricted solubilizing capability (Bardhan *et al.*, 2016; Leng *et al.*, 2017).

#### *Structure of microemulsions*

The interface is constantly and freely fluctuating in dynamic microemulsion systems. They are categorized into w/o (water in oil), o/w (oil in water) and bicontinuous microemulsions. In w/o type, oil is the continuous phase and water as droplets are dispersed in it whereas in o/w type microemulsion there is the aqueous continuous phase and oil droplets are dispersed in it. The development of the bicontinuous microemulsions proceeds in the case where the quantities of both water and oil are equal. A very huge variability of the structures and phases can be designed depending upon the altered parts of the oil, water and surfactants as soon as used together in different proportions (Oberdisse and Hellweg, 2017; Pourtabrizi *et al.*, 2018).

#### *Factor affecting the formulation of microemulsion system*

The packing ratio, the chain length, nature of co-surfactant, the property of oil phase, surfactant, type and temperature are responsive for the preparation of water or oil swollen microemulsion.

#### *Packing ratio*

Through its impact on film curvature and molecular packing, the surfactant Hydrophilic Lipophilic Balance (HLB) supports to determine the type of microemulsion. For associations of surfactant

governing to microemulsion preparation in packing ratio terms, Mitchell and Ninham (1977) and Israclachvili (1976) elucidated and analyses the film curvature and titled it as a critical packing parameter. Critical Packing Parameter (CPP) =  $v/a * l$

Where,

v is the partial molar volume of the hydrophobic portion of the surfactant, a is the optimal head group area and l is the length of the surfactant tail.

Oil in water systems (o/w) are preferred if CPP is 0-1, interface bends towards water i.e. +ive curvature.

CPP is larger than 1, interface points unexpectedly towards oil i.e. -ive curvature so water in oil (w/o) microemulsions is recommended.

Either lamellar or bicontinuous structures may be formed rendering to the film rigidity when p is equal to 1 (HLB is balanced) and curvature is zero (Muzaffar *et al.*, 2013; Singh *et al.*, 2014).

#### *Property of surfactant*

Hydrophilic and lipophilic groups are the two groups of surfactants. Cetyl ethyl ammonium bromide is a single chain hydrophilic surfactant which completely dissociates in dilute solution and has an affinity to form oil in water (o/w) microemulsion. When a high concentration of surfactant is employed or when the surfactant is in the existence of salt, the polar group's dissociation degree becomes lesser and the resultant may be w/o type system (Singh *et al.*, 2014; Chang *et al.*, 2019).

#### *Property of oil phase*

Curvature is influenced by the oil phase owing to its penetration capacity and swelling of the tail group of the surfactant monolayer, greater negative curvature is due to tail swelling results in w/o microemulsion (Singh *et al.*, 2014; Du *et al.*, 2016).

#### *Temperature*

In order to determine the size of the active head group for nonionic surfactants, the temperature is

tremendously significant. Oil in water structure is formed at lesser temperatures as its nature is hydrophilic. Water in oil structure is formed at greater temperatures as its nature is lipophilic. A Bicontinuous system is formed at an intermediary temperature due to the coexistence of microemulsion with excess oil and water phases (Singh *et al.*, 2014; Chai *et al.*, 2017).

#### *Theories of microemulsion formulation*

Various theories express the basis of microemulsion preparation as they control and affect their phase behavior and stability (Singh *et al.*, 2014; Lokhande, 2019). These theories are as follows.

#### *Thermodynamic theory*

The simple mechanism of thermodynamics is centered on the stability and formulation of the microemulsion. The free energy during microemulsion preparation depends on the alteration in entropy of the structure along with the degree, to which a surfactant reduces the surface tension at the water-oil interface, thus

$$DG_f = \gamma DA - T DS$$

Where,

$DG_f$  = Free Energy of formation,

$\gamma$  = Surface Tension of the oil-water interface,

$DA$  = Change in the interfacial area on micro-emulsification,

$DS$  = Change in entropy of the system which is effectively the dispersion entropy, and

$T$  = Temperature.

The formation of a huge numeral of minor droplets is due to a change in  $DA$  to a greater degree during microemulsion preparation. It is needed to know as the  $\gamma$  value is very small and positive at all intervals, so is balanced by the entropic constituent. The favorable dominant entropic contribution is big dispersion entropy, rising from the mingling of one part into the other one in the form of huge quantities of minor droplets. Further dynamic techniques such as monomer micellar exchange of surfactant and interfacial layer diffusion of surfactant are reasons for

favorably entropic input. The free negative energy of development is concluded, when a large lowering of surface tension is originated by favorably significant entropic change. For instance, there is spontaneous micro-emulsification and finally thermodynamically stable dispersion.

#### *Solubilization theory*

The preparation of microemulsion in water-soluble phase and oil phase by reverse micelles or micelles gently swell and become larger to a certain range of size.

#### *Interfacial theory*

The theory of interface mixed film i.e. theory of -ve interfacial tension stated that the microemulsion is capable of generating negative interfacial tension spontaneously and instantaneously in the cosurfactant and surfactant working together. The film consisting of cosurfactant and surfactant molecules assume as "two-dimensional liquid" i.e a third phase which is in equilibrium with both water and oil, a monolayer duplex film giving diverse properties on the oil and waterside. The interfacial tension  $\gamma_T$ , according to the theory of duplex film, is given by the subsequent interpretation.

$$\gamma_T = \gamma(O/W) - \pi$$

Where,

$\gamma(O/W)_a$  = Interfacial Tension (presence of alcohol reduce it).

$\gamma(O/W)_a$  is significantly lower than  $\gamma(O/W)$  in the absence of alcohol.

#### *Applications of microemulsions*

##### *Oral deliver*

Drug efficiency can be bounded by poor solubility or instability in the GI fluid so the progression of impressive oral drug delivery systems has been constantly demanding to investigators. The potential of microemulsions to overcome the bioavailability problems relating to dissolution and enhancement in the solubilization of poorly soluble drugs (especially BCS class II and IV). Hydrophilic drugs comprising macromolecules with alternating solubility can easily

be encapsulated and this is due to the existence of interfacial, polar and nonpolar domains. These microemulsion systems have been preserving the drugs incorporated against enzymatic degradation, oxidation and enhancement of membrane penetration. By enhancing the solubility in GI fluid, potentially microemulsion preparations can be useful in boosting the oral bioavailability of drugs less soluble in water (Liu *et al.*, 2019).

#### *Topical delivery*

The advantage of drug topical administration over other methods is the prevention of drug degradation in the stomach, saliva, first-pass effect and associated toxic effects. Additional is the direct target ability and delivery of the drug to affected parts of the eyes or skin. Currently, there have been numeral studies in the capacity of penetration of the drug into the skin. They are capable to unite both lipophilic drugs (finasteride, estradiol, ketoprofen etc, etc.) and hydrophilic (apomorphine hydrochloride, 5-fluorouracil, etc.) and boost their penetration. Since a high concentration of surfactant is required for microemulsion formation. The aspect of irritation of the skin is measured particularly when microemulsions are proposed to be applied for an extended period (Shukla *et al.*, 2018).

#### *Parenteral delivery*

Hydrophilic and lipophilic drug parenteral dosage formulations are difficult to establish. Oil in water microemulsions is advantageous in the case of sparingly soluble drugs for parenteral drug delivery when the suspension administration is not a requirement. The drugs require repeated administration so a relatively high concentration of these is provided using microemulsion. Additional benefits include greater physical stability in plasma than other vehicles or liposomes and the internal oil segment is more resistant to drug leaching. For parenteral drug delivery, several sparingly soluble drugs have been prepared in oil in water (o/w) microemulsion. Thoren and Von Corsewant took an alternate approach in which alcohols C<sub>3</sub>-C<sub>4</sub> were substituted with cosurfactants suitable parenterally,

ethanol / polyethylene glycol (400) / polyethylene glycol (660) 12-hydroxystearate, while retaining spontaneous curvature proximate to zero, a flexible film of surfactant to obtain nearly middle phase balanced microemulsion (Muzaffar *et al.*, 2013).

#### *Periodontal delivery*

Periodontal ailment is a joint word for a numeral of advanced oral pathological conditions as periodontal ligaments, gums degeneration, inflammation and cementum at its supportive bone. It is a chief basis of tooth damage. The discovery of Brodin comprised of a novel and innovative pharmaceutical formulation comprising oil from local anaesthetic, water, surfactant and optionally an ingredient for taste masking. The composition was a microemulsion or emulsion and had gelling properties that are thermoreversible i.e. at room temperature it was with less viscosity than a successive introduction on the mucosal membrane of a patient. Gelling properties imparted by the surfactant in the composition are thermoreversible. Favored surfactants were Arlatone 289®, Poloxamer 188® and Poloxamer 407®. As a local anaesthetic the formulation could be used for relief of pain inside the oral cavity in combination with root planning and periodontal scaling and restricted the difficulty with the current topical items (ointment, jelly or spray) such as the absence of efficiency due to short duration, insufficient penetration, and administration complications due to taste, spread, etc (Muzaffar *et al.*, 2013).

#### *Ocular drug delivery*

“The most challenging and interesting activities facing the pharmaceutical scientist is ophthalmic delivery of the drug. The biochemistry, anatomy and physiology of the eye render its structure delicately impervious to extraneous constituents. The task of the designer is to bypass the defensive barricades of the eye without enduring persistent tissue damage. The original ophthalmic suspension, ointment and solution dosage forms are no longer adequate to fight some existing contagious diseases.” The eye is a very valuable and unique organ and considered a window hinge. There are several eye infections that can upset



the body and damage to vision also. Hence, many ocular drug development systems are existing. They are categorized as new and traditional drug delivery systems. For the management of many ocular ailments, the application of drugs topically to the eye is the utmost well-accepted and popular administration route. The ophthalmic drug bioavailability is very poor due to the proficient defensive mechanism of the eye. From the eye surface, reflex and baseline lachrymation, drainage and blinking, take out quickly external bodies, even drugs. A novel ophthalmic pharmaceutical formulation such as a nanoparticle, in-situ gel, liposome, microemulsion, nanosuspension, ocular and intophoresis inserts have been established in the past three decades and increase drug bioavailability in a controlled and sustained mode (Mishra *et al.*, 2014).

#### *Tumour targeting*

For the distribution of diagnostic or chemotherapeutic agents to neoplastic cells although escaping normal cells, Maranh apo advised the service as vehicles in case of microemulsions. Neoplasm cells have a bigger quantity of low-density lipoprotein (LDL) receptors than normal cells, they apply for a technique to handle neoplasms. The microemulsions consist of a cholesterol ester nucleus and a core surrounds not other than 20% of triglycerides by free cholesterol and phospholipids and enclosed with a chemotherapeutic drug. In chemical configuration microemulsions were similar to the lipid part of LDL, however did not comprise of protein portion. When incubated along with plasma or injected into the bloodstream, these particles of artificial microemulsion incorporated (apo E) plasma apolipoprotein E on their surface. The apo E aided as a connecting component among the LDL receptors and particles of the artificial microemulsion. The microemulsions could be then assimilated into cells via LDL receptors and transported the molecules incorporated. Therefore, in the neoplastic cells, anticancer drugs in higher concentration could be achieved that have an improved receptor expression. In this manner drug, toxic effects on the normal organs and tissues could be eluded. In humans, they

detected no modification in the plasma kinetics of the microemulsion radioactively labeled containing cytosine arabinoside or carmustine thus confirming that these drug fusion did not reduce the ability of the microemulsion to bind apo E to the receptors and incorporation in the plasma (Muzaffar *et al.*, 2013).

#### *Microemulsions in enhanced oil recovery*

The approach of the techniques of EOR (enhanced oil recovery) using microemulsion and surfactant can support in finding unredeemable below ground oil. If the interfacial tension between the reservoir brine and crude oil can be minimized to about  $10^{-3}$  mN/m, a considerable portion of the residual oil in the porous media in which it is locked in and can be prepared (Singh *et al.*, 2014).

#### *Microemulsions in cosmetics*

It is supposed that the uptake of microemulsion formulation through the skin will result faster. Safety, cost, a suitable choice of components are crucial factors in microemulsions composition. Microemulsions for skincare comprise lecithin, propanol, hexadecane, tetraethylene glycol monododecyl ether, dodecyl oligoglucoside, isopropyl myristate, alkyl dimethyl amine oxide, and sodium alkyl sulfate, have been used as cosurfactants, oils and surfactants correspondingly. Microemulsions for hair care have a nonionic surfactant (an amino-functional polyorganosiloxane), a metal salt, and/or an acid. The technique of emulsion polymerization was used to produce cosmetic microemulsions of silicone oils which are translucent and transparent. Preparation of ultrafine emulsions by condensation technique has benefits in medical and cosmetic products, as they have exceptional safety and stability and droplet size can be controlled readily. Ultrafine emulsions are o/w and can be regarded as microemulsions unstable thermodynamically with droplet size parallel to microemulsion (Das *et al.*, 2020; Salager *et al.*, 2020).

#### *Characterization of microemulsions*

Principally microemulsions are very tough to characterize since they have variation in structures,

unlike their production easiness. To characterize microemulsions several techniques are required often. For improving drug delivery, an understanding of the vehicle properties is a significant necessity. Additionally, to establish the limitations and also the potential of microemulsion formulations, properties affecting stability, structure and drug release need to be understood. A range of methods, such as electrical conductivity, NMR spectroscopy, small-angle neutron scattering, self-diffusion, fluorescence spectroscopy and quasi-elastic light scattering have been engaged to characterize microemulsion systems (Agrawal and Agrawal, 2012).

#### *Microscopy*

Although the optical isotropy of the microemulsion system is confirmed by polarizing microscopy, for studying microemulsions, conventional optical microscopy cannot be employed because of the smaller size of the droplet which is typically lesser than 150 nm diameter. However, for the characterization and study of microemulsions freeze-fracture techniques in combination with TEM (transmission electron microscopy) have been applied successfully. The microemulsion structures are sensitive to temperature. Other complications are (1) microemulsion high vapour pressure, which is not compatible with microscopy low pressures (2) chemical reaction induced by electrons, thus, alteration in the structure of microemulsion and (3) lack of contrast between the environment and microemulsion structure. The techniques of freeze fracture-TEM and Cryo-TEM which have developed from these improvements, permit direct microemulsion visualization with rarer artifactual result problems (Agrawal and Agrawal, 2012; Zhao *et al.*, 2020).

#### *Nuclear magnetic resonance (NMR) studies*

The nuclear magnetic resonance techniques are used to study dynamics and microemulsion structures. Different tracer methods are used for self-diffusion measurements, generally, supply information on the mobility of the components and radiolabeling. The FT-PGSE (Fourier transform pulsed-gradient spin-

echo) procedure employs the magnetic gradient on the samples and it permits rapid and simultaneous determination of coefficients of self-diffusion of various components. (In the range of  $10^{-9}$  to  $10^{-12}$  m<sup>2s<sup>-1</sup>) (Awad *et al.*, 2018).</sup>

#### *Conductivity and viscosity*

Determination of phase inversion and nature of microemulsion is detected by using conductivity and by classical rheological approaches. Determination of viscosity also delivers valuable evidence on exactly how the drug release is influenced by colloidal systems. The possible structures existing are, for example, worm-like or rod-like reverse micelles with multilamellar layers vesicles. Water-continuous systems should have high conductivity values, while oil-continuous microemulsions display no or poor conductivity. Formerly, it has been verified that at definite volume fractions of water ( $\Phi_p$ ) microemulsions may display phenomena of percolation named the percolation threshold. The behavior of the system will be as an insulator when the water fraction is lower than  $\Phi_p$ , however water fraction values somewhat greater than  $\Phi_p$ , the operational conductivity sharply increases (Agrawal and Agrawal, 2012).

#### *Fluorescence spectroscopy*

In the microemulsions, the easiness of the fluorescent probe molecules movement is measured by Fluorescence spectroscopy. Diffusion controls it and inversely varies with the type of microemulsion and medium viscosity. In water continuous microemulsions, the excitation propagation is inhibited as diffusion of the water-insoluble fluorescent molecules (pyrene) is slow. Whereas, oil continuous microemulsions should yield a related excimer development to that of the pure oil (Agrawal and Agrawal, 2012; Hou *et al.*, 2017).

#### *Static light scattering technique*

The static light scattering technique has also been used extensively to measure microemulsion droplet shape and size. In this method, the scattered light intensity is determined generally at various angles



and for microemulsion droplets at different concentrations (Agrawal and Agrawal, 2012; Jagtap *et al.*, 2016).

#### *Dynamic light scattering*

It is similarly denoted as PCS (photon correlation spectroscopy), is used for the analysis of the fluctuations due to Brownian motion in droplet scattering intensity. The determination of self-correlation gives information on system dynamics. This system permits the measurement of z-average diffusion coefficients D (Agrawal and Agrawal, 2012).

#### *Zeta potential measurement*

It must be neutral or negative, which specify the structure is stable and droplets of microemulsion have no charge. Zetasizer is used to measure Zeta potential. Since the rate of flocculation is influenced by particle electrical charges, zeta potential is principally valuable for evaluating flocculation (Muzaffar *et al.*, 2013).

#### **Conclusion**

It is concluded that in last few years, microemulsions have been under the extensive consideration globally due to their beneficial applications, i.e. pharmaceuticals, cosmetics, food, enzymatic catalysis, metal cutting and combustion. However, it is mandatory to gain comprehensive knowledge on microemulsions that will guide about their physicochemical and biopharmaceutical properties that could be beneficial in designing the drug formulations.

#### **Conflict of interest**

There is no conflict of interest among the authors.

#### **References**

**Agrawal OP, Agrawal S.** 2012. An overview of new drug delivery system: microemulsion. *Asian Journal of Pharmaceutical Sciences* **2(1)**, 5-12.

[http://www.ajpst.com/File\\_Folder/5-12.pdf](http://www.ajpst.com/File_Folder/5-12.pdf)

**Awad TS, Asker D, Romsted LS.** 2018. Evidence of coexisting microemulsion droplets in oil-in-water

emulsions revealed by 2D DOSY 1H NMR. *Journal of Colloid and Interface Science* **514**, 83-92.

<https://doi.org/10.1016/j.jcis.2017.12.024>

**Bardhan S, Kundu K, Chakraborty G, Paul BK, Moulik SP, Saha SK.** 2016. Bioinspired Microemulsions and Their Strategic Pharmacological Perspectives. *Encyclopedia of Biocolloid and Biointerface Science* **19**, 122-44.

<https://doi.org/10.1002/9781119075691.ch10>

**Cadogan SP, Hahn CJ, Rausch MH, Fröba AP.** 2017. Study on the applicability of dynamic light scattering (DLS) to microemulsions including supercritical carbon dioxide-swollen micelles. *Journal of Colloid and Interface Science* **499**, 202-8.

<https://doi.org/10.1016/j.jcis.2017.03.111>

**Callender SP, Mathews JA, Kobernyk K, Wettig SD.** 2017. Microemulsion utility in pharmaceuticals: Implications for multi-drug delivery. *International Journal of Pharmaceutics* **526(1-2)**, 425-42.

<https://doi.org/10.1016/j.ijpharm.2017.05.005>

**Cespi M, Quassinti L, Perinelli DR, Bramucci M, Iannarelli R, Papa F, Ricciutelli M, Bonacucina G, Palmieri GF, Maggi F.** 2017. Microemulsions enhance the shelf-life and processability of *Smyrniolum olusatrum* L. essential oil. *Flavour and Fragrance Journal* **32(3)**, 159-64.

<https://doi.org/10.1002/ffj.3367>

**Chai JL, Sun B, Chai ZQ, Liu N, Pan J, Lu JJ.** 2017. Comparisons of the effects of temperature on the W/O microemulsions formed by alkyl imidazole gemini and imidazole ionic liquids type surfactants. *Journal of Dispersion Science and Technology* **38(7)**, 967-72.

<https://doi.org/10.1080/01932691.2016.1216439>

**Chang L, Pope GA, Jang SH, Tagavifar M.** 2019. Prediction of microemulsion phase behavior from surfactant and co-solvent structures. *Fuel* **237**, 494-514.

<https://doi.org/10.1016/j.fuel.2018.09.151>

**Chen J, Ma XH, Yao GL, Zhang WT, Zhao Y.** 2018. Microemulsion-based anthocyanin systems:

effect of surfactants, cosurfactants, and its stability. *International Journal of Food Properties* **21**(1), 1152-65.

<https://doi.org/10.1080/10942912.2018.1485032>

**Danielsson I.** 1981. The definition of microemulsion. Pascal and Francis Bibliographic Databases.

[\[francis.inist.fr/vibad/index.php?action=getRecordDetail&idt=PASCAL82X0076549\]\(http://pascal-francis.inist.fr/vibad/index.php?action=getRecordDetail&idt=PASCAL82X0076549\)](http://pascal-</a></p></div><div data-bbox=)

**Das S, Lee SH, Chow PS, Macbeath C.** 2020. Microemulsion composed of combination of skin beneficial oils as vehicle: Development of resveratrol-loaded microemulsion based formulations for skin care applications. *Colloids and Surfaces B: Biointerfaces* **30**, 111161.

<https://doi.org/10.1016/j.colsurfb.2020.111161>

**Du Z, Mao X, Tai X, Wang G, Liu X.** 2016. Preparation and properties of microemulsion detergent with linear medium chain fatty alcohols as oil phase. *Journal of Molecular Liquids* **223**, 805-10.

<https://doi.org/10.1016/j.molliq.2016.09.011>

**Gadhve AD, Waghmare JT.** 2014. A short review on microemulsion and its application in extraction of vegetable oil. *International Journal of Research in Engineering and Technology* **3**(9), 147-58.

<https://ijret.org/volumes/2014v03/i09/IJRET20140309022.pdf>

**Hejazifar M, Lanaridi O, Bica-Schröder K.** 2020. Ionic liquid based microemulsions: A review. *Journal of Molecular Liquids* **303**, 112264.

<https://doi.org/10.1016/j.molliq.2019.112264>

**Hou M, Dang L, Liu T, Guo Y, Wang Z.** 2017. Novel fluorescent microemulsion: Probing properties, investigating mechanism, and unveiling potential application. *ACS Applied Materials & Interfaces* **9**(31), 25747-54.

<https://doi.org/10.1021/acsami.7b05819>

**Hou W, Xu J.** 2016. Surfactant-free microemulsions. *Current Opinion in Colloid & Interface Science* **25**, 67-74.

<https://doi.org/10.1016/j.cocis.2016.06.013>

**Jagtap SR, Phadtare DG, Saudagar RB.** 2016. Microemulsion: A Current Review. *Research Journal of Pharmaceutical Dosage Forms and Technology* **8**(2), 161-70.

<http://dx.doi.org/10.5958/0975-4377.2016.00021.5>

**Lee KL.** 2011. Applications and use of microemulsions. *Chemical Physics* **13**.

<https://arxiv.org/abs/1108.2794>

**Leng L, Han P, Yuan X, Li J, Zhou W.** 2018. Biodiesel microemulsion upgrading and thermogravimetric study of bio-oil produced by liquefaction of different sludges. *Energy* **153**, 1061-72.

<https://doi.org/10.1016/j.energy.2018.04.087>

**Liu H, Mei J, Xu Y, Tang L, Chen D, Zhu Y, Huang S, Webster TJ, Ding H.** 2019. Improving The Oral Absorption Of Nintedanib By A Self-Microemulsion Drug Delivery System: Preparation And In Vitro/In Vivo Evaluation. *International Journal of Nanomedicine* **14**, 8739.

<https://dx.doi.org/10.2147%2FIJN.S224044>

**Lokhande SS.** 2019. Microemulsions as Promising Delivery Systems: A Review. *Asian Journal of Pharmaceutical Research* **9**(2), 90-6.

<http://dx.doi.org/10.5958/2231-5691.2019.00015.7>

**Mishra A, Ridhi P, Rana AC.** 2014. Microemulsions: As drug delivery system." *Journal of Scientific and Innovative Research* **3**(4), 467-474.

[http://www.jsirjournal.com/Vol3\\_Issue4\\_12.pdf](http://www.jsirjournal.com/Vol3_Issue4_12.pdf)

**Muzaffar FA, Singh UK, Chauhan L.** 2013.

Review on microemulsion as futuristic drug delivery. *International Journal of Pharmacy and Pharmaceutical Sciences* **5**(3), 39-53.

**Oberdisse J, Hellweg T.** 2017. Structure, interfacial film properties, and thermal fluctuations of microemulsions as seen by scattering experiments. *Advances in Colloid and Interface Science* **247**, 354-62.

<https://doi.org/10.1016/j.cis.2017.07.011>

**Paliwal H, Solanki RS, Chauhan CS, Dwivedi J.** 2019. Pharmaceutical considerations of

microemulsion as a drug delivery system. *Journal of Drug Delivery and Therapeutics* **9(4-s)**, 661-5.

<https://doi.org/10.22270/jddt.v9i4-s.3206>

**Pourtabrizi M, Shahtahmassebi N, Kompany A, SHarifi S.** 2018. Effect of microemulsion structure on fluorescence and nonlinear optical properties of rhodamine 6G. *Journal of Fluorescence* **28(1)**, 323-36.

<https://doi.org/10.1007/s10895-017-2195-y>

**Roohinejad S, Oey I, Everett DW, Greiner R.** 2018. Microemulsions. Emulsion-based Systems for Delivery of Food Active Compounds: Formation, Application, Health and Safety **23**, 231-62.

<https://doi.org/10.1002/9781119247159.ch9>

**Saini JK, Nautiyal U, Kumar M, Singh D, Anwar F.** 2014. Microemulsions: A potential novel drug delivery system. *International Journal of Pharmaceutical and Medicinal Research* **2(1)**, 15-20.

<https://ijpmr.org/pdf/Microemulsions-A-potential-novel-drug-delivery-system.pdf>

**Salager JL, Antón R, Bullón J, Forgiarini A, Marquez R.** 2020. How to use the normalized hydrophilic-lipophilic deviation (HLDN) concept for the formulation of equilibrated and emulsified surfactant-oil-water systems for cosmetics and pharmaceutical products. *Cosmetics* **7(3)**, 57.

<https://doi.org/10.3390/cosmetics7030057>

**Sharma N, Antil V, Jain S.** 2013. Microemulsion: A review. *Asian Journal of Pharmaceutical Research and Development* **1**, 23-36.

<http://www.ajprd.com/index.php/journal/article/view/43>

**Shukla T, Upmanyu N, Agrawal M, Saraf S, Saraf S, Alexander A.** 2018. Biomedical applications of microemulsion through dermal and transdermal route. *Biomedicine & Pharmacotherapy* **108**, 1477-94.

<https://doi.org/10.1016/j.biopha.2018.10.021>

**Singh PK, Iqbal MK, Shukla VK, Shuaib M.** 2014. Microemulsions: current trends in novel drug delivery systems. *Journal of Pharmaceutical, Chemical and Biological Sciences* **1(1)**, 39-51.

**Sujatha B, Himabindu E, Bttu S, Abbulu K.** 2020, Microemulsions-A review. *Journal of Pharmaceutical Sciences and Research* **12(6)**, 750-3. <https://www.jpsr.pharmainfo.in/Documents/Volume/s/vol12issue06/jpsr12062003.pdf>

**Talegaonkar S, Azeem A, Ahmad FJ, Khar RK, Pathan SA, Khan ZI.** 2008. Microemulsions: a novel approach to enhanced drug delivery. *Recent Patents on Drug Delivery & Formulation* **2(3)**, 238-57.

<https://doi.org/10.2174/187221108786241679>

**Winsor PA.** 1948. Hydrotrophy, solubilisation and related emulsification processes. *Transactions of the Faraday Society* **44**, 376-98.

<https://pubs.rsc.org/en/content/articlelanding/1948/tf/tf0484400376/unauth#!divAbstract>

**Zhao J, Jiang K, Chen Y, Chen J, Zheng Y, Yu H, Zhu J.** 2020. Preparation and Characterization of Microemulsions Based on Antarctic Krill Oil. *Marine drugs* **18(10)**, 492.

<https://doi.org/10.3390/md18100492>