DOI: https://doi.org/10.54393/mjz.v3i1.40

MARKHOR
THE JOURNAL OF ZOOLOGY
https://www.markhorjournal.com/index.php/mjz
Volume 3, Issue 1 (Jan-Jun 2022)

Review Article

Microemulsions; A Mini Review

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ARTICLE INFO

Key Words:
Microemulsions, Surfactant, Pharmaceuticals, Oil, Cosmetics

How to cite:
Aslam, A. . ., & Fareed Siddiqui, M. . (2022). Microemulsions; A Mini Review: Microemulsions; A Mini Review. MARKHOR (The Journal of Zoology), 3(1). https://doi.org/10.54393/mjz.v3i1.40

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Received Date: 8th May, 2022
Acceptance Date: 25th May, 2022
Published Date: 30th June, 2022

ABSTRACT

The review goes into great detail about the microemulsions' characteristics, structure, kinds, theories, characterization, and applications. They may be made easily by mixing the various ingredients together without the need for special tools or circumstances. Unlike the o/w type microemulsion, which has an aqueous continuous phase and oil droplets distributed in it, the w/o type microemulsion has oil as the continuous phase and water as droplets are disseminated in it. Microemulsions are classified into four primary categories based on different phase systems, and they are often utilized in the pharmaceutical and cosmetics sectors as well as in analytical methods. The design of medicine formulations and cosmetics may benefit from having a thorough understanding of the physicochemical and biological characteristics of microemulsions.

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 [1]. Rodawald in 1928 probably discovered the 1st 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"[2]. 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 [3-5]. 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 andtail area of surfactant is denoted by v/l_c then[6].

- 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 group. Strange behavior is show by them; initially adsorption occurs at interface, wherever they can accomplish their double duty with hydrophobic groups in air or oil and hydrophilic groups positioned in aqueous part. Furthermore, Micellization process diminishes mismatching with solvent [7]. Formation of 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

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NaCl) are also present. A co-surfactant is not needed when consuming double chain ionic (e.g., Aerosol-OT) and certain non-ionic surfactants [8]. Low viscosity, homogeneity and transparency are definite physical and chemical properties of microemulsions. Microemulsions stand transparent as the size of droplet is less than the wavelength of visible light upto 25%. Microemulsion droplet size varies from 3-50 nm [6-9]. 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. Surfactant are composite blend of phospholipids categorized with 500-700 Da molecular weight range and two primarily distinctive part 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 surfactant can perform role as co-surfactant containing alkanoids, alkylamines, and alcohol and alkanoic acids [9]. For industrial procedures especially, it is significant to characterize microemulsions accurately, in spite of their easiness of formation. Both microenvironment techniques and macroscopic measurements are involved for 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 gives 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 [3, 9-11]. Concerning the release of solubilized material microemulsion shows a rich behavior. Similarly, if the interactions among surfactant and drug and partitioning of drug between water and oil phase strongly affect the drug release, one can grasp sustained release [5, 9]. 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 are in no small part owing to their distinctive properties that are capacity 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 [12, 13].

Types of Microemulsions: Four common types of phase equilibria have been recognized by Winsor. On that base, microemulsion can be categorized into four varieties [14].

Type I: In this kind of microemulsions, O/W (oil in water) microemulsion is preferably made by solubilizing surfactant in 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 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, have 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 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.

Structure of Microemulsions: Interface is constantly and freely fluctuating in dynamic microemulsion systems. Basically, they are categorized into w/o (water in oil), o/w (oil in water) and bicontinuous microemulsions. Oil is classified under continuous phase in w/o type with water droplets dispersed in it. However, in case of o/w type microemulsion, oil droplets are dispersed in aqueous continuous phase. The development of the bicontinuous microemulsions proceeds in the case where the quantities of both water and oil are the 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 [15-17].

Factor affecting formulation of Microemulsion system: The packing ratio, the chain length, nature of co-surfactant, 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)

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elucidated and analyses the film curvature and titled it as 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 [18-20].

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. The degree of polar group dissociation decreases when a high concentration of surfactant is used, or when salt is included in the surfactant, leading to the possibility of a w/o type system [21-22].

Oil Phase: Curvature is influenced by oil phase owing to its penetration capacity & swelling of tail group of the surfactant monolayer, greater negative curvature is due to tail swelling results in w/o microemulsion [23-24].

Temperature: In order to determine the size of active head group for nonionic surfactants temperature is tremendously significant. Oil in water structure is formed at lesser temperatures as their nature is hydrophilic. Water in oil structure is formed at greater temperatures as their nature is lipophilic. Bicontinuous system is formed at an intermediary temperature due to coexistence of microemulsion with excess oil and water phases [25-26].

Characterization of microemulsions: Principally microemulsions are very tough to characterize since they have variation in structures unlike their production easiness. In order to characterize microemulsions several techniques are required often. For improving drug delivery, an understanding of the vehicle properties is a significant necessity. Additionally, characteristics impacting stability, structure, and drug release need to be addressed in order to determine the limitations as well as possibilities of microemulsion formulations. 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 [27].

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 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 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 [28].

Nuclear magnetic resonance (NMR) studies: The nuclear magnetic resonance techniques are used to study dynamics and microemulsions structures. Different tracer methods are used for self-diffusion measurements, generally supply information on the mobility of the components and radio labeling. 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^{2s-1}) [29].

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 (Φp) 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 Φp, however water fraction values somewhat greater than Φp, the operational conductivity sharply increases [30].

Fluorescence spectroscopy: Fluorescence spectroscopy is used to gauge how easily fluorescent probe molecules move in microemulsions. It is governed by diffusion, which varies inversely with the kind of microemulsion and

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medium viscosity. Excitation propagation is limited in water continuous microemulsions because pyrene, a fluorescent chemical that is not water soluble, diffuses slowly. In contrast, oil continuous microemulsions ought to produce an excimer development that is similar to that of pure oil [31-32].

Static light scattering technique: The form and size of microemulsion droplet has also been extensively measured using the static light scattering method. In this approach, the scattered light intensity is commonly calculated for microemulsion droplets at various concentrations and at various angles [33].

Dynamic light scattering: It is also known as PCS (photon correlation spectroscopy), and it is used to analyse variations in droplet scattering intensity brought on by Brownian motion. Self-correlation analysis provides details on system dynamics. This system enables the measurement of diffusion coefficients D with a z-average [34].

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 [35-36].

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