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Role of microemuslsions in advanced drug delivery

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Abstract

Microemulsions have gained significant attention from formulation scientists since the time they have been discovered, because of their excellent properties related to their stability, solubility, simplicity, and formulation aspects. The application of microemulsions is not limited to drug delivery via the oral, topical or ocular routes, but may also be seen in cosmetics, immunology, sensor devices, coating, textiles, analytical chemistry, and spermicide. Finally, the objective of this review is to discuss briefly the applications of microemulsions in advanced drug delivery.

Keywords: drug delivery, formulation parameters, microemulsions, pharmaceutical applications

Introduction

Historically, microemulsions were first discovered by Rodewald, in 1928, in the form of liquid waxes. Hoar and Schulman introduced the word microemulsion, which they defined as a transparent solution obtained by titrating a normal coarse emulsion with medium chain alcohols. Microemulsions are simple carrier systems because of their thermodynamic stability and simple technology related to the ease of their preparation (Chaudhary et al. 2014). In today's world, we can discuss the definition given by Attwood, as "a microemulsion is a system of water, oil, and amphiphilic compounds (surfactant and cosurfactant), which is a transparent, single, optically isotropic, and thermodynamically stable liquid". Microemulsions are isotropic and transparent systems, thermodynamically stable, and are comprised of oil, water, and a surfactant, mostly in association with a cosurfactant. The droplet size may vary from 10 to 200 nm (Gagandeep et al. 2014). Broadly, they are classified into 3 types: O/W microemulsion, W/O microemulsion, and a bicontinuous microemulsion with high solubilizing power. The mechanism of action of microemulsions on skin penetration is unique, since they tend to react with lipids on the skin, as a result of which the intercellular space is changed and hence the drug is transported. The main distinguishing feature between the emulsion and microemulsion is the droplet size of the dispersed phase (Shalviri et al. 2011). Microemulsions are promising tools as delivery systems, allowing both types of drug release, controlled as well as sustained, for various routes of administration. Microemulsions have various distinguishing features as a delivery system, with the main features of being less toxic, facilitating enhanced absorption of drugs, and regulating the drug release rates (Garg 2014).

Advantages of microemulsions over other dosage forms

- Microemulsions have a broad spectrum of applications in drug targeting and controlled drug release (Garg and Goyal 2012).
- They have unique distinguishing features like enhanced bioavailability, due to their ability to solubilize lipophilic drugs.
- Microemulsions can carry water-soluble drugs into aqueous phase, and hence demonstrate the ability to carry both lipophilic as well as hydrophilic drugs.
- Microemulsions have a wide range of applicability, as they can be delivered by all major routes of drug delivery (Garg and Goyal 2014b).
- Microemulsions demonstrate greater longevity as compared to other biphasic dosage forms.
- Microemulsions are designed keeping in mind the utilization of their unique properties like minimum toxic side effects and reduction in the volume of carrying vehicle.
- Ease of application makes them far better dosage forms than others.
- They provide protection from hydrolysis and oxidation.
- They facilitate increased patient compliance (Garg and Goyal 2014c).

Theories of microemulsion formation

The interfacial tension between oil and water has to approach zero, in order to form a microemulsion. Microemulsions are

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termed as the biphasic liquid dosage forms, and therefore, are distinct from molecular solutions of hydrocarbons and water (Burrows and Miguel 2001). The different theories and approaches behind the formation of microemulsions are listed in sequence below:

Thermodynamics of microemulsion formulation

The various thermodynamic properties of microemulsions, like free energy, surface tension, and interfacial area, are interdependent on each other by means of a simple algebraic equation, as given below. There is a well-defined relationship between the properties of free energy, surface tension, and interfacial area of microemulsions.

$$\mathrm{D}G_{\mathrm{f}} = \gamma \mathrm{D}A - T\,\mathrm{D}S$$

Where $\mathrm{D}G_{\mathrm{f}}$ is the free energy of formation, γ is the surface tension of the oil–water interface; DA is the change in interfacial area on microemulsification, DS is the change in entropy of the system, which is effectively the dispersion entropy, and T is the temperature. Negative values of free energy of formation are obtained where large reductions in surface tension are accompanied by positive entropy changes. Hence, microemulsification proves to be a spontaneous and thermodynamically stable process (Chandra et al. 2009).

Mixed film theory of microemulsion formation

According to the interfacial mixed film theory, there is an assumption that the film at the interface is a dual film made up of surfactant and cosurfactant, and the type of microemulsion formed depends on bending of the curvature of the this film (Schulman et al. 1959). The formation of the surfactant-cosurfactant dual film at the interface causes a reduction in oil–water tension to extremely low values. Spreading pressure of the dual film exceeds the value of the oil–water tension, and hence the negative interfacial tension causes a reduction in the size of droplets. The resulting net interfacial tension is a process that takes place at dynamic equilibrium and finally attains zero or a very small positive value (Figure 1).

Solubilization theory of microemulsion formation

The solubilization theory has very clear-cut assumptions, according to which two types of micelles exist – normal and inverse, as illustrated in the picture above. Oil is solubilized by normal micelles, and water is solubilized by reverse micelles (Gillberg et al. 1970). Solubilization is very closely and directly related to micelle concentration, as CMC solubilization is directly proportional to micelle concentration. There are numerous factors affecting the solubilization process related to microemulsions (Schott 1985). Temperature is one such important parameter (Shinoda and Kunieda 1971). Solubilization is closely related to micellization, and CMC solubilization increases in direct relation to the micelle concentration. Several important factors affect the solubilization, including temperature. Generally, solubilization increases with increased temperature. Incorporation of electrolytes as well as non-electrolytes like alcohols cause an increase in the micelle size, and hence, causes an increase in the solubilizing power (Schulman et al. 1959). Generally, two approaches have been considered in the description of microemulsion systems, to have them considered as higher swollen micelles or to involve changes that occur at the O/W interface. Microemulsion droplets are formed in the following two ways: 1. The breakdown of larger droplets on lowering of the interfacial tension. 2. Swelling of the interior of the micelle by molecular diffusion of the interior phase throws a bulk of the medium (Garg and Goyal 2014a).

Types of microemulsion systems

According to Winsor, there exist 4 types of microemulsion phases at equilibrium, and these phases are called Winsor phases (Figure 2).

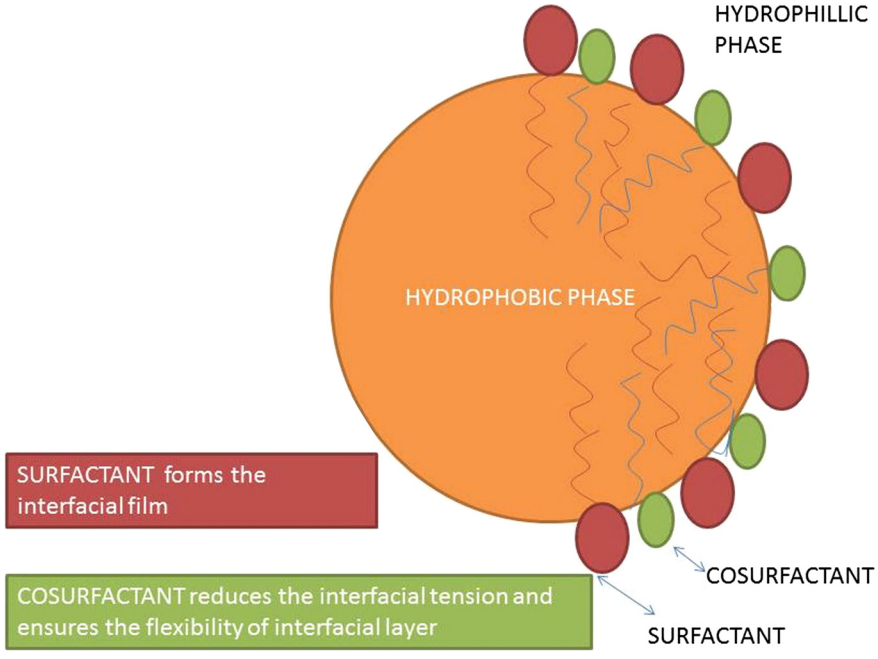

Figure 1. Arrangement of surfactant and cosurfactant at the interfacial film.

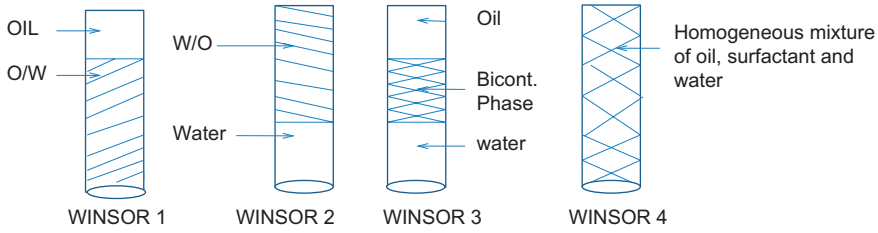

Figure 2. Types of Winsor phases.

WINSOR 1: In this type of microemulsion system, the lower O/W microemulsion phase is in equilibrium with the upper excess oil.
WINSOR 2: It exists in the form of two phases, the upper microemulsion phase (W/O) in equilibrium with the lower excess water phase.
WINSOR 3: It contains 3 phases, the middle bicontinuous phase is in equilibrium with the upper excess oil and the lower excess water.
WINSOR 4: It consists of a single phase only, that is oil, water, and surfactants are homogeneously mixed.

Microemulsion preparation techniques

Microemulsions differ from the traditional emulsions in the fact that they are made by suitable quantities of ingredients at optimum temperature (Shalviri et al. 2011). The preparation of microemulsions is a straightforward process. The method of preparation of the O/W type of microemulsion starts with the W/O emulsion containing a lipophilic surfactant. During the process, a hydrophilic surfactant is added, with stirring, which initially forms a cubical structure, but on further addition of hydrophilic surfactant results in the formation of an O/W microemulsion. The exactly opposite procedure can be adopted for the preparation of the W/O type of microemulsion (Garg et al. 2012a).

Phase titration method

The phase titration method is one of the methods to prepare microemulsions, and it can be explained with the help of a triangle-shaped phase diagram. These triangular phase diagrams are called as ternary diagrams. They are easy to interpret, being less time consuming, and have three corners, each corner representing 100% of the pure component. Ternary diagrams of water, oil and Smix are made at fixed weight ratios of Smix. The ingredients are weighed into clean and dry vials, titrated with water, and stirred. Visual inspection is used to see and confirm the formation of the monophasic or biphasic system. Samples are observed, and assumed to be biphasic in case turbidity is followed by phase separation. In case of monophasic systems, we manage to obtain clear and transparent systems after stirring. These are considered as the points in the phase diagrams. The area occupied by these points is considered the microemulsification zone. The phase diagrams are handy tools to describe the microemulsion system (Garg et al. 2014a). A simple ternary diagram shows the blending of oil, water, and surfactant. Each corner of the triangle represents a pure compound. Each corner point of the triangle represents the composition of the blend of two components, and the point inside the diagram represents the blend of 3 components. When the water content of the microemulsion is less, near the oil corner of the phase diagram, the local structure consists of swollen inverse micelles. The oil phase is continuous, and water micellar droplets are the dispersed phase. Surfactant and cosurfactant are deposited on the interface between the water and the oil phase. As we increase the water content, the shape and volume of the hydrophilic core of the hydrophilic micelles expands. At the water corner, the microemulsion looks like a direct micellar solution, because water is the continuous phase (Garg et al. 2014d). In the intermediate phase at which the water and oil phase exist in almost the same quality, the system exists as a lamellar phase (Figure 3).

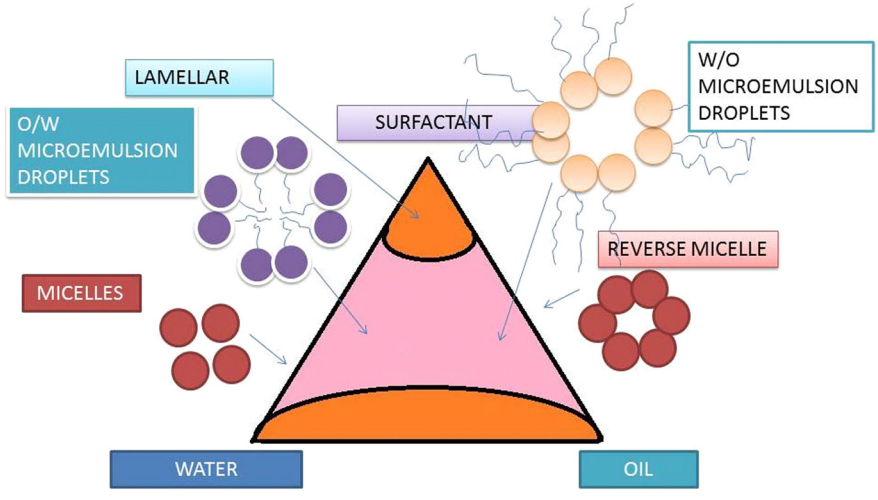

Figure 3. Phase diagram of microemulsion.

Phase inversion method

It is a method of converting the dispersed phase into a continuous phase, and vice versa. Phase inversion is a phenomenon by which the dispersed phase becomes the continuous phase, and vice versa. Surfactant arrangements at the O/W interface undergo a spontaneous change, accompanying the phenomenon of phase inversion (Chakraborty 2007). Phase inversion can be brought about by means of the 4 methods, as below:

1.Change in the temperature of the system
2.Addition of salts
3.Change in the volume fractions
4.Introduction of particular flows (Akay et al. 2005).

Change in the experimental conditions induces a sudden and dramatic change in the morphology of the emulsion system. Catastrophic phase inversion is a term that was introduced by Galindo Alvarez and coworkers. They described the influence of oil viscosity and process conditions of the phase inversion phenomenon (Sadtler et al. 2012). Another scientist, Jhanzad, showed that the formation of a microemulsion follows a catastrophic event (Jahanzad et al. 2007). Sajjadi pointed out the catastrophic phase inversion of abnormal emulsions in the vicinity of the phase inversion point, and nanoemulsion formation by catastrophic phase inversion (Jahanzad et al. 2007).

Composition of microemulsions

Microemulsions are known to increase the absorption of the applied drug at the site of application. The reason for this is the penetration enhancement effect of the carrier, mostly composed of saturated as well as unsaturated fatty acids as the oil phase.

Surfactants

Surfactants used to stabilize microemulsions may be (i) nonionic, (ii) zwitterionic, (iii) cationic, or (iv) anionic surfactants. Ionic surfactants are not used generally due to toxicologic concerns, and nonionic surfactants are considered suitable for oral ingestion (Garg et al. 2014b). Nonionic surfactants are available commercially in solubilized oral formulations, including Cremophor EL, Cremophor RH 40, Tween 20, Tween 80, TPGS, Span 80, Labrafil M-1944CS, Labrasol, Gelucire 44/14, etc. (Narang et al. 2007). Surfactants having low hydrophilic-lipophilic balance (HLB) values ranging from 3–6 are preferred for the formulation of W/O microemulsions; surfactants with high HLB values ranging from 8–18 are preferred for the formation of O/W microemulsions. Surfactants whose HLB values are greater than 20 often require the presence of the cosurfactant to reduce the HLB value to within the desired range (Garg et al. 2014c). Surfactants can be modified with the intermediate polarity groups such as polypropylene oxide and polyethylene oxide inserted between the hydrophilic head and the hydrophobic tail. With this modified structure, they are capable enough to provide enhanced interaction with both oil and water phases. This results in the formation of microemulsions with very low interfacial tension and high solubilization properties (Garg et al. 2011a).

Cosurfactant

Microemulsions often contain a cosurfactant, which is an amphiphilic molecule. It accumulates at the interfacial region, along with the main surfactant. The combination of a low HLB surfactant with a high HLB surfactant is tried, in case the HLB of the system is to be modified. A cosurfactant is used with a purpose of modifying the HLB of the system. The amount of cosurfactant used in the formulation is generally less than that of the surfactant. Alcohols can function as the cosurfactant. Similarly, nonionic surfactants can function as the cosurfactant (Narang et al. 2007). Mostly, single chain surfactants are themselves unable to reduce the O/W interfacial tension to a sufficient level, and hence, a cosurfactant is used. Substances used as natural cosurfactants are phosphatidylcholine, phosphatidylethanolamine, phosphatidylglycerol, and their derivatives, synthetic ethanol, isopropanol, propanol (short chain alcohols), transcutol, polyethylene glycol, propylene glycol, etc. (Garg et al. 2011b).

Oil phase

One of the most challenging tasks while designing the microemulsion formulation is careful selection of the oil phase. It has various advantages, as it not only solubilizes the lipophilic drug, but also enhances the absorption of the lipophilic drug from the GIT. Lipophilic drugs are preferably solubilized in O/W microemulsions. The main criterion for selection of the oil phase are that the drug should be highly soluble in it. Examples of oils are olive oil, castor oil, corn oil, coconut oil, etc. (Garg et al. 2012b).

Aqueous phase

Water used in the formulation of microemulsions is highly processed. It is deionized, double-distilled, and further purified by passing through the ion exchanger. In the aqueous phase, it may accommodate a hydrophilic active drug and some preservatives. Few formulation scientists make use of the buffer solution developed by some researchers. The droplet structure of the O/W microemulsion is retained on dilution by the biological aqueous phase, while exactly the opposite happens in case of the W/O microemulsions. As far as the W/O microemulsions are concerned, an increase in the volume of the aqueous phase leads to a decrease in the surfactant/water ratio, and hence, droplet growth. In case further dilution continues, it might lead to phase inversion or separation, or a return of the original microemulsion properties, and the integrity might be lost (Garg et al. 2013).

Buffer

As far as the use of buffers in microemulsions is concerned, phosphate and borate buffers and their mixtures are used at low concentrations. Zwitterionic microemulsions are made to be put into use to allow higher voltages for faster separation, as they decrease the intensity of current produced during the migration. Examples of zwitterionic buffers are ACES, CAPS, and CAPSO. The pH of the buffer media has a pronounced effect on the separation selectivity. Buffers have been and are being used mostly in the pH range of 7 to 9. Low pH values below 3 are applied to cancel the negative voltages that are applied through the capillaries, as a result of which

hydrophobic compounds are easily detected first. Conditions of pH above 12 have two advantages: in case of basic compounds, they are used to avoid chances of ionization, and in case of compounds like estrogens, they induce their ionization and improve their detection (Goyal et al. 2013a).

Applications in advanced drug delivery

Applications in oral drug delivery

Microemulsion formulations are normally beneficial over the conventional oral formulations for oral administration. They offer increased absorption, enhanced clinical potency, and less drug toxicity. Hence, microemulsions have been reported to be ideal delivery carriers of drugs such as hormones, steroids, antibiotics, and diuretics (Charman 2000). The oral route is the major route for drug delivery in many diseases. The major problem that we face in the delivery of oil-soluble drugs in the oral route is the poor aqueous solubility. One way to sort out this problem is to deliver the drug in the microemulsion form. Designing an effective oral delivery system has always been problematic for researchers, because of poor solubility and instability of the drugs in the GI fluid. Microemulsions have the unique ability to circumvent these problems (Goyal et al. 2013b). Microemulsions encapsulate the drugs with varying solubility because of the presence of polar, nonpolar, and interfacial domains in them. Microemulsions protect the incorporated drugs from oxidative and enzymatic degradation. Commercially available microemulsion formulations are of cyclosporin A, saquinavir, and ritonavir, available in the market (Fricker et al. 2010). A new microemulsion-based system of myricetin has been developed for oral delivery. The myricetin microemulsion improves the oral bioavailability of the drug myricetin, which was a poorly water-soluble drug. In vivo absorption studies of myricetin showed that microemulsification effectively promotes the absorption of the drug. Microemulsified forms reduce the dose of the drug and improve the bioavailability (Goyal et al. 2014a). Self-microemulsifying drug delivery systems in soft capsule form have been prepared for oral delivery for improved intestinal absorption of drugs. Forty percent of the newly discovered drugs possess little or low water-solubility and hence low bioavailability. These drugs are good candidates to be formulated in the form of SMEDDS (self-microemulsifying drug delivery system) (Gibaud and Attivi 2012). Lovastatin lowers the cholesterol level by inhibition of the enzyme involved in the synthesis of cholesterol. The oral bioavailability of cholesterol is less than 5%, because of rapid metabolism in the gut and liver. In vivo studies have revealed that there is increased bioavailability after oral administration of lovastatin in the microemulsion form (4.7 times), as compared to the commercially available lovastatin. The absorption efficiency of levofloxacin hemihydrate, a synthetic quinolone antibiotic, was found to be enhanced by the use of a water-in-oil microemulsion system (Goyal et al. 2014b).

Applications in topical delivery

Microemulsions have an excellent ability to deliver large amounts of water and topical agents into the skin, greater than the ability of water alone or other traditional vehicles such as creams and lotions, because they act as an excellent reservoir for poorly soluble drugs by their capacity for enhanced solubilization. Microemulsions of poorly soluble anti-fungal agents have been successfully developed, like miconazole nitrate (Hussain et al. 2014). Microemulsion-based gels for vaginal delivery of clotrimazole and fluconazole were developed and compared with marketed clotrimazole gel by in vitro methods. Microemulsions have proved to increase the cutaneous absorption of both hydrophilic and lipophilic medicaments as compared to the conventional vehicles like pure oils, emulsions, and aqueous solutions (Johal et al. 2014). This type of behavior of microemulsions is generally attributed to the high solubility of medicament in the microemulsions, with an enhanced concentration gradient towards the skin. Microemulsions have received great importance in terms of applications for transdermal drug delivery. The use of curcumin for treating various diseases like skin cancer, psoriasis, and scleroderma has been extensively reported (Joshi et al. 2014a). Microemulsions can be considered a suitable carrier system for the application of ascorbic acid as whitening agent. In addition, a good passage of the drug-in-drug could be interesting for the relative oxygen matrix damage. A microemulsion containing diethyl glycol monoethyl ether was found to be the best formulation to deliver the whole dose and also enhanced the skin penetration (Joshi et al. 2014b). This microemulsion showed best results in the antifungal activity test against Candida albicans. Hence, these types of microemulsions prove to be very promising for clinical evaluation. A microemulsion gel containing betamethasone dipropionate and salicylic acid provides good antiinflammatory activity for the treatment of psoriasis (Kalia et al. 2014).

Applications in ocular drug delivery

Drugs are delivered topically to treat eye diseases. O/W microemulsions have been under the radar for ocular administration to dissolve poorly soluble drugs, to increase absorption, and also to prolong the release profile (Kataria et al. 2014). Pilocarpine microemulsions were formulated using lecithin, propylene glycol, and PEG 200 as cosurfactants, and isopropylmyristate as the oil phase. Microemulsions have several excellent advantages as ocular delivery carriers, as they offer very low surface tension, thermodynamic stability, phase transition to liquid crystal state, and small droplet size, which may lead to improved ocular retention, high absorption, long duration of action, and enhanced permeation of loaded drugs (Kaur et al. 2014a). Eye drops are the most used form of dosage by the ocular route. The ocular route has two disadvantages – one is low bioavailability, and the other is the pulsed release. Microemulsions have advantageous properties like ease of sterilization, specific structures, stability, and capacity to dissolve the drugs. The results of tests on healthy volunteers in vivo have shown enhanced bioavailability (Kaur et al. 2014b). Eye drops account for 90% of the available ophthalmic formulations due to their convenience, simplicity, and suitability. Rapid precorneal loss caused by drainage and high tear fluid turnover is one of the major concerns associated with topical delivery of ophthalmic drugs.

Only 5% of the drug drops penetrate the cornea and reach the intraocular tissue (Kaur et al. 2014c). This results in the production of undesirable side effects. Microemulsions are a promising tool, with improved ocular retention, reduced side effects, and increased corneal drug absorption, maintaining the simplicity and convenience of eye drops as dosage forms. The formulations in microemulsion form are low viscosity fluids with a refractive index lending them to ophthalmic applications. The tested microemulsions have proved to be nonirritant in hen egg membrane and rabbit eye. Long-term pharmacologic effects were observed, when the drug was compared with aqueous solution in vivo (Kaur et al. 2014d).

Immunological applications

Tacrolimus is a potent immunosuppressive agent. It has limited corneal penetration. Microemulsions increase the drug's solubility and enhance drug absorption in the eye. Betamethasone-dipropionate has immunomodulatory, antiproliferative and antiinflammatory activity (Kaur et al. 2014f). The addition of corticosteroids such as BD, and keratolytic agents such as salicylic acid in microemulsion formulations, results in an enhanced and sustained corticosteroid delivery rate, leading to better antipsoriatic activity. Hydrogels as immuno therapeutics have great potential for improving the efficacy of vaccines and immuno therapeutics for diseases such as cancer (Kaur et al. 2014e).

Phytochemical applications

The delivery of plant protection agents to the leaves, and the process of their application, are still to be optimized (Kaur et al. 2014g). Till now, plant protection agents contain harmful emulsion or suspension concentrates that often contain environmentally harmful organic solvents and adjuvants (Kaur et al. 2014h). Emulsified microemulsions prepared from environmentally friendly components can be loaded with the plant protection agent fenpropiomorph up to 48% without organic solvent (Edris and Malone 2012). The solubilization behavior of a number of essential oils containing volatile phenolic constituents was investigated in 5 different micellar solutions (Kaur et al. 2014i). These oils include Eugenia caryophyllata, Thymus serpyllum, and Thymus capitates. The results of these studies showed different applications in personal hygiene, fragrance, pharmaceutical products, and cosmetics. In a new study, a microemulsion system with cassia oil as oil, ethanol as cosurfactant, Tween 20 as surfactant, and water, was made and its in vivo and in vitro activity against Geotrichum citri-aurantii was assessed (Kaur et al. 2014j). The results indicated that the microemulsion was effective in preventing postharvest diseases of citrus fruits caused by G. citri-aurantii (Xu et al. 2012).

Biotechnological applications

The microemulsion-based organogels have numerous potential biotechnological applications. A highlighting example is the use of various lipase microemulsion systems for synthetic and hydrolytic reactions (Kaur et al. 2014k). These microemulsion-based gels are media for bioorganic reactions using lipases as catalyst, formulated and optimized microemulsion-based organogels containing propanol hydrochloride, using experimental design methods (Malik et al. 2014). The results of the study concluded that the choice of lecithin/iso propyl myristate weight ratio, and the amount of drug incorporated, may be crucial in determining the performance of the organogel (Marwah et al. 2014). Enzyme catalysis in microemulsions is used for many reactions, and similarly, for the synthesis of sugar acetal, peptides, esters, transesterification, steroid transformation, and a variety of hydrolytic reactions (Modgill et al. 2014a). The most widely used class of enzymes in microemulsions consists of enzymes used for lipase catalysis. Microemulsions are used for the extraction of the proteins from fermenter liquids (Modgill et al. 2014b). These proteins and enzymes maintain and retain their normal activity. Solvent concentration, salt type, temperature, pH, and ionic strength affect the process of partition of proteins. One of the stereochemical advantages of the microemulsions is that with the help of biotechnology, we can produce the chiral epoxides using mycobacterium in W/O emulsions (Morie et al. 2014). Many biotransformation processes are difficult to carry out because of poor water solubility of substrate or product. Candida rugosa lipase has been immobilized. It has been done on gelatin-containing AOT microemulsion-based organogels, and sometimes on silica gel as well. The activity of tyrosinase was studied both in aqueous buffer solution as well as in AOT/water/isooctane W/O microemulsion, for oxidation of 4-butyl catechol to 4-butylyquinone (Pabreja et al. 2014). In case of aqueous solutions, AOT is capable of activating the enzyme at low concentrations, but inhibits the activity at high concentration. The same is true for the W/O microemulsions. It has been reported that the enzyme organophosphorus hydrolase degrades organophosphorus pesticides in water/Tween 85 + isopropanol hexane microemulsion systems. Kinetics and stability studies were conducted, which showed the partitioning of enzyme between the micelle surfactant layer and aqueous core (Rohilla et al. 2014a).

Cosmetic applications

Cosmetics are another important field where microemulsions are being used. Microemulsions have great applications in the field of cosmetics. The microemulsions have advantages like high solubilization power, thermodynamic stability, and ease of preparation. They can enhance skin permeation of loaded substances (Rohilla et al. 2014b). Microemulsion formulations reduce the toxicity and increase the product efficiency. Microemulsions have potential use as cosmetic agents and pharmaceutical drug delivery systems. Because of their high oil content, they improve the bioavailability of hydrophobic drugs. There is evidence to show that microemulsions can be used to regulate and control the release pattern of drugs within a therapeutic situation. Microemulsions are also used in the development of novel cosmetics, and are used in the process of product preservation (Friberg et al. 1994). It is believed that the skin adsorbs the cosmetics that are based on microemulsions. Cost and safety are the major criteria as far as microemulsion formulations in cosmetics are concerned, because some of the amphiphiles are not suitable for the personal healthcare products. Oligoglucoside, propanol, hexadecane, isopropyl myristate, lecithin, sodium alkyl sulfate, and alkyldimethylaminesulfate are used in microemulsion formulations for skin care (Shinoda et al.

1984). Fragrance and flavored oils are also added in microemulsion formulations. For the cosmetic use of microemulsions, vapor pressure over time and temperature is studied as a vital characteristic (Sharma et al. 2014a).

Microreactors and blood substitutes

The use of microemulsions as drug delivery vehicles has been an exciting and attractive area of research because of their many potential and extraordinary benefits. Microemulsions have found application as oral solid dosage forms as microreactors and blood substitutes (Sharma et al. 2014b).

Spermicides

Gel microemulsions are novel and non-toxic intravaginal spermicides that act as vehicles for lipophilic drug substances targeting sexually-transmitted pathogens. Spermicidal gel microemulsions have unique potential as dual-function microbicidal contraceptives to improve vaginal bioavailability of poorly soluble antimicrobial agents, without causing significant vaginal damage, as was demonstrated in an experiment conducted on contraceptive efficacy and safety studies of novel microemulsion-based lipophilic vaginal spermicides. The contraceptive activity of GM-4 with N-9 was compared, and it was concluded that the novel spermicide GM 4 formulation is quite safe and more significant than N 9 in terms of preventing contraception (Shi et al. 2007).

Analytical chemistry

The use of microemulsions for soil treatment has been reported. Rapeseed methyl-containing microemulsions have been consistently used in the extraction of the various compounds from the soil, like polychlorinated biphenyls and polycyclic aromatic hydrocarbons. Both O/W as well as bicontinuous microemulsion have been found equally reasonable and efficient in the extraction of these compounds from the soil. By making use of the chlorinated hydrocarbons and hydrophilic surfactants, these contaminants are removed with the help of microemulsions. Pesticides in O/W and W/O microemulsion forms have been used for the removal of impurities and also for detoxification of mustard compounds. A microemulsion medium at room temperature is used to measure the presence of polycyclic aromatic hydrocarbon by phosphorescence (Sharma et al. 2014c).

Microemulsions are used for two distinct purposes in the industry, i.e. coating, as well as textile finishing. They have the ability to produce monodispersion by polymerization of the W/O system, by utilizing the microemulsified monomers. They turn water-insoluble polymers into water-soluble ones. The dyeing of nylon 6.6 with azo dye has been reported, which is a novel method of dyeing and better than other traditional methods (Singh et al. 2014a). Microemulsions containing siloxanes produce a good final finish, with dispersed microemulsions. Microemulsions are good for coating and textile functions for the following reasons: increased product abrasion, high stability, good product distribution, and high internal softness, etc. (Singh et al. 2014b).

Conclusions and future prospects

There is a strong need for edible delivery systems to protect, encapsulate and release bioactive lipids within medical, pharmaceutical and food industries. Emulsion technology is the best for fabrication and design of delivery systems for encapsulating bioactives. Microemulsions find applications in sustained drug delivery, targeted delivery, controlled delivery, enzyme immobilization, enhancing bioavailability, masking taste, etc. Since orally delivered hydrophilic drugs are unstable in the GIT, like peptides and proteins (Singh et al. 2012a), new approaches consist of the use of biorecognizable moieties for active targeting in clinical trials. The advanced mechanism of action includes altering the mechanism of action of drugs with biomaterials. The cell signaling pathway, gene expression profile, and drug resistance can be altered by coupling bioactive agents with biomaterials (Singh et al. 2012b). There are different objectives behind the selection of W/O microemulsions, since they protect water-soluble drug molecules from being metabolized. There are drug molecules that are heat-sensitive, and microemulsions do not demand high temperature conditions to form. W/O microemulsions, on addition of aqueous fluids, are converted to O/W micro emulsions, and hence, release the API. This allows W/O microemulsions to be designed to selectively release API at different regions of the GIT. Microemulsions have commercially important uses. The fluid used in some dry cleaning processes is a W/O microemulsion. Some floor polishes and cleaners, personal care products, pesticide formulations, and cutting oils are actually microemulsions. Much of the work done on these systems has been used to mobilize petroleum trapped in porous sandstone, for enhanced oil recovery. A fundamental reason for the use of these systems is that a micro emulsion phase sometimes has an ultralow interfacial tension between a separate oil and aqueous phase, which may release or mobilize them from solid phases even in conditions of slow flow and low pressure gradients. Supercritical CO_2 is a handy replacement to organic solvents. Recently, efforts have been made towards making water and CO_2 microemulsions. They have tremendous applications in cosmetics, catalysts, electronics, miniaturization and ceramics. Microemulsions are used in enhanced oil recovery from the sea by means of a method called chemical flooding (Singh et al. 2014c).

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Declaration of interest

The authors confirm that the content of this article has no conflicts of interest.

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