Nanoemulsions Synthesis from Seed Oil, Characterization, and Their Applications

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Abstract Nanoemulsions are kinetically stable colloidal particle systems with an average droplet size range from 100 to 500 nm. Nanoemulsions are prepared by using different techniques using discontinuous phases from various seed oil with different types of emulsifiers and continuous phases. Of these different formulation techniques, the ultrasonication technique was the most frequent technique. The synthesized nanoemulsions can be characterized by using various parameters like droplet size, poly dispersive index, percentage transmittance, microscopic structure, refractive index, viscosity, zeta potential, and pH value. Nanoemulsions have excessive potential applications in pharmaceutics, foods, cosmetics, and biological activities such as antibacterial, and insecticidal due to their beautiful properties, such as small sizes, high surface area per unit volume, enhanced dispersion of active lipophilic components, and improved absorption. Thus it was observed that nanoemulsion proved itself as a promising alternative for improving the bioavailability of the drug. This chapter aims to give an overview of the nanoemulsions synthesis from seed oil, characterization, and their applications.

Keywords Characterization · Formulation · Nanoemulsion

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1 Introduction

Nanoemulsions are correspondingly recognized as mini emulsions, submicron emulsions, ultrafine emulsions and colloidal particulate systems. The typical droplet size range of nanoemulsions are from 1 to 1000 nm [1]. Regularly, the typical droplet diameter is between 100 and 500 nm, and the timely typical droplet size range of nanoemulsions is between 50 and 1000 nm. Commercial nanoemulsions typical droplet size range is from 0.2 to 100 μm. From this nanoemulsion particles can occur as oil-in-water (O/W) and water-in oil (W/O) forms, from the main particle is either oil or water, correspondingly [2]. In recent time nanoemulsion are categorize into three these are O/W, W/O which differ by core particles dispersed in the aqueous phase and bi-continuous (microdomains of water and oil are interspersed within the system). These three categories can be achieved for transformation by varying the components of the nanoemulsions. Both oil-in-water and water-in-oil nanoemulsions are other types of particles of nanoemulsions that present at the same time in one system in multiple emulsions. Nanoemulsions are considered kinetically stable particle sizes with 100 nm of one liquid phase dispersed in another immiscible phase [3, 4]. The dispersed phase of nanoemulsion can be stabilized by decreasing the surface tension between the two immiscible liquids by using an appropriate surfactant and co-surfactant as an interfacial film to form a particular phase. Emulsifying agents with varied features (non-ionic or ionic) had been used for nanoemulsions. Among them which widely used were sorbitan esters, polysorbates from nonionic surfactants, polymers (Spans and Tweens) and ionic surfactants (potassium laurate, sodium lauryl sulphate, sodium dioctyl sulfosuccinate and tragacanthins), cationic surfactants (quaternary ammonium halide) and zwitterions surfactants [5, 6]. Nanoemulsions have a good transparent appearance, high surface area, excellent stability, and tunable rheology are the characteristic properties of nanoemulsion, based on the above excellent properties of nanoemulsions, they are real alternatives for cosmetic, food, and pharmaceutical industries, and drug delivery applications [7]. When nanoemulsions are not stable droplets are floating on the surface, cohesion between droplets, and lastly creaming and separation. To avoid colloidal suspension the droplet's diameter needs to be greater than 0.1 μm.

Nanoemulsions are used for the capability to integrate together with lipophilic and hydrophilic drugs solubilization; improved bioavailability for many drugs; improved the degree of absorption; minimized inconsistency in absorption; defense from oxidation and hydrolysis in oil-in-water nanoemulsions; as non-toxic and non-irritant vehicles for skin and mucous membrane delivery and release control through permeation of drug through the liquid film [8]. Generally, nanoemulsion is preferable to microemulsion due to; is prepared using lower concentration surfactant, containing from 3 to 10% can be enough [9]. The aim of this chapter is to provide updated information on the formulation, and characterization of nanoemulsion by using different techniques and applications of nanoemulsion in different industries and fields.

2 Synthesis and Characterization of Nanoemulsions

Synthesis of nanoemulsions has extreme potential applications in pharmaceutics, foods, cosmetics, and biological activities such as antibacterial, and insecticidal due to their attractive properties, such as small sizes, and high surface area per unit volume. Therefore, nanoemulsions can be formulated via two wide methods these are low energy techniques and high-energy techniques [3, 4]. High-energy methods of nanoemulsion synthesis use a lot of energy (~108 W/kg) to break down huge droplets to 100 nm in size [3, 4]. High energy techniques suggest a robust method to formulate nanoemulsions with dispersed phase volume fraction as high as 40% with brute force technique [10]. Nevertheless, a lot of shear makes them incompetent and exposed to heat effects. Examples of high-energy techniques of nanoemulsion synthesis are high-pressure homogenizers, microfluidizer, and ultrasonication. on the other hand, low energy techniques of nanoemulsion synthesis feat the low interfacial tension property of a system to decrease particle size with energy input that can be attained by a magnetic stirrer (~103 W/kg), and nanoemulsions can deliver an easy and scalable route to without the use of excessive shear. High speed homogenizer, spontaneous emulsification, phase inversion temperature and phase inversion composition are examples of low energy emulsification. Oil (for solubilization of the lipophilic molecules), water, surfactant, and co-surfactant (improve the act of surfactant) are the key components for the formulation of nanoemulsions. According to Solans et al. [11] study, various methods have been realized to formulate nanoemulsion droplet diameter from 100 to 600 nm, which is suitable range for the majority of applications. Commonly, water-in-oil nanoemulsions are synthesis by using low hydrophilic–lipophilic balance (HLB) mainly from 3 to 8 HLB range of surfactants whereas, oil-in-water nanoemulsions are formulated by using high hydrophilic–lipophilic balance particularly between 8 and 18 HLB range of surfactants.

According to Moksha et al. [12] scholarship nanoemulsions were prepared by ultrasonication technique by using 80 mg (5% v/v) of coconut oil and span 80 (0.5% v/v) was placed in a beaker and stirred continuously to mix the solution. The subsequent solution was added into the aqueous phase which 5% v/v of ethanol as co-solvent and 5 present tween 80 as an emulsifier with constant stirring at 3000 r/m for 3 min. After formulation of the nanoemulsion, various physicochemical parameters of the nanoemulsion were optimized such as particle size, poly-dispersive index, percentage transmittance, morphology, zeta potential, solubility examination, and viscosity.

Moksha et al. [12] study shows that the poly-dispersive index and typical particle size of formulated nanoemulsion were measured by means of photon correlation spectroscopy method using particle size analyzer at room temperature by using tween 80 and span 80 as surfactants and the result was found to be 79.0 ± 5.7, and 0.220 ± 0.05 nm respectively. Absorption of formulated nanoemulsion was improved may be attributed in terms of a large specific area due to the small particle size of the droplet. The other property is zeta potential which is an indication of electrostatically stabilized nanoemulsion. When the zeta potential value is higher the suspension is to be stable as the charged particles repel each other and this potency overcomes the natural tendency to aggregate. From this zeta potential value of this study was found -15.54 ± 0.21 mV, due to the negative charge value of zeta potential artemether nanoemulsions indicating the presence of the anionic groups of the fatty acids and glycols in the surfactant and co-surfactant. Thus, there are negligible probabilities of aggregation of nanoemulsion in the biological environment during its shelf life.

A digital refractometer was used to characterize the refractive index value of the nanoemulsion sample by putting a few spots of formulation nanoemulsion on the transparency of refractometer at 25 °C [13]. The optimized nanoemulsion of refractive index value was 1.320 ± 0.05, from this there is no significant difference ($P \pm 0.05$) value of nanoemulsion, which was a symptom of the isotropic nature of nanoemulsion. The optimized percentage transmittance value of artemether nanoemulsion was found to be $98.20 \pm 0.7\%$ that nearer to 100% and shows that the formulation nanoemulsion was pure and clear. TEM images of particles in formulated nanoemulsion were detected as uniformly distributed, and spherical in shape with droplet diameter less than 100 nm [12].

Grounded on Kumar et al. [1] reported that nanoemulsion were synthesized by ultrasound-assisted method from sesame oil using Tween 20 surfactant with variable concentrations of oil and surfactant such as 1:1, 1:1.5, 1:2, 1:3, 1:4 and 1:5, and 30 mL of deionized water was added drop-wise in the internal phase combination to get nanoemulsion. Then the mixture of emulsion was stirred by a magnetic stirrer for 10 min at 540 r/m to get constant droplet distribution. The nanoemulsions were sonicated by ultrasonicator with 20 kHz frequency for 10, 20, 30 min respectively for individual composition. The typical particle size and PSD of nanoemulsion were characterized by using the dynamic light scattering instrument. Dynamic light scattering technique was used to measure the suspension of particles size distribution from 3 nm to 5 μm and the profile was detected as a single and narrow peak as it is mono-dispersed [14]. DLS data is detected as the plot of concentration and average droplet size [15]. For determining the average particle size accurately by DLS technique the samples should be translucent and diluted. The examination was done at 25.1 °C with 173° scattering angle. From this study, the best average droplet size range was 189.5 nm achieved at the composition of 1:3 oil to surfactant concentration. Extremely different droplet size is the result of high polydisperse emulsion. Higher stability is obtained on the lower poly-dispersive index. For sample 1:3, the poly-dispersive index was found to be the lowest at 0.514, followed by a poly-dispersive index of 0.555 for sample 1:2 oil to surfactant ratio. The value of zeta potential for 1:4, 1:3, and 1:2 showed high values, such as −23.4, −19.5 and −18.6 respectively and showed their stability. Stability test can be performed by centrifugation of the composition at 3000 rpm for 10 min and can select better stability compositions over the others (Fig. 1) [1].

Wang et al. [16] scholarship described that nanoemulsions were formulated by using dynamic high-pressure micro fluidization methods at diverse circumstances at 0–140 Mpa by using 0.03–0.18 mg/mL emulsifier with *Eucommia ulmoides* seed oil as aqueous phase solution. Tween 80/ethanol (2:1 v/v) and the from 2 to 12% volume fraction of *Eucommia ulmoides* seed oil were mixed at various proportions and stirred

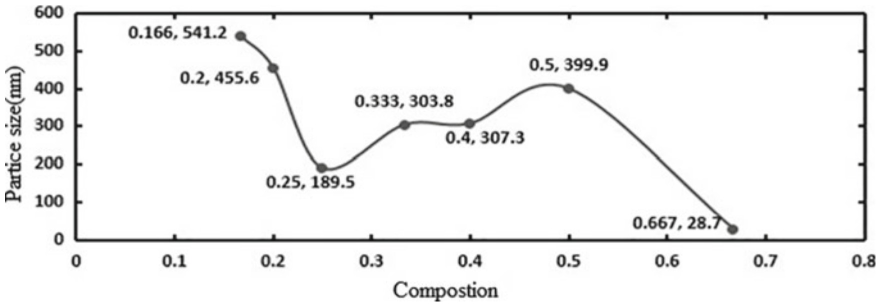

Fig. 1 Graph of average droplet size with variable composition (v/v) [1]

at 700 r/m magnetically for 10 min. Then the definite volume of distilled water was added dropwise, and the combination was, treated by ultraturrax at 10,000 rpm for 2 min. Consequently, the formulated crude emulsion was passed to prepare *Eucommia ulmoides* seed oil nanoemulsion. Rheology is the branch of physics that lessons how materials deform or flow in response to applied forces or stresses. The rheological properties of nanoemulsions are affected by the number density of the droplets, surfactants and shape, and interactions between the constituent droplets (Fig. 2) [17].

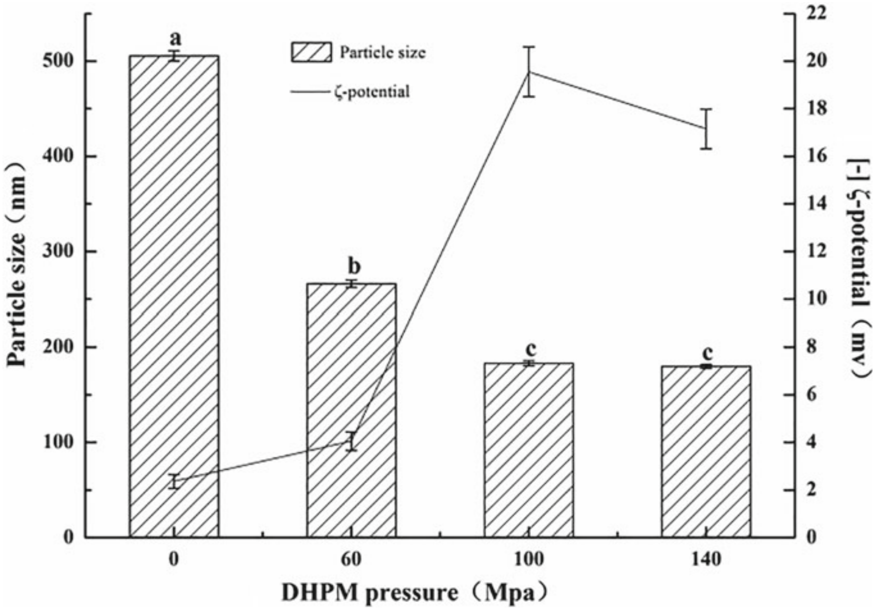

Fig. 2 Effect of droplet size and zeta-potential of nanoemulsion on dynamic high-pressure microfluidization method [16]

According to Vijayalakshmi et al. [18] nanoemulsion was synthesized using basil oil (*Ocimum basilicum*), Tween 80 and water through an ultrasonication technique that emulsified for 15 min. Stable basil oil nanoemulsion of average particle size from different concentrations was 29.3 nm droplet diameter. Based on this study the best particle charge value of the synthesized nanoemulsion was 3.70 ± 0.41 mV on the composition of 1:3 ratio and the native pH value of the nanoemulsion was 5.53 (Figs. 3 and 4).

According to Jeonghee et al. [19] report typical particle size can be minimized from 237 to 101 nm when the surfactant-to-oil combination was rise from 0.75 to 2. The poly-dispersive index decreased from 0.41 to 0.14 when the surfactant to oil proportion was a rise from 0.75 to 1.5, and then rise to 0.19 when the surfactant to oil was increased further to 2. Average droplet size is also based on the volume of surfactant, when the surfactant to oil ratio is equal to 0.75 the nanoemulsions had bimodal distributions.

Grounded on Priani et al. [20] nanoemulsion can also formulated by using ultrasonic bath. This nanoemulsion could be synthesized by the combination of *Nigella sativa* seed oil, co-surfactant (polyethylene glycol (PEG400)) and surfactant with diverse combination of oil and surfactant for self- nanoemulsifying drug delivery system. After mixing the component for few minutes, the mixture was homogenized at 40 °C for 5 min. After homogenization, the mixture was sonicated in bath sonicator for 15 min. The particle size of self- nano emulsifying drug delivery system containing *Nigella sativa* seed oil was 65.4 nm. The systems with an average droplet size below 100 nm achieve the standards of self- nano emulsifying drug delivery systems. The polydispersibility index (PDI) of *Nigella sativa* seed oil shows particle homogeneity (0–1).

Qushawy et al. [21] reported that nanoemulsion was formulated by using high pressure homogenization technique through the different compositions of Hemp seed (*Cannabis sativa*) oil, Tween 80 surfactant, Propylene Glycol and water. The droplet size range of nanoemulsion from hemp seed oil was observed from 80.7 ± 3.96 to

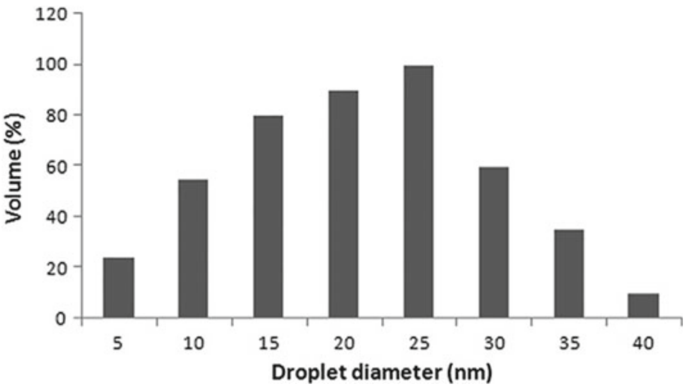

Fig. 3 Particle size of *Ocimum basilicum* oil nanoemulsion by volume [18]

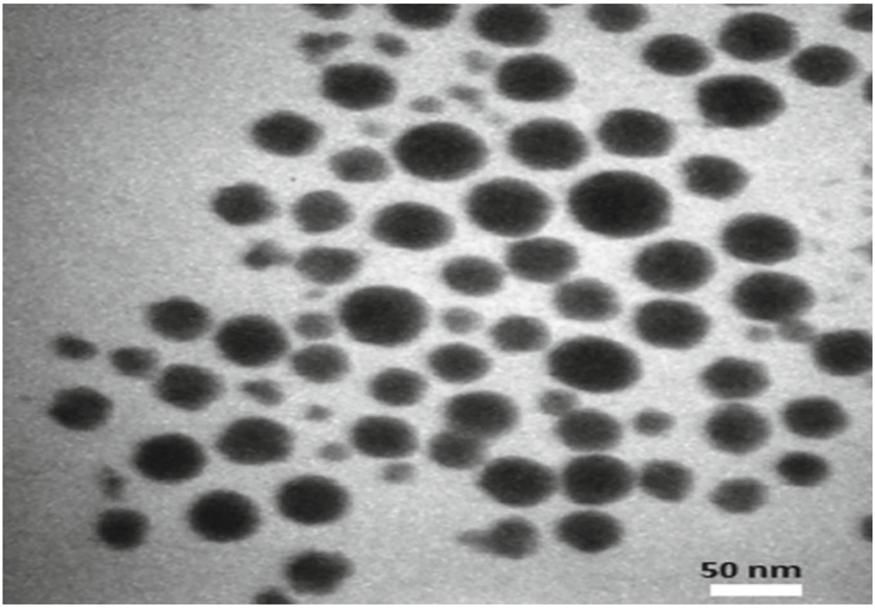

Fig. 4 TEM of *Ocimum basilicum* oil nanoemulsion with 1:3 (v/v) proportion of surfactant and oil [18]

140.9 ± 5.62 nm, polydispersity index of hemp seed oil nanoemulsions between 0.249 ± 0.06 and 0.493 ± 0.02 this result demonstrating a narrow size distribution and particle size of nanoemulsion was homogenous, zeta potential of all hemp seed oil nanoemulsions between −10.32 ± 1.35 and −21.94 ± 1.13 mV, this investigation was established that concentration of Tween 80 increased the value of zeta potential or the surface charge also increased. Minor particle size and greater surface area of oil droplets can be obtained by means of increasing Tween 80 concentration. pH value of hemp seed oil nanoemulsions was determined with a pH meter, and the value was between 5.76 ± 0.32 and 6.57 ± 0.41 pH, just like zeta potential value the pH value of nanoemulsion was enhanced with increasing concentration of Tween 80, from this opinion better stability of nanoemulsion could be obtained from better concentrations of surfactant. The viscosity of the prepared nanoemulsion formulation ranged from hemp seed oil between 3.16 ± 0.28 and 8.35 ± 0.34 cP. Lower viscosity was connected viscosity which may be attributed to higher surfactant. The electrical conductivity of the formulated nanoemulsion was between 170.93 ± 5.79 and 212.35 ± 8.46 mS/cm. TEM image of hemp seed oil nanoemulsions the best composition formulation indicates good distribution with spherical appearance and, small particle size in the nano range (Fig. 5) [21].

Based on McClements, (2010) report nanoemulsion could be synthesized by emulsion inversion point. Emulsion inversion point was formulated through water-in-oil to oil-in-water or vice versa. As its name indicates, by addition of oil or water into the water continuous phase or oil continuous phase respectively, during this time

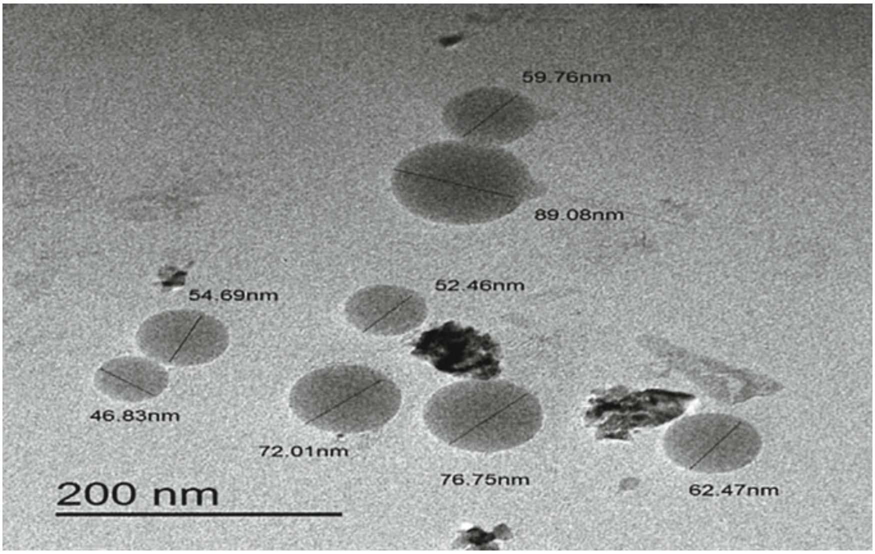

Fig. 5 The TEM image of greatest combination nanoemulsion preparation from hemp seed oil [21]

transition between distributed phases and continuous might be attained. When the addition of dispersed liquid phase reaches a critical point, the inversion mechanism occurs automatically. The emulsion inversion point could affect by surfactant-to-phase relation and degree of the distributed phase addition to the continuous phase.

McClements, 2010 reported that nanoemulsion can be emulsified by spontaneous emulsification. Spontaneous emulsification (SE) was a more suitable technique and formulated oil-in-water emulsion systems with surfactant and oil were mixed together with the help of a stirrer and then oil was dropped into the water phase. Physical and chemical properties of surfactant, type of fluids used, their solubility, degree of stirring, and surface to oil ratio (SOR) are features that disturb particle size and emulsions stability. The mechanism of SE technique system was examined on dispersed and continuous phases are established together as a distinctive phase. Whereas mixing was continued, surfactant used could pass over the water phase so that it can act as a bridge between water and oil with the help of turbulent strength. Additionally, the dispersed phase start to deport itself from the water phase. This motion can generate an enormous interfacial area between two phases. Then appropriately dispersed droplets are organized within a continuous phase spontaneously.

Niharika et al. [22] reported that nanoemulsion can also be formulated by low energy approach particularly spontaneous emulsification method by using pea protein and Tween 80 for vitamin D delivery application. The preparation procedure was 1 mg/mL of vitamin D in canola oil dissolved with Tween 80 primarily as organic phase. Then the solution was gradually titrated into distilled water with constant stirring 800 r/m on magnetic stirrer at ambient temperature [22]. Variable SOR equal to

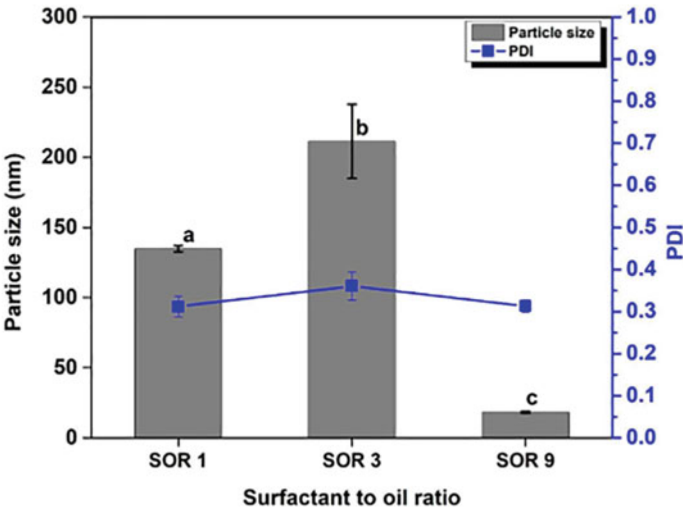

Fig. 6 SOR on the particle size and poly-dispersive index [22]

1.0, 3.0, 9.0 were adjusted and permitted to stir for 60 min followed by the addition of pea protein into the pre-formulated emulsions synthesized by 1:1 (v/v) SOR composition under constant mixing for 60 min to formulate the pea protein-Tween 80 complex nanoemulsion. To optimize concentration for emulsion production diverse SOR ratio equal to 1 with 3% w/v Tween 80 consequence was detected. After formulation of nanoemulsion average particle size and zeta-potential of the nanoemulsions were characterized by using dynamic light scattering at ambient temperature. Nanoemulsions were thinned by 1 mg/mL using double distilled water before analysis to avoid multiple scattering. From this as shown in Fig. 6, numerous surfactant molecules were presented to cover oil droplets at a surfactant to oil ratio of 8, and resulted in a minor nanoemulsion droplets size of 18.1 $\pm$ 0.7 nm. A surfactant-to-oil ratio of 1 for the formulation of emulsion also resulted in a relatively stable droplet size of 134.8 $\pm$ 2.2 nm.

3 Application of Nanoemulsion from Seed Oil

3.1 In Biotechnology

Nanoemulsions are applicable in biotechnology which have hydrophobic in nature, including dehydrogenases, oxidases, lipases, and esterases frequently purpose in the cells in micro-environments. From these numerous enzymes activate regularly stabilized by polar hydrophilic lipids and other natural amphiboles in biological systems. Nanoemulsions have been used as enzymatic catalysis for a variety of reactions, such as the synthesis of esters, peptides and sugar acetals transesterification, and steroid transformation, from these lipases are the most usually used class of enzymes [23].

3.2 Antimicrobial Activity

Nanoemulsion as antimicrobial activity is a novel and hopeful revolution because particles of nanoemulsions are thermodynamically motivated to fuse through lipid-containing organisms. From this fusion is improved through the electrostatic attraction between the positive charge of the emulsion and the negative charge of the pathogen. The energy released from both active constituent is destabilize the pathogen lipid membrane, consequential in cell lysis and death The nanoemulsion has a wide range action defined bacteria (for example *E. coli*, *Salmonella*, *S. aureus*), enveloped viruses (for example HIV, Herpes simplex), fungi (for example *Candida*, Dermatophytes), and spores (for example anthrax). The application of nanoemulsion to examine as an antimicrobial agent was encouraged through the recognized difficulty of growth of antimicrobial-resistant strains practiced with the use of present agents due to the prevalent, and occasionally unsuitable use of antibiotics, disinfectants and antiseptics. Additional research and progress of new antimicrobial agents targeting exact pathogens at the same time as being safe for the host. Since the mechanism of action of nanoemulsion seems to be nonspecific disruption of bacterial cell membranes, nanoemulsion would not consequence in the development of resistant strains. Nanoemulsion as an antimicrobial agent is a promising and new revolution. Karthikeyan et al. [24] showed that soybeans oil with cetylpyridinium chloride nanoemulsion was effective in antimicrobial activity of nanoemulsion which was greater than that of its component on cariogenic planktonic and biofilm organisms and showed 83% inhibition on *S. mutans* and *L. casei* micro-organisms. Formulated nanoemulsion from basil oil (*Ocimum basilicum*) using Tween80 surfactant and water through ultrasonic emulsification technique was assessed for antibacterial activity against *Escherichia coli* through kinetics of killing experimentation [18].

3.3 Drug Delivery Activity

Nanoemulsions have been used in furthermost topical, visual, intravenous, and oral drug delivery. Artemether nanoemulsion was better drug loading capacity of the nanoemulsion that exhibited a drug content of $98.42 \pm 0.87\%$. Nanoemulsion was used for lipophilic nature of drug to solvate water, zeta potential and rheology to synthesize aqueous solutions that can be simply distributed to patients. It is also used as a vehicle barrier against the management of drugs via the skin. Generally, formulations nanoemulsions are regularly applicable to manage drugs to improve the solubility of nonpolar compounds, pharmacokinetic profile and minimize adversative effects practiced through patients. Emulsions can be managed by patients through

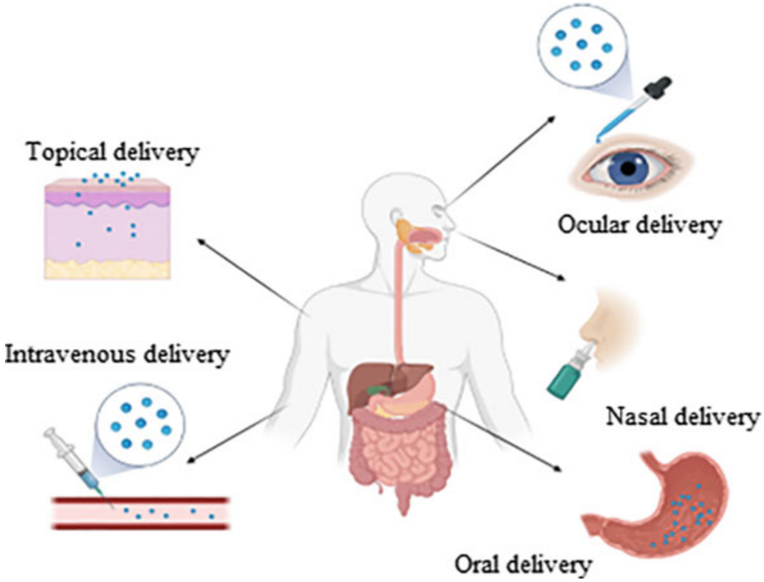

Fig. 7 Nanoemulsion management for drug delivery [25]

numerous directions that would be briefly familiarized as showed on the figure below. Generally, submicron size of nanoemulsion can be purely targeted to the tumor area (Fig. 7).

3.4 In Cosmetics

Nanoemulsion is applicable as means of transportation for measured delivery on the skin. For example, nanoemulsion formulation as kemira nanogel-based carrier system is applicable for cosmetic purposes which improve skin construction and diffusion of API. Nanoemulsion also delivers good skin feel [26]. Topical management itself has several benefits and by joining it with nanoemulsion, this formulation may impart a better way of drug delivery system. It can avoid the hepatic first-pass metabolism of the drug and related toxicity effects [27].

3.5 In Food Industry

Nanoemulsions have a broad range of applications due to their flexibility in several fields including beverage and food industries. Due to their small size, thermodynamic stability, transparency and optically transparent properties, nanoemulsion have been used as fortified soft drinks and water in food processing. Nanoemulsions can be formulated gel-like with very low particle concentrations, which can be simply applied to make low fats and novel texture products [15]. Nanoemulsions can improve the shelf-life time of industrial products due to the stability of particle aggregation and gravitational separation. Nanoemulsions could be solubilize lipophilic constituents, to encapsulate constituents into smaller size droplets, which was comparison to conventional emulsions [28]. As an innovative carrier of active ingredient, nanoemulsion has solved the difficulties of poor water solubility, easy oxidation and trouble of oil-soluble functional constituent absorption, and has attracted widespread attention in the field of food and medicine.

4 Conclusion and Future Perspectives

It has been demonstrated that synthesizing nanoemulsions from seed oil is a promising method for enhancing the solubility and bioavailability of lipophilic substances. Stable nanoemulsions with small droplet sizes and narrow size distributions have been created using a variety of techniques, such as high-pressure homogenization and ultrasound-assisted emulsification. Furthermore, these nanoemulsions have been characterized to learn more about their characteristics and stability utilizing methods like dynamic light scattering, transmission electron microscopy, and rheological analysis. The uses of seed oil-based nanoemulsions in a variety of industries, including food, cosmetics, and medicines, have also been investigated. Nanoemulsions have been utilized in the food sector to enhance the sensory qualities and shelf life of food goods. They have been utilized in cosmetics as carriers for active compounds and to enhance the skin absorption of these substances. Nanoemulsions have demonstrated potential in the pharmaceutical industry as drug-delivery devices for improving the solubility and bioavailability of medicines that are not readily soluble.

To fully utilize the potential of seed oil-based nanoemulsions, numerous obstacles still need to be overcome. To address the environmental issues related to the use of synthetic surfactants, it is important to investigate the use of natural and biodegradable surfactants and co-surfactants in addition to optimizing the formulation and processing parameters. Furthermore, the safety and toxicity of these nanoemulsions need to be thoroughly evaluated to ensure their potential use in various applications. In general, the creation of nanoemulsions from seed oil is a promising area of study with potential uses in many different industries. Unquestionably, further study in this field will result in the creation of cutting-edge, revolutionary nanoemulsion-based goods with enhanced functions.

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