



INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

REVIEW OF NANOEMULSION: FORMULATION APPROACHES AND APPLICATION OF NANOEMULSION.

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Abstract:

In pharmaceutical formulations nano emulsions are composed of practical within nanometer range. They have capacity to encapsulate drugs that are poorly water soluble due to their hydrophobic nature and also they are composed of safe gradient excipients which makes them safer and stable option to drug delivery. For several decades cancer therapy has been an issue because drugs developed to treat this disease and not always successful or and up failing, mainly due to low solubility and unspecific toxicity. This problem can be resolved by nanoemulsion because it not only solve water solubility problems but also provides specific targeting to cancer cells. This chapter includes overview about the nanoemulsion and various approaches for production of nanoemulsions which include high energy approach such as microfluidizer high pressure valve homogenization, ultrasonic homogenization. In low energy approaches, spontaneous emulsification phase inversion composition, phase inversion temperature and emulsion inversion point are discussed in detail.

Keywords: nanoemulsion, production approaches, applications

Introduction:

This review article provides detailed information about various formulation and approaches used to prepare the nanoemulsion. Emulsions could be oil-in-water (O/W), water-in-oil (W/O), and oil-in-oil (O/O) type. Emulsifier is also used as a third component playing an important role in dispersing two immiscible liquids (continuous phase and dispersed phase). Emulsions are the heterogenous system which is classified based on the nature of emulsifier used and structure of the system formed. The various structures of the emulsions system includes nanoemulsions, microemulsions, mixed, double and multiple emulsions. Nowadays, nanoemulsions have promising medicinal applications like anticancer activity and antimicrobial activity.

The major critical factor for emulsion is their breakdown processes. Ostwald ripening, Creaming, phase inversion, sedimentation, flocculation, coalescence and are the various breakdown processes which are involved in instability of the emulsion formed. microbial contamination, Oxidation, and adverse storage conditions are some of the types of chemical instability. Emulsions are characterised by various methods such as fluorescence test, dye test, dilution test, globule size analysis, conductivity, accelerated stability, and macroscopic examination.

Emulsions have wide applications range in everyday life. The concept of emulsions is widely applied in various industries. The various applications of emulsions are, agrochemicals (emulsion concentrates and pesticides, self-emulsifiable oils), oil (petroleum based and oil slick dispersions), food products (candy products, dairy, bakery products, meat products and beverages), paint (latex emulsions and alkyd resin based products), pharmaceutical (anaesthetics, creams, , chemotherapy, ointments), cosmetics (skin conditioning products and hair products), personal care (lotions, creams), dry cleaning formulations, and others¹⁻⁵.

Nanoemulsion:

In recent decades, nanoemulsions are gaining more importance due to their unique properties such as transparent nature, high surface area, robust stability and tunable rheology. The common approaches involved in nanoemulsion preparation include low energy methods (emulsion inversion point and phase inversion temperature) and high energy methods (ultrasonication and high pressure homogenization). Due to their properties, nanoemulsions are widely used in drug delivery systems, cosmetics, food, and pharmaceutical industries. Nanoemulsions are colloidal nanodispersions which is thermodynamically stable because of interfacial layer of surfactant/co-surfactant. Nanoemulsions are highly preferred over emulsions and suspensions due to higher solubilization capacity and thermodynamic stability.

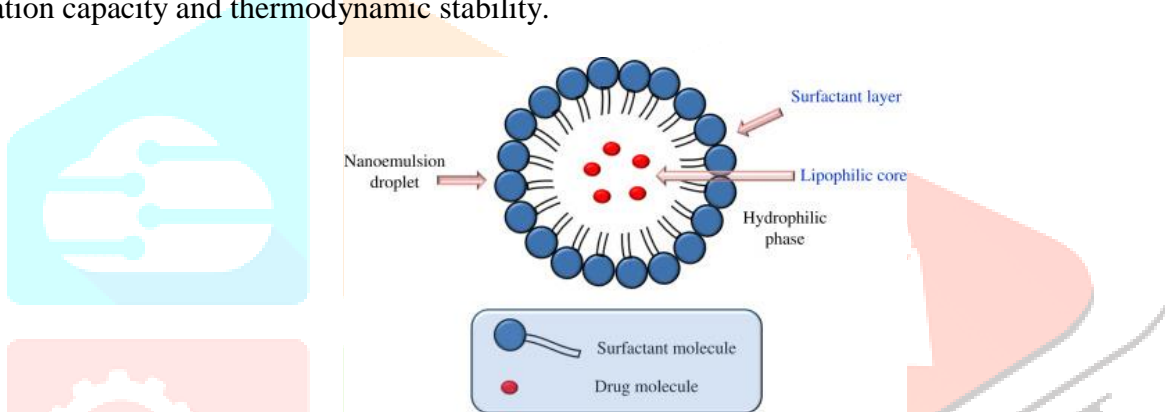


Figure 1: Nanoemulsion structure

Due to large surface area and free energy makes nanoemulsion unique delivery system. The main components of nanoemulsions are aqueous phase, oil phase and surfactant/ cosurfactants /co-solvent. Natural oils are comprised of triglyceride mixtures that contain varying chain lengths of unsaturation of fatty acids and saturated fatty acids. The selection of oil component is very important as it enhances solubilization potential of a drug candidate, and hence they enables high drug loading capacity as well. Hydrophobic Surfactants having HLB value less than 10 are (eg. Sorbitan monoesters) are tends to form the of water-in-oil type emulsion. Hydrophilic Surfactants with HLB value greater than 10 are (polysorbate 80), tends to form oil-in-water type emulsion. Sometimes, for nanoemulsion formation mixtures of both hydrophobic and hydrophilic surfactants are used. Non-ionic surfactants are mostly preferred over Ionic surfactants due to toxicological limitations. in reducing droplet size diameter surfactants plays an major role. Co-surfactant used in formulation also helps in reducing the interfacial tension between the oil-water interfaces. These co-surfactants helps to penetrate the monolayer of surfactant causing more fluidity to interfacial film and this cause break down of the rigid surfactant film formed.

Organic solvents such as glycerol, polyethylene glycol, propylene glycol, ethanol, etc., are also generally used. They helps in the dissolution of drug in lipid base or hydrophilic surfactants in large amounts by their nature of co-solvency and reduces dielectric constant of water. The ionic nature and pH of aqueous phase are given importance as they also influences droplet size and stability of nanoemulsions formed^{6,7}. Nanoemulsions have various advantages over other dosage forms and these advantages are, 1) rate of absorption increases. 2) non-irritant and non-toxic in nature. 3) improvement in bioavailability of drugs. 4) helps to solubilize lipophilic drug. 5) amount of energy required is less. 6) variety of formulations are formulated such as creams, lotions and sprays.

Formulation of nanoemulsion:

The main components involved in the formulation of nanoemulsion could be explained as follows.

Aqueous phase: In the nanoemulsion formulation, water is usually used as aqueous phase. The polar compounds may include proteins, carbohydrates, minerals, co-solvents acids and bases. The concentration of these components used and their type determines the ionic strength, pH, polarity rheology, density, refractive index, interfacial tension and phase behaviour of the aqueous phase, and this gives a direct impact on the formation, physicochemical properties and stability of the nanoemulsion formed.

Oil phase: The physico-chemical characteristics of the oil phase determine the stability, formation and properties of a nanoemulsion. The bulk physico-chemical properties of the oil phase may be viscosity, polarity, density, water solubility, interfacial tension, refractive index, phase behaviour and its chemical stability. The oil phase is usually selected from non-polar components like monacylglycerols, triacylglycerols, free fatty acids, diacylglycerols, essential oils, flavouring oils, mineral oils, waxes, fat substitutes and others.

Stabilizers: To avoid the nanoemulsion breakdown processes such as coalescence flocculation, Ostwald ripening and gravitational separation, different types of stabilizers are used to enhance their stability.

Emulsifiers: An emulsifier is capable of promoting droplet disruption, and adsorbing to the droplet surfaces prevents droplets against the formation of aggregates. Hence, the selection of emulsifiers plays a vital role. In the case of high-energy methods, yields small droplets because emulsifier causes droplet disruption by reducing the interfacial tension. In the case of low-energy methods, emulsifier have ability to produce low interfacial tension this leads to spontaneous formation of small droplets at solutions and certain environmental conditions. The small molecules are classified as nonionic, ionic and zwitterionic based on the electrical characteristics⁸⁻¹⁴.

Formulation approaches of nanoemulsion:

Nanoemulsions are non-equilibrium systems and for their preparation involves large amount of either surfactants or energy or combinations of both. Fabrications of nanoemulsion can be done by many approaches that can be classified as high energy or low energy approaches. Methods of preparation of nanoemulsion involve high energy methods (high-pressure homogenizer, microfluidizer and ultrasonicator) and low energy methods (self-emulsification, phase transition and phase inversion methods).

In The high-energy method, mechanical devices are utilizes to produce strong disruptive forces to break the water and oil phase to obtain nanoemulsions. The low-energy method, the stored internal energy utilizes for the formation of small droplets. Emulsions are obtained by changing the process parameters like composition, temperature and others that affect the hydrophilic-lipophilic balance (HLB). As compared to macroemulsions, nanoemulsions required higher energy for its production. For lowering the surface tension between the oil-water interfaces surfactants plays main role. As compared to polymeric surfactants, non ionic surfactants reduce surface tension to a greater extent.

High pressure homogenization: The use of piston homogenizer or high-pressure homogenizer produces nanoemulsions of very small droplet size of up to 1 nm range. Cavitation forces, intense turbulence and hydraulic shear act together to yield smaller droplets. Until a desired polydispersity index and droplet size is obtained we could resubject the resultant product with homogenizer. Emulsions are prepared at high volume of the dispersed phase and diluted later. But, this causes coalescence during the emulsification process, and for this purpose, surfactant could be used for effective reduction in surface tension is preferred.

Microfluidization: Through the interaction chamber that consists of small micro-channels to an impingement area this forces the product, and thus, results in fine particles of submicron range. To obtain coarse emulsion, initially the oily phase and aqueous phase together are processed in an inline homogenizer. To yield nanoemulsion formulation this coarse emulsion is then forced into a microfluidizer for further processing. This process of introducing coarse emulsion into micro-channels of microfluidizer is repeated many times till a desired particle size is attained. To formulate a stable and uniform nanoemulsion, the obtained emulsion is filtered under nitrogen to eliminate any undesired larger droplets present.

Thus at laboratory and industrial scale, both microfluidization techniques and high-pressure homogenization could be used for nanoemulsion preparation.

Ultrasonication: In ultrasonic emulsification, by ultrasonic cavitation strong shear forces are produced that produces bubbles and breaks down the particle size to nanometric range. Ultrasonication technique is mainly used at laboratory scale. For high pressure homogenization this method is used as an alternative. The method utilizes low energy and reduced surfactant concentration to yield homogenous nanoemulsion, and makes it more advantageous than conventional mechanical processes.

Phase inversion temperature: The phase inversion temperature method demonstrates a relationship between complete solubilization of oil and minimum droplet size in a bicontinuous phase that is independent of the initial phase equilibrium (multiphase or single). Phase inversion in emulsions could be of two types: catastrophic inversion and transitional inversion. The former is induced by changing factors like transitional inversion electrolyte concentration or temperature that affect the HLB of the system. Then latter at constant temperature, this induced by changing the HLB number of the surfactant.

Phase inversion temperature method employs temperature dependent solubility of non-ionic surfactants to change their affinities for water and oil as a function of temperature. In this method, water, oil and non-ionic surfactants are mixed together at room temperature. This mixture consists of oil-in-water microemulsions with excess oil, and the surfactant monolayer exhibits positive curvature. When this formation is heated gradually, the surfactant (polyethoxylated) becomes lipophilic due to dehydration of polyoxyethylene groups, and this forms the basis of nanoemulsion formation. This surfactant gets fully solubilized at higher temperatures in the oily phase. Thus, a phase inversion from oil-in-water to water-in-oil macroemulsion occurs and the surfactant monolayer demonstrates a negative curvature at this point. This method is not appropriate for thermilabile drug due to heating of components involved.

Phase inversion composition (Self-nanoemulsification): At room temperature without the use of heat energy or organic solvents nanoemulsions could be formed so this method has drawn great attention. The small droplet size of approximately 50 nm can be produced and are highly kinetically stable, though, they are not thermodynamically stable. At constant temperature, a stepwise addition of water into solution of surfactant in oil with gentle stirring yield nanoemulsions. The spontaneous nanoemulsification technique relates to the phase transitions and involves D-type bicontinuous microemulsion or lamellar liquid crystalline phases during the emulsification process.

Solvent displacement: For the preparation of polymeric nanoparticles from nano-precipitation technique the solvent displacement method is developed and used for nanoemulsion preparation. In the solvent displacement technique, the oily phase is dissolved in organic solvents (ethanol, acetone and ethyl methyl ketone). The organic phase is added to an aqueous phase containing surfactant to produce spontaneous nanoemulsion by rapid diffusion of organic solvent. The organic solvents used could be removed by vacuum evaporation or other suitable methods. Sometimes, even without the use of surfactant nanoemulsion could be formed. This method could be done at room temperature with simple stirring, and hence, used for parenteral formulations. One of the major limitations of this method is the high ratio of solvent used to yield a desired droplets range¹⁵⁻²².

Stability: Due to nanoemulsions physical and chemical stability of drugs enhanced. Regarding the development of emulsions, microemulsions and nanoemulsions stability is one of the major concerns. At refrigerated conditions and room temperature stability studies are performed by storing the samples in both conditions over a period of months. Stability is determined with respect to insignificant changes in droplet size, refractive index and viscosity during storage conditions.

Though, nanoemulsions appear physically similar as microemulsions, they have a critical difference. Nanoemulsions are kinetically stable, whereas, microemulsions are thermodynamically stable. by mechanical shear Nanoemulsions could be formed and microemulsions are formed through self-assembly. Moreover, nanoemulsions possess higher stability and have very small droplet size against sedimentation or creaming²³⁻²⁷.

Characterization of nanoemulsion: To identify the behaviour and structure of nanoemulsions, more sophisticated instrumentation such as cryo-electron microscopy .x-ray or neutron scattering, dynamic light scattering, atomic force microscopy may be required. Various parameters involved in assessing nanoemulsions are discussed as follows.

Morphology: To determine morphology of nanoemulsions transmission electron microscopy (TEM) and scanning electron microscopy and (SEM) is used. In SEM, to obtain the surface morphology of the dispersed phase, the samples are examined at an accelerating voltage of about 20 kV at various magnifications. A three-dimensional image of the particles or globules is determined using SEM. A higher resolution image of the dispersed phase is obtained through TEM. In TEM, the sample is initially negatively stained with 1% aqueous solution of phosphotungstic acid or by dropping 2% uranyl acetate solution to a 200 µm mesh size Pioloform™-coated copper grid or a microscopic carbon-coated grid. This is then observed under TEM at appropriate voltage. For qualitative measurements size and its distribution a digital image processing programme could be used. More sophisticated instrumentations like atomic force microscopy x-ray or neutron scattering, and cryo-electron microscopy are also preferred to exploit the structure and behaviour of nanoemulsions.

Droplet size and zeta potential: to measures the fluctuations in the intensity of scattering by droplets or particles due to Brownian motion Dynamic light scattering (DLS) or the photon correlation spectroscopy (PCS) can be used. Using a particle size analyzer nanoemulsion polydispersity, droplet size, and zeta potential can be assessed by PCS. The polydispersity index is a measure of the broadness of the size distribution obtained from the cumulative analysis of dynamic light scattering technique. The polydispersity index determines homogeneity of the emulsion dispersion. PCS gives z-average particle diameter. another technique used for measuring particle size is Laser diffraction.

Viscosity measurement: Viscosity is an important criterion for efficient drug release and stability. It is measured by using a viscometer. A Brookfield type rotary viscometer measures viscosity at different shear rates at various temperatures.

pH and refractive index: The pH of the formulation is determined by pH meter. Using the refractometer refractive index was measured.

Dye solubilisation: An oil soluble dye is solubilised within the oil phase of O/W and is dispersible in the W/O globule. A water soluble dye is solubilised within the aqueous phase of W/O and is dispersible in the O/W globule.

Dilutability test: the W/O type is not dilutable and undergoes phase inversion into O/W type. The O/W type nanoemulsion is dilutable with water.

In Vitro skin permeation studies: The franz diffusion cell is used for the drug release profile of nanoemulsions. The drug release is studied by dispersing a known amount of the formulation in the donor compartment of a Franz cell containing a membrane barrier, and then monitoring the appearance of the encapsulated drug in the receptor compartment (containing phosphate buffered saline, pH 7.4; 100 rpm; $37 \pm 1^\circ\text{C}$). About 2 ml of the sample is withdrawn from the receptor medium at regular intervals and is replaced with an equal amount of medium. This withdrawn sample is then filtered using 0.22- 50 µm filter and the drug released is analyzed using UV-Vis or HPLC spectroscopy at wavelength of peak absorption of the drug^{28,29}.

Applications: In the various fields, research on nanoemulsions gaining more attention for its potential applications. If the nanoemulsion formulations is prepared shortly just before the use for applications, then applications of nanoemulsions is quite effective. The direct application of nanoemulsions in the pharmaceutical field has been greatly benefited but food technology and agrochemicals have not been fully developed. The development of nanocarriers has helped in the treatment of many diseases. Some of the anti-inflammatory, anti-convulsant, antibiotic and anti-hypertensive drugs have been solubilised in nanoemulsions for use. For cancer therapy and HIV/AIDS therapy drugs which are solubilised in nanoemulsions are been investigated. Various other investigations on nanoemulsions such as applications as anti-microbial generic activity, anthrax vaccine, , efficacy of schistosomicidal compound, inactivation of Ebola virus, intestinal absorption of three model drugs and others are being carried out³⁰. The revolution in the targeted treatment of many cancer diseases occurred because of Nanoemulsions, it enable targeted delivery. Without affecting the healthy tissues tumors can be eliminated and this enhances the effectiveness of cancer therapeutic agents. They withstand multidrug resistance, enhance site specificity and efficiently delivers therapeutic agent. The folate receptors are been explored to target therapeutic compounds directly to cancer cells. Though, nanoemulsions are being explored for cancer treatment, detection and prevention, their long term effects and exact dosages on cancer therapy is yet to be studied³¹.

To improve engine efficiency nanoemulsions are used in combustion process of fuels. To improve the combustion characteristics water-in diesel nanoemulsion was formulated by blending different proportions of water with nano-AI additives. Triton X-100 was the surfactant used. The emulsion formed was of the nanometer range and the zeta potential values were neutral at water-diesel interface. Moreover, the blend was thermodynamically stable. The authors imply that the formulated nanoemulsion fuels has to be further tested for its fuel properties and engine performance to ascertain their potent application as future sustainable fuel alternative³².

Antioxidant activity: An ethanolic extract of local *Phyllanthus urinaria*, incorporated in palm kernel oil based nanoemulsion showed DPPH radical scavenging activity and could be used as a topical delivery for skin anti-ageing too³³. A transdermal nanoemulsion formulation of cummin essential oil showed effective *invitro* and *invivo* hepatoprotective and antioxidant activities³⁴. In traditional Chinese medicine *Radix Angelicae sinensis* (called as *danggui*) is a commonly used with many pharmacological activities. The essential oil of *Radix Angelicae sinensis* showed concentration-dependent antioxidant activity as investigated by ABTS radical scavenging assay, DPPH radical scavenging assay, and β -carotene bleaching test. This was mainly attributed to its component, coniferyl ferulate. The antioxidant potential was lower than those of BHA and ascorbic acid³⁵. A rice bran oil nanoemulsion protected the antioxidant effect and stability of the propolis extract in the system without interfering its activity as assayed by DPPH scavenging capacity methods³⁶.

Antimicrobial activity: The antimicrobial activity of nanoemulsions is not specific as that of conventional antibiotics. They exhibit a broad spectrum of antimicrobial activity against bacteria, spores and enveloped viruses at concentrations non-lethal to animals. Their physical kill-on-contact mechanism reduces the emergence of resistance strains. Moreover, they interact with the cell membrane and causes death of the pathogen. A soybean oil based nanoemulsion called BCTP caused 90% inactivation of *Bacillus* spores within 4h. Also, BCTP inhibits biofilm formation of *Salmonella* spp, *E. coli* 0157:H7, *Pseudomonas aeruginosa*, and *S. aureus*. Essential oils of lemon, lemongrass, oregano, lemon myrtle, thyme, rosemary, sage, clove and tea tree are known to exhibit antimicrobial activity, but excess amounts might affect organoleptic property as well³⁷. A nanoemulsion of *Thymus daenensis* essential oil produced by high intensity ultrasound technique demonstrates superior antibacterial activity with increased ability to disrupt cell membrane integrity of a food-borne pathogen, *E. coli*³⁸. Nanoemulsion of eucalyptus oil prepared by ultrasonication was impregnated with chitosan film showed increased antibacterial activity against *Staphylococcus aureus* and also could help in wound management studies³⁹. Also, eucalyptus oil nanoemulsion showed potent antibacterial activity against *Proteus mirabilis*. Thus, a topical formulation of this product could be effective against uropathogens⁴⁰. Nanoemulsions of peppermint essential oil showed prolonged antibacterial activity when compared with oil alone. Nanoemulsions of lemongrass essential oil prepared by microfluidization technique demonstrated faster inactivation kinetics in *E. coli* as compared to their sonicated nanoemulsions⁴¹.

Anticancer activity: Recent research work on natural products has increased to improve the current treatment in patients with multidrug resistance. These scientific studies mostly on natural plants have led to the development of many drugs including vincristine, taxol, vinblastine and camptothecin. There are many publication reports on the anticancer activity of essential oils. As of now, essential oils are investigated on leukemia glioblastoma, breast, melanoma, lung, and various cancers of oral, cervix, bone, colon, liver, ovary, pancreas, kidney, prostate and uterus cancers. In the recent decade, about hundred essential oils isolated from more than twenty plant families have been tested for more than twenty types of cancers. Nanoemulsions of pine nut oil was used in the encapsulation of paclitaxel (PTX), apoptotic signaling molecule C-(6)-ceramide (CER) and combinations of both PTX and CER. It was demonstrated that the combinational effects of nanoemulsion encapsulated PTX and CER showed higher cytotoxic effects in brain tumor cells as compared to administration of individual agents. Thus, CER and PTX could augment therapeutic activity in glioblastoma⁴².

Insecticidal and larvicidal activity: The plant based repellents are used traditionally to protect against host-seeking mosquitoes. Citronella oil nanoemulsion shows decrease in release rates and thereby, enhances the mosquito protection rates. Also, the microencapsulation using gelatin-arabic gum microcapsules prolongs the natural repellence of citronella. The use of these novel technologies may fasten the use of plant oil based natural repellents in markets⁴³. Nanoemulsions of neem oil enhanced the pesticidal action and bioavailability⁴⁴. A leaf and seed extract of eucalyptus oil nanoemulsion was produced into pellets and this showed fumigant toxicity against five important pests such as *Sitophilus oryzae*, *Oryzaephilus surinamensis*, *Callosobruchus maculatus* *Tribolium confusum*, and *Rhyzopertha dominica*⁴⁵. A clove oil nanoemulsion stable for about six months was developed by ultrasound technique as a green pesticide⁴⁶.

Food industry: In food industries, the formation of nanoemulsions using triacylglycerols oils like sunflower, corn, olive, soybean, safflower, flaxseed, algae or fish oils is a better owing to its low cost and abundance. Most of these oils mainly consist of long-chain triacylglycerols and thus could be used in food applications. The formation of nanoemulsions using the medium-chain and short-chain triacylglycerols present in these oils could be challenging due to their low polarity, high viscosity and high interfacial tension. An orange oil nanoemulsion prepared by ultrasonication technique showed antiyeast activity against *Saccharomyces cerevisiae*. Their activity was also evaluated in apple juices that showed complete loss of viability⁴⁷. The effects on ultrasound processing of lemon grass oil-alginate nanoemulsions is studied as it could incorporate this essential oil into the food matrix and enhance its bioavailability⁴⁸.

Cosmetics: Phytocompounds are used for decades for their potential beauty applications such as moisturizing, sunscreen, anti-aging and skin-based therapy. The nano based delivery technologies are currently used for sustained and improved delivery of phytocompounds and to overcome the low permeation and instability problems of these bioactive compounds. Nanoemulsions of plant based bioactive compounds such as polyphenols and flavonoids improve the cosmeceutical value due to very slight toxicity. Quercetin rich nanoemulsions increased skin retention of bioactive components with improved antioxidant activities in porcine skin. A multiple nanoemulsion of genistein coloaded with tocomin offers skin protection from UV, and used as sunscreen lotion. Curcumin nanoemulsion with improved transdermal availability could be used in skin care sectors. Nanoemulsions of *Achyrocline* extracts demonstrated protection against herpes virus infections. Nanoemulsions of *Aloe vera* extracts showed skin rejuvenation and anti-wrinkle activity. A rice bran oil nanoemulsion could be used as moisturizers with anti-ageing activity. Nanoemulsions of D-Limonene and tocopherol were used in skin care applications. Vitamin E enriched palm oil nanoemulsions showed improved stability and be used for further applications. Genistein loaded nanoemulsion enhances the delivery of isoflavones to skin with good skin protecting activity. A pomegranate seed oil nanoemulsion demonstrated increased skin protection against photo damage with improved antioxidant activities⁴⁹.

Drug delivery systems: Nanoemulsions play an important role in pharmacy as drug delivery systems owing to their solubilization capacity of non-polar compounds and facilitates administration through various routes. Also, nanoemulsions could serve as the ideal delivery platform for the delivery of phyto-active compounds as it shows improved permeation, absorption, and stability of certain herbal based drugs⁵⁰. Clove and cinnamon essential oils were used in encapsulation of three contemporary drugs including fluconazole (antifungal), ramipril (antihypertensive), azithromycin (antibacterial) and drugs respectively. These oils showed higher solubilization of these drugs. So, a nano-scaled drug delivery system was prepared and characterized using simple titration microemulsion technique and ultrasonication technique. Both the antifungal and antibacterial drugs showed a higher efficacy against *C. albicans* and *S. aureus* strains respectively due to the combinational effects of the drug and the co-inclusion of essential oil into the system. Moreover, this reduces the dosage concentrations of the conventional drugs used⁵¹.

Future perspectives: The advent of Nanotechnology and Nanoscience has aroused a greater expectation among pharmaceutical scientists to overcome these drawbacks. Moreover, nanoemulsions are known to have a strong impact towards antimicrobial and anticancer therapy. They exhibit wide spectrum antimicrobial action against fungi, bacteria, and viruses. They demonstrate an excellent theranostic platform for image guided therapy. Also, they serve as excellent nanocarriers of many anticancer compounds for easy permeation through small capillaries of blood vessels. So currently, researchers have pondered on the development of spice based nanoemulsion systems to improve the efficacy and to enhance their solubility of their activities as potential antimicrobial and anticancer agents. Moreover, these natural based nanoemulsions could pose bioavailability, reduced toxic effects, and biocompatibility as compared to other conventional antibiotic treatment and chemotherapy. Though, literatures are very limited, there is strong evidence concerning the improved anticancer and antimicrobial mechanistic activities of the spice based nanoemulsions⁵²⁻⁵⁴.

Conclusion:

Nanoemulsions have gained great popularity and attention during the last decade due to their exceptional properties such as appearance, transparent robust stability, high surface area, and tunable rheology. The most commonly known preparation approaches for nanoemulsions include high-energy approaches such as high-pressure homogenization, microfluidizers and ultrasonic homogenization, and low energy methods such as spontaneous emulsification, phase inversion composition, phase inversion temperature and emulsion inversion point. Nanoemulsions are considered one of the most promising systems to improve bioavailability, solubility, and functionality of nonpolar active compounds. In Food industry these systems used for the incorporation of the lipophilic functional compounds for the development of innovative food products.

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