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RESEARCH ARTICLE

STUDY ON NANOEMULSION AND MICROEMULSION OF ESSENTIAL OILS: A REVIEW

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Abstract

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Over the years, the interest in nanotechnology and its applications has been increasing, providing numerous benefits to the industries. One such nanotechnology application being used in a majority of industries is the incorporation of nanoemulsion (NE) and microemulsion (ME) in industrial products which act as a carrier/delivery system for some of the active compounds in the product. The incorporation of such emulsion systems helps increase the bioavailability, stability, and interactions of the active compounds in the product. One of the commonly used active components in NE and ME are essential oils (EO)that have a wide range of biological properties used in several fields such as food, pharmaceutical, agriculture, etc. This review intends to provide details on the formulation, stability, and components for the preparation of nanoemulsion and microemulsion. It also deals with understanding the benefits of the incorporation of essential oils into NE/ME.

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Introduction:-

Nanotechnology focuses on the manipulation of matter on a molecular or atomic scale. This manipulation leads to a change in matter with at least one characteristic dimension (the external or internal structure) to be measured in nanometers(1). The matter is converted into a size range of 1 – 100 nm that is in the nanometric scale (10^{-9}). It is observed that the matter on the nanoscale shows unique properties such as a high surface-to-volume ratio (SVR) and other novel physicochemical properties such as high absorption rate, good electrical and thermal conduction, high or better stability of the substance, increased mechanical strength, better diffusion, etc., which are not exhibited by their macroscale structures(2).The nanomaterials are synthesized using metals, metal oxides, polymers, lipids, etc. and accordingly, they form different structures such as nanoparticles, nanoliposomes, nanofibers, nanoplates, nanoemulsion (NE), and microemulsion (ME). Among these the formulation of nano/microemulsion is the easiest and is considered the best method for delivery of certain molecules i.e., they act as carrier/ delivery systems. The high surface-to-volume ratio decreased matter size,and stability are the key concepts on which most of the applications of NE and ME are based. The emulsion systems are mostly made for lipophilic or hydrophobic compounds thathave either less/or no solubility in water such as certain lipid compounds, essential oils, fatty acids, etc. The incorporation of water-insoluble compounds into the nano/microemulsion will help in solubilizing the compound into the mixture in the form of small nanoscale droplets. These small droplets of the compound will increase their bioavailability and effectiveness in the mixture due to the high surface-to-volume ratio(3).

One of the common active compounds incorporated into nano/microemulsions is essential oils. Essential oils (EOs) are hydrophobic, aromatic, volatile compounds, obtained from plants as their by-products. Every essential oil has a different composition, making it different from one another. According to the chemical composition of the essential

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oils, their aroma and properties differ. Essential oils have had great importance since ancient times in the field of medicine due to their antimicrobial activity and aroma. This property of EOs is still being used in many industries in either their original form or in a modified version, one of which is the incorporation of EO into nano/microemulsion to enhance their properties. Apart from the positive aspects of the EOs, there are negative aspects. They are prone to chemical conversion or degradation due to oxidation, rearrangement, or certain other reactions dependent on environmental conditions like temperature, light, and exposure to oxygen. Hence the incorporation of the EOs into the nano/microemulsion will not just enhance properties but also help in preventing its degradation(3, 4).

The concept of NE/ME and the use of EO-loaded NE and ME are gaining more and more interest in the field of research and several industries have started to incorporate the use of these emulsion systems.Food andpharmaceuticals are two major industries that use NE and ME as delivery systems for compounds like antioxidants, antimicrobials, flavors in food, and certain drug compounds in pharmaceuticals. In recent years, the use of NE and ME has diversified in a wide range of sectors apart from food and pharmaceuticals such as cosmetics, bioremediation, agriculture, medicine(2). This review provides an overview of the parameters of the nanoemulsion and microemulsion and the antimicrobial activity exhibited by the EO-loaded NE and ME.

Nanoemulsion Vs Microemulsion

Emulsions are the dispersion of two immiscible liquids, with the spherical droplets forming the dispersed phase, whereas the liquid surrounding it forms the continuous phase (5). Oil and water are the most commonly used liquids for emulsion formation. Multiple emulsion systems can be developed such as the water-in-oil (W/O) emulsion, oil-in-water (O/W) emulsion, and water-in-oil-in-water (W/O/W) emulsion, and oil-in-water-in-oil(O/W/O) emulsion. Among all these types of emulsion, the oil-in-water(O/W) and the water-in-oil(W/O) are the most commonly prepared formulation (5, 6). In most of the types of emulsion that are formulated a stabilizer/surfactant/emulsifier is added which can stabilize the emulsion and maintain the emulsion for a longer period The emulsions are categorized into three major groups according to the size of the emulsion droplet and the thermodynamic stability of the emulsion i.e., macroemulsion, microemulsion, and nanoemulsion (3, 7).

The macroemulsion has the largest droplet size among the other emulsions and it is called a coarse emulsion or conventional emulsion. They have a particle size of diameter > 200 nm range i.e., mostly in the millimeter to micrometer range. The macroemulsion is thermodynamically unstable and appears opaque after the preparation (7), and is mostly used in food, pharmaceutical, and cosmetics(8). Due to the large droplet size and instability, this emulsion was used in emulsification processes and not as delivery systems, hence nano and microemulsion systems were developed to achieve these functions.

According to the terminologies, microemulsion lies in the micrometric range (µm)i.e.10^{-6}, and nanoemulsion lies in the nanometric range (nm) i.e., 10^{-9}(3). Even though these terminologies suggest a difference in their size range, in most cases, it is seen that the size range overlaps each other due to similar compositions, formulation methods, etc. Several authors have defined both types of emulsions with different size ranges starting from 1 nm to a range less than 100 nm, 200 nm, 300 nm, or even 500 nm(3, 7). This creates an ambiguity in distinguishing nanoemulsion and microemulsion concerning size, hence the size of the emulsions is selected arbitrarily within the range. The commonly used size range in many experiments for microemulsion is between 5 – 50 nm and nanoemulsion is between 1 -100 nm(3).

Formulation method for Nanoemulsion (NE) and Microemulsion (ME)

The preparation of emulsion is mostly a top-down approach i.e., the breaking down of bulk material into smaller components. This top-down approach for the formulation of nanoemulsion and microemulsion requires oil, water, surfactant, and energy. According to the nature of the emulsion, oil and water can act as dispersed or continuous phases and the surfactant works at the interface between the oil and water to stabilize the emulsion. And finally, the energy is required to homogenize the components into an emulsion(9–11).The NE and ME after synthesis are checked for the size range using instruments such as dynamic light scattering (DLS) methods or particle size analyzers.

Microemulsion

Microemulsions are translucent, thermodynamically stable emulsion systems prepared from oil, water, surfactant, and sometimes co-surfactants(3). The energy required in the system is called free energy (ΔG), it is the energy available for a substance or a system to have chemical transformations. In ME not much energy is required for emulsification and uses the energy available in the system for the process, hence they carry out a spontaneous emulsification process(12).

$$\Delta G = \Delta H - T\Delta S \quad \text{(Equation 1)}$$

The free energy is dependent on the enthalpy of the system (ΔH), the temperature (T), and the entropy (ΔS), according to equation (1). As the Gibbs free energy (ΔG) decreases or becomes less than 1 i.e., ΔG becomes negative, the spontaneous emulsification is favored and the entropy or the randomness of the emulsion becomes less forming a uniform microemulsion. Even though ME can be obtained by the spontaneous process, external low energy is provided to the system for better emulsification in the form of temperature changes or external force. This external energy will change the temperature and enthalpy parameters of the system to provide a better emulsion(12, 13).

There are two-phase inversion methods used for the formulation of microemulsion that is phase inversion temperature (PIT) and phase titration method. Before carrying out the actual procedure for the preparation of microemulsion, a pseudo ternary phase diagram is constructed which will help to obtain the concentration of oil, water, and surfactant to form a stable emulsion. Varying concentrations of components are tested and the phases formed after stirring the mixture are observed visually. If turbidity followed by phase separation is observed then it is biphasic and if the transparent or translucent mixture is observed with no separation then they are monophasic mixture which forms the microemulsion (14–16).

In the phase titration method, the intended active compound which is to be loaded onto the emulsion is mixed with the oil by stirring. This active compound can be an oil itself or any active constituent of drugs, food, cosmetics, etc. which is enriched into an oil forming the oil phase. The surfactant and co-surfactant selected are mixed (S_{mix})in different ratios and then added to the oil phase, this forms different concentrations of oil and surfactant solutions. After mixing the oil phase and $S_{mix,}$ the aqueous phase i.e., the water is added slowly and mixed using a magnetic stirrer at room temperature. After each addition, the opacity of the emulsion is observed visually for the formation of microemulsion (17–19). The second method is a temperature-dependent method called the phase inversion temperature (PIT). The PIT is the temperature at which the O/W emulsion reverses to a W/O emulsion and vice versa. In this method, the quantity of composition of emulsion remains the same but the temperature varies. The oil phase is prepared and which surfactant and co-surfactant mixture (S_{mix}) is added. After mixing the oil phase and S_{mix}, the aqueous phase i.e., water is added to the mixture, and the temperature of the solution is increased. The temperature increase leads to inversion in the emulsion. After inversion, the emulsion is immediately cooled to room temperature which leads to the second inversion forming the microemulsion (20, 21).

Nanoemulsion

Nanoemulsions are transparent, thermodynamically stable/metastable emulsion systems consisting of oil, water, surfactant, and co-surfactant. In the case of nanoemulsion, the free energy present in the system is not enough for the emulsion to be formed, hence an external high-energy input is provided. The formulation of nanoemulsion can be achieved by using high-energy methods as well as low-energy methods.

High-energy approaches use intense disruptive forces, produced by mechanical devices, to break the oil droplets such as high-pressure valve homogenizers, microfluidizers, and ultrasound homogenizer methods(22). The mechanical devices generate extreme disruptive forces which must exceed the restorative forces holding the droplets into spherical shapes. The ultrasound homogenizer uses sonication energy which will disrupt or break the emulsion droplets formed from mechanical stirring into smaller droplets in the nanoscale. Similarly, high-pressure homogenizers and microfluidizers use high pressure against the emulsion and they are passed through a nanoscale orifice to form the nanoemulsion. The smallest size of the droplets formed using a high-intensity approach relies on the type of homogenizer, operating conditions of the homogenizer (e.g., energy intensity, time, and temperature), the composition of the sample (e.g., oil type, emulsifier type, relative concentrations), and the physicochemical properties of the component phases (e.g., interfacial tension and viscosity)(23, 24). The high-energy approaches sometimes use very high mechanical stress and havethe drawback of waste of energy. Hence, the low-energy approaches are also used for the formulation of nanoemulsion by incorporating more quantity of surfactants into the system compared to the quantity added to the high-energy approaches. Similar methods as mentioned for the formulation of microemulsion (as mentioned in section 2.1.1.) are used for the formulation of the nanoemulsion(25–27). In the scaling-up process in industries, the low-energyapproach is preferred due to the less energy consumption, ease in the preparation, and lower cost compared to the high-energy approaches (25).

Thermodynamic stability

The thermodynamic stability in an emulsion system is a result of the interfacial tension between the two reference phases (oil and water). The thermodynamic stability is determined by the difference in the free energy between the two reference states (oil and water)(28).

$$\Delta G = \gamma \Delta A - T\Delta S \qquad \text{(Equation 2)}$$

According to the thermodynamic equations (1) and (2), the free energy is dependent on factors like the interfacial tension (γ), the interface area (ΔA), and the entropy of the system (ΔS). For the emulsion to be in a stable state, the interfacial tension between the two reference states should be less, so that the repellent forces will be high and the attractive forces between molecules of the same reference state will be less. This will decrease the separation of the phases in the emulsion. The randomness of the emulsion (ΔS) should also decrease to increase the Gibbs free energy (ΔG) to form a uniform emulsion and increase the stability(29).

The stability of the emulsion depends on the quantity of the surfactant used for the emulsification process. The surfactant present at the interface of the two phases will maintain the stability of the emulsion by decreasing the attractive forces between the two reference states and eventually decrease the separation of the two states(30). Hence it is observed that the microemulsion has better thermodynamic stability compared to the nanoemulsion due to the use of a higher quantity of surfactants and co-surfactants for the formulation. The major distinguishing characteristic between nanoemulsion and microemulsion is their stability. Microemulsions are thermodynamically stable and kinetically unstable depending on the external conditions and nanoemulsions are thermodynamically metastable and kinetically stable/metastable. The nanoemulsionshows better kinetic stability as there is no gravitational separation and droplet aggregation due to the high energy barrier between the colloidal dispersion and the separated phases. The effect on the stability of the NE and ME for long storage conditions was studied by incubating the emulsion system for varying storage periods. An experiment was conducted by Parveen et al. and Akhtar et al. (2019) on the preparation of microemulsion loaded with Lycopersicon esculentum extract and their thermodynamic studies were carried out. The ME was subjected to different storage periods at room temperature to observe the separation and stability of the emulsion. The results showed that there was no phase separation, turbidity inversion, or any cracking of the emulsion, and no change in the globular size of the emulsion was observed during the 90 days of stability testing(31). Similarly, a glutathione-loaded nanoemulsion was prepared and their stability studies were performed for 90 days at room temperature the results showed that the nanoemulsion was stable for the 90-day storage period. Hence, from the experiments, it can be observed that the long storage conditions do not have a major effect on the emulsions, but a change in the stability was observed in ME when these emulsions were subjected to different pH ranges compared to the NE(32). Therefore, it is seen that the microemulsions even though are stable under normal conditions they are prone to destabilization by the change in environmental conditions, and nanoemulsions are not affected by such changes(33, 34).

The instability of the emulsion can be due to gravitational forces, Brownian motion, applied shear, and temperature and this instability of the emulsion can be observed by phenomena such as creaming/sedimentation, flocculation, coalescence, and Oswald ripening(3).

Surfactants and cosurfactants

Surfactants are surface-active compounds thatcanform self-assembled molecular clusters called micelles. The surfactant has a hydrophilic group and a lipophilic/hydrophobic group which are mostly alkyl chain groups. The surfactants are classified into ionic surfactants and non-ionic surfactants. The ionic surfactants are further divided into anionic surfactants and cationic surfactants according to the ions released by the molecules. The ionic surfactants are mostly hydrophilic and the non-ionic can be hydrophilic or lipophilic. In an emulsion system, the hydrophilic and lipophilic nature of the surfactant plays an important role, hence for the selection of a suitable surfactant, the hydrophile-lipophile balance (HLB) is determined. The hydrophile will attract the aqueous or water phase and the lipophile will attract the oil phase in the emulsion. The HLB values are determined for the surfactants and it is seen that the preferred HLB value for O/W emulsion is between 8 to 16 and the HLB value for W/O emulsion is 3 to 8 (Figure 1)(35, 36).

The co-surfactants are alcohols or amines ranging from C4 to C10 which help to stabilize the surfactants as well as the two reference phases (37). The co-surfactants add stabilization to the emulsion system and also support the surfactant for the formation of the micelles and the entrapment of the phases(38).

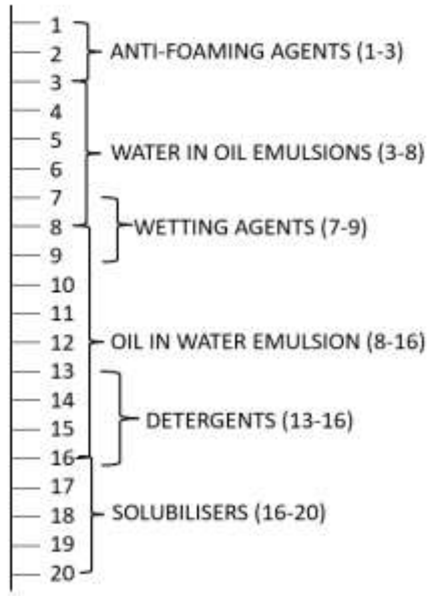

Figure 1:- Hydrophilic – lipophilic balance (HLB) chart.

The surfactant – oil ratio (SOR) plays an important role in the synthesis of nanoemulsion and microemulsion. Pavoni et al., Perinelli et al., Bonacucina et al. (2020), specified in their review that for the formulation of microemulsion, the quantity of surfactants added is more compared to nanoemulsion. The SOR for microemulsion is > 2 and for nanoemulsion is between 1 and 2(3).

PARAMETERS	MACROEMULSION	MICROEMULSION	NANOEMULSION
Particle size	1-20 mm	1-100 nm (usually 5 – 50 nm)	1-100 nm
Optical property	Opaque/turbid	Transparent	Transparent
Thermodynamic stability	Unstable	Stable	Stable/Metastable
Kinetic stability	Stable	Metastable	Stable/Metastable
Effect on temperature and pH	Stable to changes	Unstable / changes seen with a change in conditions	Stable to changes
Types of emulsion formed	Oil-in-water (O/W) Water-in-oil (W/O)	Oil-in-water (O/W) Water-in-oil (W/O) Oil-in-water-in-oil (O/W/O) Water-in-oil-in-water (W/O/W)	Oil-in-water (O/W) Water-in-oil (W/O) Oil-in-water-in-oil (O/W/O) Water-in-oil-in-water (W/O/W)
Phases	Biphasic	Monophasic	Monophasic
Preparation methods	Mechanical sheer methods	Low energy methods	High and low energy methods
Viscosity	High	Low	Low
Concentration of surfactant	High	High (lower than macroemulsion)	Low

Table 1:- Properties of the different types of emulsion.

Emulsification Of Essential Oils (EOs)

As discussed in the above sections, the NE and ME can be loaded with several different active components (mostly lipophilic/hydrophobic compounds) required in a mixture. One such hydrophobic compound is the essential oils obtained from the plants which are loaded in the NE and ME as an active compound. These essential oils show the property of antimicrobial activity which is being used in several industries.

Essential oils as antimicrobial agents

Antimicrobial agents are natural or synthetic substances that are capable of inhibiting growth (microbiostatic) or killing (microbiocidal) microorganisms such as bacteria, fungi, algae, etc.(39). The term antimicrobial agents generally refers to antibiotics, antibacterials, antifungals, antivirals, and antiprotozoals that act against specific organisms. Different antimicrobials have different modes of action to inhibit or kill the microorganisms such as by disrupting the cell membrane, affecting the biosynthesis of certain compounds, genetic alterations, etc. An ideal antimicrobial agent should have broad-spectrum activity, should be non-toxic to humans, and should not have any altered effect on the product in which it is incorporated (40). The sources of antimicrobial agents can be of natural origins such as plants, animals, and microbes, or through chemical synthesis. A majority of industries make use of synthetic antimicrobial agents for preservation and increasing the shelf life of industrial products. But nowadays, there is excessive use of chemical and synthetic antimicrobials which has several side effects in humans, and this has also led to increasing resistance of antimicrobials against microbes (41). To overcome the excess usage and toxic effects of synthetic antimicrobials, naturally derived antimicrobials are being used. Comparative studies to understand the efficiency of natural antimicrobials derived from phenolic compounds (NAPs) and synthetic antimicrobials (SAs) against biofilm and microorganisms were conducted by Martins et al (2020) and the results showed that the NAPs were less effective than SAs(chlorhexidine) for biofilm control but had a similar effect for reduction of microorganisms (42). Natural antimicrobials are derived from plants, animals, and microbes. As compared to the animal and microbial sources, plant-derived compounds showed better efficacy and ease to extract the compounds from the source. It was assumed that this effect of plant-derived compounds may be due to the presence of polyphenolic compounds which have great structural diversity and variation in their chemical composition, thus showing varied effectiveness in their antimicrobial activity against pathogens(4).

Essential oils are complex, volatile, hydrophobic compounds that are the by-products of aromatic and medicinal plants. They are extracted from different plant parts like flowers, leaves, bark, twigs, buds, roots, seeds, fruits, fruit peels, etc. They have a molecular weight of about 20-30 kDa and constitute several smaller molecular weight components (about 150-300 Da). The EOs show different properties such as antimicrobial activity, anti-cancer activity, anti-oxidant, anti-inflammatory, etc., hence they have great importance and are used in medicinal formulations. The major components of the EOs are the terpenes, alkaloids, and phenolic compounds which are said to show antimicrobial properties in the EO, but when individual compounds were tested for antimicrobial activity, the results were not as expected. Hence, it can be said that the antimicrobial activity shown by the EOs is due to the synergistic effect of the components of the essential oil (43).

Mode of action of EO

Most of the essential oils have broad-spectrum activity, they can inhibit the growth of Gram-positive bacteria, Gram-negative bacteria, fungi, yeast, etc. In comparison, Gram-positive bacteria are more susceptible than Gram-negative bacteria due to the presence of the LPS layer outside the peptidoglycan layer. The antimicrobial action of EO is linked to one of the most important EO characteristics, its hydrophobicity resulting in increased cell permeability and consequent leaking of cell constituents. The disturbed cell structure will affect other cellular structures in a cascade type of action.

1. Cell wall and membrane disturbance - It is seen that EO action results in the release of the lipopolysaccharides from Gram-negative bacteria which will consequently increase the cell membrane permeability and ATP loss. Due to an increase in permeability, the membrane potential is affected leading to the disruption of the cell membrane. A possible indirect action of EOs on the membrane is the inhibition of the secretion of toxins by the bacteria. A structural modification and energy limitation in the bacteria will block the membrane structure leading to the inhibition of toxin production and their release to the environment (44).
2. Interruption in ATP production - The production of ATP in prokaryotes occurs both in the cell wall and in the cytosol by glycolysis. Alterations can be seen in intracellular and external ATP balance which is affected due to the action of the EO on the cell membrane. Another intracellular event that may contribute to the intracellular ATP decrease is increased hydrolysis which can be due to the loss of inorganic phosphate across the compromised high permeable membrane or in virtue of the efforts made by the cell to recover the electrochemical gradient by proton extrusion driven by the ATPase(45).
3. Protein synthesis – The bacterial cells showed the synthesis of heat shock proteins on treatment with EO components. In some cells, the overexpression of a set of molecular chaperone proteins, namely DnaK, GroEL, HTpG, and the Trigger factor (Tf), outer membrane-associated proteins (OmpX and two OmpA), and proteins that are involved directly or indirectly in the citrate metabolism and ATP synthesis were also affected(40, 46).

4. pH disturbance - The pH in bacterial cells exposed to EOs showed a significant reduction. The pH homeostasis of the cell is impaired by the action of EOs on the membrane that loses its capacity to block protons(44).
5. DNA damage – The cells show mutation due to the deletion of certain regions in the DNA. In some strains, the region responsible for DNA repair is deleted and in some operons coding for certain essential growth factors or amino acids is deleted making the cells auxotrophic(40). The other mutations that can be seen are on gal2 and rfa3which affect the levels of the polysaccharide side chain of the lipopolysaccharide (LPS) that covers the bacterial surface. These mutations confer a high rough appearance to the bacterial cells and such bacteria are highly permeable(40).

Antimicrobial activity of emulsified EO

In sections 3.1 and 3.2, we have studied the antimicrobial activity shown by the essential oils and the mode of action by which they inhibit/kill the microbes. Hence, EO can be used as a potential antimicrobial agent or as a preservative in food, beverages, drugs, cosmetics, pesticides, etc. Apart from its antimicrobial activity, other properties of EOs can also be utilized in all these industries.

The combination of essential oils with the emulsion system has proven to be a better alternative to the individual use of essential oils in mixtures. Hence, researchers are studying the different essential oils obtained from several aromatic, medicinal plants and the waste products of fruits like peels of oranges, grapefruit, lemon, etc.(9, 47). Essential oils from spices and condiments are also tested for their antimicrobial activity. It is seen that the incorporation of the essential oils into NE or ME will increase their bioavailability in the mixture, especially in the case of drugs (48). As the bioavailability of the EO increases it will increase their reactivity i.e., the antimicrobial, anti-cancer, anti-fungal, or any other property for which the EO is added will be enhanced and will give a better result (49, 50). Over the years and mostly in recent years, several researchers have started to test the EOs loaded onto either NE or ME or both and compare the antimicrobial activity exhibited by them through disc inhibition assays and minimum inhibitory assay. In most cases, it is seen that the EO-loaded NE and ME showed either similar or increased antimicrobial activity as that of the individual EO (23, 42, 47, 50–53).

Application

There is a widespread application of nano and microemulsion systems in different industries. The major form in which nanoemulsion and microemulsion are used in industries is as carrier/delivery system which is used to maintain the stability or increase the reactivity of the compound by increasing its surface area in the solution/mixture.

1. Food – All three types of emulsions are used in food processing. Initially, the macroemulsion was used mostly in food manufacturing. The macroemulsion was used in the preparation of ice creams, mayonnaise, and many other food products. However, they were not capable of performing the function of a delivery system due to their instability and big size. Later on, in the production of food and beverages, nanoemulsionand microemulsion were used as carrier systems or vehicles in which food additives like nutrients, flavors, antioxidants, antimicrobial agents, etc. were incorporated (2). Chaari et al. and Theochari et al. (2017) developed and studied the encapsulation of carotenoids in nanoemulsion and microemulsion as carrier system and their properties like size, stability, and physical changes in the emulsion when stored for a longer period were evaluated. The carotenoids have antioxidant properties which have a potential preservation property in food products and certain other commercial applications. The results of the study showed that the loaded dispersion i.e., nanoemulsion and microemulsion had higher antioxidant activity compared to the use of carotene as it is (54). Similarly, several studies have been carried out to develop new advances using the nanoemulsion and microemulsion for the separation, encapsulation, and purification of certain bioactive components and to increase the stability of the compounds by incorporating them into emulsion systems that are used in the processing, preservation, and packaging of food (55, 56).
2. Pharmaceuticals and Medicine – The use of nano/microemulsion in pharmaceutical products has a potential advantage due to its ability to increase the reactivity of compounds that have medicinal properties. Hence, these properties will enhance the efficiency of pharmaceutical products like drugs, ointments, etc.(57). In most of the studies carried out to determine the efficiency of nanoemulsion and microemulsion in pharmaceutical products, it was seen that microemulsions are a better option compared to nanoemulsion due to their higher stability in the mixture. The pharmaceutical components loaded microemulsion are most commonly used in topical drugs like ointments, creams, and gels (48, 58, 59). In the oral and intranasal types of drugs mostly nanoemulsions are used as delivery systems for the administration of the drug. The use of nanoemulsion improves the solubility and stability of the drug components. It also makes the production cost-effective and reliable(57). The potential

use of nanoemulsion and microemulsion to incorporate drug components for their enhanced activity is being used in cancer treatment studies. The components extracted from either natural sources such as curcuminoid from Curcuma longa, catechin from Oolong tea leaf, etc., or components of certain drugs that can inhibit the growth of different types of cancer such as prostate cancer, colon cancer, lung cancer, etc. are loaded on to nano/microemulsion and their inhibitory activity against the cancer cells are studied. These studies lead to a better, safe, and efficient way for the treatment of cancer as they may decrease the heavy dosage issues and are an alternative to the use of synthetic drugs (10, 11, 60).

3. Cosmetics - The cosmetic industry mainly uses emulsion in oil-based products to enhance their textural properties. The textural properties and the ability of the product to carry the active and functional ingredients determine the efficacy of the cosmetic products. The nano/microemulsion is loaded with bioactive compounds, antioxidants, antimicrobials, and certain preservatives which are essential components in the cosmetics products that provide better activity of the cosmetics and increase their shelf life. The nanoemulsion used in creams or moisturizers which are for topical application on the skin provides a uniform formation of a thin lipid film, thereby enabling higher performance and bioavailability. Not just in skin-based cosmetics but also these nano/microemulsions have a significant application on hair cosmetic products like hair sprays and hair gels, etc. which helped in improving the problems regarding dry-hair appearance over a prolonged period (61–63).
4. Environmental –In recent years, the application of NE and ME has spread to solve environmental problems such as contaminations in soil, groundwater, marine sources, etc. Bioremediation is a widely used method for the remediation of several types of pollutants in the soil as well as water. Now, these bioremediation techniques are coupled with the use of NE and ME which can enhance the bioavailability of the microorganisms or any surfactants which has to be incorporated in the remediation process. The issue of oil spills in the marine ecosystem is a matter of concern and bioremediation is the method employed for the removal/degradation of petroleum. An approach using emulsification is being used in these remediation processes where the oil spills are subjected to an external force that could form the ME or NE and hence the surface area for the adherence of microorganisms to the oil will increase leading to better bioremediation. Similar approaches are used in soil remediation also, where certain compounds are incorporated into the emulsion system to enhance the bioavailability (64, 65).
5. Agriculture – The application of NE and ME is greatly increasing in the field of agriculture and farming. Pests, pathogens, and insects are a major problem in agriculture as they destroy the plants and some may cause several diseases to the plants. Hence the incorporation of pesticides, herbicides, etc. into the ME and NE is done to increase their efficiency in destroying the pests and pathogens without causing damage to the plants. An added advantage of using the NE and ME is that there will be less usage of pesticides or herbicides(66).

Conclusion:-

Nanotechnology has become an inseparable part of biotechnological approaches. Over the years newer techniques are being developed for the betterment of society. The development and the advances in the application of nanoemulsion and microemulsion are considered developments in the field of nanotechnology. Now, the majority of industries are trying to make use of these simple, efficient, and cost-effective techniques in some or other way that could enhance their productivity and market value. The use of plant-derived compounds such as essential oils and their incorporation into the emulsion is also gaining great interest. The ambiguity problem of the NE and ME is still a major concern for distinguishing the two systems, hence the development of newer formulation methods or changes in the composition can be considered as a possible future aspect for studies.

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