Nanoemulsions for health, food, and cosmetics: a review

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Abstract
Nanoemulsions are gaining importance in healthcare and cosmetics sectors as a result of the unique properties of nanosized droplets, such as high surface area. Here we review nanotechnology and nanoemulsions with focus on emulsifiers and nanoemulsifiers, and applications for drugs and vaccines delivery, cancer therapy, inflammation treatment, cosmetics, perfumes, polymers, and food. We discuss nanoemulsion safety and properties, e.g., stability, emulsification, solubility, molecular number and arrangements, ionic strength, pH and temperature.

Keywords Nanotechnology · Nanoparticles · Nanoemulsions · Emulsifiers · Applications

Introduction
Nanotechnology is developing rapidly in many sectors, especially cosmetics, pharmaceutics, agriculture and food industries (Chowdhury et al. 2017). Most of these interests are geared toward the development of lipophilic substances like fatty acids, flavors, colors, and drugs (Azmi et al. 2019). The need for using nanotechnology/nanoparticles in emulsion fabrication is crucial because emulsions have been produced from numerous ingredients and additives for so many years, creating markets and profitability. Carbohydrates, fats, proteins and other active components such as antioxidants, colorings, acidulants, flavorings, preservatives, benzoic acid, coenzyme-Q10, vitamins A and E, isoflavones, beta-carotene, citric acid, ascorbic acid, lutein, omega-3 fatty acids, minerals, among other bioactive compounds have contributed to improved taste, appearance, texture, fortification and stability, and as such innovatively inspired wide applications of nanoemulsions to foods for enhanced uptake, absorbability and bioavailability (Kumar and Sarkar 2018; McClements and Jafari 2018; Dasgupta et al. 2019a; Walia et al. 2019; Saini et al. 2020).

Research into nanoemulsions is extensive. These emulsions are disequilibrated systems of water-in-oil (W/O) or oil-in-water (O/W) emulsions (Fig. 1) within nanometer-range particle sizes and droplet diameters of 50–1000 nm (Yukuyama et al. 2016); otherwise, nanoemulsions are referred to as dispersed systems with ≤ 100 nm droplets (Azmi et al. 2019). Nanoemulsions are immiscible liquids consisting of oil and water forming a single phase by an emulsifier such as the surfactants and co-surfactants. The combination of these constituents confers high thermodynamics, stability and other physicochemical properties on the emulsion. Thus, the versatility of nanoemulsions becomes greater than that of conventional emulsions, including microemulsions and macroemulsions.

The Federal Drug Administration (FDA) has utilized molecularity and functions of some emulsifiers as the basis of approval for their use in pharmaceutical and food industries (McClements et al. 2017). Stability, emulsification and solubility of emulsions are inspired by their surface-active nature dovetailed with molecular number and arrangements, ionic strength, pH and temperature of the mixture (McClements et al. 2017). Since the preparations of nanoemulsions and their emulsifiers are crucial and paramount to the interests of key industries, the aim of the present review is to evaluate the concept of nanotechnology, the formation and the applications of nanoemulsions in the healthcare and cosmetics industries, as well as their potentials in foods and other sectors in this present century. Further considerations were also put forward. To conduct the review, web of science (WoS), google and springer search engines were used, using the words and phrases “nano”, “nanosize”, “nanotechnology”, “emulsion”, “nanoemulsion”, “applications of...
Nanotechnology and nanoemulsions

Nanotechnology is a global concept that entails the manipulation of particles within the range of 10–1000 nm using scientific, innovative and well-characterized techniques, for improved productivity and applications in agriculture, healthcare, cosmetics, defense, energy and food sectors (Kaul et al. 2018; Feng et al. 2018; Aziz et al. 2019). The world’s nanotechnology industry could worth 80 billion US dollars and could be reaching 17% growth rate by 2024. Therefore, the potential benefits and profits are huge in this emerging market (Research and Market 2018). Application of the technology to the food industry has always been towards emulsions, encapsulation and packaging technologies, of which nanoemulsions are of utmost economic importance (Dasgupta et al. 2019b).

Nanoemulsions are formed when an emulsifier is involved in the mixture of two immiscible liquids to form stable but kinetic dispersions with droplet sizes and diameters of ≤ 100 nm and 20–200 nm, respectively. The kinetic stability is achieved when nanoparticles Brownian motion surmounts the emulsions’ gravitational forces, which then stop the particles from aggregating (Wani et al. 2018). Being very minuscule in size, nanoemulsions offer great functional potentials such as enhanced stability, surface area, optical transparency, rheology and other functions associated with innovative technologies and fortification of many aqueous-based food and beverage products (Dasgupta et al. 2019b). Regarding nanoemulsions production, common methods used include high-pressure homogenization, phase-inversion temperature, ultrasonication, high-shear mixing, solvent displacement, emulsion inversion point, bubble bursting and spontaneous emulsification—all falling under the categories of low- and high-energy techniques (Mohammadi et al. 2016; O’Sullivan et al. 2018; Azmi et al. 2019; Dasgupta et al. 2019a, b).

Increasing rate of consumption of processed foods and beverages has led to increased use of food additives and processing aids such as emulsifiers, which are meant to enhance the texture, flavor, stability and shelf-life of foods (Roca-Saavedra et al. 2018; Vo et al. 2019). The hydrophilic and hydrophobic molecular groups in emulsifiers contribute to immiscibility of the formulated liquids, which then lead to much enhanced homogeneity and stability in the final products as found in butter, mayonnaise, dressings, chocolates, ketchups and yogurts (Shah et al. 2017; Vo et al. 2019). Emulsifiers have been estimated to constitute more than 70% of the world’s approved food ingredients (Shah et al. 2017), necessitating the importance and use of nanosized emulsifiers in this century.

Emulsifiers and nanoemulsifiers for nanoemulsions

Emulsifiers are surface-active molecules widely applied in the breakage of droplets into tiny and very small droplets. Emulsifiers concentration must reach the right amounts
so as to overcome the interfacial forces, and to ensure that the coating rate is rapid (Artiga-Artigas et al., 2018). This phenomenon prevents the particles from aggregating whilst enabling longer storage time and better stability. Fabricating nanoemulsions implies that the emulsifiers are well absorbed at the oil–water interface and subsequently reduce the interfacial tension in order to loosen up the particles and easily disrupt the droplets. The emulsifiers then protectively coat the oil droplets to prevent aggregation and coagulation (Das-gupta et al. 2019a).

The mixture of oil and water in the process of emulsion formulation creates two immiscible phases based on the segregation caused by coalescing globules in dispersion. The use of emulsifiers or nanoemulsifiers from the generally regarded as safe (GRAS) agents and components, such as peptides, proteins, phospholipids, micro-molecular surfactants, and polysaccharides, for the production of emulsion systems in the appropriate ratios would contribute to their efficiency and stability. Table 1 illustrates some emulsifier-stabilized nanoemulsions. This stability results from circumnavigation of processes like Oswald ripening, especially when the surfactants/emulsifiers are mixed with oil and other components in the right ratio (Gordon et al. 2003).

Over time, the formulated emulsions exhibit droplet coalescence characterized with various behavioral patterns such as heterogeneous or homogeneous growths, in which droplet sizes decrease and create early phase separation, or increase with time, respectively. Indeed, microparticulated emulsions will exhibit a higher degree of aggregation than nanoparticulated emulsions because of the irreversible droplets coalescence taking place with the former’s bigger particle size (An et al. 2014). Moreover, the properties of emulsifier used, such as functional, sensory and physicochemical characteristics, can positively or negatively affect the rheology of the nanoemulsion droplets.

The hydrophilic–lipophilic balance (HLB) system (hydrophilic range > 10, lipophilic range = 1–10) should be considered when determining the right nanoemulsifiers for nanoemulsions fabrication because the HLB system has been in use for more than half of the last century to prove optimum conditions of surfactants required for emulsions fabrication with desired characteristics (Macedo et al. 2006; Azmi et al. 2019).

Several studies on colloidal and nanoemulsion systems used emulsifiers due to their better interfacial diffusive properties compared to larger biopolymers, such as proteins and polysaccharides, but their metabolism and safety are of concern in the food industry (Adjonu et al. 2014). For protein and peptide-based emulsifiers, both plant and dairy sources have been widely investigated and applied in foods because they form a protectively strong film in the formed emulsions. They later become employed in nanoemulsions (Table 1d), with the most important of them being whey proteins. These proteins comprise 20% whey and 80% caseins with very high nutritional contents based on their essential amino acids composition. The whey proteins are basically α-lactalbumin, β-lactoglobulin, bovine serum albumin, lactoferrins, and immunoglobulins, and possess amphiphilic properties that make them crucial emulsifiers in foods (Foegeding et al. 2002; Adjonu et al. 2014; Zhao and Ashaolu 2020). Under optimal control, hydrolyzation of the proteins will yield shorter peptides with fewer secondary and tertiary structures, to expose the hidden hydrophobic core (Christiansen et al. 2004; Ashaolu 2020a, b). These outcomes increase their diffusion rate and interfacial capacity when compared to their native parent proteins. Both hydrophilic and hydrophobic mixed groups generated further increase their absorption tendencies to the oil droplets surfaces, which ensure much better stability (van der Ven et al. 2001).

In brief, the advantages of nanoemulsifiers/nanoemulsions above emulsifiers include: they are small-sized droplets that have larger surface area for enhanced absorption, with much less energy requirement (Gurpreet and Singh 2018); they play active role in solubilization of lipophilic drugs and suppression of off-flavors of the drugs (Yu et al. 2012); they are considered non-toxic and non-irritant in nature (Jaiswal et al. 2015); they stabilize chemically unstable compounds by protecting them from oxidative and light degradation (Kim et al. 2001); they can substitute liposomes with vescicles (Bouchemal et al. 2004) and improve the bioavailability of a drug (Lovelyn and Attama 2011; Yu et al. 2012), while several types of nanoemulsions can be formed in the likes of creams, liquids, and sprays. On the flip side, in order to stabilize the nanodroplets, higher concentration of surfactant and cosurfactant may be required by nanoemulsifiers (Lovelyn and Attama 2011); solubilization of high-melting substances could be limited (Azmi et al. 2019); environmental parameters such as temperature and pH could affect the stability of nanoemulsifiers (Mishra et al. 2014); and the surfactants used pharmaceutical applications must be non-toxic (Mishra et al. 2014).

Moreover, the use of nanoemulsifiers is currently limited. Adjonu et al. (2014) quite well noted certain potentials of whey protein hydrolysates as emulsifying agents in nanoemulsions. Other than protein- or peptide-based nanoemulsifiers, other groups of molecules are described in Table 1. The continuous studies on nanoemulsions and its use in food applications require a whole lot of further in-depth analyses and critical evaluations, especially for their safety validation.
Table 1 Emulsifiers in nanoemulsion systems

| Type of emulsifier                      | Homogenization technique                        | Percentage of oil used | Percentage of emulsifier used | Oil phase used                     | Droplet size diameter (nm) | Citation                     |
|----------------------------------------|-------------------------------------------------|------------------------|-------------------------------|-----------------------------------|---------------------------|-----------------------------|
| a. Non-ionic                           |                                                  |                        |                               |                                   |                           |                             |
| Polyoxylene sorbitan monolaurate       | Microfluidization/ high-pressure valve homogenizer | 0.03, 1                | 1, 10                         | Sunflower oil                     | 117–280                   | Mao et al. (2009, 2010)    |
|                                        | Microfluidization                                | 4                      | 1.5                           | Corn oil, Miglyol 812 and orange oil | 140–170                   | Qian et al. (2012)          |
|                                        | Microfluidization                                | 5                      | 1–10                          | Corn oil                          | 113–143                   | Qian and McClements (2011)  |
|                                        | Microfluidization/ solvent evaporation           | 0.3                    | 0.5                           | β-carotene in hexane               | 40–260                    | Tan and Nakajima (2005)    |
|                                        | Microfluidization                                | 10                     | 1                             | Thyme oil/Miglyol 812 oil          | 160–176                   | Chang et al. (2012)        |
|                                        | Sonication                                       | 15                     | 5.6                           | Flaxseed oil                      | 135                       | Kentish et al. (2008)      |
|                                        | High-pressure valve homogenizer                  | 3                      | 4–12                          | β-carotene in MCT oil             | 160–184                   | Yuan et al. (2008)         |
| Polyoxylene sorbitan monooleate        | Catastrophic phase inversion                     | 20                     | 10–20                         | Acetem 90–50 K                    | 100–200                   | Bilbao-Sáinz et al. (2010) |
|                                        | High-pressure valve homogenizer                  | 3                      | 4–12                          | β-carotene in MCT oil             | 161–174                   | Yuan et al. (2008)         |
|                                        | Microfluidization                                | 5                      | 0.5                           | Thyme oil/corn oil                | 164–196                   | Ziani et al. (2011)        |
|                                        | Ultrasonication                                  | 6                      | 6–24                          | Basil oil                         | 29–41                     | Ghosh et al. (2013)        |
|                                        | High-pressure valve homogenizer                  | 20/4/1                 | 1                             | PCL-liquid/Lipoid S-75/α-tocopherol | 170                      | Hoeller et al. (2009)      |
|                                        | High-pressure valve homogenizer                  | 3                      | 4–12                          | MCT oil                           | 157–178                   | Yuan et al. (2008)         |
|                                        | Microfluidization                                | 10                     | 1                             | Lemon oil                         | 217–296                   | Rao and McClements (2011)  |
| Polyoxylene lauryl ether               | Emulsification with low energy                   | 40–80                  | 4–10                          | Isohexadecane                     | 26–1277                   | Peng et al. (2010)         |
| Decaglycerol monolaurate               | Microfluidization/ high-pressure valve homogenizer | 0.03, 1                | 1, 10                         | β-carotene in sunflower oil        | 115–279                   | Mao et al. (2009, 2010)    |
| Sucrose palmitate                      | Ultra-high-pressure homogenization               | 8/2, 10                | 1                             | n-limonene, trans-cinnamaldehyde, carvacrol in sunflower oil | 130–168                   | Donsì et al. (2012)        |
| Sucrose laurate                        | High-pressure valve homogenizer                  | 20/4/1                 | 1                             | PCL-liquid/Lipoid S-75/α-tocopherol | 161                      | Hoeller et al. (2009)      |
| Sucrose monopalmitate                  | Microfluidization                                | 10                     | 1–20                          | Lemon oil                         | 15–120                    | Rao and McClements (2011)  |
Table 1 (continued)

| Type of emulsifier                        | Homogenization technique | Percentage of oil used | Percentage of emulsifier used | Oil phase used | Droplet size diameter (nm) | Citation                                      |
|-------------------------------------------|--------------------------|------------------------|-------------------------------|----------------|-----------------------------|-----------------------------------------------|
| **b. Ionic**                              |                          |                        |                               |                |                             |                                               |
| Pluronic F-68                             | Ultrasonication          | 25                     | 1–2.5                         | Olive oil      | 379                         | Wulf-Pérez et al. (2009)                      |
| Sodium dodecyl sulfate                    | Microfluidization        | 5                      | 1–10                          | Olive oil, Sesame oil, Soybean oil, Silicone oil, Corn oil/octadecane | 368, 380, 150, 92–131 | Graves et al. (2005), Qian and McClements (2011) |
| **c. Polysaccharide**                     |                          |                        |                               |                |                             |                                               |
| Low-methoxyl pectin, amidated low-methoxyl pectin | Ultra-Turrax             | 20                     | 0.5–3                         | Itraconazole in chloroform, Itraconazole in Miglyol® 812 | 200–900, > 2000 | Burapapadh et al. (2010)                      |
| Succinylated waxy maize starch/octenyl succinate starch | High-pressure valve homogenizer | 10                     | 15                            | Neobee 1053 | 140                         | Donsì et al. (2011)                           |
|                                           | Microfluidization/ high-pressure valve homogenizer | 1                      | 10                            | Neobee 1095 | 130                         | Mao et al. (2010)                             |
|                                           | High-pressure valve homogenizer | 12                     | 12                            | Peppermint oil/ MCT oil | 184–228 | Liang et al. (2012)                         |
| Maltodextrin/H-Cap                        | Microfluidization/ sonication | 5, 10, 15             | 30/10 (40)                    | Fish oil      | 174–274                     | Jafari et al. (2007a,b)                       |
| **d. Protein**                            |                          |                        |                               |                |                             |                                               |
| Pea protein                               | High-pressure valve homogenizer | 8, 10                 | 3                             | Sunflower oil | 184–218                     | Donsì et al. (2012)                           |
| Whey protein isolate-maltodextrin conjugate | Emulsification with high energy/ evaporation | 10, 15, 20, 30        | 1                             | Thymol in hexane | 67–420 | Shah et al. (2012)                        |
| Soy protein                               | Microfluidization        | 0.1                    | 1                             | β-Carotene in hexane | 196 | Chu et al. (2007)                         |
| Whey protein concentrate                  | Microfluidization/ microfluidization/ sonication | 0.1; 20, 25           | 1; 10                         | β-Carotene in hexane, α-limonene | 145; 125–387, 160–373 | Chu et al. (2007), Jafari et al. (2006)         |
| Whey protein isolate                      | High-pressure valve homogenizer | 15, 30, 45            | 4.3                           | Pea nut oil   | 146–236                     | Cortés-Muñoz et al. (2009)                    |
|                                           | High-energy emulsification/solvent evaporation | 10                     | 1                             | Corn oil      | 75–121                      | Lee and McClements (2010)                     |
|                                           | High-pressure valve homogenizer | 0.03, 1              | 1, 10                         | β-Carotene in sunflower oil | 160–373 | Mao et al. (2010)                       |
|                                           | High-pressure valve homogenizer | 20                     | 4.5                           | α-Tocopherol in palm oil | 200–500 | Relkin et al. (2011)                     |
Recent studies on the applications of nanoemulsions are described below, schematically presented in Fig. 2 and captured in Tables 2 and 3. The present coronavirus disease (COVID-19) pandemic has called for a more robust and holistic approach to solving health-related issues, the highest priority of the modern human civilization.

Nanoemulsion applications

Recent studies on the applications of nanoemulsions are described below, schematically presented in Fig. 2 and captured in Tables 2 and 3. The present coronavirus disease (COVID-19) pandemic has called for a more robust and holistic approach to solving health-related issues, the highest priority of the modern human civilization.

Health

Drugs

Nanoemulsions have the ability to dissolve nonpolar active compounds, a characteristic paramount to being choice of use as drug and bioactive compounds delivery systems. Both oral and parenteral delivery routes are employable, as the
| Citation                | Composition                                                                 | Fabrication method                                                                 | Application/activity                                                                 |
|------------------------|----------------------------------------------------------------------------|-------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|
| Arredondo-Ochoa et al. (2017) | Beeswax–starch nanoemulsions; oil-in-water | Microfluidization with Tween-80                                                   | Antimicrobial (against *R. stolonifer*, *C. gloeosporioides*, *B. cinerea*, and *S. saintpaul*); applied as edible coatings for food preservation |
| Bakshi et al. (2018)    | Non-irritant topical formulation for topical delivery of heparnoid          | Homogenization with high pressure                                                   | Therapeutic agent for superficial thrombophlebitis                                  |
| Gharibzahedi and Mohammadnabi (2017) | Jujube gum with nettle essential oil; oil-in-water | Homogenization with Tween-40                                                        | Antimicrobial; fabrication of jujube gum edible coating for Beluga sturgeon fillets   |
| Salim et al. (2018)     | Ibuprofen nanoemulsions                                                   | Phase inversion composition                                                         | Good stability; topical uses                                                         |
| Nirmal et al. (2018)    | Lemon myrtle and anise myrtle essential oil in water                       | Ultrasonication                                                                    | Antibacterial; good stability                                                        |
| Noori et al. (2018)     | Sodium caseinate and ginger essential oil; oil-in-water                    | Ultrasonication with Tween-80                                                      | Antimicrobial (*L. monocytogenes* and *S. typhimurium*); chicken breast fillet coating |
| Prakash et al. (2019)   | Linalool-based nanoemulsions; oil-in-water                                 | Ultrasonication with Tween-80                                                      | Antioxidant effect from tea polyphenols and good stability; applications in food fortification meant for commercial purpose |
| Zhang et al. (2019)     | Docosahexaenoic acid and eicosapentaenoic acid; oil-in-water               | Emulsion phase inversion with Tween-80 and 85                                     | Antioxidant effect from tea polyphenols and good stability; applications in food fortification meant for commercial purpose |
| Lu et al. (2018)        | Citral essential oil                                                      | Ultrasonication                                                                    | Antimicrobial; utilisable in cosmetics, pharmaceuticals and agrochemicals           |
| Park et al. (2019)      | Nanoemulsion powder consisting turmeric extract; oil-in-water             | High-speed homogenization, ultrasonication and spray drying with Tween-80         | Antioxidant effect and good stability in gastric model; enhanced shelf-life of fortified milk for 3 weeks |
| Teo et al. (2017)       | Phenytoin-loaded alkylbene                                                | Phase inversion method                                                             | Applied to topical wound healing                                                    |
| Farshi et al. (2019)    | Cumin seed oil, corn oil, whey protein isolate-guar gum; oil-in-water     | Ultrasonication and homogenization with Tween-80                                  | Antifungal (against *A. flavus*); food preservative                                  |
| Kaci et al. (2018)      | Coenzyme Q10                                                              | Sonication                                                                         | Topical uses                                                                        |
| Pongsompun et al. (2020) | Cinnamon essential oil; oil-in-water                                      | Ultrasonication with Tween-80                                                      | Antifungal (against *A. niger*, *R. arrhizus*, *C. gloeosporioides* and *Penicillium* sp.); food and agricultural uses |
| Sari et al. (2015)      | Curcumin and medium chain triglyceride oil                                | Ultrasonication                                                                    | Improved bioaccessibility and stability; applicable in functional foods             |
| Majeed et al. (2016)    | Purity gum ultra, canola and clove oil; water-in-oil                       | High speed homogenization                                                          | Antibacterial against Gram-positive strains; antimicrobial agent                     |
| Rebolleda et al. (2015) | Wheat bran oil-based nanoemulsions                                        | Ultrasonication with Span-80 and Tween-80                                          | Good stability, antioxidant and tyrosinase inhibitory activities; Usable in functional foods |
| Gundewadi et al. (2018) | Sapindus extract and basil oil; oil-in-water                              | Ultrasonication with saponin                                                       | Antimicrobial (against *P. chrysogenum* and *A. flavus*); applied in food safety against food spoilage pathogens |
| Anjali et al. (2012)    | Neem oil from *A. indica* and non-ionic surfactant (Tween 20)             | Ultrasonication with Tween 20                                                       | Active against *Culex quinquefasciatus*; usable as a larvicidal agent                |
| Citation                         | Composition                                                                 | Fabrication method                        | Application/activity                                                                 |
|---------------------------------|-----------------------------------------------------------------------------|--------------------------------------------|---------------------------------------------------------------------------------------|
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latter has been utilized in supplying required nutrients, controlled drug release, and vaccine delivery. Systemic antibacterial, antifungal, antiparasitic and antimicrobial activities of nanoemulsions have been reported on *E. coli*, *S. aureus*, *Candida* spp., *Dermatophytes* spp., *Plasmodium berghei*, among others (Singh and Vingkar 2008; Mansour et al. 2009).

Nanoemulsions are more advantageous than the conventional emulsions and other systems since their droplet sizes are below the micrometers range, and thus they easily pass the stringency of intravenous administration of drugs. The parenteral administration of nanoemulsions employed in nutrition of vitamins and other bioactive substances, attest to the merits they possess over other systems as their transit time, absorption, and efficacy are highly improved, while drug toxicity is reduced. Therefore, they are perfect drug delivery systems for antimicrobials, diuretics, steroids, and hormones (Sonneville-Aubrun et al. 2004; Singh and Vingkar 2008; Quintão et al. 2013).

**Vaccines**

Of equal importance is the delivery of vaccines by nanoemulsions because it is gaining much wider attention from researchers. An attenuated organism is delivered onto the surface of a mucosal in order to elicit an immune response. Nanoemulsions are used in this case as adjuvants to deliver proteins onto the mucosal surface in order to instigate rapid absorption of antigen presenting cells. Physical adsorption, encapsulation (with or without coating and targeting), and conjugation (with chemical or targeting) mechanisms are often used to load antigens into nanocarriers. In any of the mechanisms, antigens are encapsulated in nanocarriers, while the nanoparticles degrade in vivo (Zhao et al. 2014). The vaccines can be very effective and spontaneous, irrespective of the site they are introduced to in the body. For instance, the immunity of genital mucosa might be guaranteed by administering the vaccines to the nasal mucosal (Berkowitz and Goddard 2009).

Vaccine adjuvants of oil/water emulsions have notable prospects, as found in ASO3 pandemic flu and recombinant HIV gp 120 nanoemulsion-mixed vaccines (Akhter et al. 2008; Reed et al. 2009). The validation of these studies are still warranted. Moreover, the composition of emulsion, antigenicity and adjuvant specificity are paramount factors to consider when designing nanoemulsion-based vaccines. The essence of this is to ensure safety and effective immunological benefits.

**Inflammation**

Nanoemulsions could also be employed in anti-inflammatory functions. Free radicals are released by enzymes, toxic metabolites of pathogens, and inflammation mediators such as polymorphonuclear lymphocytes, leading to chronic inflammation. These same enzymes and metabolites deprive host cells of their required nutrients for growth. However, the mix of emulsifiers and oils was reportedly significant in phytochemicals absorption and treatment of inflammatory bowel disease (IBD), i.e., Crohn’s disease and ulcerative colitis (Yen et al. 2018) and periodontitis, a chronic inflammatory disease that erodes teeth’s supporting structures (Aithal et al. 2018).

Inflammatory bowel disease (IBD) is often characterized with inflamed intestinal wall where the colonic and rectal mucosa are impacted. This is continuous for ulcerative colitis while it may be transmural and discontinuous in Crohn’s disease. Host’s lifestyle, genetic make-up, oxidative stress, pathogenic attack, immune responses, and drastic changes of inflammatory mediator levels are factors associated with IBD (Head and Jurenka 2003). Meanwhile, some studies have shown the usefulness of phytochemicals in treating periodontitis and IBD, including diterpenoid and quercetin, respectively (Geoghegan et al. 2010). Due to their low water solubility, they are less bio-available and are poorly absorbed orally. To increase their absorbability, both phytochemicals were improved with emulsions (Azuma et al. 2002).

**Cancer**

Abnormal cell proliferation due to genetic coding errors generate cancer cells. Active angiogenesis and vascular density occur in order to utilize the blood supply for tumor tissues growth, and is supported by a microenvironment of the extracellular matrix, adipocytes, pericytes, immune cells, and others (Ganta et al. 2014). The use of anticancer drugs may result in inadequate solubility, toxicity to non-cancer cells, and poor selectivity of target cancer cells, while chemotherapy drugs may not be ideal in the long run due to their action on every form of proliferative cells, including hair follicles, bone marrow, red blood cells, gut epithelial cells, and lymphatic cells (Qiao et al. 2010; Mahato 2017).

Poor solubility and hydrophobicity of most anticancer drugs connote their inability to reach or effect their action on cancer cells (Sareen et al. 2012). This is where nanoemulsions are essential, as they proffer solubility to hydrophobic drugs and their stability. The resultant effect is that cancerous cells are selectively targeted earlier, leading to a high rate of successful cancer treatment. For instance, nanoemulsions could be engineered using specific ligands to target cells, tissues, or organs, all to improve the status quo in cancer therapy (Mahato 2017). Nanoparticles easily conjugate with multifunctional moieties, as found in nanoemulsions, aimed at drug delivery for cancer therapy via diagnostic means and imaging. Indeed, Tiwari et al. (2006) studied and used lipid-rich nanoemulsions containing fatty
acids (omega-3 and omega-6 fatty acids, linoleic acid), non-glucose-based calories, and vitamins E and K as colloidal carriers for chemotherapeutic drugs, whilst using diagnostic and imaging techniques. Although the in vitro study was promising, the need for a validation and safety studies cannot be undermined. Table 2 offers more examples of nanoemulsion applications in healthcare delivery.

**Cosmetics and others**

Nanoemulsions could be traced to other applications such as complex matter developments and cosmetics, based on their liquid–liquid affinity to macromolecular moieties, minute size and large surface area. As building blocks of polymers, nanoemulsions could use their hydrophobic monomeric units in the droplets to generate polymers, with vast examples demonstrated in the studies of Asua (2002), Landfester (2006) and Gupta et al. (2016). Interestingly, from the development of varying protein shell structures with silicone oil-based nanoemulsions (Chang et al. 2008), amphiphilic photoreactive surfactants (de Oliveira et al. 2011), silica nanospheres (Wu et al. 2013), photoinduced and thermoreactive polymers or organogels (Helgeson et al. 2012), essential oils-based products (Barradas and e Silva 2020), suspended magnetic nanoparticles (Primo et al. 2007), to erythrocyte-like composite hydrogels (An et al. 2013), nanoemulsions have been studied or applied.

Moreover, nanoemulsions could be used in composite and crystal formulations on the premise of size specificity and accuracy of active pharmaceutical ingredients and other products, involving a low energy-requiring process (Eral et al. 2014). Indeed, nanosized oil-loaded droplets ensure penetration of the stratum corneum, making them highly useful in alcohol-free perfume formulations (Rai et al. 2018; Barradas and e Silva 2020). Noteworthy to mention is that some oils used in nanoemulsions proffer some benefits that should not be undermined, and could be useful in the encapsulation of volatile components like aromatic compounds and essential oils.

On another note, the surface area and small size of nanoemulsion droplets increase their propensity to lesser viscousness, making them utilizable in the cosmetics sector as they could more efficiently deliver active substances to the skin. They are no flocculants, coalescing or creaming agents, and demonstrate little or no sediments, making their applications far more important than conventional emulsions in cosmetology. In this regard, *Vellozia squamata* and *Opuntia ficus-indica* (L.) Mill hydroglycolic extracts were studied and applied to fabricate nanoemulsion-based moisturizers, creams, anti-ageing agents (Quintão et al. 2013; Ribeiro et al. 2015). Similarly, oils like coconut, polyethylene glycol octyl phenyl ether and polyethylene glycol hydrogenated castor oil were included in nanoemulsions for cosmeceutical applications (Pengon et al. 2018).

Furthermore, the use of nano-gel technique for trans-epidermal water loss minimization, dermal protection, and efficacious active ingredients penetration has been suggested for inclusion in moisteners, anti-ageing creams and various sun care formulations (Mansour et al. 2009). For instance, Kemira nano-gel is a nanoemulsion-based patented cosmetics system meant to attain skin smoothness by enhancing high penetrative capacity of active ingredients and dermal cells production (Guglielmini 2008). Another patented example is that of L’Oreal (Paris, France), using nanoemulsion-based phosphoric acid fatty acid esters in cosmetics and pharmaceutical products, among others (Shah et al. 2010). Table 2 presents more on the overview of use of nanoemulsions in cosmetics and other non-food applications.

**Food**

Nanoemulsions have proven quite useful in bioavailability, bioactivity, digestibility, stability, safety, quality, and sensory enhancements of food components and natural extracts, such as lycopene-solubilized and β-carotene-based nanoemulsions (Nedovic et al. 2011; Bakshi et al. 2018), based on their wide surface area and small droplets. To remain stable, formulation of nanoemulsions requires the presence of an emulsifier, often acting as not only an additive but a preservative of the food products and/or the active components. As an example, surface-active molecules were introduced during the fabrication of basil oil nanoemulsions, and were found to exert antimicrobial activity against certain food spoiling fungi, including *Aspergillus flavus* and *Penicillium chrysogenum* (Gundewadi et al. 2018). A similar study was carried out on avocado oil-based nanoemulsions stabilized with Quillaja saponins (QS) where thermal stability was reportedly increased as QS was incorporated in the emulsions, a merit in the cause of safe and sterile emulsion-based food products development (Teo et al. 2017; Riquelme et al. 2019).

The use of nanoemulsions to stabilize essential oils in foods also assist with overcoming their high volatility, hydrophobicity, and reactivity with other food components, which could reduce their applications in the food sector. The stabilized oils or nanoemulsions thus improve the antioxid and antimicrobial activities of the processed essential oils, enhancing their compatibility, solubility, stability, physicochemical equilibrium, and behaviors (Lawrence and Rees 2000; Bai et al. 2016; Ghasemi et al. 2018; Prakash et al. 2019). Other studies that have applied nanoemulsions in foods include corn oil-based β-carotene nanoemulsions at 300 nm (Borba et al. 2019), sensory efficient nanoemulsions constituted with Brazilian propolis extracts (Seibert et al. 2019), improved digestible curcumin nanoemulsions, and
nanoemulsion-based fortified beverages with vitamin D3 (Golfomitsou et al. 2018; Maurya and Aggarwal 2019). The possibilities of nanoemulsions in foods and food products seem limitless. More examples are presented in Table 3.

Conclusion

Based on their physicochemical and functional properties, nanoemulsions have very promising multisectorial uses in healthcare, food, polymer manufacturing and cosmetics industries. Therefore, they have gained prominent attention in the scientific community. Recent uses of beeswax-starch, jujube gum, sodium caseinate, turmeric extract, linalool, docosahexaenoic and eicosapentaenoic acid, cumin seed oil, whey protein isolate, and oils like cinnamon, lemon and anise myrtle essential oils in nanoemulsion formulations (Arredondo-Ochoa et al. 2017; Gharibzahedi and Mohammadnabi 2017; Nirmal et al. 2018; Noori et al. 2018; Prakash et al. 2019; Zhang et al. 2019; Park et al. 2019; Farschi et al. 2019; Pongsumpun et al. 2020) have shown high potentials in the food industry and for the general well being. They can also deliver phytochemicals and other bioactive components in the food industry (Mahmood et al. 2017). In addition, nanoemulsions also have multifarious prospects in non-food applications shown recently in inflammatory and periodontitis treatment, agrochemical, cosmetics and pharmaceutics, texturizing agents and creams, non-steroidal anti-inflammatory drug, drug and vaccine delivery, cosmetic applications and alcohol-free perfume formulations (Aithal et al. 2018; Teo et al. 2017; Bakshi et al. 2018; Lu et al. 2018; Kaci et al. 2018; Salim et al. 2018; Pengon et al. 2018; Rai et al. 2018; Shaker et al. 2019; Kumar et al. 2019; Barradas and e Silva 2020).

Formulating nanoemulsions often employ emulsifiers/surfactants and nanoparticles, which have raised eyebrows regarding their safety because they accumulate both in the environment and in the human body (Bajpai et al. 2018). Any engineered nanoparticulates or materials attract some degree of attention due to limited comprehension of their mechanisms and health consequences, a major reason to delay further implementation of nanotechnology in the food industry (Loira et al. 2020). For instance, long-term exposure to silver nanoparticles could lead to cell damage and inflammation via oxidative stress reactions (Gaillet and ex-vivo studies. Curr Nanosci 4(4):381–390. https://doi.org/10.2174/157341308788306071

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