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Nano-Perfumes as A Fragrance Carrier: Their Brief History, Essential Aspects, Development, Preparation Methods, Characteristics, and Future Perspectives

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ABSTRACT

Nano-perfumes refer to alcohol-free oil-in-water nanoemulsion perfumes containing fragrance. Due to its favorable properties, nano-perfumes may appeal to a broader client base, including children and individuals with sensitive skin. This technology can provide an alternative solution to the low permanence of fragrances by eliminating ethanol and decreasing the amount of surfactant, co-surfactant, and solvents used in the formulation. However, relatively few studies have addressed and developed this technology to date. In this review, we examine several essential elements of nano-perfumes in order to raise some relevant questions regarding the future of this technology. The discussion focused on the brief history of nano-perfumes, essential aspects of perfume, development of nanoemulsions in the cosmetics field, nano-perfume preparation methods, significant characteristics of nano-perfumes, and their problems and prospects.

Keywords: nano-perfumes, nanoemulsions, quality by design, perfumery ternary diagram, mixture design

INTRODUCTION

In 2018, a scientific study titled "Preparation and Characterization of Water-based Nano-perfumes" coined the term "nano-perfumes" for the first time (Miastkowska et al., 2018) to refer to alcohol-free perfume in the form of oil-in-water (O/W) nanoemulsions containing fragrance without the addition of ethanol and co-surfactants (Sikora et al., 2018). This nano-perfume technology has been submitted for patent application by the group to The European Patent Office. The subject of the invention is a method of producing non-alcoholic perfumes with nanoemulsion properties. According to the invention, the solution consists of obtaining a pre-emulsion and a certain amount of oil phase consisting of a fragrance composition, emulsifier, and an aqueous phase as a mixture of water and preservative (Gut et al., 2020).

Nano-perfume technology permits the production of water-based fragrances that are clear, stable, non-toxic, non-combustible, odorless, and have excellent skin tolerance. This method can provide an alternative solution to the low permanence of fragrances by eliminating ethanol and decreasing the amount of surfactant, co-surfactant, and solvents used in the formulation. Given its advantageous features, nano-perfumes may be favored by a wider range of customers, including youngsters and those with sensitive skin. The water-based nano-perfumes have several advantages due to the eco-friendliness of water, its inflammability, and widespread acceptability. In addition, water is a far less expensive solvent than ethanol, which reduces the production cost (Miastkowska & Lasoń, 2020; Sikora et al., 2018).

The use of nanoemulsions in perfumery products has been previously reviewed by Sikora et al., who examined Nano-perfumes from the perspective of their formulation and physicochemical properties (Sikora et al., 2018). However, other crucial features of nano-perfumes, such as the optimization of fragrance components and rigorous characterization of the resulted nanoproducts have not been evaluated. In this review, we seek to fill this void and complement previous literature by discussing a brief history of nano-perfumes, essential aspects of perfume, development of nanoemulsions in the cosmetics field, nano-perfume preparation methods, significant characteristics of nano-perfumes, as well as their problems and prospects.

PERFUME: DEFINITION AND COMPOSITIONS

Perfume can be defined as a substance that emits a pleasant odor and usually is a liquid-based formulation with natural or synthetic ingredients. The word "fragrance" is typically reserved for a fragrant ingredient used in a perfume or a perfumed formulation. Perfumes consist of a mixture of aromatic chemicals and essential oils. Until the 19th century, they were usually composed of natural fragrant oils, but nowadays, most of perfumes contain chemical fragrance that are mostly synthetic (Chisvert et al., 2018). A perfume, according to Charles's pyramid, is a liquid mixture of top notes (first impact, fresh), middle notes (main perfume character), and base notes (long-lasting) in solvents (ethanol, water, matrix) (Rodrigues et al., 2021).

Perfumes used in cosmetics are complicated mixes of hundreds of elements (fragrances and other components), which collectively impart the product's distinctive aroma. They are used in virtually all cosmetics, including perfumes (also known as fine fragrances) and other perfumed cosmetic products such as general toilet products (bath gels, soaps, and deodorants), skin care products (face and body care products), sunscreens and related products (sun products, bronzing products, whitening products), hair care and related products (shampoos, conditioners, and hairsprays), and decorative cosmetics (make-up products and tinted based products) (Chisvert et al., 2018).

Perfume consists of fragrance ingredients (such as aromatic essential oils, ethanol, aroma compounds, and fixatives) dissolved in certain solvents (Sikora et al., 2018). The most prevalent solvent in fragrance products is ethanol or aqueous alcoholic solution. Low aliphatic alcohols, particularly ethanol, are chemical substances that can dissolve lipophilic fragrance compounds in a single transparent, homogeneous phase. Alcohols also have antibacterial properties (Miastkowska & Lasoń, 2020). Based on the concentration of scent, these cosmetic products are divided into *eau de parfum* (10-20%), *eau de toilette* (5-15%), *eau de cologne* (3-8 %), and aftershaves (1-3%) (Marcus et al., 2013). The purpose of including fragrances in the formulation of all these different products is to influence consumers, either by enhancing their sensorial properties or simply by signaling the product to be easily recognizable (Teixeira et al., 2013).

Essential oils or fragrance oils are the sources of fragrance compounds. Essential oils are volatile aromatic liquids extracted through steam distillation from plants. In contrast, fragrance oils refer to a blend of either synthetic fragrance compounds or natural essential oils diluted with a carrier solvent, such as propylene glycol, vegetable oil, or mineral oil (Ríos, 2016). Fragrance oils in cosmetics might induce sensitivity, irritation, and allergy in certain people (Arribas et al., 2013; Handley & Burrows, 1994; Hendriks et al., 1999; Reeder, 2020). However, using fragrance oils in the perfume industry is necessary due to the increasingly complex fragrance characteristics needed to create novelty in the perfume products, which are difficult to obtain using essential oils only. Petrichor, or the pleasant earthy scent of the first rain, is one example in which the compound of geosmin mainly generates the scent of wet soil. This compound is principally produced by *Streptomyces griseus* bacteria (Vittal, 2019). Another essential aspect to be considered in addition to the main concept of perfume and the composition of fragrances and solvents used in formulating perfume is the concept of "notes" and its optimization.

THE CONCEPT OF "NOTES" AND ITS OPTIMIZATION IN PERFUMERY PRODUCTS

The phrase "notes" in perfume refers to the scent detected after applying the fragrance. The composition of perfume notes typically relates to the perfume pyramid, which classifies notes according to their dispersion period. Top notes can be immediately recognized after the perfume is applied, followed by middle notes and finally base notes (most persistent odor) that appear close to the evaporation of middle notes and stay for the longest period compared to the other two notes (Rodrigues et al., 2021). Notes are typically used only for products in the field of delicate fragrance

(Chisvert et al., 2018). Perfume notes are a complex blend of essential or fragrance oils that give the fragrance its distinctive scent (Harrison et al., 2018). Notes are important in both conventional perfumes (alcohol-based) and nano-perfume perfumes (water-based) because they can determine consumers favors on the perfume products. Therefore, notes optimization becomes a critical step in the formulation of nano-perfumes. Unfortunately, previous studies on Nano-perfumes have not given much attention on notes optimization (Miastkowska et al., 2018; Sikora et al., 2018) as the studies were focused on selecting a suitable surfactant for the nano formulation.

To optimize the notes, the concept of "quality by design" (QBD) can be adopted. QBD is a systematic approach to product development, starting with goal setting, product and process understanding, and process control based on science and risk management. This concept emphasizes that quality cannot be tested on products alone but must be built on design (ICH, 2017). One of the tools used in applying the QBD concept is the design of the experiment (DoE). DoE is a structured and organized method for determining the relationship between factors that affect processes and outputs. This method can also be interpreted as achieving process-related knowledge by establishing a mathematical relationship between input, process, and output. Examples of statistical software used for DoE implementation are Design Expert®, JMP®, and Minitab® (Montgomery, 2017).

Generally, three main DoE implementation categories are determined by the parameters to be studied: mixture design, factorial design, and a combination of both (Armstrong, 2006; Cornell, 2002; Montgomery, 2017). Applying this concept to perfume engineering refers to the category of mixture design (MD). MD is used for the characterization and optimization of a formula. This optimization can be done if the overall amount of the composition has been determined by the formulator (Cornell, 2002).

One of the methods used in perfume engineering is perfumery ternary diagrams (PTD®). PTD® is the development of DoE, which is applied to optimizing notes or perfume composition. This method is based on the analogy between the perfume pyramid structure and the engineering of a ternary diagram. The diagram allows a quick evaluation of the odor active value (OAV) of all possible combinations of perfume notes with three fragrance components (Gomes et al., 2008; Mata et al., 2005a, 2005b, 2005c; Teixeira et al., 2013). The diagram shows each note that represents the proportion in the mixed combination, namely the top (15-25%), middle (20-40%), and base (45-55%). This proportion is responsible for the balanced tenacity of the perfume during evaporation.

PTD® concept combines three areas by placing top notes, middle notes, and base notes at the vertices of a triangle. The dots within the triangle represent all possible ternary mixtures and mappings within the area (composition range) of "notes" with a dominant odor. Every drop in the ternary chart represents a unique mix of top, middle, and base notes (the sum must equal one) (Teixeira et al., 2013). An example of perfume note optimization was previously shown by Teixeira et al. who combined three fragrance ingredients: limonene, geraniol, and galaxolide diluted in ethanol (Teixeira et al., 2009). In addition to addressing various important aspects of perfume and discussing nano-perfume in more detail, this research also reviews the development of nanotechnology in cosmetics and why nanoemulsion was chosen as a carrier technology for water-based fragrances which is a suitable alternative to conventional water-based perfumes.

NANOEMULSIONS IN COSMETICS

Consumers are increasingly attracted to a holistic and technological approach when purchasing cosmetic products. The focus of this approach is natural products derived from nanotechnology. These products were chosen because of their effectiveness, safety, and environmental factors. Nanotechnology is a field of science that manipulates atoms and molecules at the nanometer (nm) scale (Morganti, 2020). This technology has been researched extensively to design carriers of active ingredients and bioactive agents in cosmetics (Nafisi and Maibach, 2017).

The widespread use of nanotechnology in cosmetics indicates that this technology can produce distinctive properties from large-scale particles. These properties, including color, transparency, solubility, and chemical reactivity, enhance the attractiveness of this technology to the cosmetic industry (Raj et al., 2012). Various examples of the application of nanotechnology in the cosmetic field include omega fatty acid nanoemulsions for increasing the permeation of co-enzyme Q10 (Tou et al., 2019), sunflower oil nanoemulsions for sun protection (Arianto &

Table I. Types of nanomaterial used in cosmetics.

Type	**Nanomaterial form**	**References**
Polymeric nanomaterials	Nanocapsules, hydrogels, chitosan, dan liquid crystals	(Abdelghany et al., 2021; Gwak et al., 2021; Huang et al., 2022; Ling et al., 2022; Seo et al., 2022)
Nanoparticulate systems	Nanospheres, nanotopes, nanocrystals, nanofibers, dan nanopigments	(Asadi et al., 2022; De et al., 2014; Ghalehkhondabi et al., 2022; P. Mishra et al., 2021; Nafisi & Maibach, 2017; Setia Budi et al., 2022; Zarandi et al., 2018)
Carbon-based nanomaterials	Fullerene dan nanodiamond	(Karami et al., 2022; SCCS & Chaudhry, 2016; Shojaei et al., 2019; Tanzi et al., 2022)
Inorganic nanomaterials	Nanosilver, nanogold, zinc oxide nanoparticles, titanium oxide nanoparticles, dan silica nanoparticles	(Alkalbani et al., 2022; Dong et al., 2022; Fytianos et al., 2020; Gut et al., 2020; Pandey et al., 2019; Peng et al., 2020; Salama & Abdel Aziz, 2020)
Organic nanomaterials	Lipid nanoparticles (solid lipid nanoparticles and nanostructured lipid carriers), liposomes, nanosomes, niosomes, ethosomes, transferosomes, cubosomes, multiple emulsions, ultrasomes, photosomes, aquasomes, and nanoemulsions	(Allouche, 2013; Barriga et al., 2019; Daraee et al., 2016; Gopalakrishnan et al., 2013; Himeno et al., 2017; Ito et al., 2012; S. S. Jain et al., 2012; Jaiswal et al., 2015; A. Mishra et al., 2014; Morganti, 2020; Naseri et al., 2015; Opatha et al., 2020; Pepakayala et al., 2021; Sawant & Bhagwat, 2021; Shabreen & Sangeetha, 2020; Tiwari et al., 2015)
Other nanomaterials	Cyclodextrin dan dendrimers	(Nafisi & Maibach, 2017; Sakulwech et al., 2018)

Cindy, 2019), as well as the use of nanoscale pigments in sunscreen formulas as filters from the threat of ultraviolet rays (Huber & Burfeindt, 2019). Generally, nanoparticles used in cosmetics are classified into six groups (Table I), based on the different materials to compose the nanoparticles, namely polymeric nanomaterials, nanoparticulate systems, carbon-based nanomaterials, inorganic nanomaterials, organic nanomaterials, and other nanomaterials (cyclodextrin dan dendrimers) (Nafisi and Maibach, 2017).

One of the rapidly developing nanotechnologies in the cosmetic field is nanoemulsions. Nanoemulsions can be excellent carriers for the primary or cosmetic active ingredient (cosmeceutical). Ingredients used in nanoemulsions are generally safe and cannot penetrate the skin as fundamental particles or reach deep penetration of the skin, thereby requiring further attention on their chemical composition, regardless of the size (Silva et al., 2020). Nanoemulsions are a colloidal dispersion system consisting of two immiscible liquids combined with the help of emulsifiers (surfactant and co-surfactant). The emulsion consists of droplets of <200 nm in size and is physically stable, optically clear, and transparent (Abdulbaqi et al., 2019; McClements, 2011; McClements & Rao, 2011; Thakur et al., 2012).

Nanoemulsions can be categorized into oil-in-water (O/W) and water-in-oil (W/O) types. O/W nanoemulsions are oil droplets dispersed in a water medium, while W/O nanoemulsions are water droplets dispersed in an oil medium (Jafari et al., 2017). A hydrophilic emulsifier is typically used to coat the droplets in the O/W nano-emulsions. In contrast, in the W/O nanoemulsions, the droplets are covered with a lipophilic emulsifier (McClements & Jafari, 2018). Researchers have developed various types of nanoemulsions-based cosmetic products composed of natural or synthetic ingredients (Barreto et al., 2017; Brownlow et al., 2015; Dario et al., 2020; Miastkowska et al., 2018; Ngan et al., 2015; Pleguezuelos-Villa et al., 2019; Sulaiman et al., 2017).

Table II. Components of nanoemulsions in cosmetics.

Component	**Group**	**Type**	**Examples**	**References**
Oil		Triglycerides	Caprylic/capric triglycerides, avocado oil, apricot kernel oil, coconut oil	(Eid et al., 2013; Mahdi al., 2011; Pengon et al., 2018; Ribeiro et al., 201
		Terpenes	Limonene	(Bei et al., 2015)
		Fatty acids	Oleic acid	(Solè et al., 2006)
		Esters	Isopropyl myristate, isopropyl palmitate, isostearyl neopentanoate	(Hanifah & Jufri, 2018; Rodriguez et al., 2016)
		Alkanes	Isododecane, isohexadecane, vaseline, parleam	(Quemin, 2003)
Surfactant	Nonionic surfactants	Ethoxylated alkyl alcohols/alkyl acids	PEO-8 isostearate, PEO-20 stearate, Steareth-10	(Roessler et al., 2002)
		Sucrose alkyl ester	Cetearyl glucoside, sucrose distearate	(Eid et al., 2013)
		Sorbitan alkyl ester	Polysorbate 20, Polysorbate 61	(Fernandes & Yukuyam 2015)
		Polyglycerol alkyl ester	Decaglycerol monostearate	(Simonnet et al., 2003)
	Mixtures of fatty alcohols and surfactants	Phosphoric alkyl, citric alkyl ether	K cetyl phosphate, Trilaureth-9 citrate	(Simonnet et al., 2002)
	Phospholipids and peptide-based gemini surfactant	Lecithin, gemini	Soybean lecithin, dilauramidoglutamide lysine	(Tian et al., 2016; Zhou al., 2010)
	Ionic surfactants	Alkyl trimethyl ammonium,	Behenyl trimethylammonium chloride	(Okamoto et al., 2016)
	Amphiphilic oligomers	Amphiphilic oligomer	Poloxamer 231	(Tamarkin et al., 2014)
Co-surfactant	Polyols	Polyols	Glycerin, dipropylene glycol, PEG300, PEG400, poloxamer	(Walstra, 1993; Zhou et al., 2010)
Antioxidants			Ascorbic acid, alpha-tocopherol	(Rege et al., 2015)
pH adjusting agent			Sodium hydroxide or hydrogen chloride	(Ding et al., 2017)
Preservatives	Preservatives		Methyl paraben, propyl paraben	(Sikora et al., 2018)

In cosmetics, O/W nanoemulsions have been more extensively studied than W/O. Nevertheless, the system's composition must be carefully selected in parallel with the preparation parameters. The choices of the oil, or the surfactant-to-oil ratio, among others, are critical parameters in nanoformulation production. The most appropriate method depends mostly on system composition or scale-up requirements (Silva et al., 2020). Nanoemulsions consist of oils, surfactants, cosurfactants, antioxidants, pH-regulating agents, preservatives, and water (Table II). The oil phase in nanoemulsions works as an emollient and dissolves hydrophobic active ingredients. Surfactants play an essential role in droplet size reduction and nanoemulsions stability.

When choosing a surfactant, it is essential to consider its effectivity in reducing the interfacial tension between the water and oil phases and the risk of the surfactant to cause skin irritation. For this reason, nonionic surfactants are preferred in the manufacture of cosmetics (Silva et al., 2020). Co-surfactants, primarily polyols, are commonly used in conventional emulsions and various cosmetic products. This material helps the surfactant reduce the droplet size of the nanoemulsions, while simultaneously acting as a humectant and solvent for the active ingredients and even increasing the penetration of the ingredients (Nastiti et al., 2017). In addition, this material does not negatively affect the rheological properties of the final nanoemulsions (Silva et al., 2020). The aqueous phase is also crucial in enhancing the stability of nanoemulsions, as it can contain antioxidants, tonicity modifiers, pH regulators, preservatives, penetration enhancers, and viscosity enhancers, which are all combined to produce the desired final product consistency (Salim et al., 2016).

Generally, nanoemulsions are physically stable, but thermodynamically less stable than microemulsions and are highly dependent on the nanoscale droplet formation process. The low amount of surfactant in the nanoemulsions requires high energy input to achieve a stable formulation (Lopes, 2014). Nonetheless, low-energy techniques can still be used for manufacturing (Zhang et al., 2019). For cosmetic purposes, nanoemulsions can be prepared by high-energy mechanical dispersion or low-energy methods. The characterization of nanoemulsions for quality control is described in detail in the pharmacopeia and related literature. In addition, toxicity and efficacy tests that are more specific for topical nanoemulsions types should be carried out before transdermal studies (Silva et al., 2020). Nanoemulsions have the potential to be developed in various cosmetic and body care products. Oil-in-water (O/W) or water-in-oil (W/O) colloidal dispersions commonly comprise droplets with a diameter of a few nanometers to 200 nm in nanoemulsions, while the maximal particle-size range for this kind of system is occasionally increased to 1000 nm. Small droplet size in nanoemulsions has an impact on their optical properties, stability, rheology, and delivery systems that conventional emulsions cannot achieve (Sonneville-Aubrun et al., 2018). Examples of the application of nanoemulsions in the cosmetic field include fullerene-integrated nanoemulsions for the regeneration of collagen structural damage (Ngan et al., 2015), genistein-vitamin E nanoemulsions for chemoprevention against skin damage caused by UV-B rays (Brownlow et al., 2015), nanoemulsions of *Agave sisalana* by-product for increasing skin moisture (Barreto et al., 2017), *Clinacanthus nutans* L. nanoemulsions for skin antiaging (Sulaiman et al., 2017), alcohol-free perfume nanoemulsions (nano-perfumes) (Miastkowska et al., 2018), mangiferin nanoemulsions for skin regeneration (Pleguezuelos-Villa et al., 2019), and quercetin cationic nanoemulsions as photoprotection of color-treated hair (Dario et al., 2020). The various advantages of nano-perfume as a new carrier technology in fragrance products create opportunities for diversifying and differentiating existing fragrance products. Still, there are many challenges that scientists must answer through more massive studies, especially in optimization, which prioritizes nanoemulsion formulations and “notes” optimization.

NANO-PERFUMES: COMPOSITION, OPTIMIZATION, PREPARATION, AND CHARACTERIZATION

The term “nano-perfumes” refers to a water-based perfume in the form of O/W nanoemulsions with a specific fragrance composition (essential oil or fragrance oil) without the use of alcohol as a primary or co-solvent (Gut et al., 2020; Miastkowska et al., 2018; Miastkowska & Lasoń, 2020; Sikora et al., 2018). Similar to other nanoemulsions preparations, nano-perfumes has good physical stability. Nano-perfumes is transparent, non-greasy, and quickly dispersed when applied. In addition, this type of cosmetic shows the ability to protect fragrances from oxidation (Miastkowska & Lasoń, 2020).

In general, components of Nano-perfumes are also like other nanoemulsions used in the cosmetic field. The development of water-based perfumes in the form of stable nanoemulsions containing fragrance compositions (range 5-15%) stabilized by non-ionic surfactants allows the creation of safe perfume products for a wider group of consumers, including children, adolescents, and people with sensitive skin (Sikora et al., 2018). The use of various types of surfactants and co-surfactants reduces or even eliminates the use of ethanol in perfume formulas (Table III).

Table III. Surfactants/co-surfactants in water-based perfumes

Perfume form	Surfactant/co-surfactant	References
Perfume with reduced alcohol content	Glyceryl partial esters, polyglyceryl partial esters, partial sorbitan esters, partial sorbitol esters, carbohydrate esters (alkyl poly), glycosides	(Bleuez & Porcu, 2009)
Alcohol-free perfume microemulsion	Tween®20, Tween®40, Tween®60, Tween®80, Cremophor®RH 40, Cremophor®RH 60, Amerchol®, Genapol®, Poloxamer®407, Span®20, Span®40, Span®60, Span®80, Triton®X-100, Lamacit®877, LRI®, Triton®X-102, Trycol®, Tergitol®, Vicinal diol, 1,2-hexanediol, isobutyric acid-l-hydroxy-2,2,4-trimethyl-3-pentyl ester, isobutyric acid-3-hydroxy-2,2,4-trimethyl- l-pentyl ester, Brij®20, 1,2-hexanediol, sodium lauryl sulfate (SLS), PPG-24 Buteth 26, Habo monoester P90®, Lamesoft® PO 65, Plantacare® 818 UP, Plantacare® 810 UP, Plantacare® 1200 UP, Plantacare® 2000 UP, Natisol®, Symbio® Solve XC, Cremophor®RH 40, Luviquat® mono CP, Aerosol® OT	(Chung et al., 1994; Dumanois & Gueyne, 2003; Guenin et al., 1995; Manzo & Kennedy, 1998; O'rourke & Short, 1994; Piechocki & Shick, 2005; Tchakalova & Hafner, 2018; Wiedemann & Kaufhold, 2013)
Water-based Nano-perfumes	Cithrol®10GTIS, decyl glucoside, Natragem®S140, Etocas®35, polyglycerol-4 esters, sebacic and lauryl acids, polyglycerol-6 esters	(Gut et al., 2020; Miastkowska et al., 2018)

The use of a nonionic surfactant that is gentle to the skin as an emulsifier, i.e., castor oil (Etocas 35) ethoxylated with 35 moles of ethylene oxide, generates stable systems, without the need to use additional solubilizers, such as polyol ,e.g., glycerin, an oil phase component, or an oil with low polarity (e.g., isohexadecane). These formulations have low viscosity and pH suitable for the skin (Miastkowska et al., 2018).

Various studies have been carried out on the formulation of essential oils derived from various parts of plants into nanoemulsions. These studies have become an essential foundation in formulating Nano-perfumes. Examples of essential oils in nanoemulsions formulations include baccharis oil (Seugling et al., 2019), cajeput oil (Le et al., 2022), cinnamon oil (Boughendjioua & Djeddi, 2018; Liu et al., 2021; Singh et al., 2022), citronella oil (Prasad et al., 2022), citrus oil (Kang et al., 2022), clove oil (Wang et al., 2022), lavender oil(Kazemi et al., 2020), lime oil (Liew et al., 2020), myrtle oil (Falleh et al., 2021; Hagos et al., 2017), oregano oil (Christaki et al., 2022; Manaa et al., 2022), peppermint oil (Falleh et al., 2021), rosemary oil (Shahrampour & Razavi, 2023), spearmint oil (Gorjian et al., 2022), and thyme oil (Mirsharifi et al., 2023). In nanoemulsions formulation using essential oils, the main physical properties that contribute to the quality of the nanoemulsions are relative density and viscosity (Abdolmaleki et al., 2019), while the important chemical characteristic of the Nano-perfumes is peroxide number (Miastkowska et al., 2018).

The optimization of nano-perfumes and alcohol-based perfume (conventional), in principle is almost the same as the optimization of perfume notes but slightly different in the composition of the formula. In perfume notes, optimization is carried out on fragrance ingredients and alcohol (solvent), while in nano-perfumes, optimization is carried out on the ratio of fragrance ingredients (oil phase), surfactants, and co-surfactants. (Yu et al., 2022) Nanoemulsions with oil phase and surfactant in mass ratio surfactant: oil (S:O) of 0.625:0375 maintained kinetic stability in all used fragrance compositions for 12 months of storage. The droplet sizes did not exceed 30 nm and virtually did not change over 365 days

(Miastkowska et al., 2018). The role of surfactants in nano-perfume formulations is critical in forming nanoemulsions and ensuring their physical stability. Combining surfactants or adding a co-surfactant can increase the kinetic stability of nanoemulsions compared to using a single surfactant (Saxena et al., 2018). Co-surfactants can lower the interfacial tension, which helps change the curvature of the micelles. Non-ionic co-surfactants help stabilize the system by forming dynamic micelles, thereby reducing interfacial tension (Rawal & Patel, 2018; Vaidya & Ganguli, 2019) and stretching surfactant molecules (Yu et al., 2022). Various studies have been carried out on optimizing nanoemulsions formulas using DoE. These studies include mixture design, factorial design, and response surface methodology (Argenta et al., 2014; Koester et al., 2015; Salunkhe et al., 2014; Sita V G & Vavia, 2020).

The criteria for optimal nano-perfumes generally refer to the physicochemical, pharmacy technical, and biological characterizations (Gurpret & Singh, 2018). However, there are differences between Nano-perfumes as a cosmetic preparation and nanoemulsions intended as a drug delivery system (DDS). In contrast to Nano-perfumes, which focuses on transparency and fragrance protection from oxidation (Miastkowska et al., 2018; Sikora et al., 2018), DDS requires more detailed characterization on the drug release profile (i.e., release, permeation, and penetration of bioactive ingredients using membranes or synthetic skin models) (Praça et al., 2018).

Generally, the preparation of nano-perfumes has no difference from nanoemulsions, which are grouped by the level of energy used (i.e., high-pressure homogenization, microfluidization, ultrasonication, phase inversion temperature, phase inversion composition, spontaneous emulsification, and solvent displacement) (Table IV). However, the use of nonionic surfactants and manufacturing techniques using the low-energy phase inversion composition (PIC) and the high-energy ultrasonic homogenization (US) methods are recommended, related to surfactant toxicity, thermodynamic stability, and compositional flexibility (Silva et al., 2020). PIC (Cui et al., 2018; Fernandez et al., 2004; Y. Li et al., 2013; Mayer et al., 2013; Solè et al., 2010) and ultrasonic homogenization (Ghosh et al., 2013; Gut et al., 2020; Lago et al., 2019; P.-H. Li & Chiang, 2011; Mehmood et al., 2019; Miastkowska et al., 2018; Shi et al., 2015) have become an essential reference in the preparation of effective and efficient nano-perfumes. Examples of nano-perfumes preparations include the preparation of alcohol-free nano-perfumes, which are transparent, physiochemically stable, and dermatologically safe using nonionic surfactants prepared by PIC and ultrasonic homogenization (Miastkowska et al., 2018). Applying colloidal silver (AgNP) or colloidal gold (AuNP) with nonionic surfactants increases physical stability while also functioning as a nano-perfumes preservative (Gut et al., 2020).

In PIC method, the aqueous phase is continuously added the to the oil-surfactant mixture under continuous stirring. Initially, water is dispersed into the oil phase to form a W/O emulsion, but as the water fraction increases, the spontaneous curvature of the surfactant changes and transitions to form an O/W emulsion. In this method, water-soluble solvents are not used (Cui et al., 2018; Fernandez et al., 2004; Mayer et al., 2013; Solè et al., 2010). Nano-perfumes can also be produced using ultrasonic emulsification or ultrasonication (US). This technique uses a probe that emits ultrasonic waves to crush the coarse emulsion (Cheaburu-Yilmaz et al., 2019). Droplet size can be controlled by varying the time and energy input (Chime et al., 2014) and the oil-surfactant ratio (Ghosh et al., 2013). PIC, classified as Low-energy techniques, presents advantages for the industry since they do not require specialized and costly equipment, and the energy input for manufacturing microemulsions and nanoemulsions is considered low. Higher amounts of surfactant may be needed to achieve a stable formulation using low-energy methodologies, and the selection of oils and surfactants may also be limited (Silva et al., 2020). Generally, the US is mainly used in a laboratory setting for small batches. At the same time, PIC, classified as a low-energy technique, presents advantages for the industry since they do not require specialized and costly equipment, and the energy input for manufacturing microemulsions and nanoemulsions is considered low. Higher amounts of surfactant may be needed to achieve a stable formulation using low-energy methodologies, and the selection of oils and surfactants may also be limited. Even so, The optimized nano-perfume recipes obtained with different methods yielded the same physicochemical properties (stability, medium droplet size of the inner phase, polydispersity, viscosity, surface tension, pH, and density) (Miastkowska et al., 2018).

Table IV. Nanoemulsions preparation: methods, principle, advantage, and limitation

Energy level	Emulsification method	Principle of the method	Advantages	Limitations	References
High	High-pressure homogenization (HPH)	Shear, collision, cavitation	Flexibility on the composition; low process time	High cost; not recommended for sensitive products	(Đorđević et al., 2015; Falleh et al., 2021; Liu et al., 2021)
	Microfluidization	High-pressure injection	Controlled size droplets	High cost; not recommended for large scale	(Goh et al., 2015; S. M. Jafari et al., 2007)
	Ultrasonication (US)	Cavitation	Flexibility on the composition; Less expensive than HPH	Small batches	(Mehmood et al., 2019; Miastkowska et al., 2018; Sugumar et al., 2016)
Low	Phase inversion temperature (PIT)	Cooling	Low cost; easy to scale-up	Limited to nonionic surfactants	(Le et al., 2022; Ren et al., 2019; Su & Zhong, 2016)
	Phase inversion composition (PIC)	Dilution	Low cost; easy to scale-up	Requires titration	(Elgammal et al., 2015; H. Li et al., 2021; Maestro et al., 2008; Miastkowska et al., 2018)
	Spontaneous emulsification	Dispersions and condensation	Low cost; easy to scale-up	Limited amount of oil	(Liew et al., 2020; Sugumar et al., 2015; Zhao et al., 2018)
	Solvent displacement	Diffusion of organic solvent	Low cost; easy to scale-up	Organic solvents	(A. Jafari et al., 2019; Mitra Firoozy & Navideh Anarjan, 2019; Orellana et al., 2015; Trimaille et al., 2001)

One of the main concerns related to the use of nano-perfumes is their stability. The stability of nano-perfumes is related to properties and its characterization (i.e., transparency, relative density, viscosity, droplet size, polydispersity index, zeta potential, dye solubility, and fragrance permanence) (Table V.). Transparency is the main characteristic to be prioritized for the quality of nano-perfumes with acceptance criteria of light transmittance ≥ 99% (Çinar, 2017; Gurpret & Singh, 2018; Miastkowska et al., 2018; Saxena et al., 2018). Other important aspects of nano-perfumes are droplet size, polydispersity index (PDI), and zeta potential with acceptance criteria respectively of 20-200 nm, <0.2, and ± 30 mV (Gurpret & Singh, 2018; Silva et al., 2020). The characteristic distinguishes nano-perfumes from nanoemulsions in general, and refers to the criteria for conventional, alcohol-based perfumes. Nanoemulsions can lose their stability through different processes, including phase inversion, flocculation, coalescence, creaming, Ostwald ripening, and cracking. Nanoemulsions with small particle size reduce the gravitational force through the Brownian movement mechanism, thus preventing sedimentation and creaming. However, from a thermodynamic point of view, nanoemulsions are non-equilibrium systems that can cause destabilizing processes such as flocculation, coalescence, and Ostwald ripening (Eccleston, 2006).

In particular, the stability of Nano-perfumes is measured based on two types: physical stability and chemical stability (Miastkowska et al., 2018).

Table V. Nano-perfume characterization

Property	**Importance**	**Testing method**	**Acceptance criteria**	**Reference**
Transparency	Assessing the physical appearance of nano-perfumes	The wavelength was set to 570-590 nm on the Uv-Vis spectrophotometer. The sample container was emptied, and the transmittance was set to 100 percent. In the sample compartment, the cuvette was placed to hold the aquadest (blank). The blank solution was replaced with the cuvette containing sample, and it was returned to the sample compartment, and the transmittance percentage results were read.	Light transmittance ≥ 99%	(Çinar, 2017; Gurpret & Singh, 2018; Miastkowska *et al.*, 2018; Saxena *et al.*, 2018)
Relative density	Determining the density level of nano-perfumes	The 5 mL pycnometer was rinsed with acetone, the interior was dried with dry air, then the exterior was wiped with a dry towel. The pycnometer and cover were then weighed to the nearest 1 mg after calibrating to 20°C. The pycnometer was filled with freshly boiled sample, cooled to 20°C, and then immersed in a water bath where the temperature was maintained at 20°±0.2°C. The weighing results were recorded, and the relative density was calculated.	Relative density = 0.7-1.21 g/mL	(BSN, 1998; ISO, 1998a)
Viscosity	Determining the viscosity of nano-perfumes	The cone and plate viscometer were activated and left on for 5 to 10 minutes until the temperature control system reached equilibrium (the temperature was set at 25°C). A total of 2.0 mL of sample was deposited in the center of the plate and shifted into the tiny space between the stationary plate and the revolving cone, after which measurements and calculations were performed to determine the Nano-perfumes viscosity.	Viscosity ≤ 150 mPas	(BSN, 1998; Jain *et al.*, 2012; Miastkowska *et al.*, 2018)

Property	Importance	Testing method	Acceptance criteria	Reference
Droplet size, polydispersity index (PDI), and zeta potential	Predicting the physical stability of nano-perfumes	The parameters were analyzed using photon correlation spectroscopy (PCS). Sample was diluted and measured at predefined conditions correspondent to formulation properties at a constant temperature. Zeta potential was estimated from the electrophoretic mobility of droplets.	Droplet size = 20-200 nm, PDI <0.2, and zeta potential ± 30 mV	(Gurpret & Singh, 2018; Silva *et al*., 2020)
Dye solubility	Predicting dye solubility in colored nano-perfumes	Approximately 3-5 drops of water-soluble yellow eosin dye was added to 1 mL of the sample in a microtube, which was then thoroughly mixed and viewed under an inverted fluorescence microscope.	The dye was homogenously distributed.	(Bhosale *et al*., 2014; Jaiswal *et al*., 2015; Laxmi *et al*., 2015)
Microbiological assay	Determining the microbiological safety level	15 to 20 mL of agar medium was placed (temperature not to exceed 48°C) on a petri dish with a diameter of 85 to 90 mm. After allowing the agar medium to cool and harden in the incubator, at least 0.1 mL of the initial suspension and sample dilution was applied to the medium's surface. The inoculated Petri dishes was then inverted and incubated for 3 to 5 days at 25°C±2.5 °C. It was observed immediately or chilled for a maximum of 24 hours.	Maximum total plate number (TPN) = 10^5 col/g	(BPOM, 2011; BSN, 1998; Miastkowska *et al*., 2018)
Dermatological assay	Assuring safe exposure on human skin	Twenty-five test subjects (15 women and ten men, aged 19-55), under the supervision of a dermatologist, had a Nano-perfumes sample spread on the inside of the forearm with a 1 x 1 cm area, followed by a 2 x 2 cm filter paper and aluminium foil adhered with plaster. After 24 hours, the plaster was removed and the findings were evaluated to measure erythema, oedema, vesicles, and bullae. Three, four-, and five-days following treatment, further dermatological exams were performed in order to observe the response of the subject's skin to the test substance.	No adverse effects, including skin inflammation or sensitivity	Miastkowska *et al*., 2018; Praça *et al*., 2018; Spiewak, 2008)

Property	Importance	Testing method	Acceptance criteria	Reference
Oxidative stress test	Predicting chemical stability	Using an analytical balance, 100 grams of the sample were weighed and placed in the Erlenmeyer. The stopper was replaced after adding 50 mL of the acetic acid/iso-octane (3:2) solution to the flask. The mixture was shaken until it was dissolved. Using a volumetric pipette, 0.5 mL of potassium iodide solution was added to the solution. It was allowed to react for one minute, vigorously mixed three times, and then add with 30 mL of purified water. The solution was titrated with a 0.01 mol/L sodium thiosulfate solution that had been pre-standardized. It was gradually added while stirring constantly and vigorously until the yellow iodine hue has nearly vanished. To remove all iodine from the solvent layer, 0.5 mL of starch solution was roughly added and titrated with continuous agitation, especially near the endpoint. Then, sodium thiosulphate solution was added gradually drop by drop until the blue hue faded. The amount of sodium thiosulphate utilized was noted, and the peroxide number (POV) was calculated based on the results received.	The calculated values of the peroxide number (POV) indicated the level of the oil oxidation process. The lower the peroxide number differences between the fresh fragrances and those protected by nanoemulsions during storage, the higher the protective ability of the nanoemulsions and the chemical stability of the oils are.	(ISO, 1998b; Miastkowska *et al.*, 2018)

The physical stability of nano-perfumes is assessed by measuring the transparency, droplet size, PDI, and zeta potential of the Nano-perfumes stored for a certain period at room temperature (Miastkowska et al., 2018). Adding very high amounts of the oil phase to Nano-perfumes can significantly increase the droplet size resulting in Ostwald ripening and phase inversion (Reyes et al., 2021). A suboptimal ratio of surfactant and co-surfactant will result in coalescence, which is the fusion of two or more droplets into a single droplet with an irreversible increase in droplet size and volume but a decrease in interfacial area, which leads to the gradual separation of the oil and water phases (Karthik et al., 2018). The chemical stability test of nano-perfumes is typically carried out using the oxidative stress test method. This test is carried out to test the effect of nanoemulsions on the rate of oxidation of the fragrances (Miastkowska et al., 2018). This rate of oxidation is expressed as peroxide number or peroxide value (POV). The lower the difference in POV between the fresh fragrance ingredients and fragrance ingredients formulated into nano-perfumes, the higher the protective ability of nanoemulsions against fragrance oxidation/degradation (Miastkowska and Lassoń, 2020).

CHALLENGES AND FUTURE PERSPECTIVES

Several concerns have been raised regarding the use of nanotechnology in perfumes. Some of these issues are the transparency and stickiness of the products, the oil and surfactant ratio that is still optimized by trial and error, and the lack of rigorous testing of the final products including the testing for hedonic response, which is crucial in cosmetic products (Miastkowska et al., 2018). Apart from these problems, the addition of colloidal gold (AuNP) as a preservative (Gut et al., 2020) has the potential to create a vague condition (*syubhat*), especially in Muslim communities, even though there has been a fatwa basis from the relevant institutions (MUI, 2009). Some Muslim communities still think that the use of alcohol in perfume is similar to including the element of liquor (*khamr*) in this product (Hardoyono, 2017).

The trend of non-alcoholic water-based perfume formulations has grown over the last three decades. It started with alcohol reduction, alcohol-free perfume microemulsion, to alcohol-free perfume nanoemulsions (Nano-perfumes). However, research on Nano-perfumes has only been focused on the optimization of nanoemulsions as a barrier technology via trial-and-error experiments. Further research needs to address the use of the design of experiment (DoE), especially mixture design (MD) using experimental design software, such that the concept of quality by design (QbD) can be well implemented to produce an optimal Nano-perfumes final product.

CONCLUSION

Alcohol-based perfumes are now a regular solution on the fragrance market. However, ethyl alcohol can be an unpleasant solvent. In terms of the physical and chemical form of perfumery goods, alcohol-free perfumes in the form of stable oil-in-water (O/W) nanoemulsions provide an intriguing option. Nano-perfumes, which comprise fragrance compositions without the inclusion of ethanol enable the development of safe goods with good user qualities for a broader spectrum of consumers, including children, teenagers, and persons with sensitive skin.

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