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Essential Oil Loaded Nanofiber Formulations for Skin Applications

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ABSTRACT

Plant-derived formulations and products have emerged as alternative therapeutic approaches in recent years. Within this context, nanofibers—owing to their small diameters and high surface-to-volume ratios—have attracted attention as effective drug delivery systems. The electrospinning method facilitates the production of nanofibers in a cost-effective and high-yield manner. Essential oils, endowed with antimicrobial, anti-inflammatory, antioxidant, antifungal, anticarcinogenic, and analgesic properties, hold significant value in the health sector. The integration of these oils with nanofibers has yielded successful outcomes in the treatment of skin diseases. Incorporating plant essential oils into nanofiber carrier systems has demonstrated efficacy in treating dermatological diseases via topical application and has increasingly been adopted in modern therapeutic strategies. In this study, the utilization of plant essential oils within nanofiber carrier systems and their benefits in topical applications are presented with a detailed discussion of nanofiber production methods and their associated advantages.

Keywords: Nanofibers, essential oils, skin diseases, drug delivery systems

Cilt Uygulamaları İçin Esansiyel Yağ Yüklü Nanofiber Formülasyonları

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ÖZET

Bitkisel kökenli formülasyonlar ve ürünler son yıllarda alternatif tedavi yaklaşımları olarak ortaya çıkmıştır. Bu bağlamda, nanolifler, küçük çapları ve yüksek yüzey-hacim oranları nedeniyle, etkili ilaç taşıma sistemleri olarak dikkat çekmiştir. Elektro-eğirme yöntemi, nanoliflerin uygun maliyetli ve yüksek verimli bir şekilde üretilmesini kolaylaştırmaktadır. Antimikrobiyal, antiinflamatuvar, antioksidan, antifungal, antikarsinojenik ve analjezik özelliklere sahip olan uçucu yağlar, sağlık sektöründe önemli bir değere sahiptir. Bu yağların nanoliflerle entegrasyonu, cilt hastalıklarının tedavisinde başarılı sonuçlar vermiştir. Bitkisel uçucu yağların nanolif taşıyıcı sistemlere dahil edilmesi, topikal uygulama yoluyla dermatolojik hastalıkların tedavisinde etkili olduğunu göstermiştir ve modern tedavi stratejilerinde giderek daha fazla benimsenmektedir. Bu çalışmada, nanolif taşıyıcı sistemlerde bitkisel uçucu yağların kullanımı ve topikal uygulamalardaki faydaları, nanolif üretim yöntemleri ve ilişkili avantajlarının ayrıntılı bir tartışmasıyla sunulmaktadır.

Anahtar Kelimeler: Nanofiberler, esansiyel yağlar, cilt hastalıkları, ilaç taşıma sistemleri

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Introduction

Nanofibers, with diameters smaller than 1 µm and high surface-to-volume ratios, serve as effective drug delivery systems [1]. These systems offer high therapeutic efficacy at low doses and are utilized in the pharmaceutical area for wound dressings or to enhance topical drug release and penetration [2,3]. The structure of nanofibers varies depending on the used polymer solutions and the production parameters [4]. The electrospinning method is widely employed for nanofiber production due to its high yield, ease of application, and low cost [5,6]. In this method, a polymer solution is accelerated by high voltage and directed towards an electric field, forming nanofibers on a collector. The drug release performance of nanofibers prepared by electrospinning is measured by the diffusion of the active ingredient from the nanofiber structures and the biodegradability of the nanofibers on the surface of skin cells [7].

Essential oils contain bioactive compounds with antimicrobial, anti-inflammatory, antioxidant, antifungal, anticarcinogenic, and analgesic properties. Essential oils with antimicrobial properties are frequently used in nanofiber formulations [3]. The lower production cost of nanofiber systems compared to the other nanotechnology production methods makes nanofibers loaded with essential oils an attractive technology. Through nanofiber carrier systems, essential oils can be effectively targeted to human skin cells, allowing for high-dose drug application across large surface areas in a single use [8,9]. The small pore sizes of nanofibers permit the passage of liquids and gases while preventing the entry of bacteria, and providing protection against infections. Consequently, topical nanofiber formulations loaded with essential oils support wound healing by mimicking the skin’s natural function and structure during the healing process [10]. These characteristics demonstrate that the combination of essential oils with nanofiber carrier systems offers a significant advantage for topical applications [4].

In this review, an up-to-date summary of essential oil loaded nanofiber systems that exhibit antimicrobial, anti-inflammatory, antioxidant, antifungal, anticarcinogenic, and analgesic properties are presented along with the evaluations that are carried out on these formulations. In addition, the importance of nanofibers in topical skin applications and their production methods were summarized.

Essential Oils and Their Therapeutic Applications

Essential oils are aromatic volatile liquids obtained from specific parts of plants. These oils are secondary metabolites of plants and are typically named after the plant from which they are derived. They are complex liquids with characteristic scents, often colourless, but can sometimes be found in solid form. Essential oils have low densities and poor water solubility, but they are soluble in ethanol, diethyl ether, and fixed oils. They exhibit high optical activity and act as antioxidants, containing various chemical components such as phenols, ethers, esters, aldehydes, and terpenes. Due to their high vapour pressure, they are partially in a vapour state [11]. In history, essential oils were first used to enhance the flavour of foods [12]. Today, the use of essential oils has expanded in pharmaceutical fields and other various industries [13].

Essential oils are utilized in the pharmaceutical field as medicinal agents. They provide therapeutic effects for cardiovascular diseases such as cancer, atherosclerosis, and thrombosis, as well as exhibiting antibacterial, antiviral, antioxidant, and antidiabetic properties. Additionally, they are employed as natural penetration enhancers in aromatherapy and transdermal drug delivery [14]. Essential oils are favoured for their low cost and high safety profile; however, avoiding impurities during their extraction process is crucial [15]. Their side effects may include allergic reactions, skin irritation, headaches, and nausea [16]. The irritating components in essential oils can lead to inflammatory clinical conditions, and their potential for allergies is higher compared to chemical drugs [17]. They have low chemical stability, thus requiring proper storage [18]. The high concentration of active components increases the potential for reactions [17]. There is insufficient clinical research on their use during pregnancy and lactation [19,20]. The effects of essential oils are typically more pronounced in mild conditions, and they may be insufficient for moderate or severe illnesses, often serving as adjunctive therapy [21].

The Role of Nanofibers in Topical Drug Application

The term "nanofiber" is derived from the combination of "nano" and "fiber." While "fiber" refers to a slender and elongated structure, "nano" denotes a scale of one billionth. Consequently, nanofibers are fine fibers with diameters ranging from 50 to 300 nanometers [22]. Due to their large surface areas and highly porous structures, nanofibers are widely used in pharmaceutical technology. These structures are employed to extend the duration of drug action, achieve high efficacy at low doses, and enable targeted delivery of active ingredients [23].

The successful performance and versatility of ideal nanofiber compositions make them stand out in a variety of applications. In such formulations, high oxygen and air permeability are essential to ensure efficient exchange of oxygen and water vapor with the atmosphere [24]. The highly porous structure of nanofibers facilitates the incorporation and encapsulation of drugs and biomolecules. This porous structure imparts high electrocatalytic activity and rapid electron transfer properties to nanofibers, allowing them to be used as biosensors [25]. Additionally, nanofibers should offer a large surface area per unit mass or volume and possess a high surface-to-volume ratio, which provides high drug loading capacity. Nanofibers mimic the natural topographic features of the extracellular matrix of skin and create interconnected micro-porous networks. They feature extensive interconnections between pores and are made from biodegradable and biocompatible materials For use as wound dressings, nanofibers are expected to contain antibacterial materials that enhance exudate absorption and inhibit pathogenic microorganisms. Moreover, the polymers in their structures should be non-toxic and environmentally friendly [26,27].

Nanofibers are produced using various methods including bicomponent extrusion, phase separation, template synthesis, spinning, meltblowing, electrospinning, and centrifugal spinning. In industrial production, the most commonly used methods are meltblowing and electrospinning. Bicomponent extrusion involves extruding two polymers together in a specific arrangement to form fibrous structures. In the phase separation method, a polymer is mixed with a solvent before gelation, leading to phase separation due to physical incompatibility; after removing the solvent, the residual phase is frozen and dried to obtain nanofibers. Template synthesis uses a template or mold to create the desired structure, typically producing inorganic nanofibers with conductive materials. The spinning method is defined as a dry spinning process using viscoelastic materials that can withstand high degrees of deformation [22]. Centrifugal spinning produces nanofibers from polymer solutions using centrifugal force [28]. Electrospinning, on the other hand, produces fine nanofibers with diameters ranging from 50 to 800 nm and can utilize various polymer materials. In this method, long, thin nanofibers are obtained from a viscoelastic liquid using an electric current at low voltage; however, limitations exist due to its low production rate [29].

The meltblowing method is a simple, single-step process used for nanofiber production. In this method, nanofibers are produced directly from polymer resins using only the polymer melt. The polymer is fed into a mold setup with the aid of gravity at a controlled flow rate, then heated to melt and achieve the desired viscosity. The molten polymer is extruded through the mold using rotating screws and expelled from the system through a hot air-blowing nozzle. The polymer melt coming out of the nozzle encounters cold air, which solidifies it into a fibrous network, and the nanofibers accumulate on a collector. Nanofibers produced by the meltblowing technique have diameters ranging from 700 nm to 2.5 µm and generally possess larger diameters compared to those produced by electrospinning [30].

The blowspinning method is an innovative method used for producing fibers with diameters ranging from nanometers to micrometers. This method combines elements of meltblowing and electrospinning techniques. The production process begins with the delivery of a polymer solution from a liquid cone. The jet flow emerging from the solution initially progresses linearly but transforms into a turbulent flow under high electrical voltage. This flow is then stretched by a high-speed air stream to produce fibers of the desired size. The blowspinning method offers a straightforward and highly efficient production process with fewer processing steps and fewer variable parameters [31].

Nanofibers offer significant advantages in drug delivery systems due to their large surface area, high porosity, and flexibility. These advantages enable the direct application of drugs to the skin surface with high selectivity and efficacy in topical drug delivery [32]. Nanofibers can facilitate the efficient release of both hydrophilic and hydrophobic active compounds to the skin. The use of nanofiber carrier systems allows for the adjustment of various parameters, such as fiber diameter, morphology, and porosity, as well as factors like drug release profile and kinetics. This enables effective penetration of drugs through the skin barrier and enhances percutaneous absorption with biocompatible properties. Nanofiber systems can provide direct therapeutic effects to targeted areas, thereby reducing systemic side effects [33].

The soft network structure of nanofibers provides comfort in wound healing and is susceptible to morphological changes through various production methods, making them suitable for direct application to wounds. Nanofibers, which play a significant role in antimicrobial dressings and wound healing applications, also hold great potential in tissue engineering due to their similarity to the extracellular matrix structure of the skin [33]. Nanofibers enable drugs to exhibit higher efficacy at lower doses, which helps avoid frequent dosing and improves patient compliance across large populations [34].

Nanofibers for Topical Delivery of Essential Oils

Essential oils are considered potential active components due to their various effects, including antimicrobial, antiviral, antioxidant, anticarcinogenic, and anti-inflammatory properties. However, for these oils to be effective, they often need to be present in high concentrations. Nanofibers can enhance the availability of active components with low bioavailability and poor skin permeability. Additionally, nanofibers possess a high drug loading capacity, and lipophilic essential oils can be successfully integrated into these fibers using polymers with appropriate solubility. Nevertheless, obtaining stable formulations in emulsion-type carrier systems for naturally sourced active compounds is challenging, and potential safety risks arise from incompatibilities with excipients, the toxicity of surfactants in emulsions, and the skin-irritating properties of essential oils [35]. Biodegradable polymeric nanofibers offer advantages as effective carriers in active ingredient delivery due to their biocompatibility and low toxicity [36].

The high volatility and poor stability of essential oils are factors that limit their clinical applications. To enhance the stability of these oils, it is essential to optimize their volatility and release characteristics [37]. Effective encapsulation provides stabilization for the therapeutic use of essential oils and can be successfully achieved in nanofiber formulations produced by electrospinning [38].

Encapsulation enhances stability even under high-temperature conditions, enabling the attainment of potent pharmacological activities. The hydrophobic nature of essential oils particularly limits their use in transdermal applications; however, encapsulation in nanofibers increases the water solubility of these compounds [39]. Natural biocompatible bioactive substances are preferred over synthetic chemicals in wound dressings [38], and the similarity of nanofibers to the extracellular matrix structure of the skin enhances the advantages of essential oils [40].

Formulations of essential oils in drug delivery systems of micron, submicron, or nanoscale are achieved using various production methods. These methods include spray drying, coacervation, ionic gelation, and electrospinning; among these, electrospinning is one of the most preferred methods for encapsulating essential oils. Electrospinning offers the ability to produce very fine fibers with large surface areas and facilitates the functionalization of the structure, and the resulting nanofibers often exhibit good mechanical properties. This method provides flexibility and versatility in terms of scale-up [41].

Electrospinning offers the capability to create various fiber network structures. These structures include aligned or patterned fiber networks, randomly distributed three-dimensional networks, and submicron-sized coiled and wrinkled fibers. This variety demonstrates the advantages of electrospinning. Additionally, the diversity of polymer materials available for selection provides benefits in terms of adjustable fiber morphology and controllable fiber diameters [42].

Three distinct approaches can be employed to prepare nanofibers loaded with essential oils using electrospinning. The first approach involves mixing essential oils with a polymer solution and subjecting this mixture to the electrospinning process. The second approach utilizes core-shell structures, where essential oils are incorporated as the shell and the polymer solution forms the core. The third approach involves loading essential oils onto a carrier, which is then used to produce nanofibers through electrospinning [43].

Conventional electrospinning is performed using a high-voltage power supply, a metal needle, and a collector. In this method, a polymer and essential oil solution is prepared, and nanofibers are formed through electrospinning. Coaxial electrospinning produces core-shell nanofibers and offers the advantage of loading a high amount of essential oil, although it is more expensive and complex in terms of process. Emulsion electrospinning involves the use of emulsified solutions to produce nanofibers and presents challenges related to solvent and surfactant selection, making it more complex compared to conventional electrospinning [41,43].

Conventional and coaxial electrospinning methods typically present a lower risk of toxicity compared to emulsion electrospinning. The emulsion method is more complex due to its requirement for specialized mechanisms and parameters. In comparing coaxial electrospinning with emulsion electrospinning, there is a risk that the two-phase structure of the emulsion could potentially damage the essential oil structure [41].

Essential Oil Loaded Topical Nanofiber Formulations

Recent studies on the development of essential oil loaded nanofiber formulations are summarized in Table 1.

Use of Essential Oil Loaded Topical Nanofiber Formulations as Medical Wound Dressings

The effective treatment of burns and wounds remains a common problem worldwide. In this context, several studies have been conducted to develop medical wound dressing materials from low-cost and easily accessible natural resources, one of which is nanofibers. In the study by Chomachayi et al. [46], silk fibroin (SF) and gelatin (GT) polymers and thyme essential oil (TEO) were used. Synthetic antibiotics such as doxycycline monohydrate (DCMH), which is effective against Gram-positive and Gram-negative bacteria, were also used along with thyme essential oil to compare the properties of the formulations. Silk fibroin is a natural and biodegradable polymer with good oxygen and water vapor permeability, while gelatin offers biological properties similar to collagen structure and low-cost advantages. The combination of these two polymers resulted in a synergistic improvement of their properties. Thyme essential oil was added to the formulation due to its antimicrobial properties. The nanofibers were produced using the electrospinning method and the obtained nanofibers were characterized by scanning electron microscopy (SEM) and Fourier transform infrared spectroscopy (FTIR). Furthermore, other analyses such as water uptake, water drop contact angle, and water vapor transmission rate were carried out. After evaluating the antibacterial efficacy and cellular compatibility of the formulations, thyme essential oil and DCMH loaded nanofibers were found to provide longer release time and effective inhibition against both Gram-positive and Gram-negative bacteria. Furthermore, studies on mice fibroblast L929 cells revealed that these nanofibers showed high cell compatibility. However, further research is needed to find the optimal mixing ratios and stability methods, and it was noted that high stabilities are difficult to achieve in hydrophilic media. As a result, it was concluded that topical nanofiber formulations containing thyme essential oil can be used to prevent wound infections and as effective medical wound dressings.

Table 1. Essential oil loaded topical nanofiber formulations

Polymers Used in Nanofibers	Essential Oil/Drug Combinations	Diseases	Results	References
Polylactic acid (PLA)	*Zingiber cassumunar* rhizome essential oil (plai essential oil)	Skin inflammations	Reduced skin inflammations	[44]
Chitosan and polyethylene oxide (PEO)	Clove essential oil	Skin disorders: antibacterial/antioxidant/ antifungal/anti-inflammatory effects	Enhanced antibacterial/antioxidant/antifungal/anti-inflammatory effects	[45]
Silk fibroin/gelatin	Thyme essential oil and doxycycline monohydrate	Wounds	Production of biocompatible and effective wound dressings	[46]
Polyacrylonitrile (PAN)	Clove essential oil	Cutaneous and mucocutaneous candidiasis	Enhanced antifungal activity	[47]
Gelatin/polyvinyl alcohol core with aloe vera/arabinose/polyvinyl pyrrolidone shell	Ajwain essential oil	Wounds	Production of biocompatible and effective wound dressings	[48]
Polyvinyl alcohol (PVA) / chitosan	Cabreuva essential oil	Wound and burn	Production of biocompatible and effective wound dressings	[49]
Polycaprolactone-alginate	*Mentha longifolia* essential oil	Wound infections of *Pseudomonas aeruginosa* and *Staphylococcus aureus* strains	Production of biocompatible and effective wound dressings	[50]
Polyamide-6/ polyvinylpyrrolidone (PVP)	Green tea essential oil	Wounds	Production of biocompatible and effective wound dressings	[51]
Polyvinyl alcohol (PVA)	*Zataria multiflora* essential oil	Wounds	Production of biocompatible and effective wound dressings	[52]
Collagen hydrolysate-chitosan	*Melissa officinalis l.* (lemon balm) and *Anethum graveolens l.* (dill) essential oils	Wounds	Production of biocompatible and effective wound dressings	[53]
Poly(caprolactone)	Cinnamon essential oil	Wounds	Production of biocompatible and effective wound dressings	[54]
Cellulose acetate	Lemon balm essential oil	Wounds/ Skin infections of *Escherichia coli* and *Staphylococcus aureus*	Production of biocompatible and effective wound dressings	[55]
Chitosan / poly(caprolactone)	*Citrus sinensis* essential oil	Cutaneous leishmaniasis	Increased leishmanicidal effect Nanofiber networks act as protectors against environmental pathogens and prevent secondary infections	[56]
Dandelion polysaccharide	*Litsea cubeba* essential oil	Skin infections	Enhanced antimicrobial effect	[57]
Hydrolyzed collagen	Ginger essential oil	Skin infections	Enhanced antibacterial/ antioxidant/ antifungal effect	[58]
Polylactic acid	Clove essential oil	Infections	Enhanced antimicrobial effect	[59]
Polyurethane	*Lavandula angustifolia* essential oil + silver nanoparticles	Wounds	Production of biocompatible and effective wound dressings	[60]

Use of Essential Oil Containing Topical Nanofiber Formulations in Skin Infections

Essential oils are widely used in the treatment of infectious diseases of the skin. In the study by Mariana Daniela Berechet *et al*. [58], hydrolyzed collagen obtained from bovine skin by-products and ginger essential oil were used. Considering the high biocompatibility and biodegradability properties of natural polymers, it was thought that the co-formulation of collagen and ginger essential oil would give effective antifungal and antimicrobial results. Hydrolyzed collagen solution was used for electrospinning and nanofibers with diameters ranging from 464.4 nm to 665.5 nm were obtained. Nanofibers were loaded with ginger essential oil, structural analyses were carried out and microbiological analysis revealed that nanofibers loaded with ginger essential oil showed mild antimicrobial and antioxidant effects against *Escherichia coli* and *Staphylococcus aureus* bacteria. Furthermore, nanofibers loaded with ginger essential oil showed high antifungal activity against *Candida albicans*. The study emphasized that hydrolyzed collagen nanofibers loaded with ginger essential oil could be a promising formulation in the treatment of skin infections.

In another study, Hameed et al. [45] aimed to produce a non-cytotoxic nanofiber with antibacterial, anti-inflammatory, and analgesic properties. Chitosan and polyethylene oxide (PEO) polymers were combined with clove essential oil and nanofibers were produced using the electrospinning method. Since chitosan alone is not suitable for electrospinning, PEO was added and 1% clove essential oil was added by mixing the solutions. As a result of the electrospinning, nanofibers loaded with clove essential oil were obtained. In-vitro cytotoxicity studies revealed that the formulation showed a non-cytotoxic behavior in human fibroblast cell lines. The antibacterial activity of nanofibers loaded with clove essential oil was tested on Muller Hinton agar plates and found to be effective against *Staphylococcus aureus* and *Escherichia coli* bacteria. The study showed that chitosan/PEO nanofibers loaded with clove essential oil can be effectively used as potential antibacterial formulations.

Use of Essential Oil Loaded Topical Nanofiber Formulations for the Treatment of Skin Inflammations

Plai essential oil attracts attention with its anti-inflammatory properties, especially thanks to its phenylbutanoid components. In the study conducted by Wongkanya *et al*. [44], the volatile components in Plai essential oil were analyzed by GC/MS method. As a result of the analysis, it was determined that the compound E)-1-(3,4-dimethoxyphenyl) butadiene (DMPBD) from the phenylbutane group is the main bioactive component of Plai essential oil and is responsible for anti-inflammatory effects. In the formulation stage, different concentrations of Plai essential oil and polylactic acid polymer solutions were mixed to produce nanofibers. The nanofibers obtained by the electrospinning method were deposited on a metallic rotating cylindrical collector. Morphological analysis of the nanofibers loaded with different ratios of Plai essential oil (15%, 20% and 30%) was performed using SEM and smooth morphologies were observed. Structural and thermal properties of the nanofibers were analyzed by FTIR and X-ray diffraction (XRD) and it was determined that the loading capacity was quite high. *In vitro* release studies were carried out on reconstructed human epidermis and it was found that the essential oil successfully penetrated the epidermis and did not cause skin irritation. The loading of the essential oil in nanofibers was found to reduce the degradation of the oil by atmospheric oxygen and sunlight, resulting in a longer and more stable release. The high surface area and porosity of the nanofibers facilitated the efficient release of the bioactive component into the body. In conclusion, Plai essential oil loaded nanofibers were found to offer an effective solution for the treatment of inflammation with controlled release properties and DMPBD showed appropriate pharmaceutical efficacy.

Toxicity of Essential Oil Loaded Topical Nanofiber Formulations

Essential oils are composed of secondary metabolites of aromatic plants, often containing oxygenated structures and known for their therapeutic properties. Although these oils provide beneficial effects such as antibacterial, antifungal and antioxidant activities, the efficacy and safety of biopharmaceuticals are directly related to the quality and toxicity profiles of the ingredients used. Despite topical applications of essential oils are generally considered safe, in some cases they can cause skin irritation and reactions. Pharmaceutical dosage forms, including nanofiber formulations, contain excipients, which can affect the safety of the formulations. Therefore, it is important to qualitatively and quantitatively study all ingredients and analyze their toxicity profiles [61].

The toxicity risks of essential oils are generally low and many are considered low-risk ingredients. However, the toxicity profiles of these oils are analyzed in three structural classes: Class I includes oils composed of aliphatic compounds and have low toxicity; Class II includes more active components with moderate toxicity; and Class III includes reactive components with high toxicity potential. For example, the essential oil of the lemon myrtle plant shows antimicrobial activity against Gram-positive and Gram-negative bacteria but can cause toxic effects at high concentrations [62]. When lemon myrtle oil is reduced to 1% concentration, toxic effects on human skin cells are reduced and it becomes safer. The essential oils of *Ligusticum Chuanxiong* are also safe for short-term exposure but may cause skin irritation in long-term use [61].

Phenolic compounds such as carvacrol, thymol, eugenol and vanillin show a variety of pharmaceutical effects; however, some of them may also produce potentially toxic effects. Carvacrol, thymol and eugenol may produce cytotoxic effects and genotoxic effects, particularly due to oxidative stress. *In vivo* studies show that these ingredients can cause adverse effects such as skin irritation, inflammation and slowed wound healing. Vanillin is generally considered to be less toxic, but at high concentrations, it can reduce cell viability on the skin surface [63].

The use of essential oils in nanofiber form can help reduce the toxic effects that can be seen in their pure form. For example, high concentrations of lavender essential oil can cause toxic effects on human skin cells, causing damage to the cell membrane. However, since lavender oil is present in nanofibers at low weight and nanofibers made of polyurethane polymer release the active ingredient very slowly, this may reduce the toxic effects and allow for availability up to high concentrations [60].

In another study, the toxicity of the essential oil of the *Litsea Cubeba* plant, which has antimicrobial properties, was investigated on mice and rats. The dermal LD50 dose of 5,000 mg/kg was determined and it was observed that the essential oil may cause toxic effects such as skin irritation, erythema, edema, roughening and crusting. Furthermore, histological examinations at high concentrations revealed hyperplasia of the squamous epithelium and mild hyperplasia of the skin structure. In contrast, no toxic effects were observed when the essential oil of *Litsea Cubeba* was used in nanofiber form. Nanofiber formulation provides the advantages of controlled release, high pharmacological effect at low doses, large surface area and high porosity, minimizing the toxicity risks of essential oils. Thus, nanofibers can be effectively used as non-toxic therapeutic products [57, 60, 64].

Discussion and Conclusion

Essential oils are known for their antibacterial, antifungal, antioxidant and anti-inflammatory activities and are used in the treatment of skin diseases. However, these oils often have low absorption rates, may contain irritant components and can be affected by heat and light, which reduces their stability. Therefore, carrier systems are needed for the effective delivery of essential oils to the skin surface. Topical nanofiber formulations of essential oils offer the potential to reduce the toxic effects of these oils while increasing their efficacy.

Nanofibers are a new generation of drug delivery systems with a high surface-to-volume ratio and high porosity. These properties enable the controlled release of active ingredients and offer high bioavailability at low doses. Nanofibers provide physical protection of essential oils, increasing stability against external factors such as heat and light. Furthermore, nanofibers resemble the natural skin structure, supporting the wound healing process and enabling the effective application of topical drugs.

The advantages of nanofibers include the efficient delivery of essential oils to large surfaces, even at low doses, and their hydrophilic properties facilitate passage through the *stratum corneum* barrier layer. However, there are some limitations such as the high quality of essential oils, allergenic properties, stability issues and limited clinical studies during pregnancy and lactation.

In conclusion, modern topical formulations developed with nanofiber systems can increase the efficacy of essential oils while reducing toxicity risks. This review reveals that essential oil loaded nanofibers provide high efficacy in the treatment of mild to moderate skin diseases and can be an alternative to synthetic drugs.

Conflicts of interest:

There are no conflicts of interest in this work.

Acknowledge

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Ethical Approval Statement

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