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Review Article

Nanofibers: Promising Novel Drug Delivery Technology for Cosmeceuticals

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ABSTRACT

Cosmeceuticals, a merger of cosmetics and pharmaceuticals, aim to deliver functional benefits beyond traditional cosmetics while still appealing to consumers. Because of advances in cosmetics, the quality of cosmetic goods used today has improved and their diversity has expanded, just as it has in every other business. The cosmetic industry has gained a new and innovative approach by integrating nanomaterials such as nanofibers, nanoparticles, Nano liposomes and Nano pigments into the formulation of cosmetic products. Nanofibers have emerged as a promising invention in the realm of cosmeceuticals due to their unique properties of large surface area, flexibility, porous structure and versatility. Electrospinning stands out as a highly favoured method for producing nanofibers in the cosmetics industry. Nanofibers find applications in various cosmetic products and treatments. For instance, they are used in facial masks, deodorants and in addressing issues like alopecia and wound dressings. Nanofiber facial masks offer advantages in cleansing, surpassing the effectiveness of regular commercial masks in removing debris and oil from the skin. They have also been explored as a method for creating anti-acne patches, potentially providing a more efficient solution for managing acne concerns.

Keywords: Acne, Cosmeceuticals, Electrospinning, Facial mask, Nanofiber, Wound dressing.

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INTRODUCTION

Two fundamental aspects of human nature are the desire to be adored and the desire to appear beautiful. People's psychological satisfaction is increased when they appear to be clear and lovely and experience appreciation. The popularity of using cosmetics rises due to the need for personal care in addition to looking beautiful and well-groomed. Cosmetics have been used since prehistoric times.[1] Both sexes value cosmetics, which have been used by humans for a very long time and are largely utilized for regeneration purposes. They can be described as preparations that are often applied externally and that are made from a single substance or a combination of compounds that can be found in either natural or artificial sources.[2] According to the USFDA, cosmetics are defined as substances that are meant to be used on the human body. Importantly, they are designed to do all of this without significantly affecting the body's structure or how it functions.[3,4] As per the Drugs and Cosmetics Act of 1940 and its associated Rules from 1945, a cosmetic is defined as any product that is meant to be used on the human body or any of its parts. These products can be applied in various ways, such as rubbing, pouring, sprinkling, or spraying. Their purpose is typically to cleanse, enhance beauty, promote attractiveness, or change one's appearance.[5]

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Numerous personal care items fall under the category of cosmetics. Cosmetics can be divided into six categories based on the body areas to which they are applied:

- Skin-care cosmetics, including items like moisturizers and cleansers that are used for skincare routines, often to keep the skin hydrated and clean.
- Hair-care products, which encompass a range of items like hair dyes, styling products and shampoos designed for hair maintenance and styling.
- Cosmetics for the face, such as lipstick, mascara, powder and face foundation.
- Products for caring for nails, such as nail polish removers.
- Goods that contain aroma, such as cologne, deodorants, aftershave and perfumes.
- Preparations that block Ultraviolet (UV) light, such sunscreens.[6]

The quality of cosmetic goods used today has improved and their variety has expanded, just like in every other industry due to advancements in cosmetics. The cosmetic industry has embraced a novel approach by introducing nanomaterials like nanofibers, nanoparticles, nano-liposomes and nano-pigments into their product formulations. This innovation represents a fresh perspective on cosmetics, as these nanomaterials offer unique properties and advantages for improving the quality and effectiveness of cosmetic products.[7,8]

The term "nanos," derived from ancient Greek and meaning "dwarf," is used to describe measurements on the order of 10^{-9}, which signifies incredibly small scales. Materials that possess controlled dimensions of 100 nm or less fall under the category of nanomaterials. These materials are intriguing because their nanoscale sizes influence various properties like structure, mechanical characteristics, thermal behaviour, thermodynamics, kinetics and electrical attributes; often enhancing these properties.[9] Nanotechnology has a profound impact on numerous fields, including cosmetics, communication, medicine, transportation, agriculture, energy, manufacturing and consumer goods. The use of nanoparticles in cosmetics is one application for which these unique properties can be employed. Among the cosmetics that use nanotechnology are moisturizers, hair care items, makeup and sunscreen. Nanotechnology has been making its mark in the cosmetics and health product industry for over four decades now, with one of its earliest applications being the development of liposome moisturizing creams. These areas include skin wound healing, delivering drugs to the skin for anti-wrinkle and anti-aging purposes, treating conditions like alopecia (hair loss) and facilitating the topical delivery of therapeutic substances for various skin disorders.[10-12]

Nanofiber

Nanofiber refers to extremely small fibers, usually measuring from a few nanometers to around 100 nm in diameter.[13,14] These fibers can be made from different materials like polymers, carbon, or natural substances. The processes commonly used to produce nanofibers include electrospinning, template synthesis and self-assembly.[15,16]

These characteristics include their small diameter or unit length, a high surface area-to-volume ratio, remarkable strength, minimal weight, exceptional porosity and tiny pore size.[17,18]

Characteristics of Nanofiber

Nanofiber scaffold compositions exhibit good biocompatibility with both contained materials and biological tissues.

Nanofibers possess a satisfactory biodegradability history, with non-harmful by-products that are either easily expelled from the implantation site or assimilated into surrounding tissues.

Nanofiber compositions have open and linked pore structures that maximize interaction with bioactive substances.

Nanofiber compositions excel in delivering encapsulated compounds to target sites while minimizing associated adverse effects.

Nanofibers, with their superior trapping and loading capacity, enable prolonged and controlled medication release after insertion into the body.

Nanofibers don't pose a toxic risk to the body and are well-tolerated because they are designed to work harmoniously with biological systems.

Nanofiber scaffold formulations show strong binding, ensuring secure cell retention in pores or sustained, controlled drug release after implantation.[19,20]

Materials used in nanofiber

A variety of polymers and solvents play essential roles in nanofiber formulation.[21]

Polymers

Polyvinyl Alcohol (PVA): PVA is a popular choice due to its biocompatibility and ease of processing, making it widely used for nanofiber fabrication.

Polyethylene Oxide (PEO): Another biocompatible polymer, PEO, is frequently employed in electrospinning nanofibers.

Polyacrylonitrile (PAN): PAN finds its application in creating carbon nanofibers, particularly for specialized purposes.

Polyurethane (PU): PU nanofibers are versatile and used in various applications, including tissue engineering.

Polycaprolactone (PCL): Known for its slow biodegradation, PCL is utilized in drug delivery systems and tissue engineering.

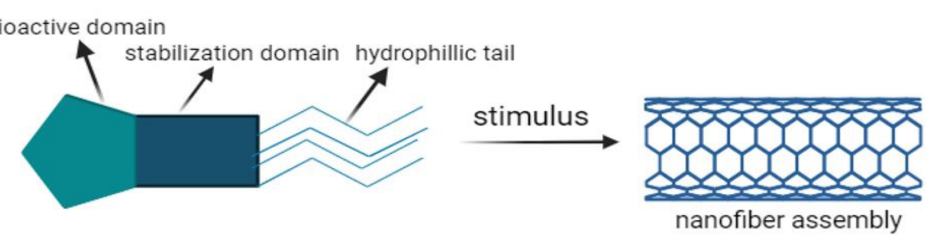

Figure 1: Self Assembly Method.

Poly (lactic acid) (PLA): PLA is a biodegradable polymer often used in medical applications and packaging.

Solvents

Dimethylformamide (DMF): DMF is a common solvent employed to dissolve a wide range of polymers in nanofiber fabrication. It's valued for its high boiling point and excellent solubility.

Dimethylacetamide (DMAc): Like DMF, DMAc serves as a solvent to dissolve various polymers for electrospinning.

Acetone: Acetone is used for specific polymers like PVA in the electrospinning process.

Ethanol: Ethanol is chosen in more environmentally friendly electrospinning processes, especially when working with biodegradable polymers.

Methods for preparation of nanofiber

Various techniques are utilized to create these nanofibers, each catering to different requirements. These techniques encompass self-assembly, drawing, melt blowing, template synthesis, phase separation, melt spinning, centrifugal spinning and electrospinning.[22] Self-assembly, phase separation and electrospinning are three approaches that have successfully been used to create nanofibrous tissue structures on a regular basis.[23,24]

Self-assembly

Intermolecular forces play a central role in bringing the smaller building blocks together. The shape of these smaller units determines the overall structure of the resulting nanofiber as shown in Figure 1. This method offers a fresh approach to designing and producing innovative materials with multiple layers.[25] Self-assembly involves arranging tiny molecules in a way that they align concentrically over time, forming the longitudinal axes of the nanofibers.[26] It's a "bottom-up" approach where the synthesis of the molecules involves a chemical reaction called convergent synthesis. The specific properties and structure of the nanofibers are governed by the intermolecular forces that bind the molecules together. This technique allows for the creation of various polymeric nanofiber topologies, including di-block copolymers, triblock copolymers, triblock polymers (comprising peptide amphiphiles and dendrimers) and bolaform structures (involving glucosamide and its deacetylated derivatives). Researchers have successfully generated diblock copolymers and triblock polymers using the self-assembly method, showcasing the versatility and potential of this approach in creating various nanofiber structures with unique properties.[27]

Table 1: Evaluation parameter of Electrospinning Process.

Parameter	Factor
Solution parameter	Viscosity, conductivity, molecular weight, polymer structure.
Processing parameter	Applied electric field, plate movement and feeding or flow rate.
Ambient parameter	Temperature of surroundings and humidity.

Drawing

In this production process, individual nanofibers are mainly created using a micromanipulator probe. Here's how it works: a small amount of a viscoelastic polymer solution is taken, and it's carefully deposited onto a flat surface. The micromanipulator probe is then brought into contact with this flat surface but at a specific distance, allowing the fibers to form as shown in Figure 2. Two critical factors in this process are the method by which the solvent evaporates and the rate at which the drawing or stretching is done.[28,29] The materials which used in drawing for formulating nanofiber like polycaprolactone, polyethylene oxide, hyaluronic acid, fish gelatin and poly-methyl-methacrylate. These nanofibers are commonly used in applications related to skin tissue scaffolds and the healing of skin wounds.[30] This technique offers a way to create nanofibers that have specific properties suitable for these medical and regenerative purposes.

Phase separation

Phase separation is a fundamental concept that involves creating two distinct phases within a solution: one rich in polymer and the other with less polymer. When the phase with fewer polymers is removed, it leaves behind a 3D fibrous structure, quite different

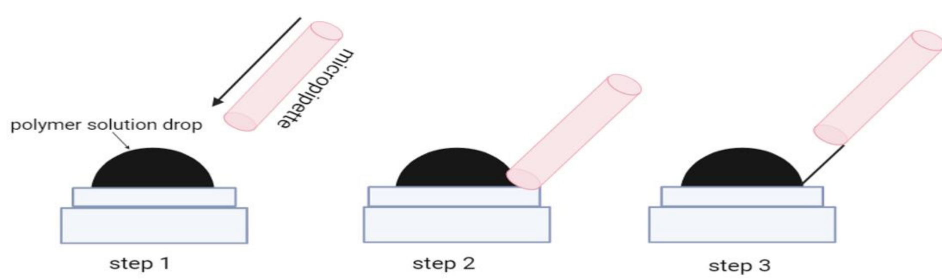

Figure 2: Drawing Method.

from traditional materials made of individual strands as shown in Figure 3.[28,31] Although there are limitations in the choice of polymers, a notable advantage is the ability to adjust the mechanical properties of the resulting structures by changing the polymer concentration. Furthermore, this method doesn't require complex equipment, making it a practical and versatile approach for creating this unique 3D fibrous structures.[32]

Template synthesis

The technique is aptly named "template synthesis," and it's used to create nanofibers utilizing biodegradable polymers. This method encompasses various approaches, including chemical vapour deposition, chemical processes, sol-gel methods and electrochemical techniques.[33] Interestingly, The size of the fiber determines the pore size of the template used as shown in Figure 4. Template synthesis is particularly useful for producing nanofibers extensively employed in applications related to tissue engineering. However, a notable drawback is that this method tends to be time-consuming.[34]

Electrospinning process

Electrospinning is a novel technique for converting polymeric biomaterials into nanofibers. Using a simple experimental setup, this technique allows for control over the composition, thickness and porosity of the nanofibers.[35] The equipment used for electrospinning, which is the primary method for manufacturing nanofibers, typically consists of three key components: I) a high voltage power supply. II) A reservoir containing the polymer solution, often connected to a syringe with a fine needle for controlled dispensing. In some cases, a flow control pump may be used. III) A metal collector screen as shown in Figure 5. The process involves six steps: 1) Initially, a charged polymer jet is created by loading the polymer solution into the reservoir and connecting it to the power supply. 2) Jet generation caused by increasing power supply causes jet distortion. 3) From the Taylor cone, the straight jet section is lengthened. 4) Deformation occurs in the straight jet portion, resulting in instability. 5) Nanofibers are solidified by evaporation or cooling of the solvent. 6) Fibers are finally collected on the collector plate.[35-40]

The method of creating nanofibers through electrospinning has an extensive range of practical applications, spanning across various fields. These applications include biomedical uses, such as wound dressing and tissue engineering, cosmetics and much more.[41] The evaluation parameter for electrospinning process as shown in Table 1.

Application

Deodorant

Nanofibers are also being used to incorporate deodorizing agents. Lee H *et. al.*, has addressed the issue of unpleasant odors in modern life by fabricating nanofibers combined with phthalocyanine. Specifically, Cu-coordinated phthalocyanine was used to target methyl mercaptan gas, a common malodorant. The researchers used two different polymers, Poly (Vinyl Alcohol) (PVA) and silk, incorporating 4 wt% phthalocyanine into the solutions of both polymers to create nanofibers. The results showed that these nanofibers effectively reduced the presence of methyl mercaptan gas. Notably, the phthalocyanine/silk nanofibers demonstrated superior deodorant performance compared to the phthalocyanine/PVA nanofibers.[42]

Facial mask and skin cleansing

Various compounds, including L-ascorbic acid (Vitamin C), retinoic acid (Vitamin A), collagen and gold nanoparticles, are commonly found in cosmetic and dermatological products due to

Table 2: Difference between conventional and nanofiber mask.

Conventional Face Mask	Nanofiber Mask
Larger molecules have trouble penetrating the skin.	Nanofibers enhance the ability of active ingredients to reach the deeper layers of the skin.
As transporters for active chemicals, aggressive molecules such as isopropyl alcohol are utilized.	Compounds that are up to three times less aggressive.
It required significant amount of time for active ingredients in products to penetrate by the skin effectively.	Active ingredients permeate the skin in a fraction of the time that traditional face masks do.
Healing is less effective.	Healing that lasts.

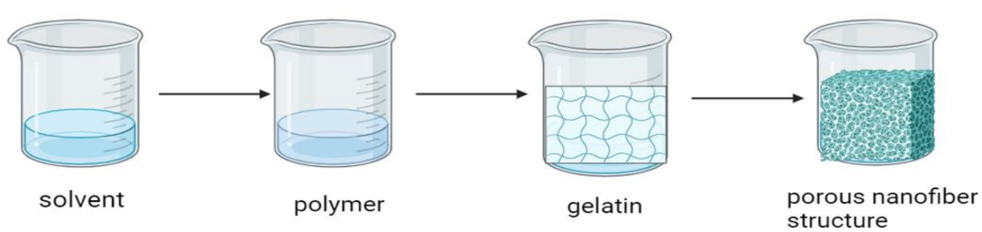

Figure 3: Phase Separation Method.

Table 3: Recent research works on nanofiber based facial mask.

Sl. No.	Researcher Name	Description
1	Sonavane G, *et al.*	Nanoparticles can penetrate rat skin and intestines, which opens up possibilities for their use in cosmetics.[47]
2	Fathi-Azarbayjani, *et al.*	They achieved this by directly spinning fibers after incorporating key ingredients like ascorbic acid, retinoic acid, collagen and gold nanoparticles into the electrospinning solution. ultimately resulting in improved skin appearance.[48]
3	Smith, *et al.*	Hold a patent for a skin care mask made of nanofibers, primarily serving as a cleanser to remove excess oil from the skin.[49]
4	Kim, *et al.*	Developed a water-soluble nanofiber layer and this nanofiber layer dissolves with water, enhancing skin adherence and ingredient removal.[50]
5	Hualei Xu, *et al.*	Created a PVA/HA/cHSP nanofiber film through electrospinning known for its moisturizing and antioxidant properties.[51]
6	K.M.N.de.S, *et al.*	Create a thin hydrogel facial mask that delivers Gold nanoparticles (AuNPs), Ascorbic Acid (AA) and Collagen (COL) through electrospinning technique and this facial mask provides anti-aging, whitening and anti-wrinkling properties.[52]

their unique properties.[43] It's often included in skincare products because of its photoprotective properties, making it useful in anti-wrinkle face masks. Vitamin C helps neutralize free radicals and oxidative agents, contributing to healthier skin.[44] Retinoic acids, a form of Vitamin A, is a key component in anti-aging cosmetic formulations. It's renowned for its effectiveness in addressing damaged skin and acne issues, making it a popular choice for people seeking to improve their skin's appearance and health.[45] Difference of Conventional and nanofiber mask is mentioned below in Table 2. Additionally, recent developments on nanofiber-based facials mask have been described in Table 3. Xu H *et al.,* developed a novel nanofiber material combining Hyaluronic Acid (HA), crude Huangshui Polysaccharide (cHSP) and Polyvinyl Alcohol (PVA) to create dry facial masks (PVA/HA/cHSP) using electrospinning. Characterization by scanning electron microscopy (SEM) revealed that the fibers were uniformly distributed with diameters under 260 nm. The mask demonstrated a high-water absorption rate of over 300% and *in vitro* tests showed effective antioxidant properties with DPPH and hydroxyl free radical scavenging half-inhibitory concentrations at 0.2781 and 1.029 mg/mL, respectively.[46]

Wound dressing and drug delivery

Delivering medications to the skin is a critical aspect of cosmetic applications, particularly in the field of derma-cosmetics.[53] Researchers are focused on not only precise delivery but also optimizing pharmacological effects through various criteria. One key goal for researchers is to administer medicine at lower doses while ensuring it acts specifically at the desired site. This approach minimizes the potential for side effects and enhances the overall effectiveness of treatment. When it comes to treating exposed wounds, there's a heightened risk of issues like toxin exposure, water loss and the actions of proteases due to bacterial infection. These factors can trigger an excessive inflammatory response, which can hinder the natural process of skin regeneration. Recent advancements in nanofiber technology

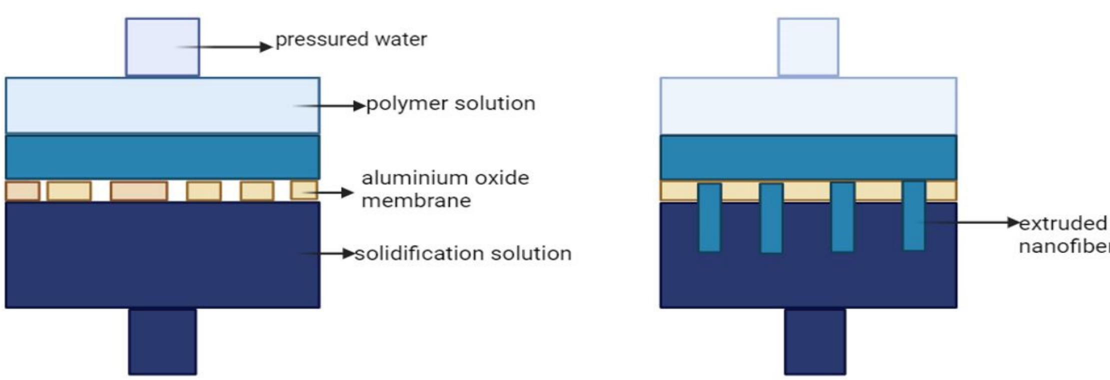

Figure 4: Template synthesis Method.

have enabled the incorporation of antibacterial agents into wound dressings, which can help combat these issues and promote a more efficient healing process. The polymer should possess both hydrophilic (water-attracting) and hydrophobic (water-repelling) properties, allowing it to effectively interact with the wound site and optimize the healing process.[54,55] Nanofibers are being increasingly used in wound dressing applications.[56] Various materials, both natural and synthetic polymers, are employed in production of nanofibers used for wound healing as described in Table 4. Silver nanoparticles have gained attention as effective antimicrobial agents in wound healing because of their ability to kill a wide range of germs, viruses and fungi.[63,64] The patent application US20240122869A1 presents a wound healing means and its method of manufacture, emphasizing the use of nanofibers in medical treatments. The invention highlights the potential of nanofibers to enhance the healing process through improved wound care products that promote faster and more efficient recovery.[65]

Topical delivery of nanofiber in treatment of acne

Acne, a common skin condition often affecting young people, is primarily caused by inflammation of the sebaceous glands due to bacterial infection. Conventionally, it's treated with antibacterial and anti-inflammatory medications. However, in recent research, nanofibers have emerged as an alternative therapeutic approach with some distinct advantages. In one study from 2022, chitosan and melittin nanofibers were developed for the treatment of acne vulgaris. And these nanofibers effectively reduced redness, inflammation and inhibited bacterial growth.[66] Another approach involved the creation of tretinoin-loaded polycaprolactone nanofibers for topical acne treatment.[67] In a different study, nanofibers made from a combination of PVA, quercetin and essential oils were developed for acne treatment. When assessed in clinical trials, these nanofibers led to a substantial reduction in acne lesions, comedones and inflammation.[68]

Treatment of alopecia

Alopecia, a common problem affecting many individuals, especially as they age, has been traditionally treated with methods like hair transplants, drugs like minoxidil and finasteride. Minoxidil sulphate, when applied topically, is a popular choice for addressing androgenic alopecia, a type of hair loss but Studies have shown that around 40% of participants experienced hair regrowth after 3 to 6 months of using minoxidil, with few side effects.[69] In a recent study they investigated the use of Polyvinylpyrrolidone (PVA) to create minoxidil sulphate-loaded nanofibers, which form a solid nano-formulation. These nanofibers serve the dual purpose of promoting hair regrowth and providing shading coverage for aesthetic purposes upon application.[70]

Patents related to nanofiber formulations

The patent US8048446B2 details a method for creating non-woven fibrous scaffolds using a blend of synthetic biodegradable polymers, such as Poly (Lactic-co-Glycolic Acid) (PLGA) and natural proteins like gelatin and elastin. These scaffolds, produced through electrospinning, exhibit a unique combination of mechanical and physical properties that promote cell penetration

Table 4: Recent research works on nanofiber technology in wound healing.

Sl. No.	Researcher Name	Description
1	Lee, *et al.*	They discovered in applications of natural polysaccharides like cellulose, chitin, alginate, chitosan and dextrose are material to be promising for biomedical applications, with the ability to accelerate wound healing.[57]
2	N Charernsriwilaiwat, *et al.*	Created chitosan-based nanofiber mats infused with extracts from Garcinia mangostana, rendering the nanofiber mats both antibacterial and antioxidant.[58]
3	Vargas, *et al.*	The use of electrospun hyper branched polyglycerol nanofibers containing Calendula officinalis extract as wound dressing materials.[59]
4	Nguyen, *et al.*	They developed electrospun fiber mats loaded with silver nanoparticles and Polyvinyl Alcohol (PVA) specifically for wound healing. These mats exhibited high antibacterial activity.[60]
5	A. Schneider, *et al.*	Approach involved using the electrospinning technique to create nanofiber mats from silk fibroin. In this case, epidermal growth factor was added to enhance the wound healing process, aiming to accelerate tissue regeneration.[61]
6	Han I, *et al.*	Nanofiber-based dressings made from poly (3-hydroxybutyrate-co-3-hydroxyvalerate) polymer. These dressings offered adequate moisture and mechanical support to the wound environment.[62]

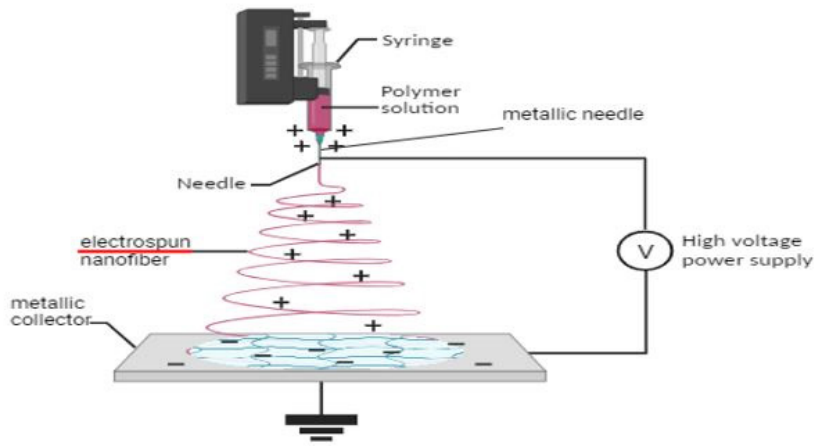

Figure 5: Electrospinning Method.

and proliferation without the need for crosslinking. The invention aims to address issues with current scaffolds, such as inadequate mechanical properties and limited cell in-growth, by providing a more porous and biocompatible structure. The electrospun scaffolds remain intact in cell culture medium for over a month and support high cell densities, making them suitable for various tissue engineering applications. The patent also describes the method of making these fibers and their potential use in medical treatments.[71] Patent US9125811B2 presents a nanofiber laminate sheet designed for cosmetic and medical applications. The sheet comprises a layer of nanofibers combined with a water-soluble polymer layer, enhancing its adhesion to skin and providing both therapeutic and cosmetic benefits. The nanofibers in this laminate can contain and delivering active ingredients, such as vitamins and medications, directly to the skin, offering improved efficacy and user experience.[72] Focused on the cosmetic industry, patent application number US20130122069A1 describes a nanofiber sheet that can incorporate various cosmetic components, such as ascorbic acid, within its structure. The electrospinning process is utilized to integrate these components into the nanofibers, resulting in a product that provides enhanced adhesion, comfort and stability. The patent also mentions potential medical applications, where the nanofiber sheet can be used for wound healing and protection.[73] The patent application US20150272855A1 describes a cosmetic sheet made from nanofibers with controlled dissolution velocity. It involves dissolving a water-soluble polymer and functional material in a solvent, then electrospinning this solution to create nanofibers. The nanofibers, with a diameter of less than 1 μM, form a sheet that dissolves upon contact with moisture, allowing for easy absorption into the skin. This sheet offers improved adhesion, comfort and effectiveness in delivering active ingredients. It eliminates the need for removal after application, enhancing convenience and usability for daily cosmetic routines.[74]

CONCLUSION

With their distinctive benefits for boosting the efficacy of skincare and cosmetic products, nanofibers have demonstrated significant potential in the field of cosmeceuticals. Electrospun nanofibers can be used in a variety of ways in the cosmetics industry. The increased drug loading capacity, site-specific action and extended drug release caused by the greater surface area have all contributed to improved active ingredient delivery and controlled release, making skincare products more potent. Nanofiber-based products have proven to be highly effective at retaining moisture, hydrating the skin and preserving the skin barrier. Researchers are focusing more on this area of study as awareness of the use of cosmetics in skin care, therapy and healing grows. It implies that nanofibers are likely to be a prominent focus of attention in this field for the foreseeable future.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

USFDA: United States Food and Drug Administration; **PVA:** Polyvinyl Alcohol; **PEO:** Polyethylene Oxide; **PAN:** Polyacrylonitrile; **PU:** Polyurethane; **PCL:** Polycaprolactone; **PLA:** Poly (lactic acid); **DMF:** Dimethylformamide; **DMAc:** Dimethylacetamide.

SUMMARY

Nanofibers emerge as a promising technology in cosmeceuticals, offering novel drug delivery methods. Techniques such as self-assembly, drawing, melt blowing, template synthesis, phase separation, melt spinning, centrifugal spinning and electrospinning are utilized for production of nanofibers. With applications in targeted delivery and improved absorption, nanofibers showcase advancements in cosmeceutical formulations. The integration of nanofibers with nano-formulations opens new avenues for optimizing skincare and beauty treatments.

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