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Electrospun nanofibers a novel treatment for localized applications: A review

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Abstract---In the present review we mainly discussed about various methods used to fabricate the electrospun nanofibers along with the localized applications are highlighted. Electrospun nanofibers are majorly used in the biomedical applications nowadays. These applications includes topical antifungal, antibacterial, anti-inflammatory as well as for treatment of burn infections, treatment of wound, reduction of deposited adipose tissues from skin, for treatment of eczema, for treatment of topical anti-glaucoma etc. The polymers are used to fabricate nanofibers by considering the various factors affecting formulation. As the size of nanofibers is less than 500nm & other advantages by means of which we can choose it for localized applications. This information can withstand for further development & up gradation of topical drug delivery system by using nanofibers.

Keywords---electrospun, nanofibers, treatment, localized applications.

Introduction

Desire therapeutic effect can be achieved by choosing correct drug delivery system. The drug release at specific site, on specific time & specific amount of drug delivery rate can be achieved by choosing the effective drug delivery system. For the localized delivery system the drug loaded electrospinning nanofibers is novel & effective system among all nano system. Nanofibers are solid polymer fibres with less than 500 nm size, ability to incorporate a wide range of drugs in an amorphous or solid form within the fibres, they are suitable drug delivery for large surface area & it also gives better biological response¹. Nowadays nanofibers studied for different biomedical applications. Because of its unique structural property that is resemblance to the structure of natural extracellular matrix. They are explored as aspirant for developing tissue templates and prosthetic devices².

Formulation of Nanofibers can be done using different techniques like, drawing method, self-assembly, phase separation, and electrospinning. Among all nanofiber production methods electrospinning is the simple, cost effective & versatile by means of which ultrafine uniform fibres are produced. Electrospinning requires simple & uncomplicated setup. In electrospinning technique electrostatic forces require producing polymer nanofibers which possess unique characteristics covers highly porous mesh with fine interconnectivity & network forming capacity and large surface area to volume ratio³.

The effective way of designing the topical drug delivery is nanofibers, because the conventional ways of topical drug delivery like dressings, bandages are of relatively large diameter ranges from 10-100 μ m. Compared to this nanofibers having diameter up to 500nm & various exemplary properties make it patient compatible⁴. Including the smooth surfaces of solid nanofibers electrospinning technique has also add some secondary structures, including those characterized by a porous, hollow, or core-sheath structure. The extrinsic and/or inner side of such nanofibers can be further featured with molecular sets or nanoparticles⁵. In the present review we focus on the fabrication and therapeutic substance loaded electrospun nanofiber for various topical applications.

Principle & instrumentation of electrospinning technique

Traditional method for fabrication of nanofibers is electrospinning. The main requirement of electrospinning during fabrication includes i) injection pump ii) syringe needle iii) high voltage power supply iv) collector plate or drum⁶. At the time of electrospinning process polymer, drug & organic solvent mixture is pumped to the tip of needle. The electric field is created between the tip of needle & collector plate which is about 10kv-22kv in the system. When the surface tension in the liquid droplet overcome by the force of electric field a droplet is formed a 'Taylor cone'. This distortion leads to an electrically charged jet ejection that gravitate at collector thus formation of a thin fibre i.e. nanofiber⁷. The setup of instrument is shown in figure no.1. However, electrospinning looks so simple & easy process but there are some processing variables, which are supposed to be controlled. The optimization of these variables attain for expected nanofibers. This optimization is done for process variables includes: i) applied voltage ii) distance between capillary & collector iii) viscosity of solution iv) flow rate of mixture v) concentration of polymer vi) solvent nature vii) conductivity of solution etc⁸.

Methods of electrospinning techniques

Different types of electrospinning techniques are getting attention as per the demand of the formulation and the stability of active molecule, so there are 5 major methods by means of which nanofibers are fabricated are: i) blend electrospinning ii) coaxial electrospinning iii) emulsion electrospinning iv) melt electrospinning & v) gas jet electrospinning.⁴

- **Blend electrospinning:** This method mostly requires two or more polymers, the viscosity of polymer solution were determined before process. In this process the active drug is used as sustained release because of its

encapsulated within polymer matrix as the drug mixed with polymer before fabrication.⁹

- **Coaxial electrospinning:** Combination of solvent & gel results into the coaxial electrospinning. In this method fibre is get the external sheath layer. Advantage of this method is absence of any chemical solvent. For fabrication of fibre by coaxial electrospinning two syringes feed with two liquid mixtures where one is inner core & other is outer sheath gives a core-shell nanofibers.¹⁰ Its a familiar choice of DDS is linear or zero-order release, which can keep drug concentrations inside a therapeutic window for a long time after delivery. As a result, patient compliance is high, and side effects are negligible.¹¹
- **Emulsion electrospinning:** It is again one of the easy & innovative method of electrospinning where again core & sheath is fabricate by meance of either type of emulsions i.e. O/W or W/O. The parameter affects the emulsion electrospinning methods like applied electric field, emulsifiers used, system of emulsion etc. Advantages of this system are sustained release of drug, encapsulation of active ingredient as well as increased in bioavailability.¹²
- **Melt electrospinning:** This is quite similar to blend electrospinning method where the drug and polymer mix together with solvent and pass through the needle jet towards the collector plate. Here instead of evaporation of solvent the molten polymer is mixed with drug once this mixture reaches to collector the molten polymer become solidify to form fine fibers.¹³
- **Gas-jet electrospinning:** In this method of electrospinning electrically driven jet is used for fabrication of nanofibers. Mostly the nitrogen gas is used in this process. Parameters affect in this process are voltage in system, flow rate of spinning fluid distance from spinneret to collector.¹⁴

Polymers used for fabrication of nanofibers

In the plastic revolutions, technology progressed in this field drastically. 20th century gives new opening of pharmaceutical practice area as well as biomedicine so the polymers are used as devices for optimizing drug delivery. In this section the various polymers used for fabrications of nanofibers are discussed briefly along with its various properties and biopolymers system used to get improved activity. For the fabrication of nanofibers natural polymers like chitosan, sodium alginate, cellulose methylated gums; gelatine, collagene as well as synthetic polymers like poly lactic acid (PLA), poly glycolic acid (PGA), poly lactic-co-glycolic acid (PLGA), tyrosine-derived polycarbonates, poly ϵ -caprolactone (PCL), polyurethane (PU), polyvinyl pyrrolidone (PVP), poly vinyl alcohol (PVA), or their various combinations are used. In some cases the combination of natural & synthetic polymers are preferred to overcome ones limitations & for better results.

The structure of the electrospun nanofibers and their diameter can be regulated by different aspects and divided into parameters of the setting, operation & solution. The electrospinning technique is thus regarded as an important candidate for a continuous nanofibers mass manufacturing strategy in which the method can be optimised for various polymer solutions.¹⁵ The characteristics of the polymer carrier influence drug release from ES fibres. While hydrophilic polymers allow for faster drug release, using a slowly dissolving or degrading

polymer, or one that is insoluble, allows for prolonged drug release over hours to weeks. ES can synthesize polymer blends, giving it a great deal of control over the specific drug release profile it delivers.⁴⁸ In selecting suitable polymers, the applications & drug distribution condition are important factors that should be taken into consideration. Hydrophobic polymers, such as poly (ϵ -caprolactone) (PCL) and poly urethane (PU) are simple to electrospun because it has high mechanical strength & elastic properties. But the hydrophobicity of electrospun nanofibers is not ideal for cell binding. To increase hydrophilicity preferable combination is natural polymers having good cell attachment & other properties.^{6,16}

Applications of electrospinning nanofibers as a topical drug delivery:

In this section various ongoing research activities both in the academia as well as in the industry related to topical drug delivery are discussed, focusing mainly on release kinetics, area of applications, drug used. Topical drug delivery system is also called as localized drug delivery system for delivery of therapeutic agents locally via skin to cure the dermal disorder. The general formulations are fabricated in forms like solid, semisolid to liquid. Dermatological products have various formulation and range in consistency. In case of nanofibers patches applied topically gives better therapeutic result than that of conventional localized drug therapy, because of its site specific activity. It also reduces the repetition of dosing. These patches currently used for various applications like antifungal, antimicrobial, wound healing, anti-inflammatory, topical treatment of glaucoma and so on.³⁰ (Table no2). Various factors are affecting the drug release while choosing nanofibers as a transdermal delivery system like i) molecular weight of drug, ii) drug concentration, iii) surface area of drug carrier etc.³⁰

Ernawaty Ginting et.al. reported transdermal patches of nanofibers loaded with diclofenac sodium made up of chitosan, polyvinyl alcohol, tripolyphosphosphate sodium shows control released activity.³¹ Tanikan Sangnim et.al. successfully loaded clindamycin in the PNPs where the polymer fabricate by using tamarind gum and the drug-loaded PNPs shows good antibacterial activity.³² Amalia Mira et.al. reported poly(methyl vinyl ether-alt-maleic ethyl monoester) (PMVE/MA-ES) nanofibers loaded with a combination of three compounds shows anti-psoriasis activities they are salicylic acid, methyl salicylate, and capsaicin. Results shows nanofibers are suitable for the development of skin adhesive dressings and allow the dissolution of the nanostructure to extract encapsulated compounds.²⁷

Elham Vatankha developed a nanofibrous matrix containing rosmarinic acid with the help of cellulose acetate and results compare anti-inflammatory activity with ibuprofen.³³ A. Gencturk et. al fabricate Donepezil hydrochloride containing polyurethane/hydroxypropyl cellulose (PU/HPC) nanofibers by the electrospinning for transdermal drug delivery which shows results that nanofiber mats can be well-tolerated and are not irritant to the skin.²⁵ Naewon Kang et.al. developed cellulose film as a topical drug delivery system by hybridizing curcumin (Cur)-loaded nanostructured lipid carriers. Films can be used as a promising topical drug delivery system for psoriasis therapy.³⁴ Priyadharsini K. et. al. fabricated poly caprolactone(PCL)nanofibers with different concentrations of antibiotic drug tetracyclinehydrochloride (TC) for the controlled drug delivery

results showed promising substrates for drug delivery applications in biomedicine and healthcare.³⁵ Jiannan Li et.al. showed dual drug delivery system composed of HCPT and Tea Polyploid-loaded nanofibers was successfully developed through emulsion electrospinning. HCPT and TP were encapsulated in the sheath and core of the nanofibers, respectively.³⁶

Sama Ghalei et.al. prepared core–sheath composite wound dressing comprising PVA nanofibers and zein nanoparticles to encapsulate diclofenac through single-nozzle electrospinning technique shows potential wound healing & anti-inflammatory activity.³⁷ Pusporini P. et.al. reported “antioxidant activity of the PVP/Green tea extract composite nanofiber mat increased with reducing the average fiber diameter because the amount of catechins in the composite nanofiber mat increased with the increase of surface area due to the reduction of the average fiber diameter.”³⁸ Pranabesh S. et.al. fabricated Polyvinyl alcohol /Chitosan nanofiber membrane incorporated with Tranexamic acid for hemorrhage control.³⁹ A. Sharma et. al. fabricated biodegradable poly(vinyl alcohol) and sodium alginate electrospun composite nanofiber based transmucosal patch and the anti-diabetic drug insulin was loaded in it which gives good results by sublingual route.²⁸ More than this nanofiber also possesses great property as they combine with building blocks for pre or post treatment process for production of biosensors.⁴⁰ Different applications of nanofibers are given in Table no:2

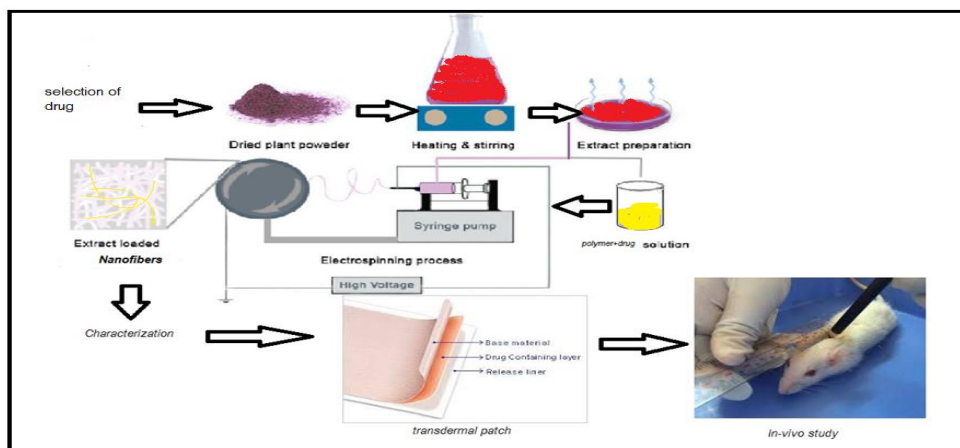


Fig 3. Schematic representation of steps involved in herbal transdermal patches formulated by electrospinning nanofibers

Table 2
Applications of nanofibers in various diseases

Sr. No.	Applications	Drug used	Ref
1	Antifungal	Sertaconazol	41
2	Antimicrobial	Silver sulphadiazine,	45
3	Skin disorders	B-carotene	42
4	Wound healing	Berberin, Turmeric, <i>Colocasia esculenta</i> , Malva sylvestris	21,22,26,25

5	Lipolysis	Levothyroxine(T4)	43
6	Antiinflammatory	Ibuprofen, Naproxen, Diclofenac	36,37,40
7	Antioxidant	Green tea	38
8	Antiglucoma (Topical)	Timolol maleate, Brimonidine tartrate, Dorzolamide hydrochloride	44,46,47
9	Antidiabetic	Insuline	28
10	Alzheimer	Donepezil Hcl.	25
11	Psoriasis	Salicylic acid, methyl salicylate & capsaicin, Curcumin	26,33
12	Antifibrinolytic	Tranexamic acid	39

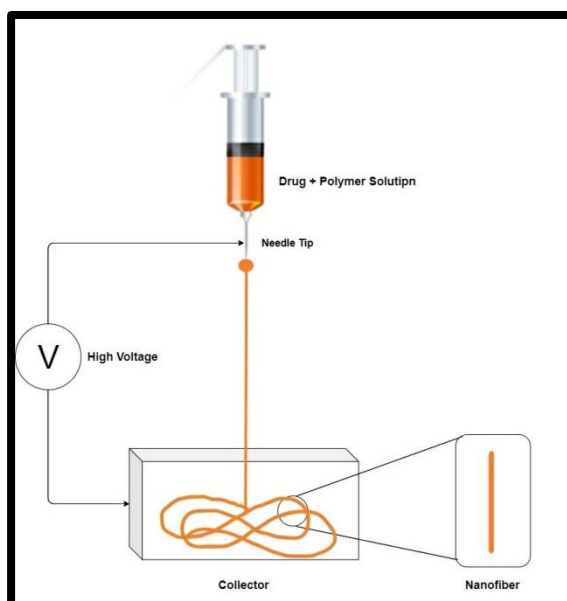
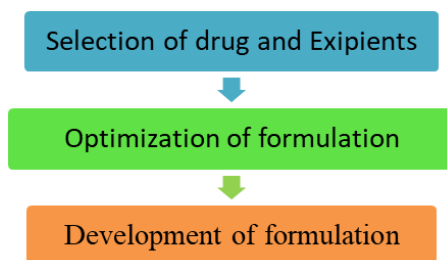


Fig 1. Diagrammatic representation of production of electrospinning nanofibers



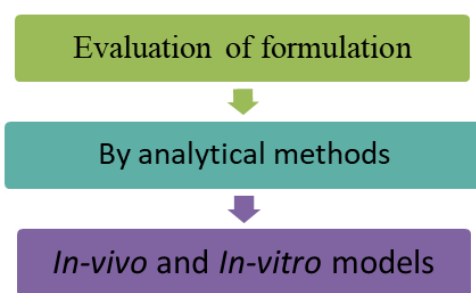


Fig 3. Schematic representation of formulation development of nanofibers containing drug

Table 1
Properties of polymers used for fabrication of nanofibers along with various drug combination

Sr. No.	Polymers	Properties of polymers	Drug	Ref no.
1	Cellulose acetate	biocompatible, biodegradable, non-toxic biomaterial, relatively low cost, less hygroscopic, excellent chemicals, & heat resistance	Naproxen, Curcumin	17
2	Polyurethane	Biocompatible, Sterilizable, chemical resistance, excellent strength, tear and wear resistance and high elastic memory for maintaining tension.	Naproxen Sertaconazol	18
3	Polyvinyl pyrrolidone	favourable, nontoxic, non-allergenic, and highly biocompatible nanofibrous membrane	Levothyroxine	19
4	Polyvinyl alcohol	biocompatible, biodegradable, nontoxic, water permeable polymer with great electrospinnability	Capsicum, Diclofenac, Green tea, Tranexamic acid	20
5	Polycaprolactone	bioresorbable, good tissue compatibility, appropriate tensile strength, and ease of electrospinning, biocompatible, tailor-made mechanical characteristics	<i>Zingiber cassumunar</i> Berberine, B-carotene	21
6	Polyethylene oxide	Enhance bioavailability & solubility of drugs because of its high aqueous solubility, non-toxic and non-irritating, unique properties in drug delivery applications	<i>Colocasia esculenta</i>	22
7	Chitosan	obtained from N-deacetylation of chitin, the second-most abundant natural polysaccharide	<i>Melilotus officinal</i> Tranexamic acid	22
8	Polyhydroxy	Biopolyesters, excellent	<i>Capsicum</i>	23

	alcanoate	biodegradability and biocompatibility	<i>Frutescens</i>	
9	PBAT*	biodegradable and flexible, which designed for film extrusion and extrusion coating		24
10	Hydroxypropylene cellulose	Non-ionic and hydrophilic cellulose derivate which is used as coating, emulsifying, stabiliser, suspending, thickener, film-coating agent	Donepezil hydrochloride	25
11	carboxymethylated gum prepared from tamarind seed	typical derivative of cellulose, is known as a biocompatible, nontoxic, biodegradable and affordable polymer with a wide range of applications	Clindamycine	26
12	poly(methyl vinyl ether-alt-maleic ethyl monoester)	biodegradable, biocompatible, bioadhesive, and low-toxic polymer	salicylic acid, methyl salicylate, capsaicin	27
13	Sodium alginate	biodegradable polymer a negatively charged polysaccharide derived from brown sea weed	Insulin	28

PBAT *- Poly (butylene-adipate-co-terephthalate)

Conclusion

Leading to the penetration of the medicinal agent through the skin and the ingestion of drugs and entry into the vascular system, TDDS has gained considerable interest. The efficient development of nanofibers begins, as defined in this review, with the combination of suitable polymers and solvents. By mixing several polymers during electrospinning processes, several desirable properties can be obtained. While new electrospinning-based drug delivery systems are being created, far more comprehensive research on various electrospinning parameters and the creation of electrospinning methods for new polymer combinations and drug loading is still required.

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