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REVIEW PAPER

A review on electrospun nanofibers for oral drug delivery

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ABSTRACT

Nowadays, polymer nanofibers have gained attention due to remarkable characteristics such as high porosity and large surface area to volume ratio. Among their fabrication methods, electrospinning technique has been attracted as a simple and reproducible approach. It is a versatile, simple and cost-effective technique for the production of continuous nanofibers with acceptable characteristics such as high porosity, high surface area to volume ratio, high loading capacity and encapsulation efficiency, delivery of multiple drugs, and enhancement of drug solubility. Due to these properties electrospun nanofibers have been extensively used for different biomedical applications including wound dressing, tissue engineering, enzyme immobilization, artificial organs, and drug delivery. Different synthetic and natural polymers have been successfully electrospun into ultrafine fibers. Using electrospun nanofibers as vehicles for oral drug delivery has been investigated in different release manners- fast, biphasic or sustained release. This article presents a review on application of electrospinning technique in oral drug delivery.

Keywords: *Drug delivery, Electrospinning, Nanofiber, Polymer*

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INTRODUCTION

Oral drug delivery is one of the preferred routes of drug administration due to its non-invasive nature, ease of use, and higher patient compliance. Moreover, oral formulations can be designed in various ways and their productions are cost effective. Compared with the other routes, the orally administered dosage form needs no expertise required and is therefore useful for chronic diseases with frequent dosage consumption.

There fore, development of medicines into oral products is preferable.

Nanotechnology has been widely investigated in oral drug delivery due to the convenience and high patient compliance associated with oral administration [1].

Recently, drug-loaded nanofibers have gained attention as potential drug delivery systems because of their unique structure. Nanofibers are solid fibers of materials with diameter in the range of micro and nano scale and with a porous structure which makes them a very high surface area. Properties of nanofibers including increase in the surface to volume ratio, small pore size and high pore volume, improved mechanical properties and flexibility in surface functionalities make them suitable materials in different scientific fields [2-5]. Widespread applications of polymeric nanofibers in numerous fields such as computer technology, fabric formation, nanocomposites, cosmetics, separation industries and electronics have been attempted [6]. In the medical field, nanofibers have been used in tissue engineering [7-9], wound dressing [10], enzyme immobilization [11], artificial organs [12], ophthalmology [13], dentistry [14-16], bone repair [17, 18] and drug delivery [19-22].

Different techniques including drawing [23, 24], template synthesis [25, 26], phase separation [27,28] and self-assembly [29] have been used for fabrication of polymer nanofibers (Fig. 1). However these methods have disadvantages such as time-consuming process, material limitation, and difficult scale-up.

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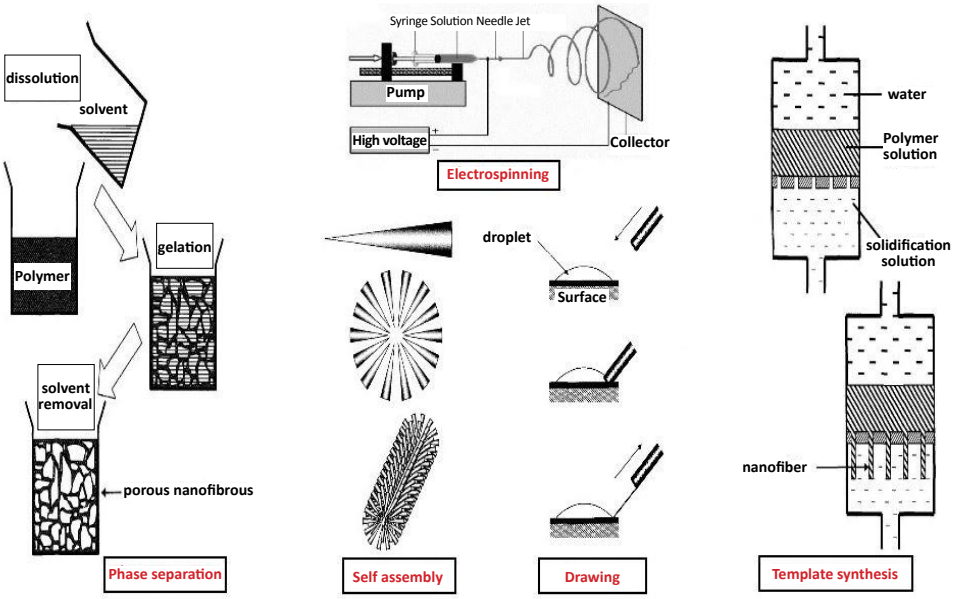

Fig 1. Different methods for fabrication of nanofibers

Electrospinning is a straightforward method for production of nanofibers by feeding a polymer solution in a high electric field. A thin jet is made from the solution droplet and drawn by the electrostatic field while the solvent evaporates and solid nano-or micro-scale fibers can be prepared. Fig. 2 schematically illustrates the mechanism of nanofiber production by electrospinning method. Fabrication of ultrafine fibers by an electrostatic force firstly reported in 1934 [30]. Meanwhile, in recent year's academic and industrial research have been dramatically increased in production of electrospun nanofibers because of the remarkable characteristics of simplicity, versatility, and potential uses in diverse fields. The high loading capacity, high encapsulation efficiency, delivery of multiple drugs, enhancement of drug solubility, ease of operation, and cost-effectiveness have been the reasons for trends to application of electrospun nanofibers in drug delivery [31, 32]. Various drug delivery systems with different drug release profiles such as fast, pulsatile and biphasic have been successfully achieved based on electrospun nanofibers [33]. This article presents a review on the developments of electrospinning and studies on applications of electrospun nanofibers in drug delivery.

Basics

The electrospinning equipment is basically composed of an electrical supply for generation of high electrical voltage, a syringe filled with polymer solution, a pump and a grounded conductive rotatable or static collector all enclosed within a chamber. When the process starts the solution is ejected from the nozzle of the syringe by the pump. Then the droplet is subjected to a high voltage and difference in electrical voltage present between the nozzle and the collector with the counter charge and the resulted electrical voltage causes a cone-shaped deformation of the droplet known as a Taylor cone. When the voltage surpasses a threshold value, the electric force overcomes the surface tension of the droplet and a charged jet of solution is ejected from the needle of the syringe. On the way to the collector solvent evaporation of the charged jet occurs and the solid material is collected as a solid continuous small fiber [34].

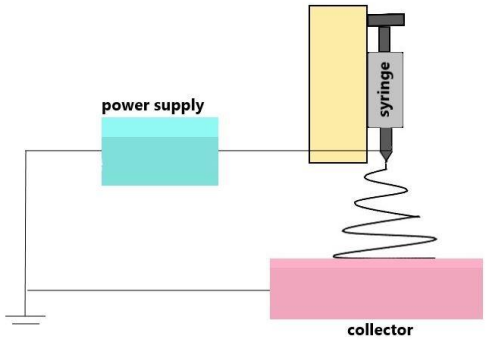

Fig 2. Schematic of electrospinning method

Both the dissolution and the electrospinning are essentially conducted at room temperature under the atmosphere condition.

Electrospinning parameters

The process of electrospinning and the formation of electrospun nanofibers with acceptable characteristics depend on several factors. Careful control of these parameters can lead to the production of highly porous structures of smooth and bead free nanofibers. These parameters are classified as solution properties, electrospinning parameters,and environmental parameters.

The solution parameters include the polymer concentration, type of solvent, viscosity and solution conductivity.The viscosity of polymer solution is low at the lower polymer concentration and the entanglement of polymer which needs for fiber formation does not happen. Instead, in this state particles are formed and the phenomenon is called electrospraying [35]. In a study it was shown that the boundary concentration between electrospray and electrospinning depends on the solvent used [36]. Also, Rieger et al., studied a correlation between precursor solution properties and nanofiber morphology for polymer solutions electrospun with or without hydrophobic oils. They demonstrated that transition from bead-on-string to cylindrical nanofiber morphology occurred by increase in polymer concentration [37]. Another investigation on poly vinyl alcohol based electrospun nanofibers revealed specific correlations between solution properties and the final electrospun product which could be useful for prediction and optimization of electrospinning method [38].

Type of solvent is another effective solution parameter. Erdem et al., showed that the morphologies of polyurethane nanofiber membranes could be significantly changed by solvent type and mixing ratios of the solvents for the electrospinning [39]. Also, solvent volatility has a significant effect on the morphology of the resulting nanofiber. When a solvent with low volatility is used, solvent evaporation is low and the solidification process could be retarded. On the otherhand, for volatile solvents, fiber formation will not be complete due to the early solidification of the polymer jet.

Solution conductivity is the other parameter of solution which affects the nanofiber formation. Increasing the solution conductivity increases the Taylor cone formation and also reduces the diameter of the nanofibers [40].

The electrospinning parameters include the applied electric voltage, needle diameter, distance between the tip of the needle and counter electrode (collector), and flow rate. An increase in applied voltage causes a change in the shape of the Taylor cone and therefore affects morphology of the nanofibers. A critical electric voltage is needed for the formation of ultrafine nanofibers [41]. The higher applied voltage beyond the critical value will result in the formation of beads and non-uniformity of nanofibers. The distance between the tip of the needle and collector is another essential electrospinning parameter affecting the morphology of electrospun nanofibers. Decrease in the distance between the tip and the collector enlarges diameter of nanofibers [42]. Another important parameter is flow rate which in the critical point leads to the formation of a uniform electrospun nanofiber. This critical value varies with the polymer system. Increasing the flow rate beyond a critical value produces nanofibers with larger diameter and pore size and also increases the bead formation [43].

The environmental parameters include relativity humidity (RH) and temperature which are crucial for production of ultrafine nanofibers with acceptable morphology. Relative humidity affects the formation of pores on the fiber surface

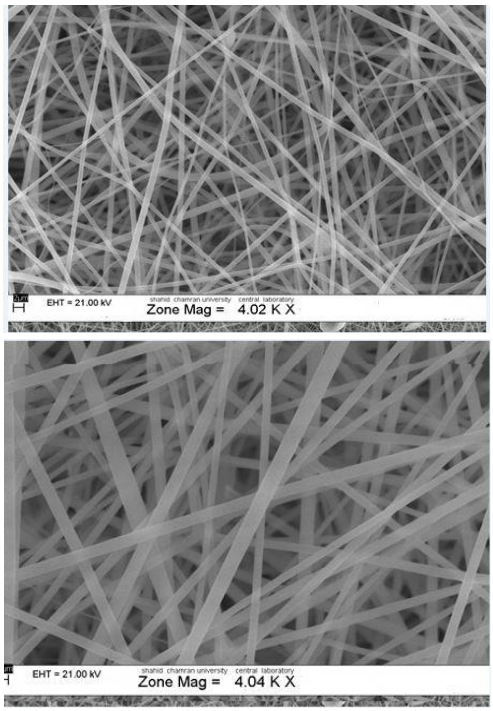

Fig 3. SEM of loratadine-loaded PVP nanofibers prepared by different feed rates; (a) 1 mL/h and (b) 6 mL/h

Table 1. Different polymers used for fabrication of nanofibers with various drug release kinetics

Polymer	Drug	Drug release behavior	Reference
polyvinylpyrrolidone (PVP)	paracetamol/caffeine	fast	[56]
PVP/cyclodextrin (CD)	meloxicam	fast	[63]
polyvinyl alcohol (PVA)	nebivolol	fast	[52]
PVA	caffeine	fast	[55]
polycaprolactone (PCL)	dexamethasone	controlled	[96]
PCL	ampicillin	controlled	[78]
PVP/ethyl cellulose	ketoprofen	biphasic	[73]
PVP/zein	ketoprofen	biphasic	[74]
Cellulose acetate	diclofenac	controlled	[97]
Eudragit L	mebeverine	delayed	[80]
hydroxypropyl methylcellulose (HPMC)	piroxicam	controlled	[79]
Eudragit S	5-fluorouracil	biphasic	[87]
Eudragit S	budesonide	delayed	[92]
Eudragit S/Eudragit RS	indomethacin	controlled	[88]
shellac	ferulic acid	controlled	[85]

via solvent evaporation. In an investigation it was shown that the porosity and pore diameter of polystyrene fibers produced from tetrahydrofuran solution increased with increasing humidity above 30% RH [44].

Temperature also has important effects on fiber formation by changing the rate of evaporation of solvent and viscosity of the polymer solution and subsequently affecting the size of electrospun nanofibers. The effect of humidity and temperature on the fiber properties of two different polymers, cellulose acetate and polyvinylpyrrolidone have been investigated [45].

As a consequence, by optimization of the cited parameters achieving more uniform nanofibers with suitable physicomechanical properties will be easier. Also, regarding the application of fibers one can obtain nanofibers with various shapes and sizes by changing the mentioned effective parameters which in the field of drug delivery will be useful for different delivery systems.

Polymers used in electrospinning

A number of synthetic, semisynthetic and natural polymers have been applied for production of electrospun nanofibers. Compared with natural sources, synthetic polymers have great flexibility in synthesis and modification. Meanwhile, natural polymers exhibit better biocompatibility and safety. Natural polymers have also some unique properties such as antibacterial characteristics. There are various types of natural polymers including polysaccharides, proteins, DNA and their derivatives which have been used in electrospinning process [20, 46, 47]. Synthetic polymers and copolymers such as poly (lactic acid) (PLA), poly (lactic-co-glycolic acid) (PLGA), poly(ε-caprolactone) (PCL), poly(vinyl pyrrolidone) (PVP), and poly(ethyleneoxide) (PEO) have been used to produce for tissue engineering and drug delivery. In the field of drug delivery, different parameters of polymers such as molecular weight, polymer composition and ratio of amorphous to crystalline segments of the polymer could affect drug release from nanofibers.

The polymer composition is an important factor which is effective in drug loading and release from nanofibers. Hydrophilic and amphiphilic copolymers could increase drug loading and inhibit burst drug release [48]. It was also shown that high crystallinity of polymer decreases drug release rate because of limitation of crystalline regions for water uptake compared to amorphous regions [49].

Depending on the polymer carrier used, drug release from electrospun nanofibers can be in a rapid, immediate, delayed, or extended manner. Therefore, selection of the polymer is a crucial factor to achieve a desirable drug release profile. Various polymers and their related solvents used for production of electrospun nanofibers aimed for drug delivery are listed in Table 1.

Electrospun nanofibers in oral drug delivery

Fast release

Many pharmaceutical companies and scientific researchers have recently produced novel dosage forms that rapidly disintegrate in the oral cavity and make comfortable usage. These called orodispersible or fast-dissolving drug delivery systems (FDDDSs). Orodispersible drugs can easily dissolve or disintegrate in the mouth very rapidly, without requiring any water to aid in swallowing.

Therefore, higher bioavailability and rapid onset of action of drug can be achieved by these dosage forms [50]. Electrospun fibers are good candidates for FDDDSs due to very large surface area which causes immediate disintegration in water solution and faster drug release.

In a study on the Angelica gigas Nakai(AGN) extract-loaded fast-dissolving by poly (vinyl alcohol) (PVA) and Soluplus (SP)-based nanofiber mat, nanofibers were fabricated using an electrospinning method. AGN/PVA/SP NF with a 170-nm mean diameter and over 80% entrapment efficiency was fabricated. It was shown that using electrospinning for fabrication of nanofibers converts the solid state of AGN extract in nanofiber structures from the crystalline to the amorphous state, and consequently improves aqueous solubility and rapid dissolution in the aqueous media [51]. Transition of crystalline to amorphous state of drug due to electrospinning process was also demonstrated in another investigation [52]. This crystalline-amorphous conversion along with the increase in surface area of nanofibers caused a rapid and complete dissolution of nebivolol-loaded electrospuns. It was also shown that dissolution of the nanofibers was not affected by pH of the media [52].

Vigh et al. fabricated fast release nano- and microfibers of spironolactone using hydroxypropyl-b-cyclodextrin. Conversion of crystalline to amorphous state of drug during electrospinning process was demonstrated. Total drug release from nanofibers was 1 min, while adding PVP K90 led to the gel formation of the webs after wetting and consequently affected drug release via hindering drug diffusion and aiding the crystallisation of the amorphous drug [53].

In another investigation, PVP nanofibers loaded with loratadine were produced using the electrospinning method. A full factorial design was used to evaluate the formulations, including the variables, polymer concentration, the ratio of drug to polymer, the feed rate, and the applied electric voltage. It was demonstrated that increase in the feed rate from 1 to 6 mL/h increased the diameter of electrospun nanofibers, as shown in Fig. 3. It was also shown that increasing the voltage applied to the polymeric solution up to an adequate amount creates uniform nanofibers with smaller diameter. Fig. 4 depicts the disintegration process of nanofibers. As shown, the optimum formulation disappeared at a time of less than 40 seconds. Compared to solid dispersion formulations, electrospun nanofibers of loratadine disintegrated faster and it could be due to a higher surface to volume ratio of nanofibers along with the high porosity of nanofibers [54].

Electrospun polyvinyl alcohol (PVA) nanofibers were prepared as a FDDDS for caffeine and riboflavin. Drug release profiles showed a burst release to the extents of 40% and 100% within 60s for riboflavin and caffeine, respectively [55].

Using electrospun nanofibers as vehicles for taste masking products have also been investigated. In a study, paracetamol and caffeine loaded electrospun nanofibers were fabricated by electrospinning. The resulted fibers were uniform in shape and completely disintegrate within 0.5 and 150 s in the simulated saliva solution and dissolution media, respectively. Also a flavoring agent could easily be incorporated into the formulation aimed for drug taste masking. Therefore, it was a suitable dosage form useful for children and elderly [56]. Loading of electrospun nanofibers in the minitablets were also investigated [57].

In recent years, use of cyclodextrins (CDs) in the preparation of electrospun nanofibers has been explored [58, 59]. CD inclusion complexes have also been carried out to modify drug release properties and to enhance in vivo functionality [60-62]. Samprasit et al., produced meloxicam loaded polyvinylpyrrolidone (PVP)/cyclodextrin (CD) nanofibers using an electrospinning approach. They found that drug is composited into the nanofiber mats in the amorphous state. The presence of CD in the structure of fibers managed the high physical stability of electrospuns. Also, the results demonstrated that incorporating meloxicam into the nanofibers increases the palatability of dosage forms along with a fast release in the mouth [63].

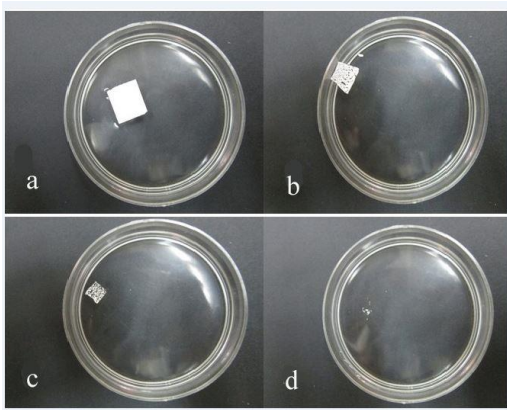

Fig 4. Photos of the disintegration process of loratadine-loaded PVP nanofibers after (a) 0s, (b) 10s, (c) 20s and (d) 40s

Buccal formulation of ketoprofen-loaded Eudragit L and Eudragit S nanofibers by electrospinning technique was obtained. The effect of various factors including polymer concentration, applied voltage, flow rate and drug loading was evaluated in the development of nanofibers. It was demonstrated that Eudragit L100 nanofibers loaded with drug is effective in the management of the inflammatory response associated with mucositis [64]. In another work, gelatin nanofibers for oral mucosal drug delivery were successfully prepared and photo-reactive polyethylene glycol diacrylate (PEG-DA575) was added as a cross-linker to improve the structural stability of the nanofibers [65]. Use of the other polymers such as polycaprolactone (PCL) [66] or combination of electrospinning with the other approaches like inkjet printing [67] have also been tried for development of oromucosal dosage forms.

Controlled release

Controlled drug delivery systems (CDDS) have been widely investigated for treating many diseases. Electrospun nanofibers have a great potential for applications in the field of topical and oral drug delivery regarding their unique features, including versatility of drug incorporation, high porosity, high loading efficiency, large surface area, flexibility in surface functionalities and cost effectiveness. In the field of oral drug delivery, they have been used as controlled drug release system which includes delayed, burst, biphasic and sustained release [68, 69]. First report was conducted on electrospun fiber mats made from poly (lactic acid) (PLA), poly (ethylene-co-vinylacetate) (PEVA) and a mixture from two polymers as vehicles for controlled drug release of tetracycline. The drug release rate was controlled mainly by diffusion, with the slow degradation of PLA and the non-degradable property of PEVA [70].

In a study, amyloid-like bovine serum albumin (AL-BSA) with ampicillin sodium salt (amp) was developed as a controlled drug release system. It was shown that in the first 24h, nanofibers fabricated with 5% (w:w) amp:BSA demonstrated ideal controlled release of ampicillin, but for the large diameters of the 10% and 20% (w:w) amp:BSA membranes, the diffusion lengths increased [68]. Also PVA and curcumin nanofibers or PVA with a cyclodextrin–curcumin complex prepared by electrospinning to produce a sustained release system. It was shown that a controlled drug release profile with two sequential stages of drug release over 5h can be achieved [71]. In another investigation, multi-layered electrospun fibers were fabricated by sandwiching the drug loaded gelatin layer between another gelatin nanofiber matrix without drug acting as diffusion barrier, sequential crosslinking and a combination of both. A desirable zero order release profile for 48h was observed for piperine as a model drug [72].

Biphasic release

Many of drugs such as non-steroidal anti-inflammatory drugs (NSAID) are better to administrated in the form of biphasic release system because of their relieving effect in the shortest time after administration and avoiding repeated administration, which is good for the patients' convenience. For this purpose, coaxial electrospinning was carried out to prepare core/sheath ketoprofen-loaded nanofibers that could provide biphasic drug release profiles, using

PVP as the sheath polymer and ethyl cellulose as the core matrix. Dissolution profiles showed a biphasic release profile consisting of an immediate and sustained release [73]. In another investigation conducted on ketoprofen nanofibers the shell part of nanofiber was PVP, but the core matrix was zein. The electrospun nanofibers showed an immediate drug release of 42.3%, followed by a sustained release over 10h [74].

Lee et al., fabricated a tri-layered nanofiber mash composed of zein and PVP as the top/bottom and middle layers, respectively. It was shown that each component has distinct release feature and the whole system showed a time regulated biphasic release of ketoprofen [75]. A biphasic release profile with initial rapid drug release followed by a slow release was observed from gelatin-ciprofloxacin [76] and resveratrol nanofibers [77]. In the case of low compatibility of the drug and polymer a modified coaxial electrospinning was used in which a partially electrospinnable shell solution containing 4% (w/v) polycaprolactone (PCL) and a fully electrospinnable core fluid containing 10% (w/v) PCL and 2% (w/v) ampicillin were used in order to fabricate ampicillin-loaded PCL nanofibers layered with a PCL shell. The shell layer was responsible for slow releasing pattern while burst release was observed for single electrospinning of the core

[78]. Paaver et al., combined solid dispersion and controlled release techniques in fabricating supersaturating controlled-release drug delivery systems for a poorly water-soluble drug, piroxicam. Electrospinning was carried out as a new technique in preparing high-energy amorphous solid dispersions of drug and hydroxypropyl methylcellulose (HPMC) as an amorphous-state stabilising carrier polymer in nanofibers. The electrospun nanofibers showed a short lag-time, the absence of initial burst release and zero-order drug release [79].

Delayed release

The encapsulation of drugs in the core of enteric polymers has been investigated for oral delivery of peptides and proteins and also for the treatment of diseases such as ulcerative colitis.

Electrospun mebeverine hydrochloride-loaded nanofibers prepared with the polymers PVP and Eudragit R L100-55 delivered the drug to the GI tract in a sustained manner and protected it in the stomach [80]. In another investigation, hydrophilic electrospun gelatin fibers as the carriers for prolonged release rate of a hydrophobic drug i.e. piperine were used which could modulate the release rate of the drug by the degree of cross-linking of the carrier and variation of the pH of the site of release [81]. Hamori et al., prepared nanofiber-based capsules using eudragit S 100 for two model drugs; uranine as a water-soluble and nifedipine as a water-insoluble drug. The in vitro and in vivo results showed that electrospun nanofibers with polar or non-polar physicochemical properties can be successfully achieved [82].

Nanofiber-based tablets of acetaminophen were produced using direct tableting of electrospun nanofibers of eudragit S 100. Process of tableting was performed easily without the lubricant. Nanofiber tablets released drug in a pH-dependent manner and therefore could be useful as an ultra-long-acting dosage form [83].

Colon drug delivery

Nowadays, different approaches have been examined for oral drug delivery to the colon, including pH-sensitive polymers, controlled release through the use of a matrix system, pro-drugs, and timed-release systems.

In a study, Eudragit L 100-55 nanofibers containing diclofenac sodium were fabricated by electrospinning. Drug release from the resulted nanofibers was pH-dependent and therefore nanofibers showed promising for colonic drug delivery of diclofenac [84]. In another study, shellac nanofibers loaded with ferulic acid were fabricated using a coaxial electrospinning process. It was shown that drug is amorphously distributed in the fibers. Drug release at pH 2.0 was minimal, where a sustained release was observed in the neutral dissolution medium through an erosion mechanism. During the dissolution processes, the shellac fibers were gradually converted into nanoparticles as ferulic acid was freed into solution [85].

Zhou et al., conducted a long-term research to get better clinical results for treatment of IBD by combining anti-inflammatory therapy with physical mucus layer restoration. According to this study, they designed nanofibers of self-assembled de novo glycoconjugates, consisted of anti-inflammatory drugs and glycopeptides [86].

At the specific times, pH-responsive drug delivery systems could set up drug releasing rate by changing the pH values for treatment of diseases. Illangakoon et al. designed a pH-sensitive electrospun drug delivery system for 5-fluorouracil (5-FU). 5-FU was loaded in core/shell electrospun fibers in which shells were made of Eudragit S100 (ES-100), while drug-loaded cores were PVP, ethyl cellulose, ES-100, or drug alone. Low molecular and high acid solubility of the drug leaded to diffuse through pores in the ES-100 coating. Transmission electron microscopy showed smooth and cylindrical fiber shape and the active ingredient existed in the amorphous form in the fibers. Also the fiber formulations showed two distinct phases of release: burst release in stomach and second phase of release upon transfer into small intestine [87].

Combination of two polymers with different effects on drug release for fabrication of electrospun nanofibers aimed for colon targeting has also been explored. In a study, electrospinning was used for preparation of indomethacin-loaded nanofibers using different blends of eudragit S (ES) (ERS) as a pH-dependent polymer and eudragit RS as a controlled release polymethacrylate. The effect of solvent and viscosity on the characteristics of nanofibers was studied. The results showed that indomethacin is evenly distributed in the nanofibers in an amorphous state. It was shown that drug-loaded ERS and ES nanofibers could

be fabricated by proper selection of variables such as type of solvent, drug to polymer ratio and viscosity of the spinning solution [88]. For example, scanning electron micrographs (SEM) of drug-loaded nanofibers (Fig. 5) showed that the increase in drug level in the composition of the formulations affected the morphology of nanofibers and created some beads in the structure of fibers (Fig. 5b). The optimized formulations were capable of drug loading up to 66% and could be useful for further studies on possible colonic delivery of indomethacin [89]. Use of combination of polymers to achieve more appropriate drug release kinetics for colonic drug delivery of nanofibers have been investigated in the other studies [90, 91].

Colon-targeted drug delivery is not only for local delivery to treat diseases of the colon but also a good approach to increase the bioavailability of poorly water-soluble drugs. Therefore, electrospinning technique was considered for production of nanofibers of low water-soluble drugs such as budesonide. Drug-loaded eudragit RS100 fibers were fabricated.

The physicochemical investigation and FTIR measurements indicated that hydrogen bonds take place between budesonide and the polymer. Dissolution experiments showed no significant drug release at pH 1.0 while a sustained release at pH 7.2 occurred. Therefore, this system could be useful for drug targeting to terminal ileum and colon with the aim of improving the local efficacy of this drug [92]. Using electrospun nanofibers for colon specific delivery of protein drugs have also been investigated [93, 94].

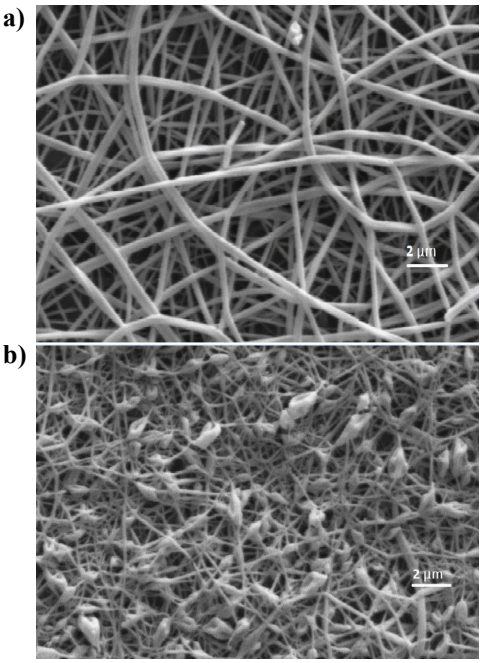

Fig 5. SEM of two different indomethacin electrospun nanofibers containing ES:ERS (1:4) with drug loading of (a) 47% and (b) 54.5%

Dual drug delivery

An example of using electrospun nanofibers as dual drug delivery systems was zein/eudragit composite nanofibers entrapped with aceclofenac and pantoprazole.

Due to the insolubility nature of eudragit S 100 in acidic solutions the release of the drug was prolonged up to 8h in this medium. Also, a sustained drug release profile was observed from the zein fibers because of its hydrophobic nature. As an overall result, a dual drug delivery system was successfully developed with reduced side effects [95].

CONCLUSION

Electrospinning is a simple, versatile, and cost-effective technology for the fabrication of continuous nanofibers with suitable characteristics such as high porosity and high surface area to volume ratio.

Due to these properties electrospun nanofibers have been extensively used for different biomedical applications including tissue engineering, wound dressing, enzyme immobilization, artificial organs, bone repair and drug delivery. Formation of the electrospun nanofibers significantly depends on various parameters such as properties of the polymer, solution viscosity and conductivity, type of solvent, applied voltage, tip-to-collector distance, and relative humidity. Optimizing these parameters is crucial for obtaining electrospun nanofibers with desirable properties.

In the field of drug delivery, different electrospinning methods such as direct method or coaxial electrospinning have been successfully used for fabrication of nanofibers with various drug release behavior including fast, biphasic, delayed or controlled release.

This article highlighted the effect of various parameters and polymers on fabrication of nanofibers by electrospinning technique. It also summarized the applications of electrospun nanofibers in drug delivery and especially oral dosage forms with different release manners.

However, the physical and chemical stability of these systems along with understanding of the detailed drug release kinetics have not yet been thoroughly explored and therefore will be a challenge for future investigations. With overcoming these challenges, electrospinning will remain a promising technique for developing oral drug delivery dosage forms.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.

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