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Electrospun diclofenac sodium loaded Eudragit® L 100-55 nanofibers for colon-targeted drug delivery

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ABSTRACT

Eudragit® L 100-55 nanofibers loaded with diclofenac sodium (DS) were successfully prepared using an electrospinning process, and characterized for structural and pharmacodynamic properties. The influence of solvent and drug content on fiber formation and quality was also investigated. Fiber formation was successful using a solvent mixture 5:1 (v/v) ethanol:DMAc. XRD and DSC analysis of fibers confirm electron microscopic evidence that DS is evenly distributed in the nanofibers in an amorphous state. FTIR analysis indicates hydrogen bonding occurs between the drug and the polymer, which accounts for the molecular integration of the two components. *In vitro* dissolution tests verified that all the drug-loaded Eudragit® L 100-55 nanofibers had pH-dependent drug release profiles, with limited, less than 3%, release at pH 1.0, but a sustained and complete release at pH 6.8. This profile of properties indicates drug-loaded Eudragit® L 100-55 nanofibers have the potential to be developed as oral colon-targeted drug delivery systems.

1. Introduction

Electrospinning is a simple and straightforward method to produce nanomaterials and nanostructures, that can be combined with other technologies to expand its applications in a wide variety of fields (Xie et al., 2010; Zhang et al., 2009; Yu et al., 2010a). The main strategy for endowing the nanofibers produced from a single fluid electrospinning process with a particular function is to directly make the functional component (drug, inorganic nanoparticle, sensor, etc.) highly distributed in the filament-forming polymer matrix (Ribeiro et al., 2005; Sawicka et al., 2005; Thakur et al., 2008; Yang et al., 2008). By exploiting nanofiber properties (such as small diameter, large surface area, high porosity, and assembling randomly in a non-woven mat with a continuous three-dimensional web structure), the functions of the incorporated materials can potentially be improved and may even gain enhanced functions due to nano-effects (Sill and von Recum, 2008; Greiner and Wendorff, 2007; Rutledge and Fridrikh, 2007; Lu et al., 2009; Natu et al., 2010). Another strategy for enhancing function is to treat nanofibers after preparation by processes such as cross-linking and coating (Ding et al., 2005; Sell et al., 2008).

Since being first reported in 2002 (Kenawy et al., 2002), active pharmaceutical ingredient (API)-loaded nanofibers have attracted great interest. This is in part due to the possibility of developing novel drug delivery systems (DDS) for commercialization (Yu et al., 2009a). For applications of nanofibers in the drug delivery area, two trends may be noted. First, much of the literature simply describes the preparation and characterization of API-loaded nanofibers (Yu et al., 2009a, 2010a,b), with fewer reports on the final DDS product and the possible commercialization (Yu et al., 2009b; Wu et al., 2010). Second, due to the polymer matrix properties, most of the API-loaded nanofibers reported are for treatment to external surfaces of the human body, e.g. auxiliary therapy, transdermal DDS and wound dressing (Wu et al., 2010; Katti et al., 2004).

Relatively little work has focused on creating API-loaded nanofibers for oral DDS (Ignatious et al., 2010; Yu et al., 2009b, 2010c,d), which is the preferred route of drug administration due to its convenience, patient compliance, and cost-effectiveness and is the most common format in the drug delivery market (Jelvehgari et al., 2010; Yamanaka and Leong, 2008). However many filament-forming polymers are not suitable for oral administration and only a few polymer excipients approved by the FDA have both good filament-forming properties for electrospinning and can meet the pharmaceutical requirements for developing oral DDS.

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Yu et al. have developed electrospun fibers for application to oral delivery using polyvinylpyrrolidone (PVP), a hydrophilic filament-forming polymer with a wide variety of applications in medicine, food, pharmacy, and cosmetics (Yu et al., 2009b, 2010c,d). The PVP fibers formed the basis of a fast dissolving DDS capable of forming solid dispersions and improved dissolution profiles of poorly water-soluble drugs for possible oral delivery applications. To the best of our knowledge, there are few reports in the literature describing electrospun drug-loaded nanofibers made from pharmaceutical polymer excipients, targetted for oral, and particularly colon, drug delivery.

A series of enteric soluble cellulose polymers and methacrylic acid co-polymers have been extensively studied for development of oral colon DDS (Silva et al., 2009; Donini et al., 2002; Wang et al., 2010). Among them, Eudragit® L 100-55, a well known pharmaceutical excipient developed by the Röhm Company in Germany, has been widely used for the formulation of different oral dosage forms (e.g. tablet coating, tablet matrix, microspheres, nanoparticles) for colon-targeted drug delivery (Oosegi et al., 2008; Zakeri-Milani et al., 2009; Moustafine et al., 2006; Jelvehgari et al., 2010; Cetin et al., 2010).

Nano-packaging of medicines can increase drug efficacy, specificity, tolerability, and therapeutic index, and polymer-based nano DDS can also potentially further protect drugs from degradation and reduce the toxicity or side effects (Maghsoodi, 2009; Kumari et al., 2010; Merisko-Liversidge and Liversidge, 2008). As a special type of nano DDS, nanofiber-based DDS should have significant potential in this area because their unique characteristics (diameter in the microscopic scale but length in the macroscopic scale) endow them with both the merits possessed by the DDS at the nanometer scale in altering the biopharmaceutical and pharmacokinetic properties of the drug molecule for favorable clinical outcomes, and also the advantages of conventional solid dosage forms such as easy processing, good drug stability, and ease of packaging and shipping (Yu et al., 2010c).

Non-steroidal anti-inflammatory drugs (NSAIDs) are globally the most widely used class of therapeutic drugs and are good candidates for the development of controlled release preparations, particularly through the oral route (Warner et al., 2006). The NSAID diclofenac sodium (DS) has potent anti-inflammatory, analgesic, and antipyretic properties, but also generates severe adverse effects with risks of toxicity, and nanoparticles of DS in Eudragit® L 100 have been reported to reduce these drawbacks (Sena et al., 2004; Cetin et al., 2010).

The present study describes the preparation by electrospinning of DS-loaded nanofibers using Eudragit® L 100-55 as the filament-forming matrix, aimed for oral colon-targeted delivery. The influence of solvents and drug loading on the formation of nanofibers, the physical state and interactions of components in the fibers, and the drug *in vitro* release profiles are described.

2. Experimental

2.1. Materials

Eudragit® L 100-55 (average molecular weight approximately 135,000) was supplied by Rohm GmbH&Co. KG (Darmstadt, Germany). Diclofenac sodium (DS) was purchased from Hubei Biocause Pharmaceutical Co., Ltd. (Hubei, China). Analytical grade N,N-dimethylacetamide (DMAc) and ethanol were purchased from the Sinopharm Chemical Reagent Co., Ltd. Water was distilled before use. All other chemicals and reagents were of analytical grade.

2.2. Preparation of spinning solutions

Four different spinning solutions of Eudragit® L 100-55 were prepared by dissolving 20 g Eudragit® L 100-55 in 100 mL methanol, ethanol, DMAc or a 5:1 (v/v) mixture of methanol:DMAc. The solutions were degassed with a SK5200H ultrasonator (350W, Shanghai Jinghong Instrument Co., Ltd. Shanghai, China) for 15 min before electrospinning.

Three different spinning solutions of DS and Eudragit® L 100-55 were prepared by first dissolving 2, 4, and 10 g DS into 100 mL of methanol:DMAc 5:1 (v/v), and then adding 20 g Eudragit® L 100-55. The drug content in fibers was 9.1%, 16.7%, and 33.3%, respectively. The solutions were degassed before electrospinning as described above.

2.3. Electrospinning process

The spinning solutions were loaded in 10 mL syringes. The feeding rate was controlled by a syringe pump (Cole-Pham®, USA) and was fixed at 1.0 mL/h. A high voltage supply (Shanghai Sute Electrical Co., Ltd., China) fixed at 10 kV was applied to the metallic needle (0.5 mm inner hole diameter), and a piece of aluminum foil was used to collect the ultrafine fibers with a horizontal distance of 12 cm from the needle tip. All electrospinning processes were carried out under ambient conditions (temperature $24 \pm 1\,^{\circ}C$, relative humidity $68 \pm 3\%$). The electrospun fibers were dried at 40 °C under vacuum (320 Pa) in a DZF-6050 Electric Vacuum Drying Oven (Shanghai Laboratory Instrument Work Co. Ltd., China) to facilitate the removal of residual organic solvents and moisture. The drug-loaded fibers in which the percentages of DS were 9.1%, 16.7%, and 33.3% were denoted F_1, F_2 and F_3, respectively. The Eudragit® L 100-55 fibers prepared from mixed solvent were denoted as F_0.

Physical mixtures (PM) of DS and Eudragit® L 100-55 with a drug-to-polymer ratio of 1:5 were prepared as controls by accurately weighing, pulverizing to pass through a mesh sieve (125 μm) and then thorough mixing using light trituration for 3 min in a mortar until a homogeneous mixture was obtained (Yu et al., 2009b).

2.4. Characterization

2.4.1. Morphology

The surface morphologies of electrospun fibers were assessed using a JSM-5600LV scanning electron microscope (SEM, Japan Electron Optics Laboratory Co. Ltd.). Prior to the examination, the samples were gold sputter-coated under argon to render them electrically conductive. The pictures were then taken at an excitation voltage of 15 kV. The average fiber diameter was determined by measuring diameters of fibers at over 100 points from SEM images using Image J software (National Institutes of Health, USA).

2.4.2. Physical state of the components in the drug-loaded fibers

Differential scanning calorimetry (DSC) analyses were carried out using an MDSC 2910 differential scanning calorimeter (TA Instruments Co., USA). Sealed samples were heated at 10 °C/min from 20 to 160 °C. The nitrogen gas flow rate was 40 mL/min.

Wide-angle X-ray diffraction analyses (XRD) were obtained on a D/Max-BR diffractometer (RigaKu, Japan) with Cu Kα radiation in the 2θ range of 5–60° at 40 mV and 300 mA.

2.4.3. Compability between the components of drug-loaded fibers

Fourier transformed infrared spectroscopy (FTIR) was conducted using a Nicolet-Nexus 670 FTIR spectrometer (Nicolet Instrument Corporation, Madison, USA). The samples were prepared using the KBr disk method (2 mg sample in 200 mg KBr) and the scanning range was 500–4000 cm^{-1} with a resolution of 2 cm^{-1}.

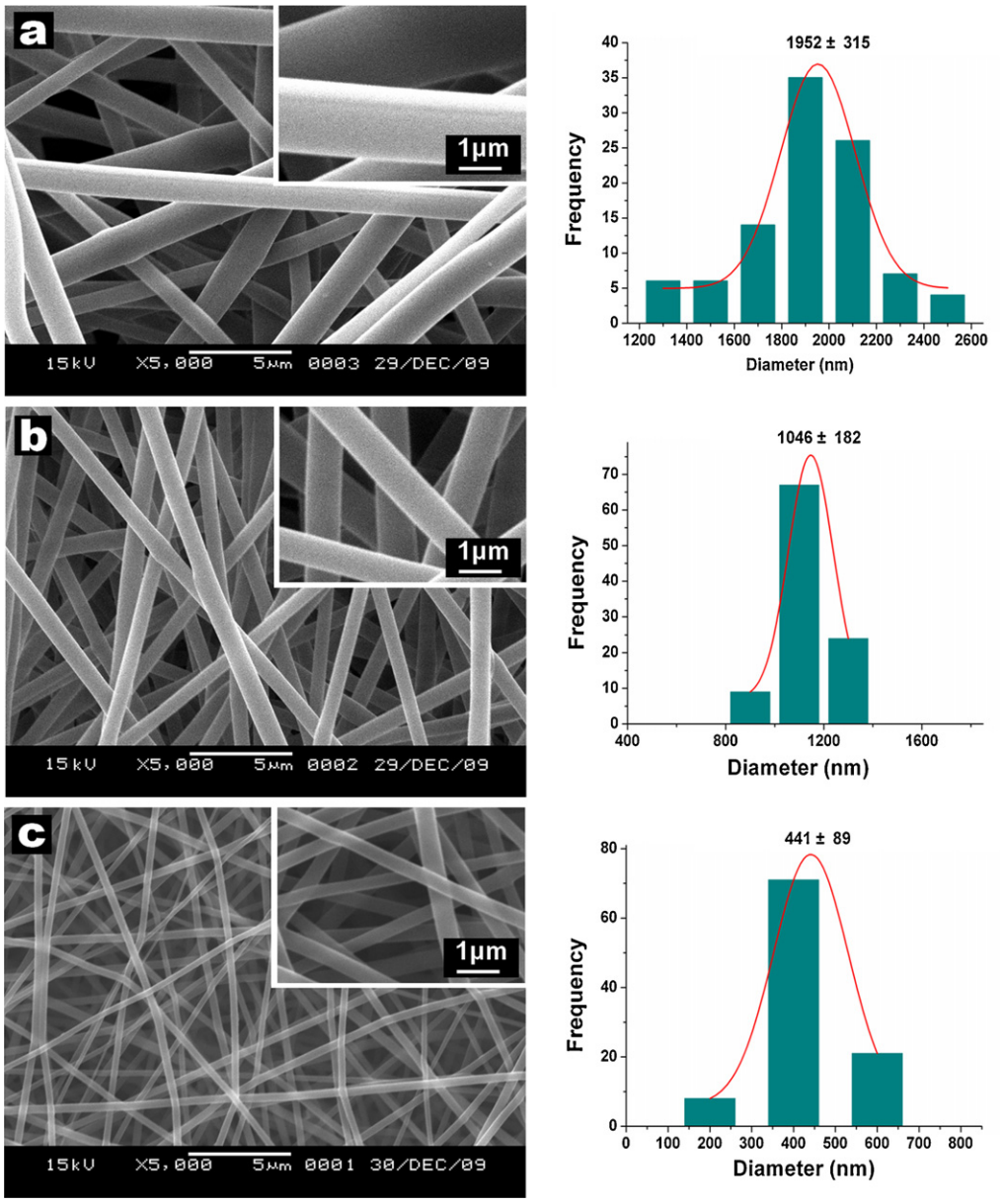

Fig. 1. SEM images of Eudragit® L 100-55 fibers prepared at a concentration of 20% (w/v) in solvents: (a) methanol, (b) ethanol and (c) ethanol:DMAc with a volume ratio of 5:1. The inset in each picture is an SEM image of the same fibers taken at a magnification of 10,000. The graphs on the right of each panel show the distribution of fiber diameters measured from each SEM image.

2.5. In vitro drug dissolution tests

The *in vitro* dissolution of DS-loaded fiber and PM was performed according to the Chinese Pharmacopoeia (2005 Edn.) by a paddle method using a RCZ-8A dissolution apparatus (Tianjin University Radio Factory, China). All experiments were conducted at 37 °C and 50 rpm in 900 mL 0.1 N HCl for 2 h, followed by 8 h in 900 mL of phosphate buffer (PBS, pH 6.8, 0.1 mol/L). At predetermined time intervals, aliquots of 5 mL were withdrawn for sampling and replaced by an equal volume of PBS to maintain a constant volume. After filtration through a membrane (0.45 μm), the sample solutions were analysed at a wavelength of 276 nm by a UV spectrophotometer (Unico Instrument Co. Ltd., Shanghai, China). The amount of DS present in the sample was calculated using a calibration curve constructed from reference standards (Chinese Pharmacopeia 2005 Edn.). DS dissolved at specified time periods was plotted as percentage released versus time. All measurements were conducted in triplicate and results are reported as average values.

3. Results and discussion

3.1. Preparations of drug-loaded nanofibers

Suitable selection of solvent is one of the most important factors for successful preparation of electrospun polymer nanofibers (Moghe and Gupta, 2008; Qi et al., 2010; Liu et al., 2010), and for preparation of drug-loaded nanofibers. The solvent should be able to dissolve the drug easily as well as maintaining electrospinnability of polymer solutions. Eudragit® L 100-55 could be electrospun into fibers when methanol or ethanol was used as the solvent and both of them can dissolve DS. However, the prepared electrospun fibers always had a relatively large diameter (>1 μm), non-uniform structure and an unsmooth surface due to the high vapor pres-

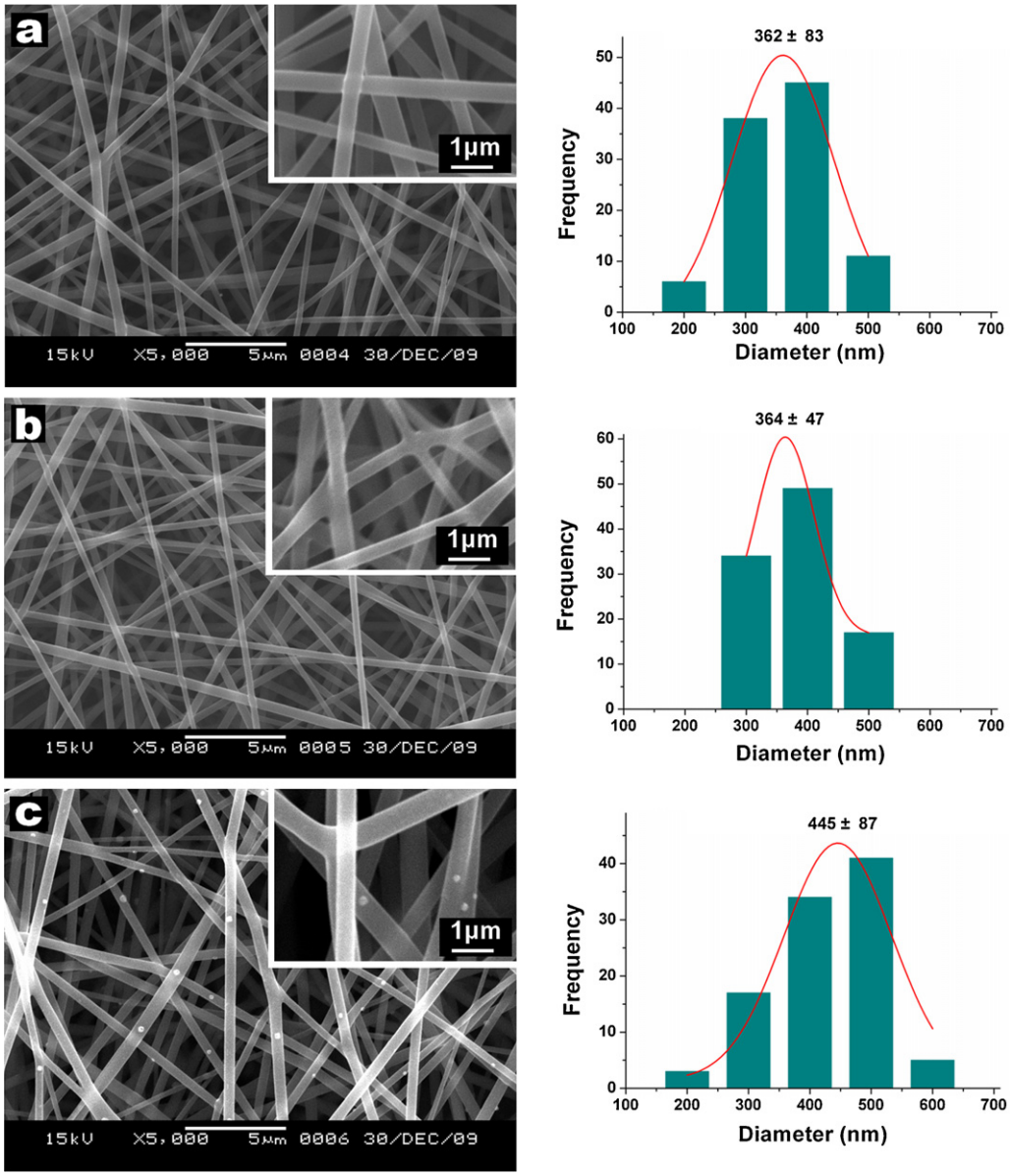

Fig. 2. SEM images of DS-loaded Eudragit® L 100-55nanofibers with varying drug content: (a) F_1 – 9.1%, (b) F_2 – 16.7% and (c) F_3 – 33.3% (w/w) respectively. The inset in each picture is an SEM image of the same fibers taken at a magnification of 10,000. The graphs on the right of each panel show the distribution of fiber diameters measured from each SEM image.

sure of ethanol and methanol (Pornsopone et al., 2005). Thus in the present study, the use of DMAc as a solvent was investigated, due to its high boiling point (166 °C) and its ability to dissolve DS to a high concentration.

All the Eudragit® L 100-55 solutions in methanol, ethanol, DMAc and a mixture of ethanol and DMAc are transparent. The Eudragit® L 100-55 solutions in DMAc were unspinnable. Only discrete droplets were observed when they were subjected to the electrospinning process. Fig. 1a–c shows SEM images of Eudragit® L 100-55 fibers prepared from methanol, ethanol and 5:1 (v/v) ethanol:DMAc, respectively. Eudragit® L 100-55 fibers prepared from ethanol have an average diameter of 1046 nm, smaller than that of fibers prepared from methanol, 1952 nm. Occasionally, the spinneret was clogged during the electrospinning process due to fast evaporation of ethanol/methanol. The skin-like clump that forms must be removed manually for a continuous process.

However, when a mixture of ethanol and DMAc was used as the polymer solvent, the electrospinning process always proceeded un-interrupted. The presence of the high boiling point DMAc in the solution favors the formation of a stable Taylor cone and prevents the gel-forming on the jet surface, effectively preventing the spinneret from clogging, which has noted elsewhere (Moghe and Gupta, 2008).

The average diameter of Eudragit® L 100-55 fibers from a 5:1 (v/v) ethanol:DMAc mixture was sharply decreased compared with ethanol alone, to only 441 nm. The slower evaporation of DMAc would keep the jet in a fluid state for a longer time and allow it to be subjected to a longer drawing time under the electrical field in the instability region, and thus in turn results in thinner nanofibers.

Based on the above results, a 5:1 (v/v) ethanol:DMAc mixture was used as the solvent for preparing drug-loaded Eudragit® L 100-55 nanofibers. Drug-loading capability is an important parameter for evaluating drug-loaded nanofibers, since high drug-loading often has a negative influence on the nanofiber morphology and the state of the drug in the fibers.

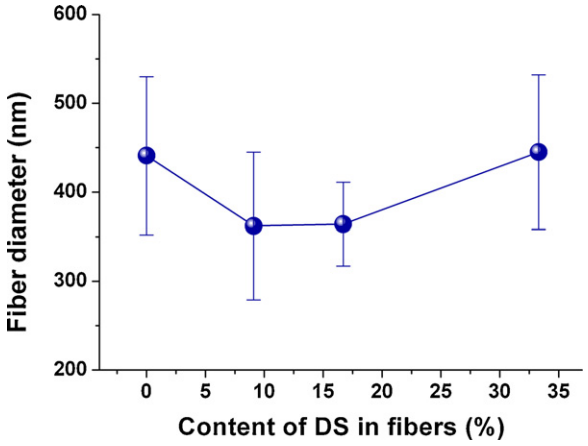

Fig. 3. The relationship between fiber diameter and drug content. Data are the mean ± SD of 100 diameter measurements.

Fig. 2a–c shows SEM images of drug-loaded Eudragit® L 100-55 nanofibers with a content of DS at 9.1% (F_1), 16.7% (F_2) and 33.3% (F_3) (w/v), respectively. F_1 and F_2 have almost the same average diameter, and are smaller than F_0 (Fig. 1c). DS is a diclofenac salt and can increase the solution conductivity and thereby enhance the electrical drawing effects on the jet fluid. However, when the drug loading was further increased, not only did the fiber diameter increase (Fig. 2c), but also the smooth surface of the fibers was lost, with some particles separated out on them. As the concentration of DS increased, the solution viscosity also increased, and this counteracted the influence of conductivity increases, and gradually had a greater influence on nanofiber diameter compared to electrical forces. The relationship between fiber diameter and drug content is shown in Fig. 3.

3.2. Physical state of components in the nanofibers

The physical state of the drug in the fibers is important for achieving the desired drug release profiles. In the present study, DSC and XRD analysis was undertaken to determine the physical status of the components of the composite nanofibers.

DSC thermograms are shown in Fig. 4. The DSC curve of pure DS exhibited a single endothermic response corresponding to a melting point of 289 °C (Fig. 4a). The F_0 composed of pure Eudragit® L 100-55 exhibited a broad endotherm ranging from 170 to 230 °C due to the glass transition (T_g), suggesting that the Eudragit®

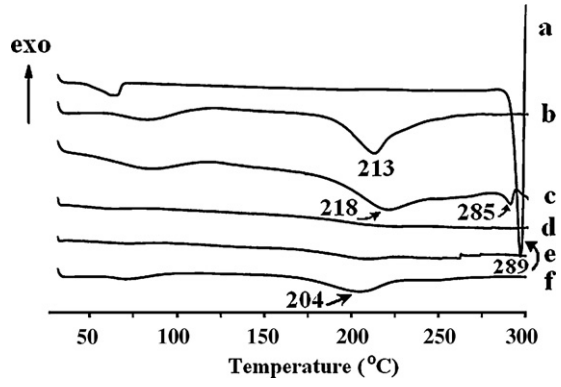

Fig. 4. DSC thermograms of drug and polymer preparations: (a) DS – diclofenac sodium, (b) F_0 – nanofibers with no DS, (c) PM – physical mixture of DS and Eudragit® L 100-55, (d) F_1, (e) F_2, (f) F_3 nanofibers with 9.1%, 16.7%, and 33.3% (w/v) DS, respectively.

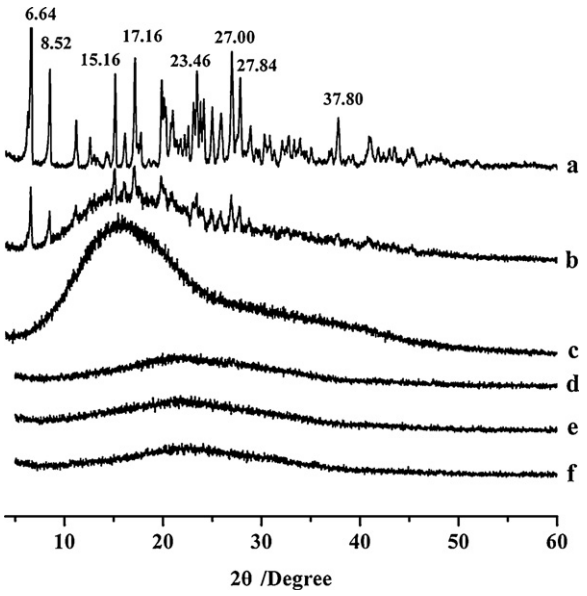

Fig. 5. X-ray diffraction patterns of drug and polymer preparations: (a) DS – diclofenac sodium, (b) F_0 – nanofibers with no DS, (c) PM – physical mixture of DS and Eudragit® L 100-55, (d) F_1, (e) F_2, (f) F_3 nanofibers with 9.1%, 16.7%, and 33.3% (w/v) DS, respectively.

L 100-55 is an amorphous material (Fig. 4b). For the PM, there were two clear phase transitions, as shown in Fig. 4c. The first one at 218 °C corresponded to the glass transition temperature of Eudragit® L 100-55, and the second one at 285 °C can be attributed to melting of DS. The lowering of the melting point of DS may be caused by the presence of the Eudragit® L 100-55 that resulted in a loss of the crystalline content of DS. The DS-loaded Eudragit® L 100-55 fibers did not show any DS melting points (Fig. 4d–f), suggesting that all the DS present in the composite nanofibers was in an amorphous state, having lost its original crystalline state. In addition, the curve of F_3 showed a broad endotherm ranging from 150 to 220 °C with the peak of T_g lower than that of pure Eudragit® L 100-55, which should result from a plasticizing effect of DS. The structural similarities of NSAIDs make them good plasticizers of the polymer matrix (Kaushal et al., 2004; Yu et al., 2009b).

The presence of numerous distinct peaks in the XRD patterns of the fibers indicated that DS was present as crystalline material with characteristic diffraction peaks (Fig. 5a). Eudragit® L 100-55 exhibits only a hump characteristic of amorphous forms (Fig. 5c). The PM XRD pattern shown in Fig. 5b has all the characteristic diffraction peaks of raw DS particles, albeit with decreased intensity, indicating that DS is present in the PM in a crystalline state. In contrast there are no peaks of crystalline DS detectable in the XRD patterns of the three DS-loaded Eudragit® L 100-55 nanofibers (Fig. 5d–f), indicating that all the DS loaded in the fibers was no longer present as crystalline material, but had been totally converted into an amorphous state.

The XRD results concurred with the findings from DSC, similarly demonstrating that DS molecules were highly distributed in the Eudragit® L 100-55 nanofiber matrix and were present in a complex manner in which the original structure of the pure, crystalline material was lost. Although particles separated from the nanofibers were visible in the SEM images (Fig. 2c), the DSC and XRD results suggested that the components of separated particles are also in an amorphous form, but the compositions of the particles may be different compared with the composition within the bulk of the nanofibers.

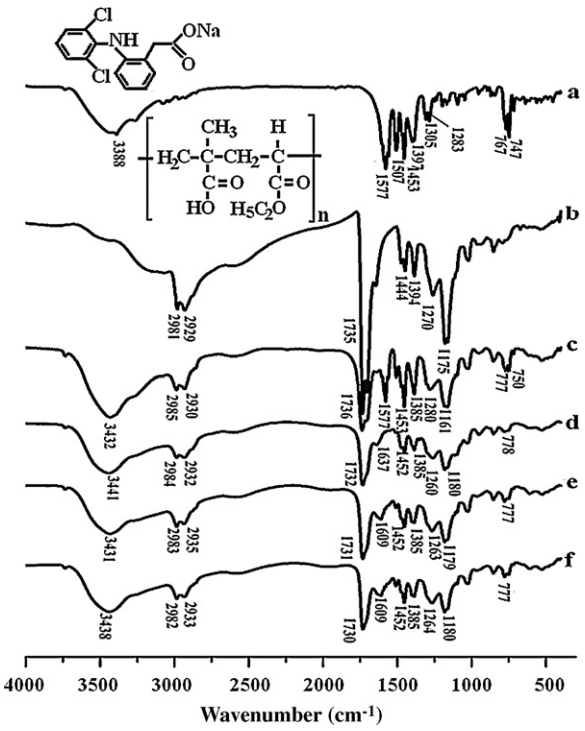

Fig. 6. FTIR spectra of drug and polymer preparations: (a) DS – diclofenac sodium, (b) F_0 – nanofibers with no DS, (c) PM – physical mixture of DS and Eudragit® L 100-55, (d) F_1, (e) F_2, (f) F_3 nanofibers with 9.1%, 16.7%, and 33.3% (w/v) DS, respectively.

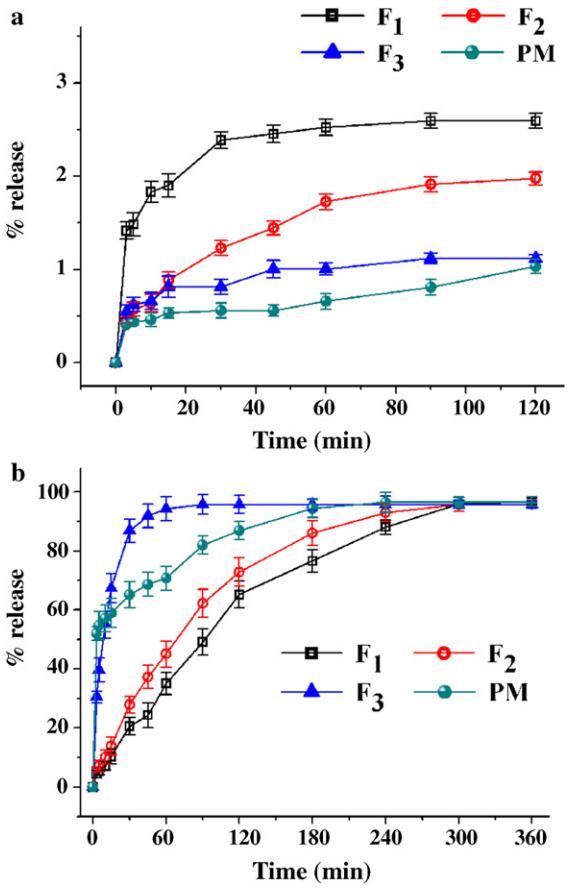

Fig. 7. *In vitro* dissolution profiles of drug-loaded nanofibers (F_1–F_3) and a physical mixture of DS and Eudragit® L 100-55 (PM) in different media. Drug release in: (a) 0.1 N HCl and (b) pH 6.8 PBS. Data are the mean ± SD of three measurements.

3.3. Compatibility of nanofiber components

The compatibility of components is important both for the formation of nanofibers during the electrospinning process and for the stability of the composite nanofibers, which may otherwise be prone to solid phase separation. Often secondary interactions such as hydrogen bonding, hydrophobic interactions, and electrostatic forces increase the compatibility of the components in the fibers (Chen et al., 2008; Yu et al., 2010b). We probed secondary interactions of the different components and composites using IR spectroscopy, shown in Fig. 6. The spectrum of DS has bands characteristic of secondary amine groups (N–H stretch vibration) at 3388 cm^{-1}, and phenyl groups (C=C stretch vibration) at 1577 cm^{-1} and substituted phenyl group stretch at 748 cm^{-1} (Fig. 6a) (Sagar and Pradeep, 2009). The spectrum of Eudragit® L 100-55 has a broad band characteristic of hydroxyl groups (O–H stretch vibration) in the range of 3400–2200 cm^{-1}, characteristic bands of methyl and methylene (C–H stretch vibration) at 2981 cm^{-1}, 2929 cm^{-1}, a strong band due to carbonyl groups (C=O stretch vibration) at 1735 cm^{-1} and two bands due to ester linkages (C–O stretch vibration) at 1270 cm^{-1} and 1175 cm^{-1} (Fig. 6b).

The spectrum of the PM appears to be an overlap of that of DS and Eudragit® L 100-55, with all the characteristic bands of DS and Eudragit® L 100-55 still distinct (Fig. 6c). This indicates few interactions occur between the two components when mixed physically. In contrast, there are significant changes in the spectra of the three drug-loaded composite nanofibers (Fig. 6d–f), including (1) the disappearance of the characteristic peaks of the phenyl group (C=C stretch vibration) at 1577 cm^{-1}, and of the substituted phenyl group stretch at 748 cm^{-1}; (2) the characteristic peaks of the carbonyl groups (C=O stretch vibration) at 1735 cm^{-1} have shifted to 1732, 1731 and 1730 cm^{-1} for F_1, F_2, and F_3, respectively. All these changes can be attributed to hydrogen bonding between DS and Eudragit® L 100-55, including (1) between C=O of DS and O–H of Eudragit® L 100-55, and (2) between the C=O of Eudragit® L 100-55 and the N–H of DS. The latter hydrogen bondings disrupt the p–π conjugation in the DS molecules generated between the aromatic ring and secondary amino group which has an isolated electron pair at the N atom, and thus accounts for the disappearance of characteristic peaks of DS in the drug-loaded nanofibers. The interactions between the DS and Eudragit® L 100-55 may promote them to mix at a molecular level in the nanofibers, reflecting the good compatibility between them and would favor the stability of the composite nanofibers to avoid solid phase separations.

Additionally, because (1) numerous researches have demonstrated that the active ingredients (even sensitive biomedical API such as pharmaceutical proteins) undergo the electrospinning process without any change of their structural integrity or any loss of their effectiveness as an active pharmaceutical agent (Chew et al., 2005; Li et al., 2008; Maretschek et al., 2008; Chen and Yu, 2010); (2) The filament-forming matrix Eudragit L100 is a common excipient for drug delivery in pharmaceutics presently, it can be assumed that the model drug DS used in the present should retain its stability during the electrospinning process.

3.4. In vitro drug dissolution tests

To evaluate DS release profiles from the drug-loaded nanofibers, *in vitro* dissolution tests were carried out under acidic conditions in 0.1 N HCl for 2 h and subsequently at pH 6.8 in PBS for 6 h, to mimic gastrointestinal conditions. PM of DS and Eudragit® L 100-55 with a weight ratio of 1:5 was also used as a control.

The drug release profiles of PM and composite nanofibers in the two different dissolution media are shown in Fig. 7. In 0.1 N HCl the

in vitro drug release rates were very slow, with no more than 3% of the loaded drug released from all the samples in 2 h (Fig. 7a). All the nanofibers exhibited a bigger drug release rate than that of PM, in the order $F_1 > F_2 > F_3$ (Fig. 7a). That the PM gave the smallest release rate was mainly due to DS being present in the PM in a crystalline physical state and which has very poor solubility in acid conditions. In the nanofibers, all the DS is present in an amorphous state, such that no high lattice energies need to be overcome for dissolution, and thus in turn resulted in a relatively larger release rate. However, because Eudragit® L 100-55 is insoluble in an acid environment, it should prevent dissolution of DS. The small release of drugs from the fibers may reflect the drug content present on the drug-loaded nanofiber surface.

At a pH of 6.8, PM showed the fastest dissolution rate, due to the solubility of DS at neutral pH. The drug-loaded nanofibers exhibited a more sustained drug release profile. The release rates of DS follow the order: PM> $F_3 > F_2 > F_1$, which, for release from nanofibers, reflects the content of DS. Although Eudragit® L 100-55 is soluble in media of pH higher than 5.5 (Sauera et al., 2009), the dissolution process always takes relatively longer because polymer dissolution usually involves the processes of absorption of water, swelling, and disentanglement, before release of free drug into the media. Accordingly, the greater percentage of Eudragit® L 100-55 in the fibers, the longer the time taken for release of DS (Fig. 7b).

The mechanism of release of drug from composite nanofibers in PBS can be characterized by analysis of the dissolution data using the Peppas equation (Peppas, 1985) $Q = kt^n$, where Q is the percentage of drug released at time t, k is a kinetic constant and n is the diffusional exponent indicative of the release mechanism.

The diffusion index n was 0.7323, 0.6688 and 0.4787 for F_1, F_2, and F_3, respectively. When the value of n is between the ranges of 0.5–1, a Fick diffusion mechanism does not determine the rate of drug release. Drug release from F_1 and F_2 was likely controlled by a combination of diffusion and erosion mechanisms. The n value for F_3 indicates that rate of drug release was determined by a Fick diffusion mechanism. Since DS is soluble in neutral media, channels would develop during the dissolution process along the nanofibers from the surface to the inside of the fiber. The high content of DS in F_3 would result in a sufficient number of channels to allow most of the DS to be released by diffusion before complete erosion of the Eudragit® L 100-55 matrix.

4. Conclusions

Eudragit® L 100-55 nanofibers containing diclofenac sodium have been successfully prepared by electrospinning DS solutions in a 5:1 (v/v) mixture of ethanol and DMAc. Fibers with DS content up to 33% (w/w) were prepared and in all cases DS and Eudragit® L 100-55 were integrated at the molecular level. SEM analysis showed that particles separated out on the nanofibers surface only when the DS content reached 33.3%. Nevertheless, DS in all the composite nanofibers was present in an amorphous state, as confirmed by the DSC and XRD analysis. FTIR spectra suggested that DS and Eudragit® L 100-55 have good compatibility due to hydrogen bonding between them. *In vitro* dissolution tests verified that all the drug-loaded Eudragit® L 100-55 nanofibers had a pH-dependent drug release profile, and nanofibers with a suitable DS content have a sustained drug release profile in neutral media, controlled by both diffusion and erosion mechanisms. The drug-loaded Eudragit® L 100-55 nanofibers described here therefore have the potential to be developed as an oral, colon-targeted DDS.

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