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Synthesis and characterization of bio-composite nanofiber for controlled drug release

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ABSTRACT

In the present study, nanofiber mats of polyvinyl alcohol (PVA), polyvinyl acetate (PVAc) and 1:1 (w/w) PVA & PVAc (multi-component composite) have been developed and evaluated for the sustained release of broad spectrum antibacterial drug 'ciprofloxacin HCl'. These nanofiber mats were developed through electrospinning the solutions of these non-toxic and biocompatible polymers (i.e. Drug PVA and PVAc) individually, as well as in 1:1 (w/w) mixed condition (i.e. composite). Prior to the electrospinning (about 1.5 h), 5%, 10% and 15% w/w ciprofloxacin HCl (CipHCl) was also homogeneously mixed in these polymer solutions. Results indicate that the average diameter of PVA, PVAc and multiple-component composite (PVA/PVAc) fibers without drug loading was 59.5, 93.3 and 183.7 nm, respectively. Moreover, the average diameter for drug multiple-component composite (1:1) fibers with increasing drug concentration (i.e. 5%, 10% and 15%) was 171, 163.5 and 162.4 nm, respectively. XRD analysis of these nanofiber mats showed higher surface property, which is indicated by only weak signals for the characteristic peaks with increasing drug concentration. For 5% CipHCl loading, the drug released from drug-multiple-component composite was intermediate (~29%) as compared to PVA (~50%) and PVAc (~13%). However, the drug multiple-component composite mats exhibited the property of extended drug release for 10 days as compared to complete drug release of 6 days in case of both drug PVA and PVAc nanofiber mats. It indicates that the addition of PVAc promotes the sustained release of drug via its enhanced water stability, and reduced fiber swelling and initial burst of drug release.

1. Introduction

Wound dressing materials play an important role in optimal wound healing and cosmetic appearance of the healed wound. It is particularly important in case of burns, split skin graft donor sites, sores, and diabetic ulcers which require long healing time [1]. In such chronic conditions, applications of anti-microbial drug directly on the wound sites for longer duration are chosen over systemic administration [2,3]. Optimal wound healing takes place due to selective targeting, improved drug availability, decreased frequency of dressing, minimal tissue damage and decreased possibility of development of bacterial resistance along with patients comfort [4,5]. The selection of drug carrier material plays a very crucial role in the wound healing. The drug carrier materials must have oxygen permeability for tissue respiration and excellent swelling capacity to absorb the exudates from the wound sites [3,4]. Films, sponges and foams are widely used in this context since long time [5–7]. In recent times, nanofiber-based mats developed from electrospinning are emerging as novel wound dressing materials [4,12], which act as vehicle for the drug delivery to wound sites. Moreover, methods such as bubble electrospinning and bubbfil spinning [8,9] are being used for bulk nanofiber production. However, limited information is available in the literature on the controlled delivery of drugs from such polymeric nanofiber dressing materials

The use of electrospun nanofiber mats have found their potential applications in a wide variety of fields [10,11], such as energy, environment, wound dressings [12], tissue engineering [13] and drug delivery [15,16] etc. Their use as wound dressing materials has many benefits. It includes their semi-permeability for cell respiration, better conformation to exposed tissue surface for scarless healing, absorbability and maintaining homeostasis with tissue fluid [14]. Many such nanofiber polymers are being used in the field of medicine in recent times. One commonly used non toxic, biocompatible and non-carcinogenic natural polymer having excellent mechanical properties [1,5] is polyvinyl alcohol (PVA). It has been successfully employed in soft

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contact lenses, artificial organs, cartilage skin and cardiovascular devices [17]. Another polymer having wide application in the field of medicine is polyvinyl acetate (PVAc) due to its good biocompatibility with blood, body fluids and tissues. It contains acetate functional group which is common in metabolites of biological system [18].

The two frequent bacterial species causing wound infection are *Staphylococcus* sp. (Gram positive) and *Pseudomonas* sp. (Gram negative). Anti-microbial agents are used against these microbes during would healing, which have variable spectrum of the targeted microbes. For example, narrow range antimicrobial drugs are effective against few selected bacterial species, whereas broad range antimicrobial agents effectively kill many pathogenic bacteria species. The broad range antibiotics ciprofloxacin (having low minimum inhibitory concentration) loaded with the nanofiber mats have been widely studied against *Staphylococcus* and *Pseudomonas* infections in would heal studies. However, ciprofloxacin release from the multiple-component composite nanofiber (PVA & PVAc composite) mats has not been studied. Therefore, ciprofloxacin release from multiple-component composite nanofiber mats in synthetic phosphate buffer saline (pH 7.4) has been evaluated in the present study for its effectiveness in sustained drug release.

2. Experimental details

The general steps involved in the synthesis of nanofiber mats with ciprofloxacin drug in 3 polymers namely, PVA, PVAc and multiple-component composite using electrospinning method is depicted in the flow diagram (Fig. 1)

2.1. Electrospinning equipment

Electrospinning system consisted of a 40 kV high voltage power supply (Model AYRA N801, Goldstar, New Delhi, India), a syringe pump (model NE300, New Era Pumps, USA), a metallic needle and an electrically conductive collector plate [20].

2.2. Polymers and drug

PVA (MW = 70000, Da 98% hydrolyzed, Sigma Aldrich), polyvinyl acetate (MW = 50,000 Da) and drug Ciprofloxacin HCl (CipHCl) were purchased from Alfa Aesar (India). Analytical reagent (AR) grade chemicals and solvents were used wherever required.

2.3. Synthesis of pure and drug-loaded nanofiber

PVA (0.6 g) was suspended in 10 ml of 1:1 acetic acid: double distil water and stirred at 60 °C for 30 min till the formation of a homogeneous solution [19]. Similarly, 1.6 g PVAc was dissolved (alcohol and acetic acid) in a different flask and stirred for 17 h at room temperature. Further, these two polymer solutions were mixed in 1:1 (v/v) ratio for preparing the multiple-component composite nanofibers. Further, the drug CipHCl (5%, 10% and 15% w/v ratio) was added to these polymer solutions (i.e. PVA, PVAc and multiple component composite) and mixed homogenously using magnetic stirrer for 1.5 h before electrospinning. The electrospinning was done using 22 gauge needle with a flow rate of 0.8 ml/h. Moreover, the needle tip was kept at a distance of 15 cm from the collector plate, and 18 kV voltage was maintained between the needle tip and the collector plate. Full details of the electrospinning set up are discussed in the literature [20,21].

2.4. Degree of swelling and percentage weight-loss

Degree of swelling and weight loss (%) of nanofiber mats was determined in the release medium phosphate buffer saline (PBS) at 37 °C. Nanofiber mat of initial mass M_i was submerged in the release medium. The weights [M] of the swollen mats were measured at time intervals of 1, 4, and 24 h after gentle pat drying with the help of filter paper denoted by M [19]. These pat dried swollen mats were subjected to vacuum drying at 40° till constant weight (M_d) is reached. Degree of swelling and% weight loss are calculated using Eqs. (1) and (2).

$$\text{Degree of swelling}(\%) = \frac{(M - M_d)}{M_d} \times 100 \quad (1)$$

$$\text{Weight Loss}(\%) = \frac{(M_i - M_d)}{M_i} \times 100 \quad (2)$$

2.5. Drug release from nanofiber-mat

Ciprofloxacin HCl loaded electrospun nanofiber mat of 6 cm^2 was immersed in flasks having 20 ml PBS of pH 7.4 at 35 °C. The drug

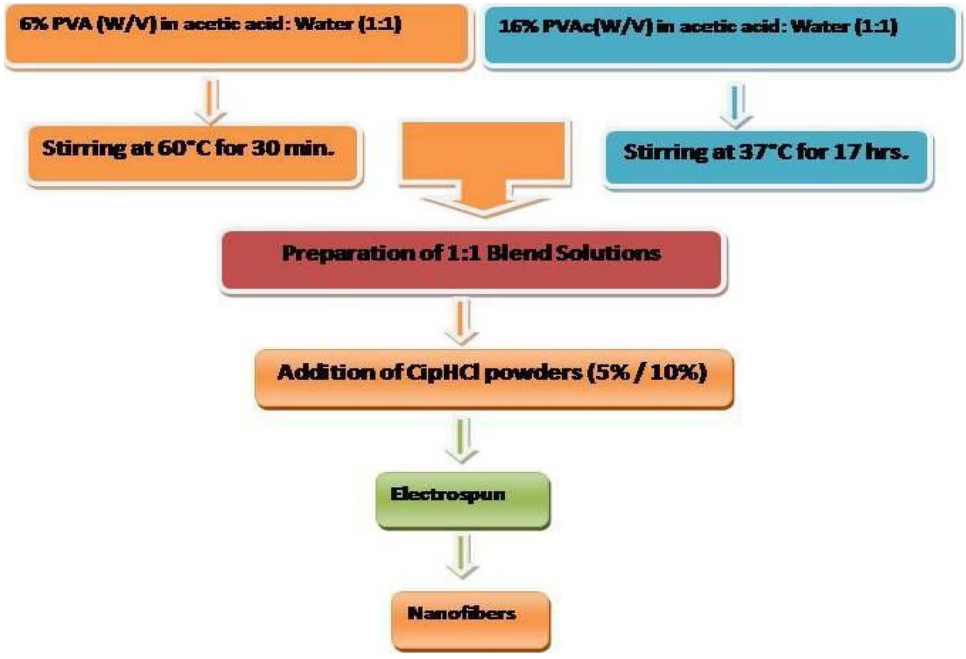

Fig. 1. Flow-sheet for synthesis of PVA/PVAc nanofiber mats.