Studies on Development and Characterization of Biomaterials for Drug Delivery

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Abstract. Although there are many methods used for synthesis nanofibers such as drawing, template Synthesis, phase separation, self assembly, and electro spinning. In these techniques, electrospinning is a manifold method to move polymers into continuous fibers with diameters within range of a few micrometers to a few nanometers. Poly Vinyl Alcohol (PVA) is a popular hydrogel polymers. Because of its good water permeability, biocompatibility, non-toxicity and specially electro spinnability it is easily sustained release of the transdermal drug delivery. The nanoparticle was prepared to reduce hypertension using Residronate sodium drug incorporated to PVA. The Electrospinning method was used PVA solution mixed with Residronate sodium to form the drug loaded electro spun PVA nanofibers. These nano fibers was characterized by Scanning electron microscopy (SEM), UV-Visible spectroscopy analysis, Fourier transform infrared spectroscopy (FT-IR), X-ray diffraction method (XRD), and Thermo gravimetric analysis (TGA). In vitro drug release at different time interval and different pH was analysed using acetate buffer method.

Keywords: Poly vinyl alcohol, Nanofibres, Electrospinning. Transdermal drug delivery. Residronate sodium.

1. Introduction
The goal of drug delivery is to attain a controlled release of pharmaceutical compounds to specific target tissues. Precise delivery of the drug is necessary to maximize the therapeutic effect of the drug while simultaneously minimizing the undesirable side effects [1]. Many excellent researchers reported that the advanced aspects of polymeric controlled release [2]. Electrospinning is a technique to develop nano fibers of polymer or polymer composite substances from respective solutions or melt. In the electrospinning procedure a high degree of voltage is taken to develop an electrically charged jet of polymer solution or melt. Advances in the polymer science have led to many new drug delivery systems being developed. Considering about proper surface and bulk characteristics may assist in structure of polymers for different applications for drug delivery[16-20]. Biodegradable polymers are commonly used in the production of drugs, since they may be reduced to non-toxic monomers within the body[15-17]. The evaluation of biomedical polymers is a crucial move in defining and proving the applicability and protection of products [18]. ISO10993 in Europe and Food Drug Administration (FDA) blue book memorandum G95-1 in the United States regulates the biodegradable evaluation of medical equipments in terms of processes defining and modifying the biological hazards that occurs with biomedical materials. [6]
Hydrogels are polymeric substances that do not mix in water at physiological temperature and pH, but do swell well in an aqueous medium and are commonly considered as drug and protein produce carriers due to their fine tissue stability, easy changes under swelling conditions, and solute permeability [10, 11]. Poly (vinyl alcohol) (PVA) is one of the most common Hydrogel polymers. PVA is a semi-crystalline, hydrophilic polymer with good thermal and chemical stability [19–21]. Its biocompatibility, non-toxicity, good water permeability and, in particular, excellent electrospinnability make PVA interesting here. In recent years, several researchers have been investigating different conditions influencing the morphology of electro spun PVA fibres, e.g. concentration and flow rate of solution, hydrolysis degree, applied electrical potential, collection size, ionic salt addition, PVA molecular weight, and pH [13]. And investigating the purpose of electrospun PVA fibers to carry a TDDS is quite important. A TDDS has tremendous potential to prevent first-pass metabolism of the hepatic, sustain stable blood rates for a longer time, decrease side effects and increase compliance. Hydrates are especially important in pharmaceutics, since water is popular in manufacturing. An active pharmaceutical ingredient can undergo phase changes in the solid state, including water being incorporated into or released from the molecule. [22].

Residronate sodium (RS) is a drug without steroid used to get relief from pain for hypertension diseases. RS is freely soluble in water and also it has high dissolution and stain permeability. So, it was beneficial to develop mats of electro spun PVA nanofibers that carries the drug delivery of RS. Development and synthesis of new polymer compositions will extend the reach of future new drug delivery systems. In this experiment, mats of PVA of nanofibers were made by Electrospinning and such electro spun fiber mats have been taken as drugs carrier for a TDDS. The purpose of this experiment is to synthesis and characterization of Residronate sodium drug attached on PVA. This study is also includes the drug releasing efficiency using acetate buffer in vitro studies [23-25].

2. Materials and Methods

Merck Chemicals (India) supplied polyvinyl alcohol (PVA; white powder; degree of polymerisation = 1600 and degree of hydrolysis = 97.5-99.5 mol percent). All other chemicals were used analytical grade.

2.1. Preparation of neat and RS-loaded PVA fiber mats and films

A measured volume of PVA powder was dissolved at 80 0C for 3 h in distilled water to make a PVA solution at a constant concentration of (10 per cent) 1gm at 10 ml as soon as the solution reached room temperature. One type of drug was mixed into the PVA solution under fixed stirring for 4 h. On the basis of dry weight of PVA [%wt] was mixed in to PVA solution. The electro-spinning of the made solutions was accomplished by joining a positive polarity removing electrode from a power supply with high voltage DC. For the solutions put in a standard 2 ml syringe, the syringe nozzle 0.5mm thickness. The electro-spinning of the formed solutions was accomplished by joining a positive polarity removing electrode from a high-voltage DC power supply.

2.2. Drug content analysis

The drug loaded electrospun mat was taken in square disc about 2x2cm² squares. 4ml of dimethylsulfoxide (DMSO) was taken and dissolved the drug mat. Then, 0.5ml of the solution was pipette and mixed into 8ml of acetate buffer solution [14]. At wavelengths of 262 nm this wavelength corresponds to the average wavelength for drug, the drug solution was tested for quantity of drug taking a UV-Visible spectrometer.

2.3. Drug release in various pH

Acetate buffer 20ml was taken in three different beakers adjusted the pH (3.5, 5.5 and 7.4). Solution from the each beaker was taken in separate Petri dish kept in incubator at 37°C. After those 22 hours & 81 hours & 94 hours were taken in UV-spectrometer for different pH figures land 2 and 3 show the residronate sodium release profiles from electrospun mat and polymer films.
2.4. Morphology study

A high resolution scanning electron microscope (HRSEM) from these pictures observed the morphological presence of both the neat and the RS-loaded as-spun PVA fiber mats selected and were sputtered or coated with gold and micro to nano structure. To observe the orientation pattern of the fibers and to see the surface of the individual fibers using the software section based on the SEM images. A thermo gravimetric analysis was taken to examine thermal quality of drug, the electro spun PVA mats, as well as the RS-loaded as-spun PVA mats (10% wt). The TGA analysis (equilibrated with an indium standard, the specimen weighed 1.37mg) was found while heating from 0 to 700°C at a rate of 20°C min⁻¹. Fourier transform infrared studies have established the functional groups using a BRUKER 66V FT-IR spectrometer within 4000-400cm⁻¹ range. Mixed samples with KBr spectroscopy and placed into disks.

3. Result and Discussions

3.1. Morphology of neat and drug-loaded as spun PVA mats

The 10% weight by volume of PVA solution was prepared with distilled water and known quantity of RS drug was added. Then this mixture was subjected to electrospinning under 22 kW power at a collection distance of 22 cm and system was runned for 2 hrs. The morphological structure of PVA-drug mat was presented in Fig. 1. The SEM picture 10,000 magnification of the spurned PVA fibers clearly showing cross section ally rounded fibers with smooth surface. The maximum fiber diameter was approximately 130 nm. On the basis of the quality of spun fibers was found, 10% w/v PVA solution was taken as basic solution; in to that the single drug was added. This solution was later electro spun, and selected SEM images of the drug-loaded as-spun PVA fibers are shown below. The maximum diameter of such fibers was about 283 nm as calculated.

Figure 1. SEM analysis of Residronate sodium drug with 10% w/y of PVA solutions.

3.2. FTIR spectrum of pure PVA

It obviously shows that most of the peaks associated with poly (vinyl alcohol) fig. 2 shown that For example, it could be seen C-H broad alkyl stretching band (n = 2852.9-2921.0 cm⁻¹) and typical strong hydroxyl bands for free alcohol (nonbonded -OH stretching band at n = 3350.8 cm⁻¹), and hydrogen bonded band (n = 3787.1cm⁻¹). Because of strong hydrophilic forces intermolecular and intermolecular hydrogen bonding is expected to occur among PVA chains. A large absorption peak at n = 1096.6 cm⁻1 was verified[9]. This band was used as a poly (vinyl alcohol) structure assessment device b, it is a semi-crystalline synthetic polymer capable of forming certain domains depending on many process parameters.
Figure 2. FTIR analysis of PVA

Table 1. Characteristic infrared peaks for PVA

| Wave number (cm\(^{-1}\)) | Band assignment   |
|---------------------------|-------------------|
| 3350.8                    | OH stretching     |
| 2852.9 – 2921.0           | CH\(_2\) stretching |
| 1665.7                    | C=\(=\)C stretching |
| 1441.6                    | CH\(_2\) stretching |
| 1096.6                    | C-C stretching    |
| 848.7                     | CH\(_2\) stretching |

3.3. FTIR spectrum of pure PVA and drug
The reaction mechanism can be further testified via the FTIR spectrum of the obtained noncable, which is almost the same as that of pure PVA and drug. Fig. 3 shows that both spectra have characteristic infrared peaks for PVA and drug in table 3.

Table 2. Characteristic infrared peaks for PVA and drug

| Wave number (cm\(^{-1}\)) | Band assignment   |
|---------------------------|-------------------|
| 3307.9                    | OH stretching     |
| 2939.8                    | CH\(_2\) stretching |
| 1660.5                    | C=\(=\)C stretching |
| 1440.9                    | CH\(_2\) stretching |
| 1378.7 – 1331.1           | CH\(_2\) stretching |
| 1143.3                    | C-C stretching    |
| 1094.9                    | C-C stretching    |
| 851.3                     | CH\(_2\) stretching |
3.4. Drug Release in Different pH

The drug release at different pH was analysed using acetate buffer method. In vitro resindentate sodium release from electrospun fibers with 10% of pH 3.5 was in different time.

3.5. X-RAY DIFFRACTION ANALYSIS (XRD)

The analysis were done with a Brucker DS X-ray diffractactometerfurnished with a scanning attachment and a proportional counter with Ni-filtered Cu Kα radiation. The Scherrer equation is given as:

\[ \tau = \frac{k \lambda}{\beta \cos \theta} \]

Based on the Scherrer Equation, the \( \tau = 5.4156 \text{ Å}, 4.7634 \text{ Å}, 4.8638 \text{ Å}, 2.4512 \text{ Å} \) and \( 3.0056 \text{ Å} \).

| Table 3. X-Ray Diffraction Analysis |
|------------------------------------|
| Pos. [°2] | Height [cts] | FWHM [°2 Th.] | d-spacing [Å] | Rel. Int [%] |
|----------|--------------|---------------|---------------|-------------|
| 43.1183  | 144.36       | 0.2755        | 2.09801       | 17.71       |
| 44.6409  | 671.78       | 0.3149        | 2.02992       | 82.43       |
| 50.0918  | 132.52       | 0.3149        | 1.82107       | 16.26       |
| 51.9889  | 404.54       | 0.6298        | 1.75899       | 49.64       |
| 73.4497  | 814.96       | 0.5760        | 1.28818       | 100.00      |

3.6. THERMO GRAVI METRIC ANALYSIS (TGA)

Thermo gravimetric analysis is generally applied in research and testing to calculate properties of substances and polymers like absorbed moisture content, degradation temperatures, level of inorganic parts[3]. PVA-drug nano fiber 1.373 mg was taken while heating from 50°C to 700°C at 20°C/min under nitrogen purge 200ml.min⁻¹. TGA thermograms for neat and drug laden electro spun PVA mats is shown in the following figure. From the results, for the neat as spun PVA mat. Two steps of losing the weight were seen, the first included the temperature around 50°C to 225°C corresponding to the moisture loss second and the third covered the temperature spectrum of around 225°C to 445°C.

4. Conclusion

An electrospinning technique was successfully prepared using drug-loaded poly(vinyl alcohol) (PVA) electro spun mats. The morphology of the electro spun mats based on the characteristics of theresidronate sodium drug-having PVA solutions. The high electrical potential didn’t influence the chemical composition of the drug. The characterization of the SEM was identified for 283 maximum nano fiber present and all other fibers were below 283 nanometer. And FTIR test estimated for
identified correct PVA electro spun fiber and PVA with residronate sodium drug functional groups were presented. In vitro drug release graph identified for long time duration and sustained drug release. The drug release rate reduced as the drug release time increases. The TGA and XRD analysis was carried out for drug loaded PVA loaded PVA electro spun mat.

5. References
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