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Research Article

Fabrication and Characterization of Olopatadine Hydrochloride Loaded Bionanofibers as a Platform for Drug Delivery

Gitanjali Mehetre*, Vishal Pande

Sanjivani College of Pharmaceutical Education and Research, Kopargaon, Ahmednagar, Maharashtra, India.

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Abstract

Bionanofibers drug delivery systems are able to improve therapeutic efficacy, reduce toxicity, and increase patient compliance by delivering drugs at controlled rate over a period of time to the site of action. Bionanofibers were individualized from *Moringa oleifera* gum by a chemical process and then mechanically separated into nanofibers using high- intensity ultrasonication. The obtained bionanofibers were characterized on the basis of fiber length and diameter, morphology, entrapment efficiency and drug release behavior. FE-SEM images showed that the length of obtained bionanofibers is about 10µm with 94nm in diameter. DSC data showed that the endothermic peak at about 253ºC for drug shifted to lower temperature in drug polymer blend. FTIR analysis shows no any significant interaction between drug and polymer. The in-vitro release study demonstrated that there is a controlled release pattern of drug from bionanofibers.

Keywords: *Moringa oleifera* gum, Bionanofibers, Olopatadine hydrochloride, Entrapment efficiency, In-vitro drug release etc.

INTRODUCTION

Nanofibers, generally defined as fibers with a diameter below 100nm [1,2]. Because of their unique characteristics such as high surface area-to-volume ratio, high tensile strength, low coefficient of thermal expansion and high Young's modulus [3]. Nanofibers are different from micro-sized fibers with regard to their mechanical, optical and dimensional properties [4].

Bionanofibers mainly based on bio-based materials to process into nanobjects using chemical treatment on the cellulose based materials or polysaccharides [5]. Bionanofibers are an exciting new class of material and having a wide range of applications from medical to consumer products and industrial to high- tech applications such as drug delivery involves colonic drug delivery [6], for wound dressing [7], air and liquid filtration, energy storage, composite, aerospace, battery separators, optical and chemical sensors.

The use of natural gum for pharmaceutical applications because of its properties such as biodegradable, biocompatatible, easily available, nontoxic, economic and capable of chemical modifications [8, 9] mainly used in drug delivery as suspending agent, disintegrant [10], emulsifying agent [11], binder and release retardant [12].

The major aim in designing nanostructures as delivery system is to deliver pharmacologically active molecules with accurate dose at targeted sites [13]. Several studies have been conducted on use of nanostructured biopolymers from renewable resources. Among that, the polysaccharides are the most abundant and renewable natural polymers. Cellulose is used as raw material in the production of bio-based nanofibers due to their ability to form transparent and strong fibers [14].

Olopatadine hydrochloride, IUPAC name is {(11Z)-11-[3-(dimethyl amino) propylidene]-6, 11-dihydrodibenzo [b, e] oxepin-2-yl} acetic acid. It is an anti-histaminic with histamine H1receptor antagonist action used for treatment of allergic conjunctivitis, erythema, chronic urticarial, psoriasis vulgaris, eczema dermatitis. By blocking the action of histamine olopatadine bind to H1 receptors and mostly acts on smooth muscles, bronchi, and capillaries. It's having ac-

tivity as ocular mast cell stabilizer also [15, 16].

In present research work, we developed bionanofibers as a carrier for drug delivery. The fabrication of bionanofibers from *Moringa oleifera* gum by using acid hydrolysis and ultrasonication treatment yield fibers with average diameters in sub- micrometer to nanometer range. Because of very small nanoscale diameter and high surface area significantly higher drug content can be loaded in a very small volume.

Materials and method

Materials

Moringa oleifera gum powder, Conc. Sulfuric acid (wt. %), Olopatadine Hydrochloride, Acetone

Isolation of Moringa Oleifera gum

The gum was extracted from injured sites of trees was dried and to form fine powder. The purification of gum was done with distilled water using centrifugation. The resultant suspension was then treated with acetone to precipitate materials and then dried [17].

Fabrication of bionanofibers

Bionanofibers were produced by acid hydrolysis and probe sonication treatment by using *Moringa oleifera* gum as a natural polymer. Aqueous solution of sulfuric acid with different concentration (20, 33, 40, 60 wt. %) was placed in desired quantity of *Moringa oleifera* gum powder. The suspension was stirred on electromagnetic stirrer for sufficient time at 2, 4, 6hrs. After that, suspension was centrifuged to remove unreactive sulfate groups and subject against distilled water to maintain pH (7). The obtained suspension was then sonicated for 20 min using probe processor (Model no. 750FL) at 15-20 KHz an output power of 700W using an ice bath to isolate the nanofibers [18, 19].

Drug loading in bionanofibers

Loading of olopatadine hydrochloride onto the suspension of nanofibers was carried out by mixing (10mg/ml) of olopatadine hydrochloride (dissolved in water) with (5mg/ml) of nanofibers suspension at Ph 7 overnight. Then next day, unbound excess olopatadine hydrochloride was removed by repeated washing and ultrafiltration through a 0.45µ filter. The concentration of olopatadine hydrochloride loaded onto nanofibers solution was measured by the absorbance peak at 206nm after subtracting the absorbance of bionanofibers at that wavelength [20].

Characterization of bionanofibers [21]

Scanning Electron Microscopy

The morphological features of nanofibers were examined by scanning electron microscopy (Philips XL 30 ESEM). Samples were prepared for coating before examination.

Particle Size

Determination of particle size, polydispersity index was determined using a photon correlation spectrometer (Zetasizer ZS 90, Malvern Ltd., UK) based on laser light scattering phenomenon. Diluted samples were placed into the module and measurement was done.

Differential Scanning Calorimetry (DSC)

The DSC system was controlled by (STAR SW 10.00) instrument using Nitrogen was used as the purge gas. The samples were characterized with a heating rate of 10ºC/min at various ranges to measure thermal properties (crystalline or amorphous).

FT-IR Studies

Fourier- transform infrared spectra were obtained using an FT-IR spectrometer (Shimadzu 8400S, Japan). The small quantity of samples was mixed with KBr to form discs by compressing powders in a hydraulic press, which were analyzed between ranges of 600-4000cm^{-1}.

Drug entrapment

Entrapment efficiency is the efficiency of the preparation technique to incorporate drug into carrier system. The entrapment efficiency of nanofibers was calculated by keeping drug loaded nanofibers at overnight. The amount of drug was then analyzed by UV- spectroscopy.

***In-vitro* drug release study**

The drug release was carried out using Franz diffusion cell with cellulose acetate membrane. Firstly, cellulose acetate membrane was kept in pH7.4 for activation at 24 hr. before starting experiment. The receptor compartment was filled with phosphate buffer 7.4 and maintains temperature at 37± 0.5ºC. Samples (5ml) were taken at different time intervals and amount of drug release was analyzed using UV spectroscopy at 206nm [21].

Result and discussion

Scanning electron microscopy

Length and shape of fibers was measure by SEM. The length of all nanofibers was found to be 10µm and with 94nm in diameter. The drug loaded nanofibers showed same length as compared to blank. Because of high surface area to volume ratio relatively more quantity of drug can be loaded into fibers.

Particle size

The average diameter of olopatadine hydrochloride loaded bionanofibers was evaluated with Malvern Zetasizer. The average particle size was found to be 94nm with diameter with polydispersity index 0.2 which indicates uniformity of particle size. The graph was found to be bell shaped with even distribution range.

Differential Scanning Calorimetry (DSC)

Differential scanning calorimetry (DSC) is a thermal analysis technique which measures the temperature and heat flow related with transitions in materials as a function of temperature. It gives information about physical and chemical changes that involved endothermic/exothermic processes. DSC thermo gram of olopatadine hydrochloride shown in fig. and it show sharp endothermic peak at 253.11ºC with decomposition.

DSC thermo gram of drug loaded bionanofibers was show glass transition appears at 88.48ºC depends on materials. The sharp endothermic peak appears at 250.40ºC showing no interaction between drug and polymers.

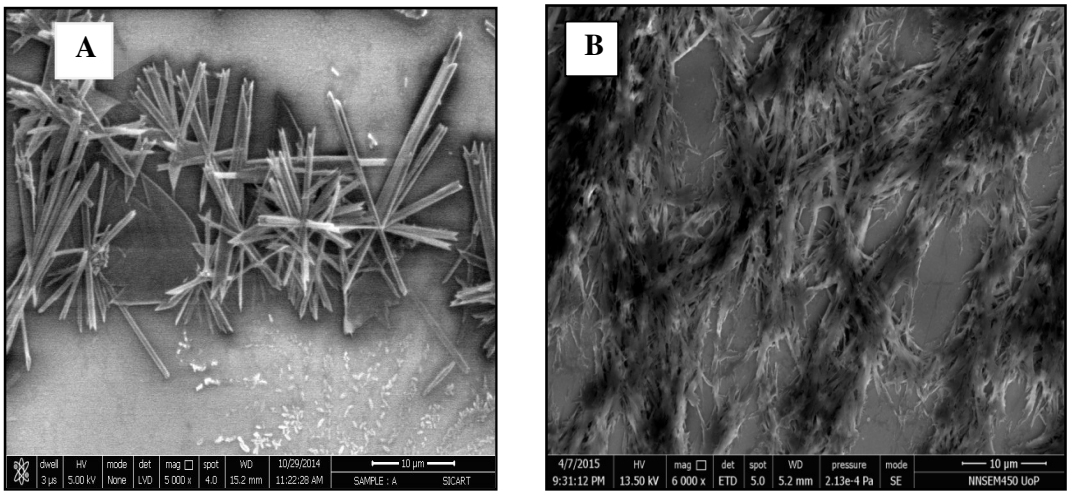

Figure 1 SEM images of (A) Nanofibers and (B) Drug loaded nanofibers

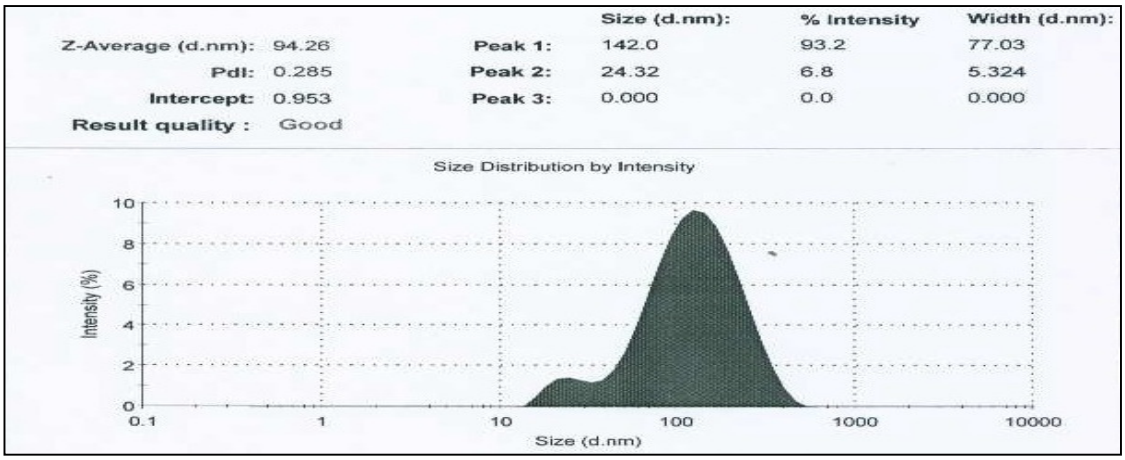

Figure 2 Particle size distributions of drug loaded bionanofibers

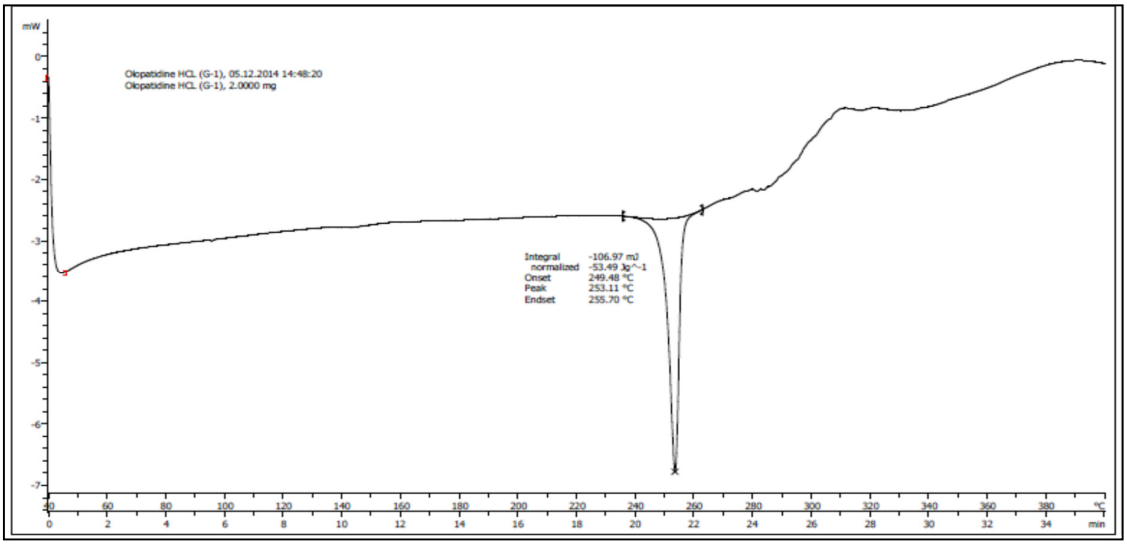

Figure 3 DSC pattern of Olopatadine hydrochloride

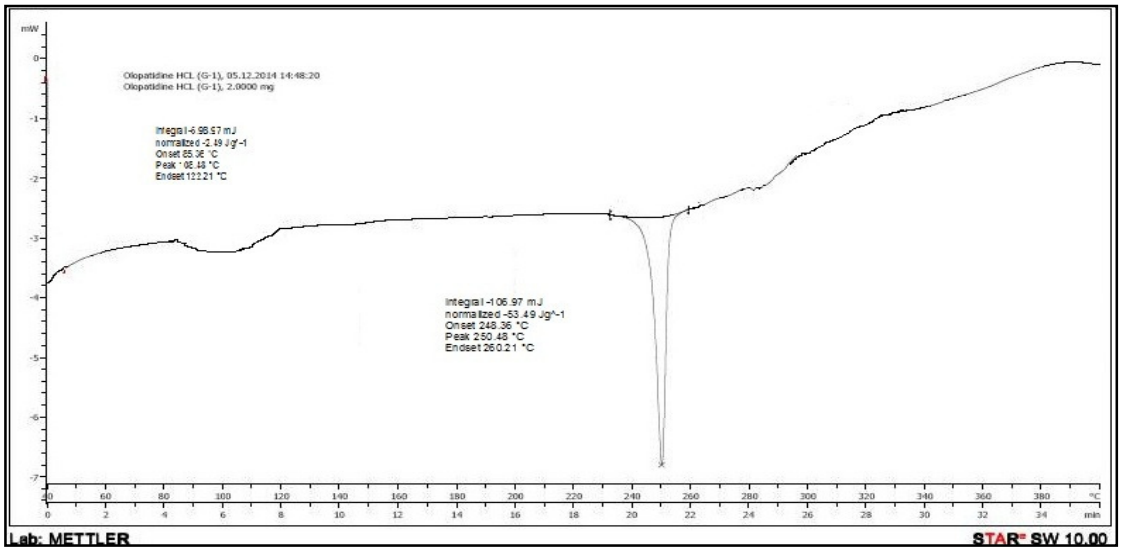

Figure 4 DSC pattern of drug loaded bionanofibers

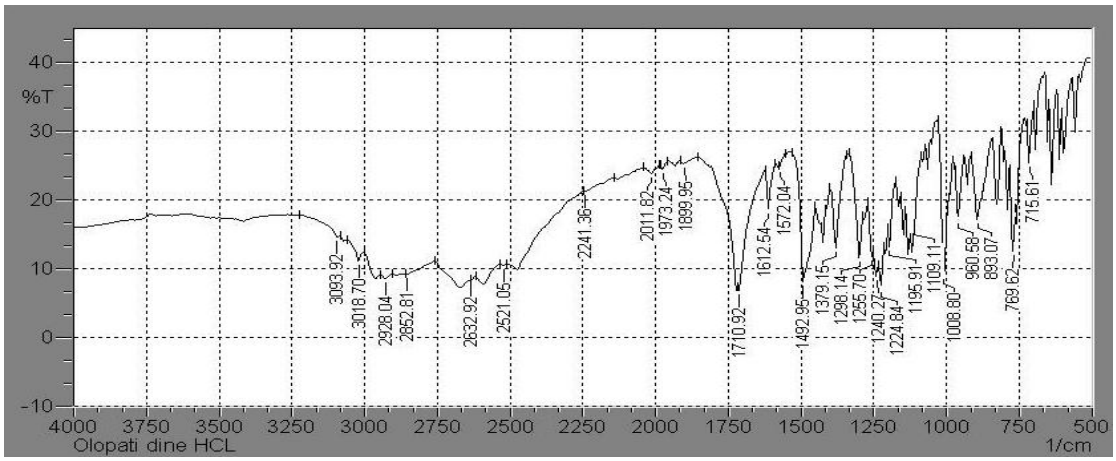

Figure 5 FT-IR spectra of Olopatadine hydrochloride

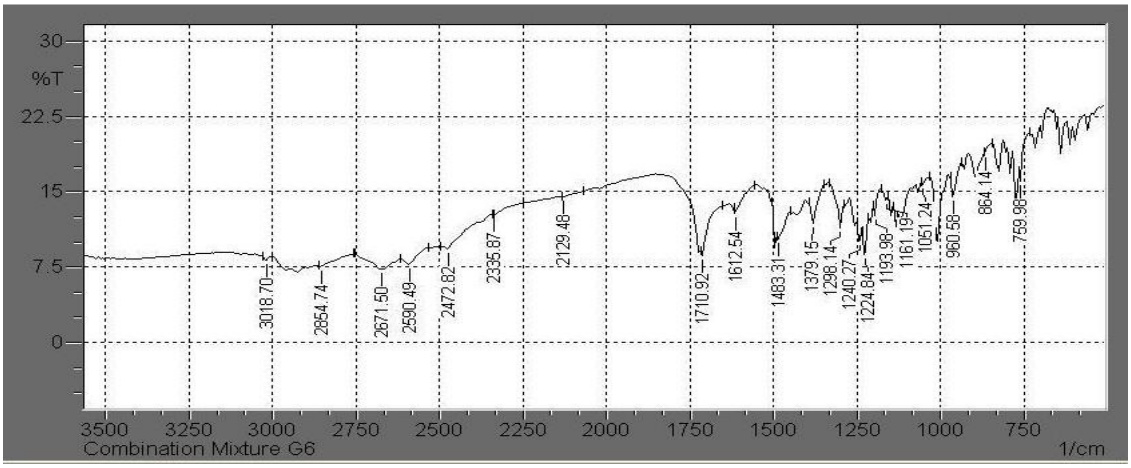

Figure 6 FT-IR spectra of combined mixture (drug+polymer)

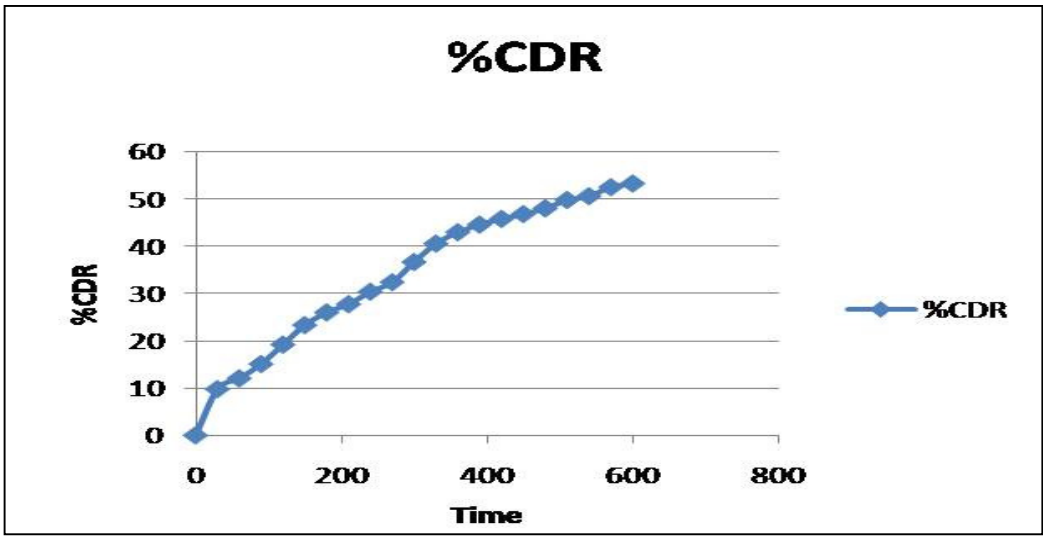

Figure 7 The release profile of olopatadine hydrochloride bionanofibers

Fourier Transformed Infrared Spectroscopy (FTIR)

The IR spectral analysis of olopatadine hydrochloride has shown principle peak obtained at wavenumber of 3018, 3093, 2928cm^{-1}showing CH stretch for aromatic, 2852cm^{-1}CH stretch for aliphatic, 715-960cm^{-1}oop's bending, 1612cm^{-1}C=C stretch, 1710cm^{-1} show COOH group, 1492$cm^{-1}$$CH_3$ bending.

The major functional groups observed in figure 6 showed C-H stretching at 2854cm^{-1}; C=C stretching at 1612cm^{-1}; COOH group at 1710cm^{-1}; C-N amine stretch at 1051cm^{-1}; C-O-C stretching at 1224, 1240cm^{-1} indicating no interaction between drug and polymer and compatible to each other.

***In-vitro* drug release and entrapment efficiency**

In-vitro release study showed that the fabricated bionanofibers are capable of controlled drug delivery. There was an initial burst release of drug because of enormous surface area of the nanofibers followed by controlled release of drug. The release behavior was investigated in pH 7.4 as medium showing % CDR was found to be 53%. The loading ratio of olopatadinehydrochloride bionanofibers was calculated to be 62% estimated from the weight ratio between drug and carrier.

Conclusion

In the present research work bionanofibers were successfully developed by using acid hydrolysis

and ultrasonication treatment. Chemical structure, morphology, thermal stability of bionanofibers was investigated by SEM, DSC, and FTIR etc. Experimental results show bionanofibers having diameter as 94nm while length of 10µm. FTIR measurements shows no any interaction in between drug and polymers. DSC exhibits the sharp endothermic peak at 253ºC of drug and small shifting of drug loaded nanofibers. After drug loading surface area and roughness of nanofibers was decreases. The in-vitro activity showed a controlled release pattern of the drug from bionanofibers. Thus, present investigation gives direction of delivering drug through nanofibers at targeted site.

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