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ORIGINAL ARTICLE

# Fabrication of electrospun nanofibres of BCS II drug for enhanced dissolution and permeation across skin

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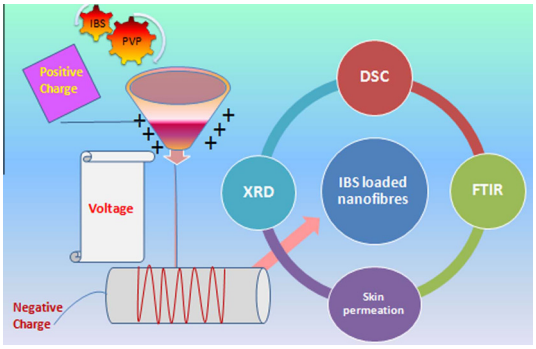
## GRAPHICAL ABSTRACT

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## ABSTRACT

The present work reports preparation of irbesartan (IBS) loaded nanofibre mats using electrospinning technique. The prepared nanofibres were characterized by scanning electron microscopy, Fourier transform infrared spectroscopy, differential scanning calorimetry, X-ray diffraction analysis, *in vitro* diffusion and *ex vivo* skin permeation studies. FTIR studies revealed chemical compatibility of IBS and polyvinyl pyrrolidine (PVP K-30). SEM images confirmed formation of nanofibres wherein IBS existed in amorphous form as revealed by DSC and

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XRD analyses. The prepared nanofibre mats of IBS were found to be superior to IBS loaded as cast films when analysed for *in vitro* IBS release and *ex vivo* skin permeation studies since the flux of IBS loaded nanofibres was 17 times greater than as cast film. The improvement in drug delivery kinetics of IBS loaded nanofibres could be attributed to amorphization with reduction in particle size of IBS, dispersion of IBS at molecular level in PVP matrix and enormous increase in the surface area for IBS release due to nanonization. Thus transdermal patch of IBS loaded nanofibres can be considered as an alternative dosage form in order to improve its biopharmaceutical properties and enhance therapeutic efficacy in hypertension.


## Introduction

One of the commonest disorders responsible for cardiovascular mortality and morbidity in large population is hypertension [1]. Various routes including oral and parenteral are reported for delivery of drugs to the patients suffering from hypertension. In most of the cases, oral route is preferred over any other routes of drug delivery owing to its advantages such as ease of administration and patient compliance. However, the oral drug delivery system also proposes drawbacks such as uneven biodistribution of drug, lack of drug targeting and specificity, requirement of large doses in order to achieve therapeutic plasma drug levels and adverse side effects associated with such high dose. The transdermal route of drug administration can deliver drugs locally as well as into the systemic circulation. Thus it is recognized as one of the potential routes of drug delivery. Owing to the advantages such as bypassing first pass effect, sustained drug release, reduced side effects with frequency of drug administration and patient compliance, transdermal drug delivery systems have attracted most of the researchers [2].

Irbesartan (IBS) is BCS II drug with low solubility and high permeability. It is primarily used for the treatment of cardiovascular diseases including hypertension, cardiac insufficiency and cardiac arrhythmia [3,4]. It is an angiotensin II receptor type 1 antagonist and also reported to delay progression of diabetic nephropathy. Moreover, it is also indicated for the reduction of renal disease progression in patients with type II diabetes. However, its low solubility and in turn bioavailability act as a hurdle in development of dosage form. Additionally, it shows side effects such as the gastric irritation, stomach upset when administered orally. Thus various approaches for solubility enhancement of irbesartan have been reported which include formulation of nanocomposites [5], solid dispersions [6], self emulsifying systems [7] and β, γ-cyclodextrin complexes [8,9]. There is lacuna in the literature on the preparation of IBS-loaded transdermal nanofibre mats to enhance its dissolution and permeation across the skin.

Formulation scientists have been working on development of drug loaded nanofibres since they offer advantages such as high ratio of surface area to mass or volume, high porosity and extremely small pore size within fibres. Further, nanofibres can be useful in targeting drug molecules to specific sites since they present large possibilities for surface functionalization. Electrospinning has been used most commonly to produce drug loaded nanofibres owing to their advantages such as simple and continuous technique having ability to produce nanofibres from a large variety of polymers with an ability of industrial scale-up [10]. In the electrospinning process, a sufficiently high voltage is applied to a liquid droplet containing polymer inducing the charge (positive or negative) in the same. The droplet is stretched due to attraction by the oppositely charged collector thus forming a stream of liquid from the surface at a critical point which is known as the Taylor cone. The charged liquid jet dries in flight leading to formation of fibres which are collected on the rotating drum (collector) [11].

Considering the drawbacks associated with irbesartan and the superiority of transdermal drug delivery, formulation of irbesartan loaded nanofibre mat having an ability to provide optimum amount of drug to control the disease condition with minimum side effects is the need of hour. Further, it is believed that such system can also lead to cost effectiveness of healthcare treatment for long-term management of hypertension [12,13]. In current work, irbesartan loaded nanofibres of polyvinyl pyrrolidone (PVP) were prepared using electrospinning technique and characterized for drug content, FTIR, DSC, morphology, XRD, *in vitro* diffusion and *ex vivo* permeation studies using Franz diffusion cell.

## Material and methods

### *Materials*

Irbesartan was generously gifted by Lupin Research Park, Pune, India. Polyvinyl pyrrolidone (PVP K-30) was purchased from Loba chemi, Mumbai, India. Methanol and N, N-dimethylacetamide (DMAc) were purchased from S.D. Lab and Labscan (Asia), Mumbai, India, respectively.

### *Methods*

#### *Preparation of spinning solutions*

An accurately weighed PVP powder was dissolved in methanol/DMAc (3:1 v/v) mixture to obtain a PVP solution (15% w/v). Irbesartan (20% by weight of dry PVP) was added into the base PVP solution under constant stirring for 4 h at 200 rpm (Heidolph mixer RZR 2051 control, Heidolph India, Hyderabad, India).

#### *Preparation of nanofibres*

The prepared solutions were loaded in 5 mL syringe with 18 gauge needle (Resource Pharmaceuticals, Vadodara, India). The feeding rate (0.5 mL/h) was controlled by a syringe pump. A high voltage supply fixed at 12 kV was applied to the metallic needle. A piece of aluminium foil kept at horizontal