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Novel Repurposed Nano-Facial sheet masks For Dermatological Disease

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KEYWORDS

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SHORT SUMMARY

Drug repurposing has become one of the most valuable strategies that works on overcoming the tedious process of long-term drug discovery. Moreover, nano-drug delivery systems technology has proven its crucial role in maximizing the benefits of repurposed drugs via its role in customizing the release pattern of the repurposed drugs. Drug repurposing also has the ability to target new sites of action for the repurposed drugs and disposition of the repurposed drugs in new routs of administrations. Spironolactone is a repurposed drug with many off label (repurposed) uses for many dermatological diseases. In this study, spironolactone was formulated into polymeric electrospun nanofibrous sheet masks to maximize its activity, negate its systemic side effects and target skin diseases. Electrospinning method was used in the preparation process. Characterization of the prepared nanofibrous sheet masks were done, and the obtained results proved that the fiber diameters in the nano-range with no beads. It also showed that there was compatibility between the whole ingredients of nanofibrous sheet mask, in addition to successful incorporation between the drug and nanofibrous mats. The release pattern was also tested and an improvement in the amount released was obvious compared to pure drug. An animal Ex-vivo test was also completed and has proven the successful delivery of topical spironolactone using nanofibrous sheet masks.

EXTENDED ABSTRACT

INTRODUCTION

Spironolactone (SP) is an aldosterone antagonist that is commonly used as potassium sparing diuretic drug in the management of heart failure, edema associated with liver cirrhosis, arterial hypertension, and many systemic diseases [1]. In addition to those FDA- approved uses, it has been used as repurposed drug in many dermatological diseases via oral route which is always accompanied by serious side effects [2] Polymeric nanofibers have been emerged as one of the promising nano-drug delivery systems that can target skin and avoid drugs' systemic side effects. They also work on enhancing the efficacy of drugs via entrapping the drug molecules in polymeric solution that would be further electrospun and can be formulated as dry facial sheet masks which provide drug stability and more patient compliance [3]. The aim of this work is to reformulate spironolactone in the form of PVP electrospun nanofibers to target skin disorders especially facial skin disorders.

METHODS

Preparation of drug loaded nanofibrous sheets

An optimized PVP solution was mixed with drug solution via continuous stirring till the formation of homogenous mixture. That mixture was electrospun using electrospinner device under the condition of voltage between 19-25 KV, feed rate

0.4 ml/hr and suitable needle diameter the fibers collected on foil collector. The produced nanofibers were dried under vacuum oven.

Characterization of the nanofibrous sheets

The surface morphology of the nanofibrous masks was detected using field emission scanning electron microscopy (FESEM). Fiber diameters were also calculated using ImageJ software.

Compatibility and interactions:

The compatibility between the drug and polymer was examined using Fourier transform infrared spectroscopy to ensure that there is no significant change in the drug's functional groups after formation of the nanofibrous masks.

In-vitro drug release

In-vitro release of the drug from nanofibrous masks was studied using the total immersion method. Predetermined drug loaded nanofibers' samples were immersed in phosphate buffered saline, PBS, Ph 7.4 at 37°C ± 0.5°C. Then, it was placed on shaking water bath at 100 rpm. UV spectrophotometer was used to detect the amount of drug released after withdrawal of each sample and compared with the release from pure drug form.

Ex-vivo skin permeation study

Franz diffusion cells with donor and receptor compartments were used to evaluate the drug permeated through skin. The excised rat skin was fixed at Franz cells and the fibrous sheet was mounted on the upper donor chamber while the lower receptor chamber filled with phosphate buffer saline Ph 7.4. Aliquots were withdrawn from the receptor medium and the amount of drug were detected via UV spectrophotometer in comparison with the results obtained from pure SP gel [4].

Skin retention study

After ex-vivo permeation study, the remaining formulations were removed from the skin, then the skin was washed and minced then digested in a test tube contains a mixture of PBS and HCl (0.1 M) for 24 hours. Centrifugation of all skin samples done using cooling centrifuge. The supernatant was collected, and drug content was measured at predetermined λ_{max}.

RESULTS

Spironolactone loaded nanofibers masks showed non-beaded fibers with diameter range less than 400 nm (Figure1).

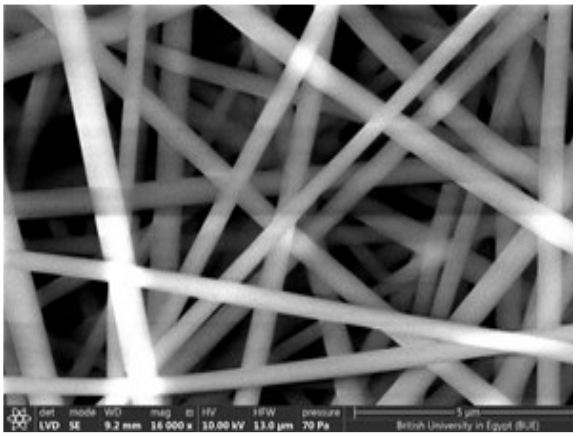

Figure1: SEM image for the optimized PVP nanofibers loaded with the SP.

FTIR results

The characteristic peaks of pure Spironolactone were detected in the pure drug spectrum. Also the pure polymer spectrum showed its characteristic peaks. The spectrum of the physical mixture showed no significant change in the characteristic peaks of the drug indicating compatibility and absence of interaction between them. Drug peaks also did not change significantly after loading on nanofiber scaffold.

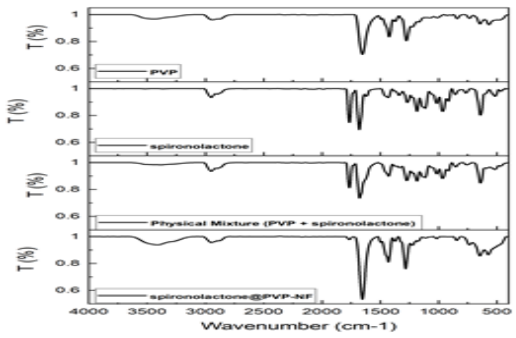

Figure 2: FTIR spectra of PVP, SP, Physical mix. and SP-PVP nanofibrous sheet mask.

In-vitro release results

As shown in figure 3, spironolactone release from the PVP nanofibers is biphasic. It shows initial fast release followed by more controlled pattern with improvement in the amount released compared to the pure drug release.

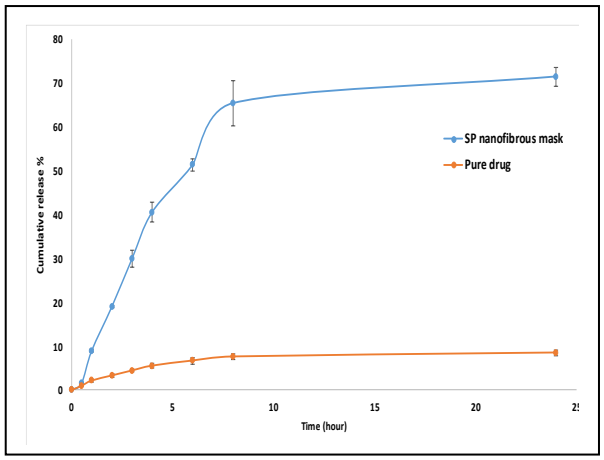

Figure 3: In vitro release of drug from nanofibrous sheet mask compared to pure drug

EX-vivo study results

Ex-vivo penetration of the drug from the nanofibrous masks was superior in comparison with its flux from gel form as shown in figure 4.

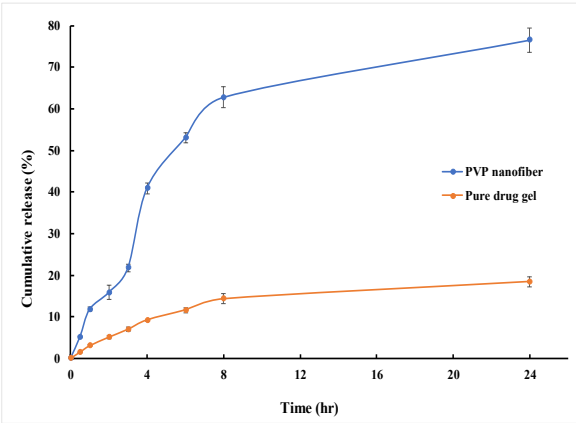

Figure 4: Ex-vivo permeation of drug from the nanofibrous sheet mask compared to gel

Skin retention study

the percentage of drug retained in the skin in case of PVP nanofibrous mask is higher than that retained from gel with nearly 66 times (Figure 5).

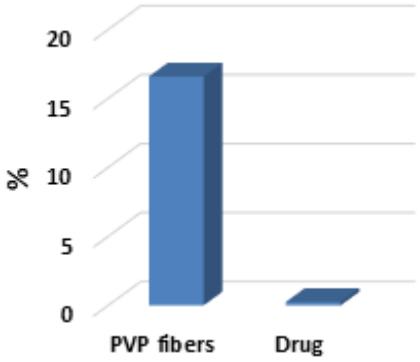

Figure 5: Percentage SP retained in the skin from SP loaded nanofibrous sheet mask and SP gel.

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