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FABRICATION AND EVALUATION OF GLIMEPIRIDE *FICUS BENGHALENSIS* FRUIT MUCILAGE MATRIX TRANSDERMAL PATCHES

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ABSTRACT

The main purpose of the present study was to develop matrix type transdermal patches of glimepiride with *Ficus benghalensis* fruit mucilage and to study the permeability patterns. Transdermal patches were prepared by solvent evaporation technique. The prepared patches were evaluated for physicochemical characteristics viz. thickness, mass and drug content, which were uniform in prepared batches. The study proved that glimepiride can be developed as a transdermal patch with *Ficus benghalensis* fruit mucilage. *In vitro* permeation studies were performed using rat abdominal skin as the permeating membrane in Keshary-Chien cell.

Key words: Glimepiride, *Ficus benghalensis*, Transdermal delivery, Matrix.

INTRODUCTION

Glimepiride belongs to sulfonylurea drug, a class used to treat type II diabetes. The recommended daily dose of glimepiride is 1-8 mg/ day; 2 mg q.i.d or 4 mg b.i.d. The biological half life ($t_{1/2}$) of glimepiride is reported as 2.3± 0.8 h after a single dose of 3 mg and increasing to 5.3± 3.0 h after multiple dosing[1]. In this study, *Ficus benghalensis* fruit mucilage was used as a matrix polymer for controlled release of glimepiride.

EXPERIMENTAL

Materials

Glimepiride was obtained as a gift sample from Dr. Reddy's Laboratories, Hyderabad,

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India. *Ficus benghalensis* fruits were obtained from the locally growing plants in and around Anantapur, India and authenticated by the Botany Department of Sri Krishnadevaraya University, Anantapur, India. Glycerin, propylene glycol, methyl paraben, propyl paraben and Span-80 were procured from S.D. Fine Chemicals, Mumbai, India. All the reagents used were of Analytical Reagent grade. The drug samples were characterized by means of UV spectrophotometric method along with determination of solubility and pH for their authentication.

Methods

Extraction of mucilage[2]

The fruits were thoroughly washed with water to remove dirt and debris and cut into two pieces. The seeds were removed. The pulps of the fruits were crushed and soaked in water for 5–6 h, boiled for 0.5 h and left to stand for 1 h to allow complete release of the mucilage into the water. The mucilage was filtered using a multi layer muslin cloth bag to remove the marc from the solution. Acetone (three times the volume of filtrate) was added to precipitate the mucilage. The mucilage was separated, dried in an oven at 40°C, collected, ground, passed through a # 80 sieve and stored in desiccator at 30°C and 45% relative humidity till use.

Preparation of transdermal films[3]

Various proportions of *Ficus benghalensis* mucilage were taken in a beaker, Propylene glycol (plasticizer), Span-80 (penetration enhancer) propyl paraben, methyl paraben (preservatives) and glimepiride (16 mg) were added with continuous stirring using teflon-coated magnetic bead placed in magnetic stirrer for 0.5 h at 500 rpm. The above mixture was poured within the glass bangles (6.1 cm diameter) placed on mercury surface in a petri dish. The rate of evaporation was controlled by inverting a funnel over the petri dish. After 24 h, the dried films were taken out and stored in desiccator. The quantities in the formulae were showed in Table 1.

Table1: Different formulae of transdermal patches

Ingredients	GPFB-1	GPFB-2	GPFB-3	GPFB-4	GPFB-5
Glimepiride (mg)	16	16	16	16	16
Ficus benghalensis fruit mucilage (g)	1	2	3	4	5

Cont…

Ingredients	GPFB-1	GPFB-2	GPFB-3	GPFB-4	GPFB-5
Glycerin (mL)	0.3	0.3	0.3	0.3	0.3
Propylene Glycol (mL)	0.18	0.18	0.18	0.18	0.18
Span-80 (mL)	0.06	0.06	0.06	0.06	0.06
Methyl paraben (g)	0.02	0.02	0.02	0.02	0.02
Propyl paraben (g)	0.01	0.01	0.01	0.01	0.01
Water up to (mL)	20	20	20	20	20

Stability studies[4]

The formulations were stored at 27ºC, 35ºC, 45ºC and 60ºC for 3 months. The samples were withdrawn every week and the amount of intact drug remaining was estimated.

Evaluation of skin irritation potential of transdermal patches

The primary skin irritation studies were carried out using modified Draize test [5]. The hair of rabbits were removed by shaving from the dorsal area on both sides 24 h before test, one side of the back of each rabbit i.e. untreated skin area serves as the control for the test. Medicated patch was secured on experimental side using adhesive tape and the non-medicated patch was adhered on the control side of six rabbits. These patches were covered with occlusive covering to approximate the condition of use. The medicated patches were changed after 48 h and the fresh patches were secured at the same site. However, the patches on the control side were not changed. The patches were secured on the back for seven days. After removal of patch after a week, each of the areas were examined for any sign of erythema or edema.

In vitro skin permeation studies of transdermal patches

The transdermal patches were subjected to *in vitro* evaluation across rat dorsal skin. After removal of epidermal hair, skin was cleaned for removing any adhering subcutaneous tissue and blood vessels. The skin was mounted over night (12 h) on receptor phase to remove any water soluble (UV absorbing) material. The *in vitro* skin permeation of glimepiride from various transdermal patches was studied using locally fabricated Keshary-Chien type of diffusion cell [6]. The diffusion cell consists of two parts; the upper part i.e. the donor compartment and contains the active ingredient and the carrier adhesive patch, the

bottom part contains the receptor solution, the water jacket for temperature control and the sampling port. The effective permeation area of the diffusion cell and receptor cell volume was 1.0 cm^2 and 17.5 mL, respectively. The temperature was maintained at 37±0.5°C. The receptor compartment contained 17.5 mL of phosphate buffer IP (pH 7.4) stirred by magnetic stirrer. The permeability studies were carried out across both rat and cadaver skin[7]. Samples (1.0 mL) were withdrawn and replaced with the same volume of fresh receptor solution, through the sampling port of the diffusion cell at predetermined time intervals till 48 h. Absorbance of the withdrawn samples were measured at 230 nm. The experiments were done in triplicates. The values are shown in Fig 1.

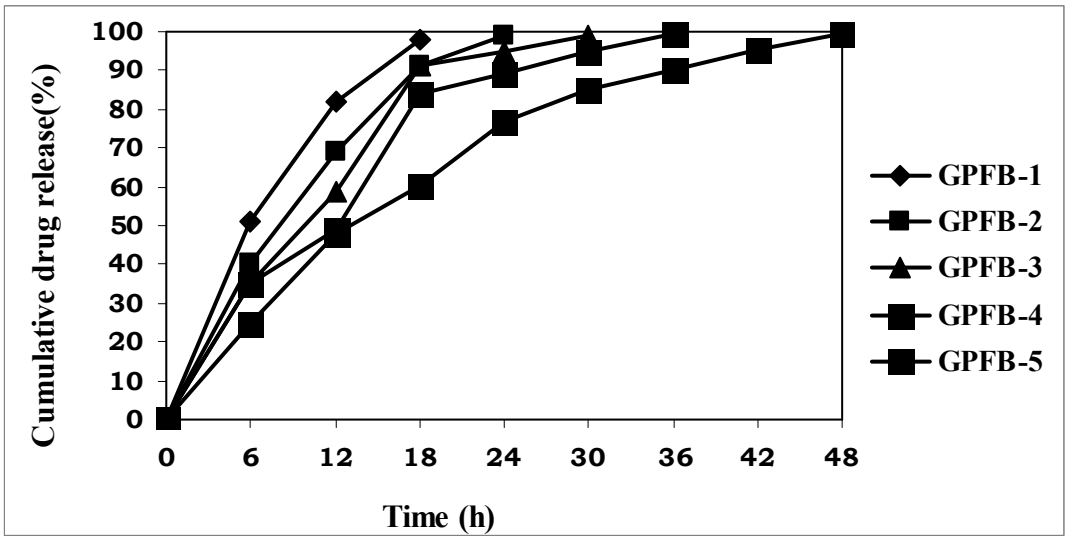

Fig 1: *In vitro* permeation profile of glimepiride from transdermal patch

RESULTS AND DISCUSSION

The results of physico-chemical evaluation of *Ficus benghalensis* films showed uniform drug content and minimum batch variation. The thickness of the patches varied from 625 to 775 µm. The physical appearance of the patches and the effect on ageing indicated that the patches need to be stored in properly sealed air tight packing to keep them protected from extremes of moisture that may alter their appearance; thus, the properties were found to be within limits and satisfactory.

CONCLUSION

It can be concluded that the prepared transdermal patches were having satisfactory

physical parameters and permeation profile. Hence, it is concluded that glimepiride transdermal patches can be prepared with *Ficus benghalensis* fruit mucilage, which is economical and effective.

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