*Int. J. Chem. Sci.: 8(1), 2010, 681-686*

# FORMULATION AND EVALUATION OF RAMIPRIL TRANSDERMAL PATCH

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## ABSTRACT

Transdermal patch are self contained discrete dosage forms, which when applied to the intact skin, deliver the drug through the skin at controlled rate to the systemic circulation. Ramipril transdermal patch was prepared by acrylic (2-ethylhexyl acrylate) based polymer. Methyl acrylate (monomer), vinyl acetate (copolymer) in ethanol as solvent and ramipril was dissolved or suspended in mixture of solvents constituted by one litre of propan -2-ol and 1.5 liter of ethyl acetate. The mixture was stirred, until a homogeneous mass was obtained, and this was evaporated. The composite medicated foil form the final transdermal patch. Evaluation was done by physical appearance, folding endurance, water vapour transmission, drug diffusion study, permeability studies, content uniformity and *in vitro* drug release.

**Key words**: Ramipril., 2-Ethylhexyl acryl ate, Acrylic acid, Sodium lauryl sulphate, Ethyl acetate.

## INTRODUCTION

At present, the most common form of delivery of drugs is the oral route. While this has the notable advantage of easy administration, it also has significant drawbacks -- namely poor bioavailabiltity due to hepatic metabolism (first pass) and the tendency to produce rapid blood level spikes (both high and low), leading to a need for high and/or frequent dosing, which can be both; cost prohibitive and inconvenient.

## EXPERIMENTAL

### Materials and method

Ramipril, 2-ethylhexyl acrylate, acrylic acid, vinyl acetate, ethanol, sodium lauryl

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sulphate, urea and ethyl acetate

**Formulation procedure**

A quantity of 50 g of ramipril was dissolved or suspended in mixture of solvent constituted by one litre of propane-2-ol and 1.5 liter of ethyl acetate This solution was added, with stirring, to the mixture of copolymer (prepared). The mixture was stirred, until a homogeneous mass was obtained, and this was evaporated. To produce a mixture with consistency, appropriate spreading was done on the appropriate liner. Then the adhesive mixture containing the active ingredients was spreaded on to the foil of silicone–coated paper or polyester and dried at between 30$^{o}$C and 80$^{o}$C to form a film matrix weight about 98 g/m$^2$ of the dry matrix. Finally, a polyester foil about 15 μm thick was sucked on matrix to form the outer cover covering of the patch. Individual circular patches contain area of 18 cm$^2$, each containing about 4 mg of the active ingredients was cut from the composite medicated foil to form the final transdermal patch

**Evaluation of trandermal patches**

**Physical appearance**

The free films prepared were evaluated for physical appearance by visual observation.

**Thickness uniformity**

The thickness of the films was measured by a dial caliper. The means of the observations were calculated.

**Folding endurance**

The folding endurance was measured manually for the prepared films strip of the films. 2 x 2 cm$^2$ was cut evenly and repeatedly folded at the same place till it broke. The number of films could be folded at the same place without breaking give the exact value of the folding endurance.

**Water vapour transmission**

For this study, vials of equal diameters were used as transmission cells. These cells were washed thoroughly and dried in oven. About 1 g of calcium chloride was taken in the cell and the polymeric films measuring 3.14 cm$^2$ areas were fixed over the brim with the help of an adeshive. The cell's initial weight was recorded. These were kept in a desiccator

containing saturated solution of potassium chloride (about 200 mL). The humidity inside the desiccator was measured by hygrometer, and it was found to be in between 80-90% RH. The cells were taken out and weighed. Then water vapour transmission rate was calculated.

Water vapour transmission rate (W.V.T) = WL/S where W = Water vapour transmission in g and L = Thickness of the film in cm and S = Exposed surface area

**Drug diffusion study**

Drug diffusion study was conducted using vertical type diffusion cell. The receptor compartment was filled with 15 mL of phosphate buffer having pH 7.4 as diffusion media. Polymeric film was mounted on the donor compartment with the help of an adeshive. 10 mL of the 2% w/v drug solution was poured into the donor compartment. A magnetic stirrer was set at 100 rpm and whole assembly was set at temperature at 37 ± 2$^{o}$C. The amount of drug release was determined by withdrawing 1 mL of sample at regular time intervals for 3 hrs. The volume withdrawn was replaced with equal volume of fresh buffer solution. Samples were analysed for drug content using a UV spectrophotometer at 290 nm.

**Permeability studies**

From the drug diffusion data, the permeability coefficient for the varies films were calculated using the formula-

$$P_m = K_{app}. H/A \quad \ldots(1)$$

Where $K_{app}$ = Drug diffusion rate constant calculated from the slope of liner drug diffusion profile.

H = Thickness of the film, and

A = Surface area of the film

**Content uniformity**

Drug content uniformity was determined by dissolving each patch in 10 mL of ethyl alcohol and filtering with Whatman filter paper. The filtrate was evaporated and the drug residue was dissolved in 100 mL of phosphate buffer (pH 6.8). The 5 mL solution was diluted with phosphate buffer up to 20 mL, filtered through a 0.45 μm Whatman filter paper, and analysed by UV Spectrophotometer at 290 nm. The experiments were performed in triplicate and average values are reported.

### Surface pH study

Following method was used to determine the surface pH study of patch. A combined glass electrode was used for this purpose. Each patch was allowed to swell by keeping it in contact with 1 mL of distilled water for 2 hours at room temperature. The pH was noted by bringing the electrode into contact with the surface of the patch and allow it to equilibrate for 1 min. The experiments were performed in triplicate and average values are reported.

### *In vitro* drug realese

The rotating paddle method was used to study release from the patches. 200 mL of phosphate buffer (pH 6.8) was used for dissolution medium, at 37 ± 0.5$^{o}$C and rotation speed of 50 RPM. One side of the patch was attached to glass disk with instant adhesive. The disk was put in the bottom of the dissolution vessel. Samples were withdrawn at half–hour intervals and replaced with fresh medium. Samples were filtered through Whatman filter paper and analysed. The experiments were performed in triplicate and average values are reported.

## RESULTS AND DISSCUTION

According to the results, the ramipril transdermal patch has maximum antihypertensive effect due to high liphophilicity of ramipril and acrylic based polymer matrix type of ramipril. Transdermal patches were prepared by using acrylic based polymer and evaluated. The results of the parameters such as thickness uniformity, *in vitro* drug realese and surface pH study permeability studies showed that ramipril transdermal patches have an effective controlled release activity to cure hypertension. There is a scope to formulate antihypertensive ramipril transdermal patches.

### Summary and coclusion

The result of the study shows that ramipril transdermal patches are very effective in given doses and blood pressure. The results showed that ramipril transdermal type therapeutic system will give suitable therapeutic effect. This study holds promise for the clinical studies.

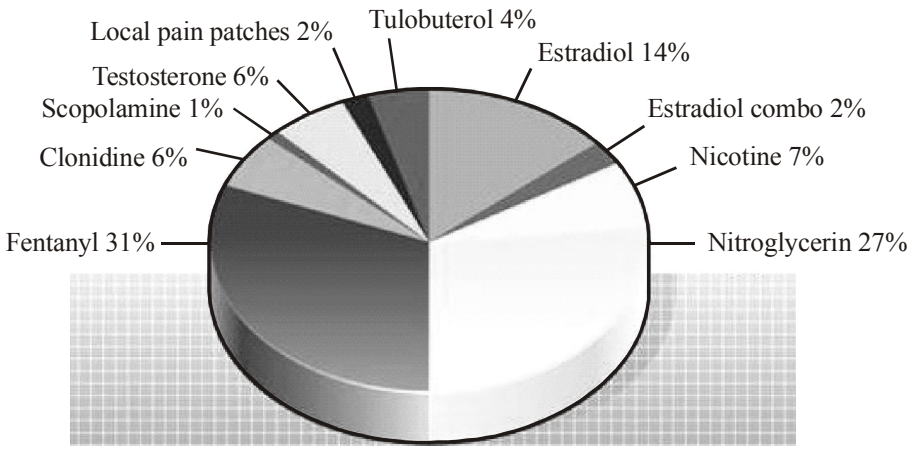
### Advance development in TDDS

Drug in adhesive technology has become the preferred system for passive transdermal delivery Two areas of formulation research are focused on adhesives and excipients. Adhesive research focuses on customizing the adhesive to improve skin adhesion

over the wear period, improve drug stability and solubility, reduce lag time, and increase the rate of delivery. Because a one-size-fits-all adhesive does not exist that can accommodate all drug and formulation chemistries, customizing the adhesive chemistry allows the transdermal formulator to optimize the performance of the transdermal patch.

A rich area of research over the past 10 to 15 years has been focused on developing transdermal technologies that utilize mechanical energy to increase the drug flux across the skin by either altering the skin barrier (primarily the stratum corneum) or increasing the energy of the drug molecules. These so-called "active" transdermal technologies include ionophoresis (which uses low voltage electrical current to drive charged drugs through the skin), electroporation (which uses short electrical pulses of high voltage to create transient aqueous pores in the skin), sonophoresis (which uses low frequency ultrasonic energy to disrupt the stratum corneum), and thermal energy (which uses heat to make the skin more permeable and to increase the energy of drug molecules). Even magnetic energy, coined magnetophoresis, has been investigated as a means to increase drug flux across the skin.

**Global TDD product sales by segment**

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*Revised : 24.10.2009* *Accepted : 28.10.2009*