

Abstract

This Study evaluates in-vitro transdermal delivery of a proprietary drug molecule, R053, which contains a benzothiazole group. Three in-vitro permeation studies were performed to evaluate the effect of acrylic and silicone adhesive concentrations, the effect of permeation enhancers, Oleyl alcohol and Dipropylene Glycol (DPG), and the effect of the occlusion of backing materials on the permeation rates. The results show that increasing the acrylic adhesive concentration results in a decrease in the permeation rate; Oleyl alcohol enhances the permeation but DPG does not; the degree of occlusion of backing materials has no effect on the permeation rate.

Purpose

Skin is an effective barrier against micro-organisms and chemicals from entering the body. Therefore, therapeutic delivery of drugs through the skin barrier is a challenge for transdermal formulation development. Some molecules have been successfully delivered by passive transdermal systems such as; Estradiol, Progesterone, Methylphenidate, and Scopolamine. However, there is not yet a commercial passive transdermal system which delivers a drug molecule that contains a benzothiazole group. This study will evaluate the transdermal delivery of R053, a proprietary molecule which contains a benzothiazole group. The study evaluates the effect of adhesives, the effect of permeation enhancers, and the effect of occlusion of backing materials on permeation rates.

Methods

Formulations

The transdermal systems are comprised of a backing layer, a drug-in-adhesive matrix layer, and a protective release liner layer.

Study #1 has 3 formulations. Formulation 1, 2 and 3 have the acrylic adhesive to the silicone adhesive ratios at 1:3, 1:1, and 3:1 respectively. Each formulation contains 5% R053 and 10% Poly-vinyl-pyrrolidone (PVP). The backing is a 2 mil polyester/ethylene vinyl acetate film and the release liner is a 5 mil thick polyester film with fluorocarbon release surface.

Study #2 also has 3 formulations. Formulation 1 has 5% Oleyl alcohol, Formulation 2 has 5% DPG, and Formulation 3 has no Oleyl alcohol or DPG. Each formulation contains 5% R053, 10% PVP, and 1:3 ratio of silicone to acrylic adhesive. The backing is a 2 mil polyester/ethylene vinyl acetate film and the release liner is a 5mil thick polyester film with fluorocarbon release surface.

Study #3 has 2 formulations. Formulation 1 contains an occluded backing, polyester/ethylene vinyl acetate film and Formulation 2 contains a semi-occluded backing, polyurethane/polyvinyl alcohol film. Both formulations also contain 5% R053, 10% PVP, and 1:1 ratio of silicone adhesive to acrylic adhesive. The release liner is a 5mil thick polyester film with fluorocarbon release surface.

Figure 1

Effect of Acrylic/Silicone Adhesive Ratios

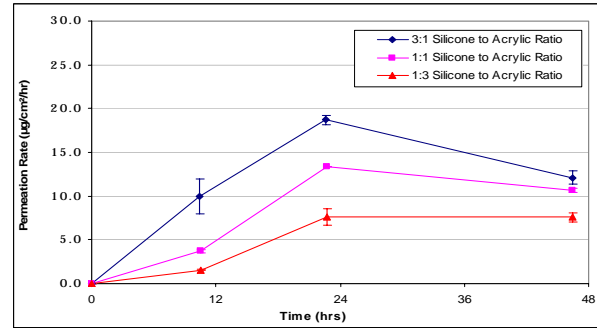


Figure 2

Effect of Permeation Enhancers

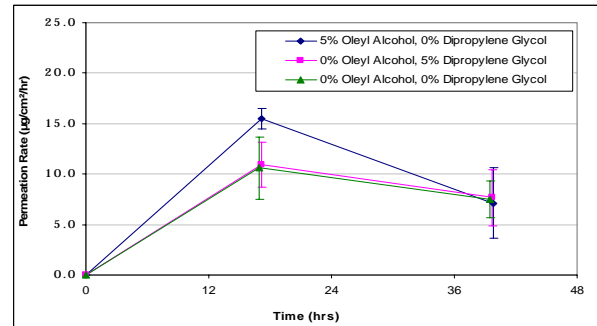
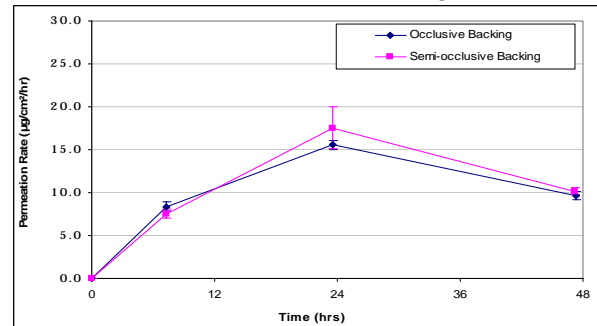


Figure 3

Effect of Occlusion of Backings



In-Vitro Study

Modified Franz diffusion cells and human cadaver skin were utilized in the evaluation of the in-vitro drug delivery. The epidermis layer of human cadaver skin was used as the permeation barrier. These diffusion cells had a defined receiving volume and delivery area. The receiving solution was normal saline with an anti-microbial agent.

The diffusion cells were stored in an incubator at approximately 32 °C. Samples were taken from the receiving solution within 48 hours from the initial time. HPLC was used to analyze for the R053 concentrations. The results of the permeation rates are in Figure 1, Figure 2, and Figure 3.

Results

Study #1 - Effect of Adhesives

This study was designed to evaluate the effect of the silicone to acrylic adhesive ratios on the permeation rates of the R053. The ratios of silicone to acrylic adhesive were varied 1:3, 1:1, and 3:1. The results in Figure 1 illustrates that the permeation rates are increased as the silicone adhesive ratios are increased.

Study #2 - Effect of Enhancers

This study evaluates the effect of DPG, which is a hydrophilic enhancer and Oleyl alcohol, which is a lipophilic enhancer, on the permeation rate enhancement. The study compares the permeation rates of 5% DPG formulation and 5% Oleyl alcohol formulation with the permeation rate of the formulation that has no enhancer. As the results shown in Figure 2, DPG has no effect on the permeation rate while the Oleyl alcohol helps increasing the permeation rate.

Study #3 - Effect of Occlusion of Backing

This study evaluates the effect of the occlusiveness of the backing materials on the permeation rate. The permeation rate of the occluded backing formulation, polyester/ethylene vinyl acetate film, is compared with the permeation rate of the semi-occluded backing formulation, polyurethane/polyvinyl alcohol film. Figure 3 shows the results that the permeation rates of the two formulations are not different.

Conclusion

Three in-vitro studies show that the occlusion of the backing has no effect on the R053 permeation rates, Oleyl alcohol enhances the permeation but DPG does not, and the silicone/acrylic ratios affect the delivery rate. Overall, the research shows that a drug molecule with the benzothiazole group could be developed and delivered by a passive drug-in-adhesive transdermal system.