

# Acrylic Polymer Backing Films for Controlling In-Vitro Permeation and Delivery Profile of Estradiol from Transdermal Drug Delivery Systems

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## ABSTRACT

In previous work, utilization of backing films comprised of polyester (PET) and acrylic polymers to control the permeation rate and drug delivery profile of drug-in-adhesive transdermal drug delivery systems (TDDSs) was investigated for low molecular weight amine drugs, i.e. d-amphetamine base[5][6]. The purpose of this study was to evaluate the effect of acrylic polymer backings on controlling permeation rate and drug delivery profile of estradiol. The permeation studies were performed with TDDSs consisting of drug, permeation enhancers, solubility modifiers, acrylic pressure sensitive adhesive (PSA), and silicone PSA [1][2]. Control of estradiol delivery profile can be achieved by the use of different moieties in the acrylic polymer backing. The coat weight of the acrylic backing film had a more substantial effect on the permeation rate of estradiol rather than the delivery profile. Varying the thickness and/or moiety of the acrylic polymer backing can modify the drug delivery profile and permeation rate of estradiol.

## I. PURPOSE

This investigation was initiated to evaluate the delivery of estradiol from TDDSs utilizing acrylic polymer backing films. The parameters explored include drug delivery profile and permeation rate for a single drug-in-adhesive matrix laminated to various backing films comprised of PET and acrylic polymers. The drug-in-adhesive matrix consisted of estradiol, povidone, a fatty alcohol, a glycol, acrylic PSA and silicone PSA. The ability to control the drug delivery profile and permeation rate with the acrylic polymer backings allow the formulator another approach in creating and experimenting with development of TDDSs.

## II. EXPERIMENTAL METHODS

### A. Formulations

#### Drug Permeation / Profile : Study 1

Three acrylic polymer backings were laminated to the drug-in-adhesive matrix as described above. The three acrylic polymer backings utilized different moieties of acrylic polymer in their composition: Example 1 contains an acid functional moiety, Example 2 contains a non-functional/non-reactive moiety, and Example 3 contains a hydroxyl (-OH) functional moiety. The acrylic polymer of the backing had a target coat weight of 5.0 mg/cm<sup>2</sup> on PET. The drug-in-adhesive matrix had a targeted coat weight of 5.0 mg/cm<sup>2</sup>. The objective of this study was to determine acrylic reactivity and its influence on permeation rate and delivery profile of estradiol from the TDDSs. Vivelle Dot® was utilized as a control for the study.

#### Drug Permeation / Profile : Study 2

Previous work has shown significant permeation and delivery profile effects of increasing coat weights of the acrylic backing films. These formulations were investigated and discussed in a prior paper and included here for comparison between two different drug actives[6]. A single acid functional acrylic polymer backing varying the coat weight was utilized. Coat weights for the acrylic backing were 2.5 mg/cm<sup>2</sup>, 5.0 mg/cm<sup>2</sup>, and 7.5 mg/cm<sup>2</sup> for examples 4, 5, and 6, respectively. These acrylic backings were laminated to the drug-in-adhesive matrix comprising 20% d-amphetamine base, acrylic PSA, and silicone PSA. The objective was to determine if backing thickness with the same acrylic moiety had an influence on permeation rate and delivery profile of d-amphetamine from the TDDSs. Methylphenidate transdermal system [MTS] was utilized as a control for the study.

#### Drug Permeation / Profile : Study 3

To study the phenomenon that occurred with the formulations from Study 2, the same study was performed with a different drug, estradiol. A single acid functional acrylic polymer backing was prepared varying the backing thickness. Coat weights for the acrylic backing were 2.5 mg/cm<sup>2</sup>, 5.0 mg/cm<sup>2</sup>, and 10.0 mg/cm<sup>2</sup> for examples 7, 8, and 9, respectively. The drug-in-adhesive matrix was laminated to the backing layer as described above. The objective was to determine if backing thickness with the same acid functional acrylic moiety had an influence on permeation rate and delivery profile of estradiol from the TDDSs. Vivelle Dot® was utilized as a control for the study.

### B. In-Vitro Permeation Studies

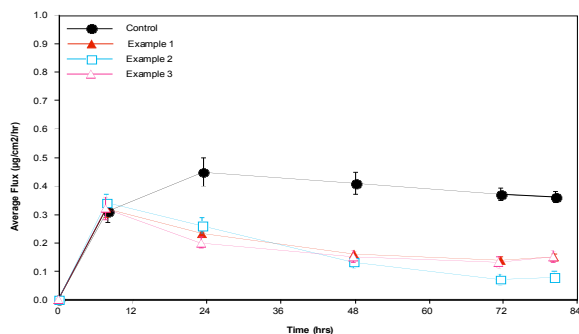
Determination of the permeation properties of the described formulations were conducted on a modified Franz Diffusion Cell through a disc of stratum corneum obtained from human cadaver skin. The formulations were die punched, mounted on the disc, and placed on the cell containing an isotonic saline solution. The cells were stored at 32°C for the duration of the permeation study while having the solution stirred at a constant rate of approximately 300 rpm. Aliquots of the solution were taken during the course of each study (approximately 84 hours for estradiol and 8 hours for d-amphetamine/methylphenidate) to determine the permeation characteristics for each formulation. The estradiol, d-amphetamine, and methylphenidate concentrations in each cell were determined by HPLC. The previous work with d-amphetamine and methylphenidate were evaluated with 5 cells per formulation[6]. All other formulations were run with 4 cells per formulation.

## III. DISCUSSION OF RESULTS

### A. Drug Permeation / Profile : Study 1

Figure 1 illustrates the results for the three moieties of acrylic polymer backings utilized. Acid functional and hydroxyl functional acrylic polymer backings had a similar effect on the delivery profile of estradiol. The non-functional/non-reactive moiety in the acrylic backing exhibited a decrease in the delivery profile after 48 hours of delivery compared to the acid functional and hydroxyl functional acrylic backings. It was surmised more of a pronounced effect should have been noted in the delivery profiles between the acrylic backing layers based on reactive properties with the drug. Further investigations will need to be conducted to explore the cause and effect delivery profile caused by the layers of acid functional and hydroxyl functional acrylic polymers in the backing composition.

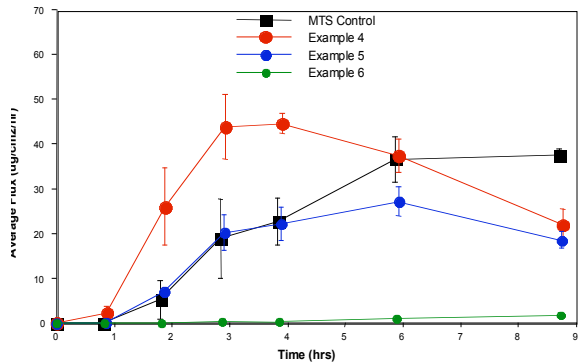
FIGURE 1



### B. Drug Permeation / Profile : Study 2

Study 2 is included here for comparative purposes only. This experiment was performed and discussed in previous work by Kanios et al[6]. Figure 2 illustrates the permeation rate decreasing as the acid functional acrylic backing thickness increases. Furthermore, as the acrylic backing layer increases the drug delivery profile reaches a near-zero order delivery.

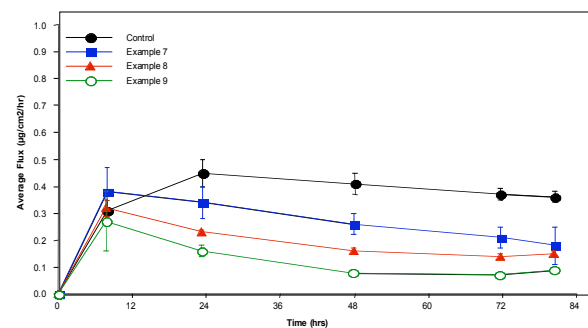
FIGURE 2



### C. Drug Permeation / Profile : Study 3

Figure 3 illustrates the permeation rate and delivery profile of estradiol for variation of acrylic backing coat weights, utilizing the acid functional acrylic polymer backing from Study 2. The graphical presentation indicates permeation rate increases as the backing film thickness decreases while the delivery profile appears to be the same for all three coat weights. Further investigation is required to determine if the same or different attributes are a result of the use of acrylic backings described in Study 1.

FIGURE 3



## IV. CONCLUSION

The results of the in-vitro permeation studies indicate manipulation of the acrylic backing polymer through changes in moiety and thickness allow for flexibility in formulation to attain a desired permeation rate and delivery profile for estradiol. This study confirms the previous work by Kanios et al[6] utilizing a different drug molecule, estradiol. As the functional moiety and thickness change, the permeation rate and delivery profile can be changed to create a transdermal patch with a multitude of delivery profiles and rates for a selected therapeutic target. Further evaluation into acrylic backing moieties and thicknesses needs to be done to verify and confirm the modifications to delivery profile and permeation rate for this drug and other drug actives both *in vitro* and *in vivo*.

## V. REFERENCES

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