

Abstract

This study evaluates the relationship between water vapor transmission rate (WVTR) of the backing materials and the delivery rate (flux) of Clonidine from a drug-in-adhesive transdermal matrix system. Three transdermal systems were developed, which backings have the WVTR of 15g/m²/day, 100g/m²/day, and 1500 g/m²/day. To evaluate in-vitro delivery rate, modified Franz diffusion cells and human cadaver skin were utilized. The results show that as the WVTR is increased, the delivery rate of Clonidine is decreased and sustained.

Purpose

In the formulation development for a drug-in-adhesive transdermal delivery system, ingredients such as adhesive matrix, enhancer excipients, and drug concentrations are some critical variables that affect the drug delivery rate. Moreover, the backing materials, which are part of the delivery system, also have significant effect on the delivery rate. This study illustrates the relationship between the water vapor transmission rate, which is a physical property of the backing materials, and the in-vitro delivery rate of Clonidine.

Methods

Three drug-in-adhesive matrix transdermal systems with backing of different WVTR values were constructed. These systems were evaluated for the in-vitro delivery of Clonidine.

Transdermal Systems

The transdermal systems were composed of a layer of protective release liner, a layer of drug-in-adhesive matrix, and a layer of backing. The protective release liner was 5 mils thick polyester film that is coated with silicone polymer as the release surface. The adhesive matrix layer was a homogeneous mixture of 7% Clonidine base and 93% acrylic adhesive. The Clonidine was completely dissolved in the adhesive. The coat weight of the adhesive matrix layer was 10mg/cm².

The backing of System #1 was a 2 mils thick polyester (PET) and ethylene vinyl acetate (EVA) film. The adhesive matrix was laminated onto the PET side of the backing. The WVTR of the backing was 15g/m²/day

System #2 was a 2 mils thick polyurethane (PU) and vinyl alcohol (EVOH) film. The adhesive matrix was laminated to the PU side, and the WVTR was 100g/m²/day.

The backing of System #3 was a 1 mil thick PU film. It was a monolayer backing, and its WVTR was 1500g/m²/day.

In-Vitro Study

To evaluate the delivery rate in-vitro, modified Franz diffusion cells and human cadaver skin were utilized. These diffusion cells had a defined receiving volume and delivery area. The receiving solution was

normal saline with an anti-microbial agent. The epidermis layer of human cadaver skin was separated from the dermis, and was used as the permeation barrier.

The diffusion cells were stored in an incubator at approximately 32 °C. Samples were taken from the receiving solution at approximately 12, 24, 48, 72, 96, 120, 144, and 168 hours from the initial time. The samples were analyzed by HPLC for the Clonidine concentration. With the Clonidine concentration, the sampling times, the receiving volume, and the delivery area, the delivery rates were calculated. The results were plotted in Figure 1 and Table 1.

Figure 1

In-Vitro Delivery Rate of Clonidine

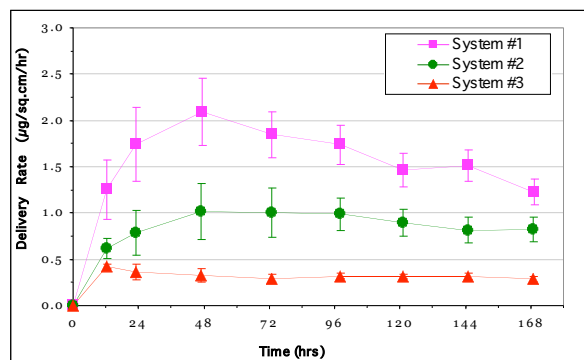


Table 1

Effect of WVTR on Clonidine Delivery Rate

	WVTR (g/m ² /day)	Clonidine Delivery Rate (µg/cm ² /hr)
System #1	15	1.69
System #2	100	0.93
System #3	1500	0.32

Results and Discussion

Table 1 shows that System #1, with the backing that has the WVTR of 15g/m²/day, has the highest average Clonidine delivery rate, 1.69µg/cm²/hr. As the WVTR is increased to 100g/m²/day in System #2, the delivery rate decreased 45%, which is 0.93µg/cm²/hr. As the WVTR of the backing is increased furthermore to 1500g/m²/day in System #3, the delivery rate decreased by 81%.

The results show a clear trend that as the WVTR is increased, the delivery rate is decreased. Looking at the mass transfer of the whole delivery system, the drug concentration in the patch is much higher than the drug concentration in the skin, which creates a concentration gradient. This concentration gradient forces the drug to diffuse from the patch through the skin and into the body. At the same time, water diffuses from the other side of the skin into the drug and adhesive matrix layer then diffuses out of the matrix through the backing. The water diffusion is opposite direction of the drug diffusion. As the water diffuses through the skin layer, the drug and adhesive matrix layer, and the backing layer, the momentum of water diffusion counter act with the momentum of the drug diffusion. The result of this interaction is the inversed delivery rate of the drug and the water vapor transmission rate of the backing.

To evaluate the delivery profile, Figure 1 shows that System #1 has the maximum delivery rate of 2.09 µg/cm²/hr at 48 hr of the delivery and has the minimum delivery rate of 1.23 µg/cm²/hr at the end of the 7th day. The delivery rate of this System changes 41% from high to low. System #2 has the maximum delivery rate of 1.02 µg/cm²/hr and the minimum delivery rate of 0.82 ug/cm²/hr. The delivery rate changes 20% from high to low. System #3 has the delivery rate change 19% from high to low.

The results show that the delivery rate of System #1, which has the lowest WVTR value, is less sustained than System #2 or System #3. System #1 gradually decreases its delivery rate after 48 hours of delivery because of the depletion of the drug concentration in the adhesive matrix. In the contrary, System #2 and System #3 can reserve their drug concentrations in the adhesive matrix due to low delivery rate, which results in a sustained delivery profile.

Conclusion

This study illustrated the water vapor transmission rate of the backing materials have an affect on the transdermal Clonidine delivery rate. As the WVTR value of the backing materials are increased, the drug delivery rates are decreased but sustained. This affect could provide the transdermal formulators a variable to control the delivery profile of other drug molecules.

References

- Sablotsky S and Gentile C.; Breathable Backing: US Patent 4,994,278