Carbosil® membrane was investigated, in order to attain a diffusion mechanism of drug transport.

**INTRODUCTION**

Ibuprofen is a non-steroidal, anti-inflammatory drug (NSAID), known as the propionic acid derivatives, or profens. Profens are ionized at physiological pH and are more lipophilic than other NSAID’s. Because of the lipophilicity (log P of 3.6) of ibuprofen, it has the ability to form a reservoir in the stratum corneum, where it is exposed to the effect of evaporation. The Franz cells were left open and the donor solution was continuously stir the receptor phase inside a Grant® water bath at 32 °C, simulating the temperature of human skin.

Saturated solutions of ibuprofen in the different solvents or combination of solvent vehicles were prepared an hour before the experiment. The saturated solutions were kept at 32 °C before application to the membrane. Depending on the experiment conducted a specific volume of saturated solution was applied to the membrane. The volumes that were tested were as follow: 2, 5, 10, 20, 50 and 150 µl. A separate experiment was done for each donor phase vehicle with a certain volume. Out of the twenty four Franz cells that were used per diffusion experiment, the receptor phase of the first four cells were extracted after 1 h and were not refilled. After 2 h the second 4 Franz cells were extracted. The aforementioned was done hourly until 6 h have passed and all the receptor compartments were empty. The main reason for doing the experiment this way was to ensure that the diffusion area stays as consistent as possible; due to the fact that when the cell is turned upside down to refill the receptor compartment; the diffusion area will change for volumes that does not cover the entire diffusion area of the Franz cell. By leaving the cell unmoved until extraction ensures that the diffusion area stays the same for the duration of the experiment. Therefore, as a result of the design of this experiment it was not possible to use cumulative concentrations or flux. The Franz cells were left open and the donor solution was exposed to the effect of evaporation.

**EXPERIMENTAL METHODS**

Twenty four glass vertical Franz diffusion cells with a diffusion area of 1.075 cm² and receptor capacity of approximately 2 ml were used during this study. Presoaked Carbosil® membrane was cut into circles big enough to cover the area available for diffusion of the Franz cell. The membranes were placed on the lower half of the vertical Franz diffusion cell, the donor compartments were placed on top, sealed with Dow-corning® vacuum grease and clamped with metal horseshoe clamps. A small stirrer bar was placed in each receptor compartment.

The receptor compartment was filled with PBS (pH 7.4 at 37 °C), taking care not to allow bubbles in the receptor compartment. The diffusion cells were placed in a tray on a Variomag® stirrer plate in order to continuously stir the receptor phase inside a Grant® water bath at 32 °C, simulating the temperature of human skin.

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**RESULTS AND DISCUSSION**

In Figure 1 the permeation profiles of the lipophilic drug, ibuprofen, with hydrophilic penetration enhancer solvents, i.e. propylene glycol and water individually and in combinations is summarized and it is evident that the application of finite doses of the single penetration enhancer solvent, propylene glycol, achieved the highest penetration enhancement effect, with the ibuprofen concentration of diffused ibuprofen being the highest with this solvent. The concentration of diffused ibuprofen that had been delivered from application of a finite dose of the water delivery vehicle could not be measured, due to the lipophilic nature of ibuprofen (log P of 3.6) and the low solubility of ibuprofen in water, resulting in permeation concentrations that were immeasurable.
Concentration (µg/cm²) effect for ibuprofen, compared to all other mineral oil and combination achieved the best penetration enhancement. Solvents and solvent mixtures containing 100% Miglyol®, 50/50 (v/v) and 80/20 (v/v) mineral oil/Miglyol® all showed similar penetration enhancement effects with finite dose applications.

CONCLUSION

From the findings in this study it became evident that the lipophilic/hydrophilic nature of both the solvent and the permeant would significantly have an impact on the absorption of a permeant through Carbosil® membrane. If the membrane is hydrated with a lipophilic delivery vehicle while carrying a lipophilic permeant, a higher percentage of the applied dose may diffuse through the membrane in comparison to a hydrophilic delivery vehicle. Ibuprofen showed higher permeation levels with small application volumes of 100% Miglyol® as well as with mixtures of Miglyol® and mineral oil (lipophilic) delivery vehicles. When a lipophilic permeant was applied in a hydrophilic delivery vehicle, i.e. ibuprofen in propylene glycol and water, the diffusion was lower.

REFERENCES


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Figure 1: Finite dosing of ibuprofen (µg/cm²) that diffused over 6 h through the Carbosil® membrane using propylene glycol and water as delivery vehicles (n = 4)

Figure 2: Finite dosing of ibuprofen (µg/cm²) that diffused over 6 h through the Carbosil® membrane using mineral oil and Miglyol® as delivery vehicle (n = 4)

Figure 2 illustrates that the results for finite dose applications of these solvents clearly showed that the binary vehicle of 20/80 (v/v) mineral oil/Miglyol® combination achieved the best penetration enhancement effect for ibuprofen, compared to all other mineral oil and Miglyol® solvents, individually and in combination. Because of the lipophilic nature of these solvents it might be that when it was applied to the membrane it increased the hydration levels of the membrane and decreased the barrier function of the membrane. For this reason higher levels of the lipophilic drug (ibuprofen) penetrated the membrane. The results can also be explained by the synergistic action of the combination of the two enhancers. Solvents and solvent mixtures containing 100% Miglyol®, 50/50 (v/v) and 80/20 (v/v) mineral oil/Miglyol® all showed similar penetration enhancement effects with finite dose applications.