Comparative study of Different Skin Penetration Delivery Vehicles for Retinol, Resveratrol, Epigallocatechin gallate, and Vitamin C
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ABSTRACT SUMMARY
There are many commercially available penetration enhancers on the market that claim to help actives penetrate through the stratum corneum in order to reach cells in the epidermis and dermis. In this study we selected three vehicles that can be obtained commercially and claim penetration and carried out a comparative study with four model compounds. It was found that the different carriers provided penetration to different levels spanning four orders of magnitude in efficiency.

INTRODUCTION
The stratum corneum, uppermost layer of the skin, is an effective barrier that protects the underlying tissue from external aggressors. Because of this, delivery of active ingredients that can provide benefits to skin cells often needs permeation enhancers to effectively reach the target area.

In this study, we investigated the penetration capabilities of a variety of carriers in order to get a better understanding of the existent technologies in the field and to identify adequate carriers for topical delivery of active compounds to skin cells. We investigated the delivery of four active compounds commonly used in skin care products: Retinol, Resveratrol, Epigallocatechin gallate (EGCG), and Vitamin C (Vc). Three carriers were studied: commercially available loaded liposomes, Natipide®, and Transcutol®.

EXPERIMENTAL METHODS
Permeation studies were performed using the skin substitute Strat-M membrane from Millipore® on a Franz Cell platform with an opening of 0.9 cm diameter. 1 mL of each donor solution was added to the donor cell. The receptor cells were 5 mL in volume filled with phosphate buffered saline (PBS) for the case of all the donors except for retinol, which had PBS and 6% Oleth 20 in order to help solubilize the retinol in the receptor. Tests were carried out for 24 hours. A 500 µL sample was removed from the receptor every hour for the first 8 hours and replaced with PBS (or PBS with Oleth 20). After the 8 hours a sample was removed every 2 hours until 12 hrs and then once again at 24 hrs. The samples were analyzed using HPLC. All donors were at a concentration of 1-2% in the carrier.

RESULTS AND DISCUSSION
After 24 hours, it was found that Transcutol® could provide penetration through the membrane for all tested compounds, but to varying degrees (160 µg for resveratrol, 37.6 µg for retinol, 5 µg for Vc, and 2 µg for EGCG or normalized for the area: 250 µg/cm² for resveratrol, 94 µg/cm² for retinol, 38 µg/cm² for Vc, and 3 µg/cm² for EGCG) (Figures 1-4). On the other hand, Natipide was most successful at providing penetration for the hydrophilic active, Vitamin C (800 µg or 1250 µg/cm² in 24 hrs) (Figure 1). It also provided penetration for the other compounds to varying degrees after 24 hours (10 µg or 16 µg/cm² for Retinol and 1.3 µg or 2 µg/cm² for EGCG) (Figures 1-4). However, Natipide did not facilitate penetration of resveratrol by the 24 hour time point (Figure 3). The commercially available loaded liposomes were not successful at providing penetration of tested compounds through the synthetic skin substitute (Figures 4-5). In our study, the most difficult molecule to deliver was EGCG (maximum was 2 µg or 3 µg/cm² in 24 hrs with Transcutol ®) (Figure 2). This can be for a variety of reasons, molecular weight being one of them or perhaps there was degradation that has not been accounted for. Each compound was delivered to a different extent, and whether that amount is enough will depend on the level...
needed to have an effect on the targeted skin cells and what amount may be cytotoxic to the cells. Studies still must be done to verify that formulation levels of the carrier which would typically be used in a product can also cause penetration.

**CONCLUSION**

Our findings indicate that when selecting carriers to topically deliver active compounds for skin care applications, careful consideration must be taken in terms of the individual characteristics of each compound, as delivery efficiency varies across the different carrier technologies. The carrier that is selected will depend on the amount needed to deliver to the skin.

**REFERENCES**


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