Skin Penetration of Caffeine from Marketed Eye Creams

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Introduction

Everybody experiences symptoms of aging as they grow older. Some of these changes include increased dryness, changes in facial shape, appearance of lines and wrinkles, as well as changes in hair growth.[1] The extract of the fruits of the coffee plant (*Coffea arabica*) has been shown to exhibit antioxidant activity mediated by potent antioxidant polyphenols. This extract showed an improvement in fine lines, wrinkles, pigmentation, and overall appearance.[2] Due to this evidence, there are many anti-aging products on the market today that contain caffeine.

Anti-aging products may be cosmetics or drugs in the United States (US) depending on their intended use.[3] All three products selected to be tested in this project were cosmetics. Caffeine is a popular anti-aging ingredient in the US, therefore, we decided to focus on this ingredient. We selected two prestige anti-aging eye creams for women, and a prestige anti-aging eye cream for men, all containing caffeine.

Objective

The objective of this project was to determine the amount of caffeine that permeated through a skin-like synthetic membrane from marketed anti-aging eye creams.

Materials

The anti-aging eye creams selected included:

- **Product 1 for women** – Product L
- **Product 2 for women** – Product LP
- **Men's product** – Product C

Product	L	LP	C
Top Claims	• Experience advanced action against the signs of aging • Now, 360-degree action around the eyes for smoother, firmer skin in just 4 weeks.	• Visibly reduces the appearance of crow's feet wrinkles and the look of dark circles. • Caffeine visibly reduces the appearance of dark circles.	• This hydrating treatment combats eye-area lines and wrinkles for a younger look. • Quick-absorbing formula strengthens the moisture barrier.
Caffeine	#15 of 31	#11 of 23	#26 of 57

Methods

Market Research

Various websites, including Sephora.com, Ulta.com, Target.com, and Walgreens.com were researched, using the keyword 'caffeine'. The search was filtered to beauty products and skin care products.

Physiochemical Characteristics

pH was tested with a pH meter (InLab Science®, Mettler Toledo, Columbus, OH). Appearance was studied by visual observation. Droplet size was measured by dynamic light scattering (Anton Paar Litesizer™ 500, Ashland, VA). 0.10 g of each cream was diluted with 2.5, 5, and 10 mL of water for the readings.

***In Vitro* Permeation Testing (IVPT)**

Strat-M® membrane (EDM Millipore, Darmstadt, Germany) was used for the IVPT. This membrane correlates very closely to human skin[4] and is commonly used for *in vitro* screening of transdermal formulations.

Three 12 mL Franz cells (Fig. 1) were used for each product. These were held at a constant temperature of 32 ± 0.2°C using a water bath and a circulator.

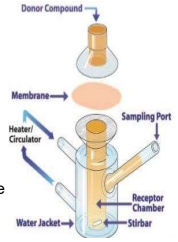


Figure 1. Franz cell[5]

Phosphate Buffer Solution was used at a pH of 7.4 as the receptor fluid. Samples of 300 µL were taken at pre-determined time points during the 24-h study and then analyzed for drug content.

High Performance Liquid Chromatography (HPLC)

An HPLC (Waters Alliance e2695 separation module, Milford, MA) equipped with a 2998 PDA detector and a reverse phase 5 µm Biphenyl 100 Å liquid chromatography column (50 x 4.6 mm) was used. Caffeine was measured at 273 nm. The mobile phase consisted of water and 0.1% formic acid, and methanol and 0.1% formic acid (70:30) was pumped at a flow rate of 1.0 mL/min.

Caffeine Extraction

In order to quantify how much caffeine permeated through the membrane, we analyzed the caffeine content of the three marketed products.

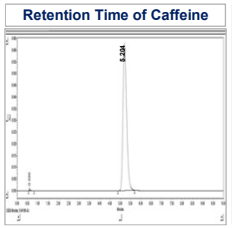
Approx. 1 g of each sample was stirred at room temperature in dichloromethane (DCM) overnight. Caffeine was extracted into DCM. The aqueous layer was titrated out. DCM was dried over anhydrous sodium sulfate and decanted into a round bottomed flask which was then placed on a rotary evaporator (Heidolph HEI-VAP with a G3 Condenser, Elk Grove Village, IL) and reduced in volume. The resulting solid was transferred into a clean vial and a small sample was taken and dissolved in HPLC grade methanol for analysis by HPLC.

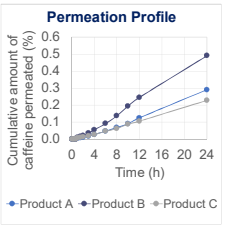
Results – Physiochemical Characteristics

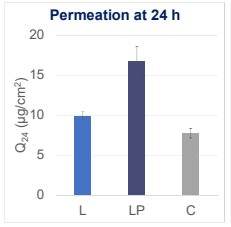
Product	pH (n=3)	Droplet size (n=3)	Caffeine Content of the Eye Creams
L	6.11 ± 0.01	1.03 µm ± 0.16	4.11%
LP	5.98 ± 0.01	1.33 µm ± 0.36	1.54%
C	5.89 ± 0.03	3.49 µm ± 0.51	1.35%

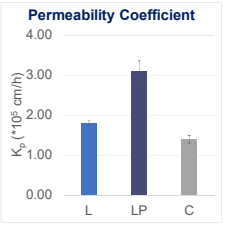
APPEARANCE			
Product	L	LP	C
Description	Thick, glossy, off-white, opaque cream	Very thin, glossy, white, opaque cream	Very thick, light-tan, opaque cream

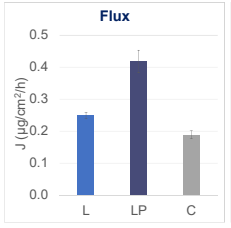
Results - IVPT

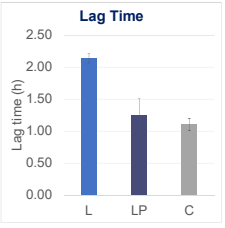












Conclusions

The appearance of the eye creams slightly differed among the three brands, their pH was similar. The eye creams were monodisperse, the average droplet size varied between 1-3.5 µm, depending on the brand.

Product L contained the highest amount of caffeine, the other two creams contained a similar amount. Caffeine permeation (Q) through the Strat-M® membrane was the highest from Product LP in this 24-h study (0.49±0.04%), followed by Product L and Product C. The same trend was observed in the case of flux (J) and permeability coefficient (K_p). Product L had the longest lag time, the other two creams had a similar, shorter lag time.

Although Product L contained the highest amount of caffeine, the highest permeation was observed for Product LP. This may be due to the other ingredients in the creams as they can have a significant effect on the permeation of caffeine.

Future Studies

Eye creams containing caffeine will be formulated using *in silico* modeling (Formulating for Efficacy™) and tested for *in vitro* release and *in vitro* permeation. Data from this preliminary study will guide in designing the creams.

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