BRIDGING THE GAP BETWEEN LONG LASTING AND ACTIVE INGREDIENTS DELIVERY IN COLOR COSMETICS: AN IN-DEPTH STUDY USING IN VITRO AND IN VIVO PERMEATION TECHNIQUES

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Abstract

The interest for multipurpose make-up has grown and consumers are looking for formulations that go beyond decoration. This work aims to study the influence of silicone-based film formers on the delivery and long-lasting properties of skin care actives added to color cosmetic formulations.

Niacinamide (nicotinamide) was elected as the active ingredient of reference for method validation. Scanning electron microscopy was used to evaluate the effects of film-forming technologies on the morphology of the formulations.

ATR-FTIR and tape stripping data revealed that niacinamide is delivered faster from an aqueous solution compared to a water-in-silicone emulsion. When silicone-based film formers are added, niacinamide appears to be distributed more homogeneously in the stratum corneum and the concentration of niacinamide recovered from the top layer of the epidermis is reduced. Tape stripping data showed that Dimethiconol/Trimethylsiloxysilicate Crosspolymer acts as a booster. Rub-off experiments confirmed the ability of the film formers to hold niacinamide on the skin surface, maximizing the benefits of the active ingredient.

This work demonstrated that silicone-based film formers improve the delivery of niacinamide and prevent its loss from abrasion. Morphology of the films were also significantly improved. It is believed that this study opens up a new frontier with valuable knowledge for the development of color cosmetics with skincare benefits.

Keywords: color cosmetics, multipurpose formulation, active ingredients, film formers, in vitro and in vivo correlation.

Introduction. The skin is the largest organ of the body with a total surface area of about 2 m^2 in adults. It fulfills regulatory and sensory functions. The skin also protects the body against the outside environment, preventing water loss as well as the entry of harmful substances and microorganisms. In particular, the stratum corneum, the outermost skin layer, is a formidable barrier which must also be overcome for the delivery of active molecules through the skin. A good understanding of the barrier properties is important for development, optimization and testing of topical products in cosmetics [1,13].

Cosmetic compositions used to make up a user's skin must be able to impart color with little to no transfer. They must also provide good wear properties. The transfer resistance and wear of cosmetic compositions are usually obtained through the use of film forming resins such as silicone film forming resins [3,4]. Silicones are synthetic polymers containing Si─O─Si bonds and are used in many industries for their water repellency, ability to wet-out surfaces, high permeability to gases, stability in extreme temperatures, and resistance to thermal, radiation and chemical degradation [2, 9].

With the increase of interest for multipurpose or hybrid make-up in the last few years, the world is evolving at a faster pace and pushing beauty trends at the same speed. Consumers are more concerned and looking for multi-functional cosmetics. Color cosmetics are more than ever linked to skin care and the search for makeups that go beyond decoration is rising and must be urgently addressed. It is well known by the skilled in the art that silicone-based film formers [10] are key ingredients to achieve long lasting in color cosmetics [2], however, what role will it play in the delivery of anti-aging actives when these are added to color cosmetics? Little is known about it.

This work aims to address this puzzling question by determining the influence of silicone-based film formers [9] on the delivery of skin care actives [11,13,16] added to color cosmetic formulations and it´s long-lasting properties.

Materials and Methods

A. Materials. Niacinamide was purchased from DSM Personal Care at 99% purity. Four different silicone and silicone-acrylate film formers supplied by The Dow Chemical Company were evaluated in this study: Dimethiconol/Trimethylsiloxysilicate Crosspolymer [SiOH/MQ crosspolymer], Dimethicone (and) Acrylates/Polytrimethylsiloxymethacrylate Copolymer [Silicone Acrylate], Polypropylsilsesquioxane (and) Isododecane [T-propyl] and Trimethylsiloxysilicate [MQ]. The percentages of active film former varies and are described in Table 1. Dimethicone 2cS, Dimethicone (and) Dimethicone PEG/PPG-18/18 were also supplied by The Dow Chemical Company, the later one supplied at 36% active level. Isododecane was obtained from Vantage at 98% purity. A combination of the pigments, Titanium dioxide and Iron oxides with the following surface modification: Aluminum Dimyristate (and) Triethoxycaprylylsilane (and) Disodium Stearoyl Glutamate [Hybrid-grafted] supplied from Miyoshi Kasei and ungrafted CI 45410 (Red 27 lake) obtained from Sun Chemical were also used in the experiments. Pigmented formulations can be found in Table 2.

Table 1. Quantitative unpigmented formulations included in this study

Phase	Ingredient	Formulation (%wt.)				
		Placebo	Silicone Acrylate	SiOH/MQ Cross-polymer	MQ	T-Propyl
A	Trimethylsiloxysilicate (100% actives)				5.0	
A	Dimethicone				5.0	
B	Isododecane	20.0	20.0	20.0	20.0	20.0
B	Dimethicone	25.0	12.5	12.5	15.0	18.3
B	Dimethicone (and) PEG/PPG-18/18 Dimethicone	5.0	5.0	5.0	5.0	5.0
B	Dimethicone (and) Acrylates/Polytrimethylsiloxymethacrylate Copolymer (40% actives)		12.5			
B	Isododecane (and) Trimethylsiloxysilicate/Dimethiconol Crosspolymer (40% actives)			12.5		
B	Polypropylsilsesquioxane (and) Isododecane (75% actives)					6.7
C	Water	47.0	47.0	47.0	47.0	47.0
C	Niacinamide	3.0	3.0	3.0	3.0	3.0

Table 2. Quantitative pigmented formulations included in this study

Phase	Ingredient	Foundation (wt.%)					Liquid lipstick (wt.%)				
		No FF	Silicone Acrylate	SiOH/MQ Cross-polymer	MQ	T-Propyl	No FF	Silicone Acrylate	SiOH/MQ Cross-polymer	MQ	T-Propyl
A	Dimethicone	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0
A	Isododecane	0.2	0.2	0.2	0.2	0.2	-	-	-	-	-
A	CI 77499 (IRON OXIDES)	7.0	7.0	7.0	7.0	7.0	-	-	-	-	-
A	CI 77891 (TITANIUM DIOXIDE)	2.5	2.5	2.5	2.5	2.5	-	-	-	-	-
A	CI 77492 (IRON OXIDES)	0.4	0.4	0.4	0.4	0.4	-	-	-	-	-
A	CI 77491 (IRON OXIDES)	-	-	-	-	-	10.0	10.0	10.0	10.0	10.0
A	CI 45410 (RED 27 LAKE)	25.0	12.5	12.5	15.0	18.3	25.0	12.5	12.5	15.0	18.3
A	Dimethicone	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0
A	Dimethicone (and) PEG/PPG-18/18 Dimethicone	-	12.5	-	-	-	-	12.5	-	-	-
A	Dimethicone (and) Acrylates/Polytrimethylsiloxymethacrylate Copolymer (40% actives)	-	-	12.5	-	-	-	-	12.5	-	-
A	Isododecane (and) Trimethylsiloxysilicate/Dimethiconol Crosspolymer (40% actives)	-	-	-	10.0	-	-	-	-	10.0	-
A	Trimethylsiloxysilicate (100% actives)	-	-	-	-	6.7	-	-	-	-	6.7
A	Polypropylsilsesquioxane (and) Isododecane (75% actives)	37.0	37.0	37.0	37.0	37.0	37.0	37.0	37.0	37.0	37.0
B	Water	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0
B	Niacinamide	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0

B. Methods. Cosmetic formulations are complex systems due to the presence of numerous chemical ingredients, making it difficult to isolate and investigate individual contributions [2,17,18]. Thus, it is important to control variables that can interfere in the permeation kinetics of the active molecule. Key formulation ingredients were identified and their concentrations were assigned based on conventional use levels in color cosmetic products: Niacinamide, emulsifier and film former concentrations were kept constant at 3.00%, 1.25% and 5.00%, respectively. Oil to water phase ratio was kept constant at 1:1. Formulations are described in Tables 1 and 2.

However, there are other variables which can potentially influence how niacinamide can be delivered [11,13,16] to the skin or to a test membrane and must also be controlled: phase and pigmentation. Niacinamide is a water-soluble molecule, and it is hypothesized that inversely emulsifying a niacinamide aqueous solution can inhibit its delivery as it would be present in the internal phase of the emulsion. It is also hypothesized that inorganic particles, like titanium dioxide and iron oxides, can represent a physical barrier once deposited on the skin, potentially inhibiting permeation.

To mitigate these two equally important variables, permeation studies were carried out in four stages: in the first one, an aqueous solution of niacinamide was evaluated by ATR-FTIR [12] and tape stripping/HPLC [6,7,8,11,14]. It represents positive control; the situation where optimal delivery is expected. Secondly, this aqueous solution was inversely emulsified (W/Si) in the absence of any film former and permeation was studied using the same techniques utilized in the first stage. For the third stage, silicone and silicone-acrylate film formers were added separately to the W/Si emulsion and niacinamide permeation was studied, once again, by ATR/FTIR and tape stripping/HPLC. And finally, as the fourth and final stage, W/Si emulsions were pigmented and studied by means of Franz Cells using synthetic membranes.

The influence of phase could be objectively determined by comparing in vitro and in vivo data from stages one and two, meanwhile the influence of film formers could be objectively determined by comparing data from stages one to three. As the technique employed in the fourth stage was different, data had to be analyzed separately to determine the influence of pigments in the permeation of niacinamide.

B.1. In Vitro ATR/FTIR Spectroscopy. The ATR-FTIR permeation experiments [19,20] were conducted on a Perkin Elmer Spectrum 100 system, fitted with an ATR ZnSe crystal accessory and controlled by Spectrum software. The substrate of choice was Vitro-Skin®, purchased from IMS Inc., USA. The membrane was prepared by cutting a piece of 5.4 cm x 2.7 cm and hanging it inside a sealed chamber containing a reservoir with 4L of a (40:60) (glycerin:water) solution for at least 24 hours prior to the analysis. An aliquot of 20 uL of the test formulation was poured from a micropipette on the membrane and spectras were acquired in triplicates from 700 cm^{-1} to 4000 cm^{-1} with 12 accumulations at times 5, 10, 15, 20, 25, 30, 45, 60, 90 and 120 minutes to build the permeation curve. The area under the curve of the band peaking at 1700 cm^{-1} was calculated.

B.2. In Vivo Tape Stripping. Three panelists were recruited for this analysis and 3 circular areas with a diameter of 4.40 cm were marked on each forearm, corresponding to an area of 60.80 cm^2. A total of six areas were analyzed, one per treatment. Each testing formulation was applied at 4.0 mg/cm^2 from a micropipette on the testing area and spread with a disposable latex finger cot with 120 circular movements to distribute the product homogeneously [14,15]. The mass of the disposable cot was controlled to determine the amount of formulation not transferred to the skin. Panelists were kept in a controlled environment for 2 hours to allow niacinamide to permeate.

D-Squame® standard stripping tapes were purchased from Clinical & Derm LLC, removed from skin at constant speed, added to Falcon tubes in groups of three or five for extraction with 5 mL of ammonium acetate buffer:isopropyl alcohol (50:50). Solutions were filtered using PVDF 0,45 μm membrane and transferred to a 2 mL glass vial. Niacinamide was determined by high pressure liquid chromatography in an Agilent system coupled with a diode array detector set up at 264 nm. The separation was carried out using an Eclipse C8 column (250 x 4,6 mm 5μm) maintained at 25ºC in a 1,0 mL . min -1 gradient flow with acetonitrile and ammonium acetate buffer as a mobile phase.

B.3. In Vitro Franz Diffusion Cells. Finite dose studies were performed in quadruplicates in a Logan Automated Transdermal Dry Heat Diffusion Cell Sampling System coupled with a Waters Acquity H-Class UPLC-UV. Formulations were poured down on Strat-M®

membranes at 4.0 mg/cm^2 and niacinamide concentration in the receptor compartment containing 0.05 M acetate buffer was acquired at times 0.5, 1, 2, 4, 6, 8, 10 and 12 hours to build the permeation curve.

B4. Film Morphology. Films were cut and placed on an adhesive tape on a stub (45° angled). In order to prevent sample charging each sample was coated with a thin layer of Au/Pd and analyzed in a Jeol IT300 LV SEM with a 10 mm working distance and an aperture of 2. Digital images were acquired with secondary electron mode. Energy dispersive spectroscopy (EDS) analysis was conducted using a Bruker Xflash 6|30 EDS microanalysis system, which is attached to the SEM. Spectra were acquired using a 10 mm working distance and an aperture of 2.

B.5. Rub-off Resistance. A washability tester from Elcometer, model 1720, was used to rub-off the films against felt bands attached to the test site. A silicone membrane supplied by The Dow Chemical Company was cut in circles with 5.31 cm of diameter and an aliquot of 42.48 uL of test formulation was poured on it from a micropipette. The formulation was spread using a previously weighted latex finger cot by doing 120 circular cycles and subsequently put inside an oven at 45ºC for 30 minutes. The latex finger cot was weighted again to determine the amount of formulation not transferred to the membrane and rubbed-off 25 times at minimum speed. Niacinamide was extracted from the silicone membrane and quantified by HPLC using the same procedure as described in section B.2.

Results and Discussion

A. In Vitro ATR/FTIR Spectroscopy. The ATR/FTIR spectroscopy technique enables the direct identification and quantification of a permeant concentration in a membrane in situ and in real time, as long as a distinguishable absorbance band can be assigned to it. Niacinamide has a characteristic band at ~1700 cm^{-1} assigned to the stretching of the carbonyl bond, which does not overlap significantly with any of the bands assigned to Vitro-Skin®. Besides that, normalization and subtraction of the membrane spectra are

performed in the software to eliminate any possible interference. Once niacinamide is micro pipetted on the substrate, it progressively permeates until it reaches 2 µm away from the membrane-crystal interface, which is the expected depth of penetration of the IR beam in the ZnSe ATR cell. It happens fast and absorbance is registered after 1 minute of contact of the solution/emulsion with the membrane (Figure 1).

As time elapses, absorbance shows a logarithmic increase with time as niacinamide builds up in the membrane until a plateau is reached. At this point, it is believed the interface membrane-crystal is saturated with niacinamide and absorbance no longer increases - the time needed to reach saturation varies according to the formulation being experimented. No information about a gradient of concentration at different depths of the membrane can be obtained, this is an inherent limitation of the technique.

Smoothed curves of the area under the peak at ~1700 cm^{-1}, which correlates with concentration of niacinamide, versus elapsed time are shown in Figure 1.

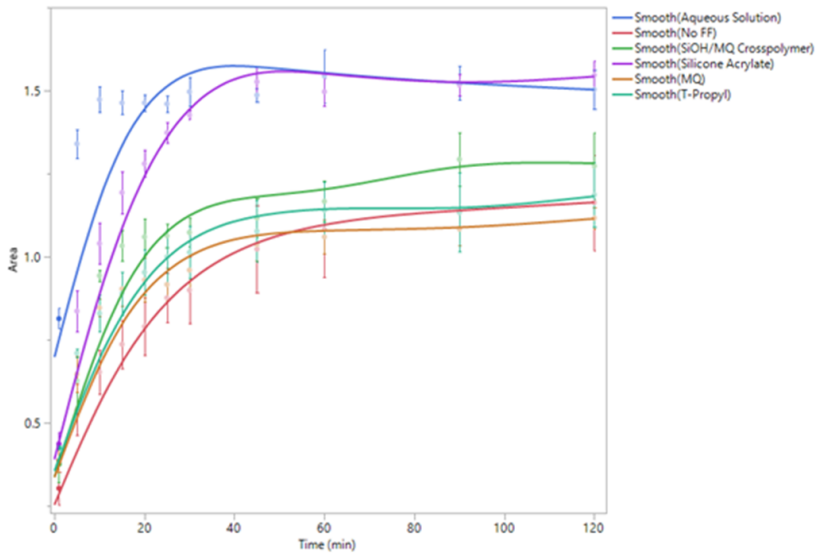
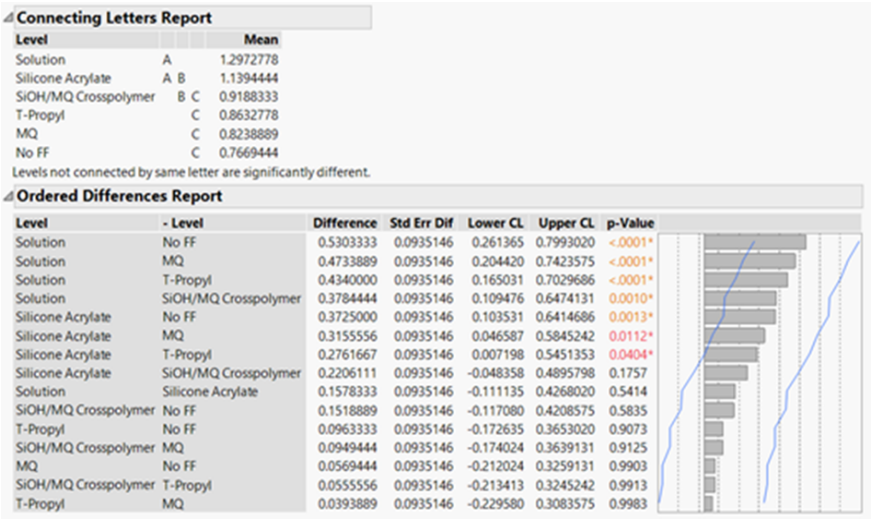


Figure 1. smoothed average curves of area vs time for all formulations containing niacinamide

It is observed a rapid permeation of niacinamide during the first twenty minutes of the experiment from when it starts slowing down as the concentration gradient decreases inside the membrane. The ascending region can provide information about how fast niacinamide can be delivered to the membrane, and the asymptote (or plateau) can provide information

about the maximum concentration that can permeate the membrane, given the physical barrier imposed by the ATR crystal.

Significance analysis among treatments was obtained by comparing means using Tukey HSD and is reported in Figure 2, including the connecting letter report.



Connecting Letters Report

Level		Mean
Solution	A	1.2972778
Silicone Acrylate	A B	1.1394444
SiOH/MQ Crosspolymer	B C	0.9188333
T-Propyl	C	0.8632778
MQ	C	0.8238889
No FF	C	0.7669444

Levels not connected by same letter are significantly different.

Ordered Differences Report

Level	- Level	Difference	Std Err Dif	Lower CL	Upper CL	p-Value
Solution	No FF	0.5303333	0.0935146	0.261365	0.7993020	<.0001*
Solution	MQ	0.4733889	0.0935146	0.204420	0.7423575	<.0001*
Solution	T-Propyl	0.4340000	0.0935146	0.165031	0.7029686	<.0001*
Solution	SiOH/MQ Crosspolymer	0.3784444	0.0935146	0.109476	0.6474131	0.0010*
Silicone Acrylate	No FF	0.3725000	0.0935146	0.103531	0.6414686	0.0013*
Silicone Acrylate	MQ	0.3155556	0.0935146	0.046587	0.5845242	0.0112*
Silicone Acrylate	T-Propyl	0.2761667	0.0935146	0.007198	0.5451353	0.0404*
Silicone Acrylate	SiOH/MQ Crosspolymer	0.2206111	0.0935146	-0.048358	0.4895798	0.1757
Solution	Silicone Acrylate	0.1578333	0.0935146	-0.111135	0.4268020	0.5414
SiOH/MQ Crosspolymer	No FF	0.1518889	0.0935146	-0.117080	0.4208575	0.5835
T-Propyl	No FF	0.0963333	0.0935146	-0.172635	0.3653020	0.9073
SiOH/MQ Crosspolymer	MQ	0.0949444	0.0935146	-0.174024	0.3639131	0.9125
MQ	No FF	0.0569444	0.0935146	-0.212024	0.3259131	0.9903
SiOH/MQ Crosspolymer	T-Propyl	0.0555556	0.0935146	-0.213413	0.3245242	0.9913
T-Propyl	MQ	0.0393889	0.0935146	-0.229580	0.3083575	0.9983

Figure 2. significance analysis by comparing means using Tukey HSD and connecting letter report for studies with ATR/FTIR

Permeation of niacinamide through the Vitro-Skin® membrane significantly varies when it is inversely emulsified compared to its aqueous solution. Permeation is slower and the saturation is achieved at a lower concentration, indicating a detrimental and important effect of the phase, as hypothesized.

There is no significant difference in the permeation kinetics and saturation concentration when any of the silicone film formers are added to the continuous phase of the W/Si emulsion ([MQ], [SiOH/MQ Crosspolymer], [T-Propyl]). On the other hand, adding Acrylates/Polytrimethylsiloxymethacrylate Copolymer to the W/Si emulsion significantly changed the permeation kinetics of niacinamide, mitigating the detrimental effect of having it in the internal phase of the emulsion and generating statistical correlation with the curve obtained for the niacinamide in aqueous solution, which is the positive control.

For an in-depth analysis of the curves, data was fitted to an Exponential 3P model in the JMP software, which conforms to the following formula:

$$a + b\text{Exp}(cx)$$

Where:

a = asymptote

b = scale

c = growth rate

x = time

The exponential 3P fit model is characterized by a continuous increase, but the rate of growth slows so that the model has an asymptote, which correlates to the saturation concentration at the membrane-crystal interface. Fitted curves, grouped and ungrouped, are illustrated in Figure 3. Fitting returned a R^2 of 0.9292.

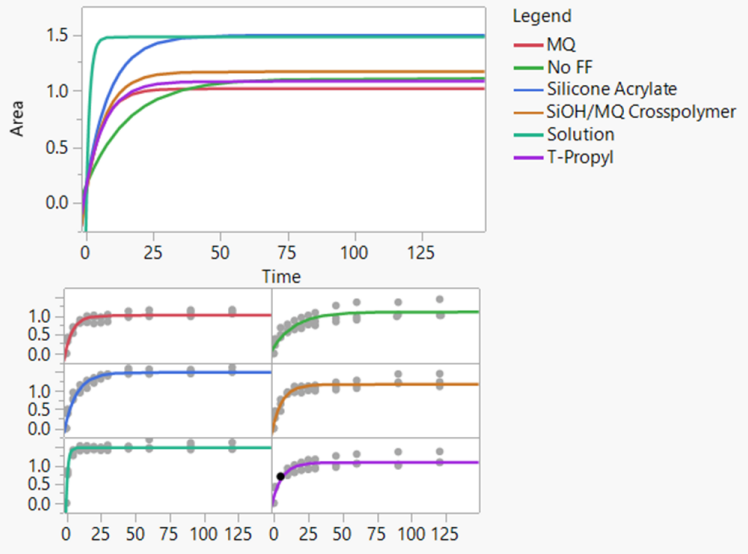


Figure 3. curves fitted to Exponential 3P model in JMP software, grouped and ungrouped

Equation parameters can be tested for equality across the formulations by an Analysis of Means (ANOM), represented by the decision limits shaded in blue in Figure 4. If the result

for a given formulation in a parameter exceeds the limits, the parameter is different from the overall mean. Alpha level for this analysis was set at 0.05, representing a 95% confidence level. It is a good tool to analyze the influence of film formers in the speed of the delivery of Niacinamide by analyzing the growth rate, and the saturation level by analyzing the asymptote, testing the findings from the smoothed curves and HSD Tukey significance test (Figures 1 and 2).

Niacinamide delivered from a W/Si emulsion free of film formers has a lower asymptote and a higher growth rate, confirming the findings from Figure 1 and the hypothesis that inversely emulsifying the active inhibits its delivery to the membrane. Fitted data also confirms silicone acrylate mitigates this detrimental effect by boosting the delivery of Niacinamide.

None of the silicone film formers inhibited the delivery of niacinamide from the W/Si emulsion.

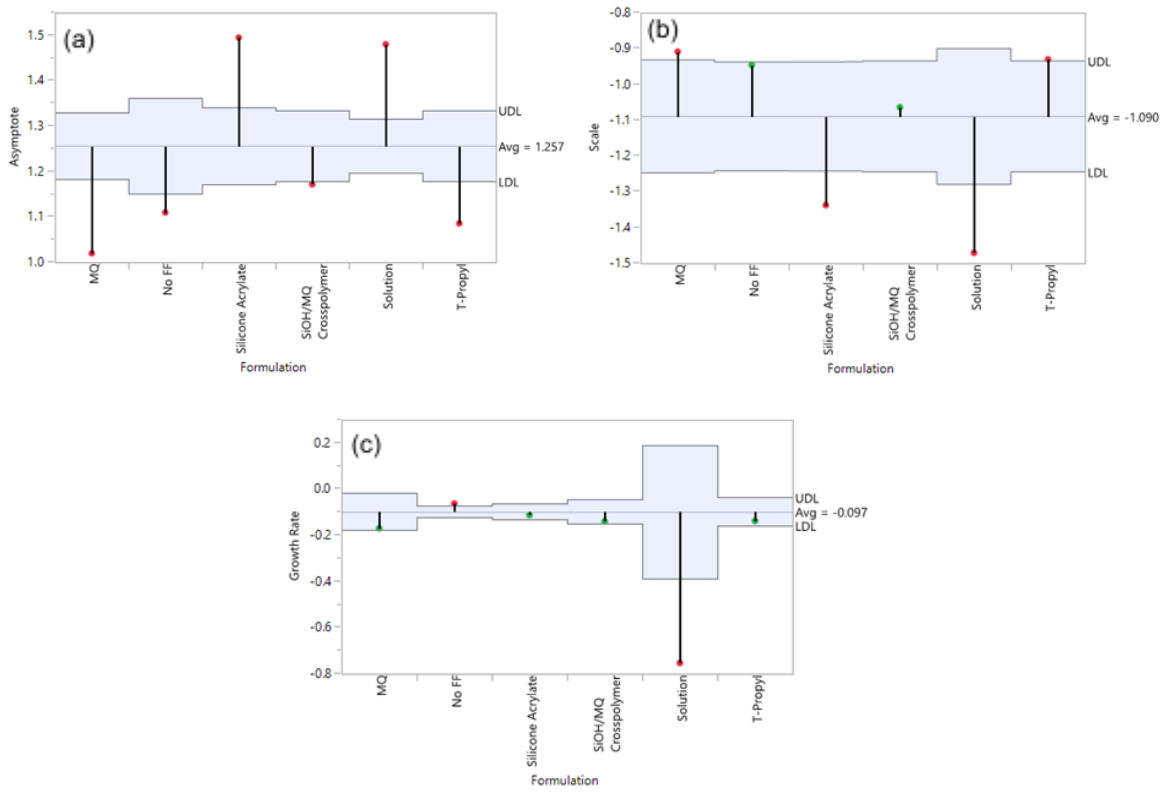


Figure 4. parameters estimate for the Exponential 3P fit model (a) Asymptote, (b) Scale, (c) Growth Rate

B. In Vivo Tape Stripping. tapes went through the extraction process in groups of five to maximize signal-to-noise ratio in the HPLC analysis. An exception was made for the first 3 tapes, which are expected to contain a higher concentration of niacinamide. Data for the three panelists are averaged and permeation curves are constructed as concentration of niacinamide, either individually or cumulatively, by groups of tape, as represented in Figure 5.

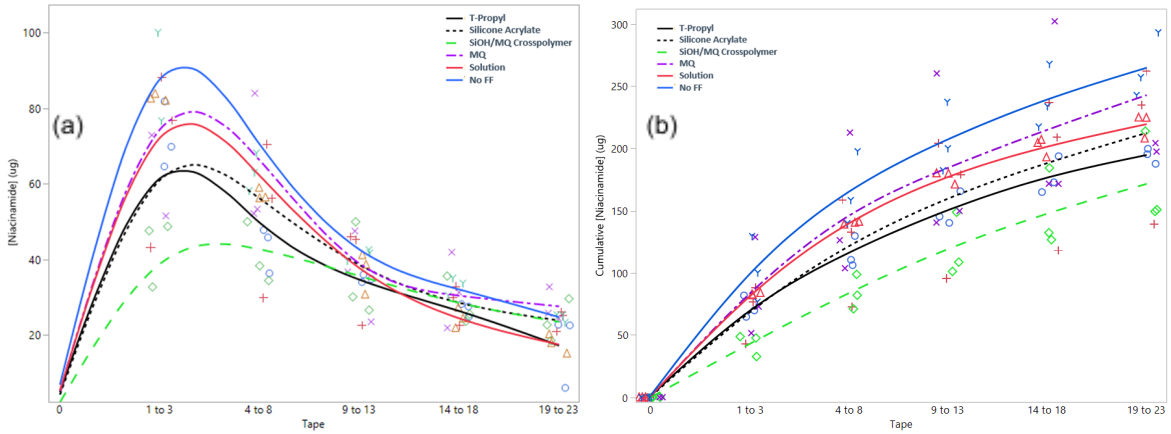


Figure 5. concentration of niacinamide recovered (a) individually by groups of tapes, (b) cumulative by group of tapes

One can think of groups of tapes as different depths of the epidermis, as tape stripping involves the removal of sequential macroscopic layers of the *stratum corneum*. As observed in Figure 5a, a significantly higher concentration of niacinamide is present on the outer layer of the skin and may serve as a reservoir for a long term delivery. The same data is represented in Figure 6a as the weight percentage of total niacinamide applied on the skin. Delivery of niacinamide is not as fast as observed in the ATR/FTIR technique, possibly due to limitations of the membrane to mimic human skin. The presence of SiOH/MQ Crosspolymer in the continuous phase of the W/Si emulsion significantly decreases the concentration of niacinamide in the reservoir, pushing it faster towards the epidermis. It also causes a more homogeneous distribution of the active in different skin layers/groups of tapes, as seen in Figure 5b. The mechanism involved is unknown and not a subject of this research project. An apparent similar performance is seen for T-Propyl and Silicone

Acrylate, however, statistical significance was not achieved due to a low number of panelists involved in this study.

Figure 5b shows the cumulative concentration of niacinamide. Curves show that the steady-state has not been reached after 2 hours of permeation, indicating niacinamide takes longer to completely permeate the *stratum corneum* and to reach deeper skin layers. The presence of a high concentration reservoir corroborates this assessment.

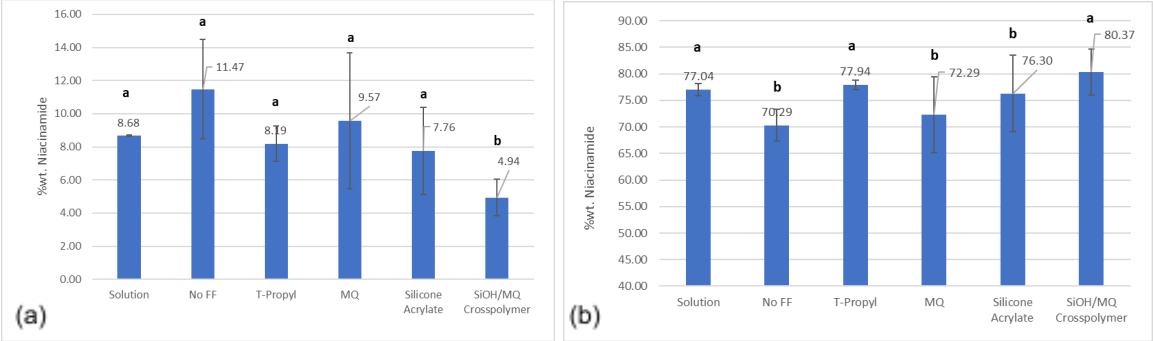


Figure 6. percentage of mass of niacinamide recovered (a) from the first 3 tapes; (b) delivered to the skin, calculated as (total niacinamide applied - total niacinamide recovered)

Recovery rates of niacinamide ranged from 20% to 30%, depending on the formulation. It is fair to believe that the unrecovered active has been successfully delivered to the skin within the 2 hours period. Weight percent of total niacinamide delivered is reported in Figure 6b and demonstrates that a lower concentration is obtained from a W/Si emulsion compared to its aqueous solution. However, when SiOH/MQ Crosspolymer and T-propyl are added to the emulsion, it presents statistically equivalent performance to the aqueous solution of niacinamide, boosting the delivery of the active.

C. In Vitro Franz Diffusion Cells. Pigmented formulations were analyzed with the objective of understanding the influence of inorganic and organic particles associated with silicone film formers in the diffusion of niacinamide into a synthetic membrane. Cumulative penetration data was acquired up to 12 hours for both foundations and lipsticks and kinetic curves are presented in Figures 7 and 8, respectively. Film formers are plotted separately to facilitate visualization and analysis.

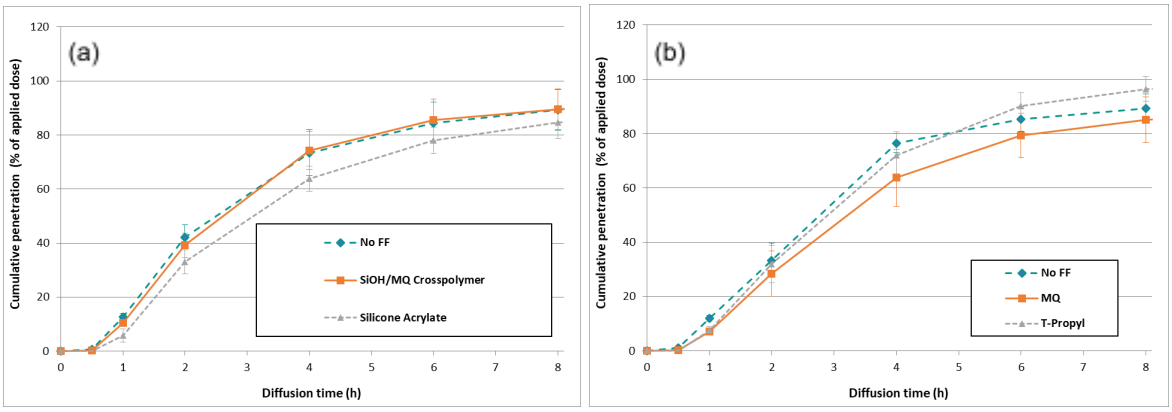


Figure 7. cumulative permeation curves of niacinamide from foundations into Franz cells containing (a) no film former, SiOH/MQ Crosspolymer and Silicone Acrylate, (b) no film former, MQ and T-Propyl

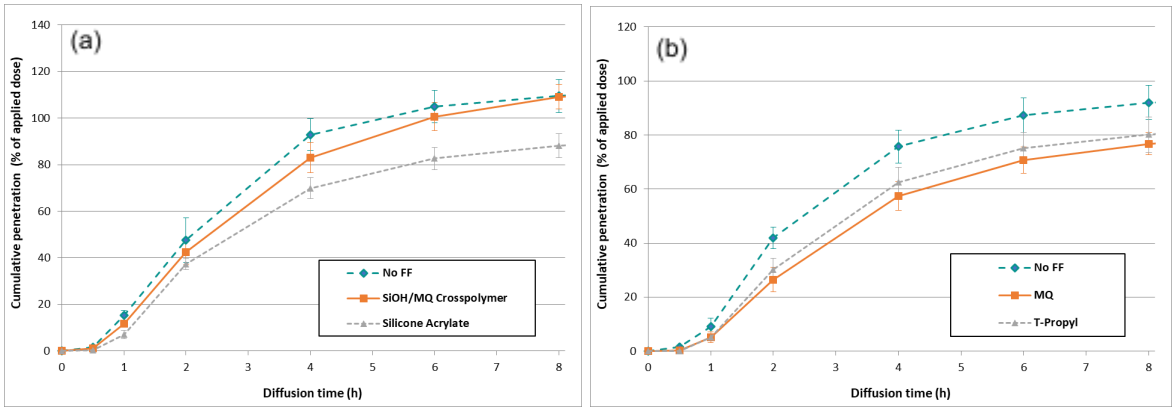
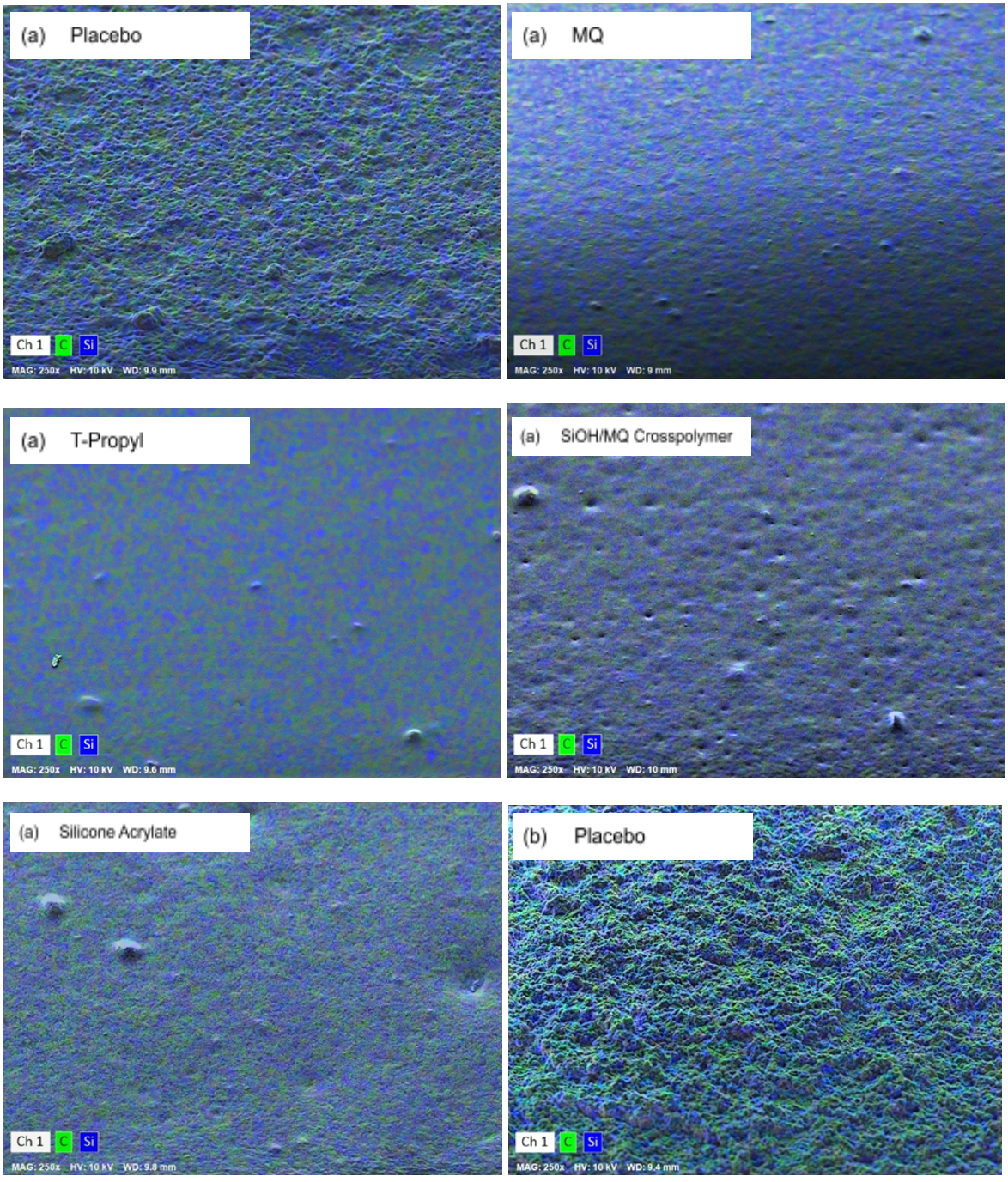


Figure 8. cumulative permeation curves of niacinamide from liquid lipsticks into Franz Cells containing (a) no film former, SiOH/MQ Crosspolymer and Silicone Acrylate, (b) no film former, MQ and T-Propyl

Permeation is reported as percentages of applied dose to correct eventual variations in the weight of product applied on the membrane. No significant differences among film formers and placebo emulsion were identified, neither for foundations or liquid lipsticks. Permeation kinetics of niacinamide among treatments are equivalent. Positive effects from silicone acrylate and SiOH/MQ Crosspolymer identified by ATR/FTIR and tape stripping, respectively, did not replicate with pigmented formulations.

At the same time, it is possible to conclude that silicone/silicone acrylate film formers and pigments, both organic and inorganic, do not inhibit the permeation of niacinamide.

D. Film Morphology. Thin films of lipsticks and foundations in Table 2 were prepared on Strat-M membranes and visualized by Scanning Electron Microscopy (SEM). Images for different film formers and formulations can be seen in Figure 9 along with elemental distribution for C and Si obtained by Energy Dispersive Spectroscopy (EDS).



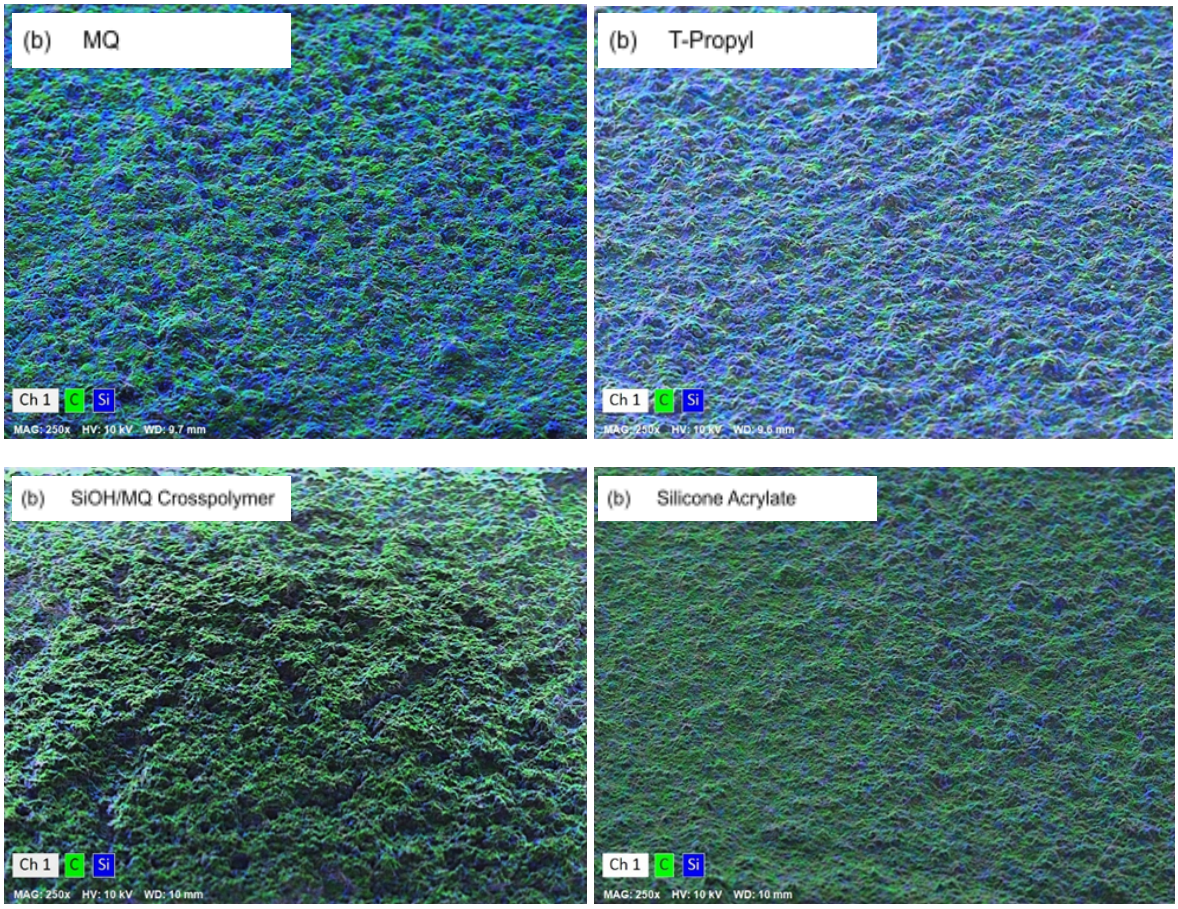


Figure 9. SEM images of films with different silicone and silicone-acrylate film formers (a) foundations; (b) lipsticks

All films observed in Figure 9 are continuous and homogeneous, however, the ones made of lipsticks are inherently rougher compared to the ones made of foundations. As expected, a high presence of Silicon can be observed from the EDS contrast images and this element is homogeneously distributed along the films. All silicone and silicone-acrylate film formers significantly improved film morphology by decreasing surface roughness, with remarkable performance of Silicone Acrylate in the lipstick formulation and T-propyl in the foundation.

E. In Vivo and In Vitro Correlation. Each of the methods explored in this study have its own difficulties and limitations. In vitro relies on synthetic membranes that can mimic certain properties of human skin, but cannot fully replicate it. ATR/FTIR deals with a physical barrier composed of a membrane-crystal interface, which forces the correlation of a plateau to the final active concentration in the substrate. The tape stripping technique is time/resource consuming and demands a high number of individuals to minimize effects of human-to-human variability in the statistical power of the study. And finally, Franz diffusion cells also operate with synthetic membranes, which are still not close to mimicking human skin.

This present study allows ATR/FTIR data to be directly compared with the in vivo because the same formulations were tested. Both techniques validated 2 important hypotheses: inversely emulsifying niacinamide is detrimental to its permeation (speed and final concentration), and silicone film formers do not inhibit the delivery of niacinamide. Here, in vitro did a great job and correlated very well with in vivo. However, differences between techniques were observed when analyzing film formers individually - data from ATR/FTIR pointed Silicone Acrylate as a booster, meanwhile in vivo indicated SiOH/MQ Crosspolymer as a booster. It proves that in vitro may not have enough accuracy to discriminate among film formers and correlate with in vivo.

Data from Franz diffusion cells cannot be directly correlated to in vivo as non-pigmented formulations were not tested. As future work, pigmented formulations will be analyzed by means of ATR/FTIR and non-pigmented formulations by Franz diffusion cells, allowing methods to be directly compared.

F. Rub-off Resistance. Silicone and silicone acrylate film formers are polymers capable of forming a cohesive and continuous film on keratinous surfaces with optimum adhesion and flexibility, being fundamental ingredients in color cosmetics to achieve long lasting. Thus, it is fair to hypothesize that such polymers may have the ability to support the effectiveness of color cosmetics containing a skin care active by protecting it from being rubbed-off throughout the day, minimizing losses from unwanted frictions, washes or any other aggression. To test this hypothesis, formulations were tested as described in section B.4 and results are presented in Figure 10.

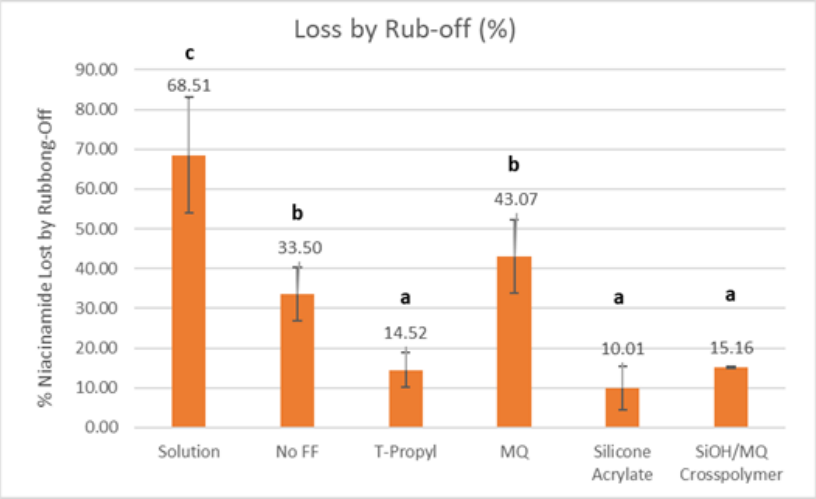


Figure 10. percentage loss of niacinamide by rubbing-off a silicone membrane against a felt band, 25 cycles

Most of the niacinamide (68.51%) was removed from the silicone membrane when delivered in solution, meanwhile loss significantly decreases when delivered from a W/Si emulsion (33.50%). MQ silicone film former did not significantly decrease the loss of niacinamide compared to placebo emulsion – the film formed was rigid and broke down during the rub-off cycles, facilitating its removal. On the other hand, SiOH/MQ Crosspolymer, T-Propyl and Silicone Acrylate significantly decreased the loss of niacinamide from 33.50% down to 15.16%, 14.52% and 10.01%, respectively.

Silicone and silicone acrylate film formers, except for MQ, significantly improved rub-off resistance of the tested formulations, potentially enhancing the long-term delivery of niacinamide to the skin by protecting it from being rubbed-off.

Conclusion. This work demonstrated that silicone-based film formers improve the delivery of niacinamide from water-in-silicone emulsions and prevent its loss from abrasion. Morphology of the films were also significantly improved. It is believed that this study opens up a new frontier for makeup with valuable knowledge for the development of color cosmetics with skincare benefits. New insights for the development of sunscreen formulations with physical filters and skincare attributes can also be correlated.

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Conflict of Interest Statement. NONE.

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