Case Studies for the Use of Silicone Chemistry in Topical Formulations

Marc Eeman, Morgane Le Meur, Laurie Maes
Dow Corning Europe S.A., Seneffe, Belgium

Hyder Aliyar
Dow Corning Corporation, Midland, Michigan, USA

Xavier Thomas
Dow Corning France, S.A., Lyon, France
Abstract
This report demonstrates the benefits of silicone-based polymers for enhancing pharmaceutical drug delivery to skin, by means of three independent studies.

The first revealed that an anhydrous semisolid formulation with a cross-linked silicone polymer offers faster and higher skin delivery of the nonsteroidal anti-inflammatory drug ibuprofen (IBP) compared to similar formulations based on organic excipients, as well as to a commercial benchmark.

The second study focused on ascorbic acid (AA), a depigmenting agent used to treat hyperpigmentation disorders. This study combined a cross-linked silicone polymer and a silicone emulsifier to develop an anhydrous glycerin-in-silicone system that stabilized AA for a significantly longer time compared to a commercial benchmark. Preservation of the chemical stability of the drug was shown to have a direct impact on its depigmenting activity.

The third study focused on betamethasone dipropionate (BDP), a corticosteroid used to treat itching in chronic skin disorders. This study showed that a silicone resin crosspolymer film-forming emulsion provides significantly higher substantivity than a commercial benchmark based on an oil-in-water emulsion without impacting the delivery of BDP to skin.

Introduction
Silicones are polymer compounds with a molecular structure formed by a chain of alternating silicon and oxygen atoms. The most common are various forms of polydimethylsiloxane (PDMS), where the strong polar backbone of Si-O bonds is surrounded by a nonpolar “cloud” formed by organic methyl groups attached to the silicon atoms. The length of the Si-O chain determines the viscosity of the silicone fluid, with the highest molecular weights related to gum-like materials[1, 2]. A broad variety of silicone materials can be derived from PDMS, including silicone gum blends, elastomers, resins, and their emulsion forms. Silicone materials have a use history of more than 60 years in health care applications because of their wide biocompatibility profile, confirmed biodurability, and versatility of their properties. These characteristics continue to stimulate emerging applications.

In today’s health care market, the flexibility of silicone materials coupled with market change suggests potential for novel applications related to topical products. The current global regulatory landscape is evolving rapidly, driven in part by increased consumer focus on self-care, and resulting efforts by government agencies to lower public risk. Interest is growing in treatments that contain less to no active pharmaceutical ingredients (APIs), a development that stands to increase the use of semisolid delivery forms not licensed as drugs. In these instances, products would be commercialized and registered as medical devices if their intended effects could be obtained by physical means. At the other end of the spectrum, trends in modern dermatology suggest development based on novel excipients acting as new delivery forms, offering innovation as well as greater efficiency with existing active pharmaceutical ingredients.

The aim of the three studies described here was to assess the utility of silicone-based polymers to enhance the skin delivery and chemical stability of drugs used for pain management and for the treatment of skin conditions such as hyperpigmentation disorders and psoriasis. Given the range of silicone material options available, it is useful to examine the formulating process more closely, as well as to assess the ability of these materials to deliver topical treatments. In addition, based on the evolving regulatory landscape for topical applications, these materials may suggest broader potential for formulating options.

Study 1: Enhanced delivery of anti-inflammatory drugs
Although ibuprofen (IBP) is commonly formulated with alcohol, water and a gelling agent, experiments were conducted to investigate the benefits of silicone as a primary polymer in topical semisolid pharmaceutical formulations. In this context, an anhydrous formulation based on a novel cross-linked silicone polymer network material containing 5 wt% IBP was developed and the delivery of IBP was assessed by means of both in vitro and in vivo methodologies. Performance of the silicone-based system was compared to similar formulations prepared using petrolatum, an acrylic, or a cellulose polymer as well as to a commercial benchmark.
Materials and Methods

Materials
The cross-linked silicone polymer network used in this study is a developmental silicone material for health care applications and was obtained from Dow Corning Corporation (Midland, MI, USA). This material comprises high-molecular-weight polyglycol cross-linked silicone polymer network particles swollen in isododecane with an average solid content of 15.00 ± 0.75%[3].

The EUDRAGIT® L100 Type A NF acrylic copolymer was obtained from Evonik Industries (Hanau-Wolfgang, Germany). The ETHOCEL™ Standard 10 Ethylcellulose NF premium was obtained from The Dow Chemical Company (Midland, MI, USA). Ibuprofen (IBP, USP grade) was obtained from Spectrum Chemicals Manufacturing Corporation (New Brunswick, NJ, USA). The commercial benchmark used for both the in vitro and in vivo permeability experiments was a hydroalcoholic gel product with the following ingredient composition: isopropyl alcohol, solketal, poloxamer 407, miglyol 812, water, lavender oil, neroli oil, and IBP (5 wt%).

Formulations
All formulations were prepared with 5 wt% IBP (see Table 1). The required amount of IBP was weighed into a SpeedMixer™ cup and dissolved by the addition of liquid components with gentle mixing/swirling. The silicone material or petrolatum was then added to the IBP-containing solution and mixed in a SpeedMixer (AM501T; Hauschild, Hamm, Germany) at 3000 rpm until a homogeneous formulation was obtained. For the formulations based on the acrylic or cellulose polymer, the polymer in a powder form was dissolved in isopropyl alcohol and added last during the preparation of corresponding formulations.

In vitro permeability testing
The in vitro permeability of ibuprofen was assessed at 32°C through epidermis tissues prepared from custom harvested full-thickness human cadaver skin (National Disease Research Interchange, Philadelphia, PA, USA). Tissues were placed on manual Franz diffusion cells (volume: 5 mL) filled with a phosphate-buffered saline solution (PBS, pH 7.4). For each formulation, the applied dose was 15.5 ± 0.5 mg over a permeation area of 0.63 cm².

Three cells were prepared for each formulation. The experiment was carried out for 8 hours, and 1 mL of sample was collected from the receptor chamber at 0.5, 1, 2, 4, 6, and 8 hours and replaced with fresh PBS solution. Sink conditions were maintained for IBP in the PBS throughout the experimental period. All samples were analyzed using a Waters ACQUITY™ ultra-high performance liquid chromatography (UPLC) system (Waters Corporation, Milford, MA, USA) to determine the IBP concentration.

In vivo permeability testing
The in vivo permeability of IBP was assessed using 11 cannulated Fischer rats (age: 8-10 weeks minimum; weight: 225 g - 250 g) (Charles River Laboratories Inc., Wilmington, MA, USA): five animals received the anhydrous silicone-based formulation, five animals received the commercial benchmark, one animal was dosed with a placebo version of the anhydrous silicone-based formulation.

The formulation dose was 424.7 mg (placebo), 470.5 ± 25.3 mg (silicone-based system) and 504.9 ± 25.9 mg (benchmark). The application site was the back of the animal, with an application...
area of 10 cm². There was no occlusion. IBP was assayed from the blood drawn from the animals at several time intervals (0.25, 0.5, 1, 2, 4, and 8 hours post application) as well as from the excised skin from the application site of the animal at the end of the experiment (8 hours).

The in vivo animal study complied with all applicable sections of the final rule of the Animal Welfare Act regulations (9 CFR, part 1, 2, and 3).

Results and Discussion

The in vitro permeability of IBP was assessed using human cadaver epidermis. Figure 1 shows in vitro IBP permeability profiles of the silicone-based formulation compared to the commercial benchmark (A) and to similar formulations prepared using either petrolatum, the acrylic polymer or the cellulose polymer (B). The permeability experiment was carried out for all the formulations at the same time on the same skin donor (in triplicate). Compared to all the other formulations, the silicone-based anhydrous system exhibited much higher flux at 1, 2, 4, 6 and 8 hours with a maximum flux during the 2-hour to 4-hour period. In addition, the silicone-based system provided a cumulative 246.1 μg.cm⁻² of IBP in 8 hours, which was 2.4, 2.5, 6.3, and 8.6 times higher than the petrolatum-based formulation (103.2 μg.cm⁻²), the formulation based on acrylic polymer (98.5 μg.cm⁻²), the formulation made from cellulose polymer (39.0 μg.cm⁻²), and the commercial benchmark (28.6 μg.cm⁻²), respectively.

To confirm the efficient IBP delivery observed in the in vitro study from a silicone-based formulation, an in vivo study was conducted on cannulated rats. The in vivo study was performed only for the commercial benchmark and the silicone-based system. A placebo version of the silicone-based formulation was used for reference. As illustrated in Figure 2, the silicone-based system provided a much higher IBP concentration in the blood over the commercial benchmark with the highest average concentration obtained at 1 hour. At this sampling time, the silicone-based system delivered an average of 8.7 times IBP compared with the benchmark. The higher IBP delivery was also confirmed when quantifying the drug in the skin tissues excised at the end of the study (8 hours); although the silicone-based system showed an average 264 ± 59 μg.g⁻¹ of IBP in the animal skin tissues, the animals dosed with the benchmark displayed a 2.5 times lower concentration (102 ± 5 μg.g⁻¹).
Study 2: Delivery of actives sensitive to oxidation

The second study focused on ascorbic acid (AA), a compound that is recognized for its strong antioxidant properties\(^4\) and its use as a skin depigmenting agent\(^5\) for treating hyperpigmentation disorders such as melasma, lentigines and post-inflammatory hyperpigmentation.

To address the high vulnerability of AA to oxidation\(^6\), an anhydrous glycerin-in-silicone system capable of stabilizing up to 10% AA was developed (Table 2). It consists of a two-phase formulation made in one case from the combination of a cross-linked silicone polymer and a silicone emulsifier, and another from an AA solution in a polyol such as glycerin or propylene glycol. The addition of appropriate amount of polyol in such system protects AA from oxidation by reducing the water activity in the immediate vicinity of the active compound\(^7\).

Although having a high concentration of glycerin or any other polyol in an anhydrous formulation protects AA from oxidation, it impacts negatively the sensory characteristics of the formulation. By adjusting the silicone chemistry, and more specifically by formulating the polyol into a cross-linked silicone polymer, it is possible to improve considerably the sensory characteristics of the final formulation, which becomes lighter and less greasy than the formulations without silicone.

The benefits of the silicone-based system on AA stability, skin penetration and skin depigmenting efficacy are described in the following section.

Materials and Methods

Materials

All silicone-based ingredients used in the glycerin-in-silicone systems are commercialized products from Dow Corning Corporation (Midland, MI, USA). L-AA (AA) and glycerin were purchased from Sigma-Aldrich (Saint-Louis, MO, USA). Isododecane (Creasil\(^\text{®} \) ID CG) was purchased from Cosmetics Innovations and Technologies Sarl (Dreux, France). dl-\(\alpha\)-tocopheryl acetate was kindly provided by DSM Nutritional Products Ltd (Heerlen, The Netherlands).

Formulations

The anhydrous glycerin-in-silicone formulations were prepared first by blending AA with glycerin at above 90°C and by adding under high shear the glycerin/AA blend to a silicone phase containing a silicone emulsifier, a silicone carrier and a silicone elastomer as well as alpha-tocopheryl acetate. The composition of glycerin-in-silicone systems is described in Table 2.

The performance of the anhydrous glycerin-in-silicone formulation was compared to a commercial benchmark and a pure blend of AA and glycerin. All formulations contained 5 wt% ascorbic acid.

The commercial benchmark was a solution of L-AA in glycerol at pH 6.0 emulsified in a silicone base and prepared under nitrogen atmosphere. It is sold in aluminum tubes for preventing contact with air, and its stability is said to be longer than three years at room temperature. It has the following ingredients: water, glycerin, cyclopentasiloxane, ascorbic acid, propylene glycol, nylon-12, sodium hydroxide, citric acid, PEG/PPG-18/18 dimethicone, propylparaben, acrylates copolymer, fragrance, disodium EDTA, and methylparaben. Table 2 provides the composition of the formulation.

Stability of ascorbic acid

The stability of AA was assessed visually and using a UPLC system from Waters Corporation (Milford, MA, USA) following prolonged
storage at room temperature and at 50°C. Formulation aging was performed in translucent closed jars.

**In vitro skin permeability**

The in vitro permeability of AA was assessed through full-thickness pig skin tissues using a receptor medium made of 0.5% acetic acid in ultrapure water. Experiments were done over a 6 h period, and diffusion cells were sampled every hour via a Logan 912 auto-sampler system with volume replacement (Logan Instruments Corp., Somerset, NJ, USA). Temperature was set to 32°C. Permeated samples were directly analysed by UPLC (Waters Corporation, Milford, MA, USA) to limit AA oxidation. At the end of the diffusion period, the different skin layers (stratum corneum, epidermis, and dermis) were separated for AA recovery analysis. Stratum corneum was removed from the skin by 12-15 consecutive tape-stripping using circular D-Squame® skin sampling discs (CuDerm Corp., Dallas, TX, USA). An appropriate volume of 0.5% acetic acid in ultrapure water was added for extracting AA from the stratum corneum strips. Epidermis was mechanically separated from dermis using curved tweezers. Both epidermal and dermal compartments were placed in distinct glass containers together with an appropriate volume of extraction medium. Extraction of AA in the different skin layers was carried out for 1 hour.

**In vitro skin depigmenting study**

In vitro reconstituted pigmented human epidermis tissues (Bioalternatives, Gençay, France) were used to evaluate the depigmenting efficacy of AA contained in the formulations under investigation. Before Day 7, tissues were grown in AA-containing culture medium, whereas from Day 7 to Day 16 they were cultured in AA-depleted medium to better emphasize the depigmenting efficacy of AA contained in the test formulations. Tissues were topically treated with formulations of interest at Day 7 and at Day 12. Applied dose was 5 mg/cm². Both a non-treated control condition (negative control) and a control condition treated with a positive control were run in parallel. The positive control formulation had the following ingredients: water, glycerin, butylene glycol, butylene glycol, dl-α-tocopheryl acetate (vitamin E acetate), L-AA (vitamin C), silicone elastomer powder or blend (Dimethicone crosspolymer, dimethicone, vinyl dimethicone crosspolymer, etc.), and polyol (glycerin, propylene glycol, butylene glycol). At Day 16, the content of melanin in pigmented human epidermis tissues was evaluated by extracting it using a solution of Soluene 350 (PerkinElmer, Inc., Waltham, MA, USA). Optical density of extracting solution was measured at 405 nm, and melanin content was calculated using a calibration curve obtained for a series of melanin standards (0 μg/mL to 250 μg/mL). A control of the melanin content at Day 7 was also performed to calculate the percentage of synthesis inhibition of melanin from Day 7 to Day 16. All experimental conditions were performed using six tissue replicates (five tissues being used to quantify AA, one tissue being used to assess tissue viability).

**Results and Discussion**

The impact of glycerin on AA stability is demonstrated in Figures 3 and 4. Although the partial or complete substitution of glycerin by water in the internal phase of a glycerin-in-silicone system reduced considerably the concentration of pure AA in the formulation, it had a detrimental effect on the visual appearance of the preparation, which turned rapidly yellow or brown upon AA oxidation (Figure 3).

As illustrated in Figure 4, after 28 days, the benchmark samples held at room temperature and at 50°C both showed significant evidence of discoloration associated with oxidation, although the glycerin-in-silicone formulation exhibited only slight yellowing effect at 50°C.

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**Table 2. Composition of formulations containing ascorbic acid.**

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>(%, w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water-in-silicone emulsifier (PEG-10 dimethicone, PEG/PPG-19/19 dimethicone, etc.)</td>
<td>0-6</td>
</tr>
<tr>
<td>Carrier (caprylyl methicone, isododecane)</td>
<td>0-20</td>
</tr>
<tr>
<td>Silicone elastomer powder or blend (Dimethicone crosspolymer, dimethicone, vinyl dimethicone crosspolymer, etc.)</td>
<td>4-30</td>
</tr>
<tr>
<td>dl-α-tocopheryl acetate (vitamin E acetate)</td>
<td>0-1</td>
</tr>
<tr>
<td>L-AA (vitamin C)</td>
<td>1-10</td>
</tr>
<tr>
<td>Polyol (glycerin, propylene glycol, butylene glycol)</td>
<td>40-75</td>
</tr>
</tbody>
</table>

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penetration rate observed for AA with the pure blend of AA and glycerin can be explained by both its higher bioavailability in the topical formulation and the skin absorption properties of glycerin.

It is interesting to note that in the case of anhydrous glycerin-in-silicone system, most of the

While the above data show clearly the benefits of a glycerin-in-silicone system to stabilize high concentration of pure AA, it was very important to demonstrate as well that the incorporation of AA in a silicone matrix made from a cross-linked silicone polymer does not impact its percutaneous penetration and ultimately its depigmenting activity.

Although similar percutaneous penetration profiles of AA were obtained for the three formulations evaluated (with about 10 wt% of the applied quantity having been released from the formulations after the six-hour period), the absorption of AA into the different skin compartments was formulation-dependent (Figure 5). With the pure blend of AA and glycerin, a significant amount of the released AA was found in the dermal compartment and the receptor chamber of the diffusion cells after 6 hours of diffusion. At the opposite, both the glycerin-in-silicone system and the commercial benchmark showed a higher proportion of AA in the upper skin layers. No difference was observed between those two formulations. The faster penetration rate observed for AA with the pure blend of AA and glycerin can be explained by both its higher bioavailability in the topical formulation and the skin absorption properties of glycerin.

It is interesting to note that in the case of anhydrous glycerin-in-silicone system, most of the
AA remaining in the donor compartment was still biologically active, while for the pure blend of glycerin and AA and in a greater extent for the commercial benchmark, a significant proportion of the AA present in the donor chamber was degraded and could no longer be detected by UPLC. This observation strongly indicates that the entrapment of AA in a cross-linked silicone matrix is a way of ensuring a long-term stability of this light-sensitive active, without compromising its delivery to the skin layers and its biological activities while it is available on the skin surface.

The efficacy of AA-containing anhydrous glycerin-in-silicone formulations for treating hyperpigmentation disorders was evaluated using in vitro reconstituted pigmented human epidermis tissues (RHEm). The performance of the silicone-based system was compared to the leading commercial product and a pure blend of AA and glycerin, as well as to a positive control containing 4-butylresorcinol which has been reported to be a strong tyrosinase inhibitor and to decrease melanin synthesis[8], and to exceed by far the potency of very common skin-whitening agents such as hydroquinone, arbutin and kojic acid[9].

The study first confirmed that ascorbic acid is a strong depigmenting agent as shown by the large inhibition of melanin synthesis (47% inhibition of synthesis) obtained when a pure blend of glycerin and ascorbic acid is topically applied on RHEm (Figure 6). Although glycerin is responsible for the improved chemical stability of ascorbic acid and does not prevent both the release and penetration of ascorbic acid in skin, a pure blend of glycerin and ascorbic acid does not represent a suitable delivery system for topical application. Indeed, a very high level of glycerin has a detrimental effect on the sensory attributes of a formulation, leading to low patient compliance and interruption of the treatment. In addition, successive application of a topical treatment containing very high levels of glycerin could ultimately alter the architecture of the stratum corneum and as a result the barrier function of the skin.

As demonstrated above, the incorporation of ascorbic acid into a glycerin-in-silicone system preserves its chemical stability. Compared to a pure blend of glycerin and ascorbic acid, the anhydrous silicone system offers significantly improved sensory characteristics.

From an efficacy standpoint, as illustrated in Figure 6, the silicone-based system does not prevent the release of ascorbic acid and leads to a significant decrease in melanin synthesis (34% inhibition of synthesis), unlike the commercial benchmark which marginally (13%) impacts the melanin synthesis.

**Study 3: Delivery of drugs from substantive silicone films**

A third component of the study focused on the use of substantive silicone film-forming technologies to provide long-lasting delivery of drugs to the skin. In this case, the drug model was betamethasone dipropionate (BDP), a corticosteroid with anti-inflammatory and immunosuppressive activities[10]. This API is used in formulations designed to treat itching in chronic skin disorders such as eczema and psoriasis.

![Figure 6. Inhibition of melanin synthesis in melanocytes-containing reconstituted human epidermis treated with ascorbic acid-containing formulations and a positive control formulation](image)

(Numbers in parentheses represent levels of confidence; ns=no significant difference versus control.)
Topical preparations used to deliver drugs to or through the skin are mainly limited to semi-solid formulations and transdermal patches, respectively. Although traditional semisolid formulations can be obtained using simple and affordable processes they do not provide in general sufficient substantivity on skin and are therefore not recommended to provide a long-lasting delivery of drugs to the skin. Moreover, semisolid formulations aiming at improving skin conditions such as eczema and psoriasis are usually heavy petrolatum-based preparations resulting in low patient compliance[11]. At the opposite, transdermal patches offer high skin adhesion making them suitable to deliver drugs to the systemic circulation. However, their preparation requires complex and costly processes, and their poor aesthetic (although strongly improved during the last decade) makes them very unattractive and inappropriate when it comes to the treatment of skin disorders such as eczema and psoriasis.

Benefits of using film-forming polymers to deliver drugs to the skin include higher dosing flexibility and potentially longer-lasting benefits, leading to higher patient compliance compared to the traditional formulations described above[11].

This study investigated the potential benefits of a developmental silicone-based film-forming technology as an alternative to traditional formulations to deliver BDP to the skin.

**Materials and Methods**

**Materials**
The silicone-based film-forming technology used in this study is a developmental silicone material for health care applications and was obtained from Dow Corning Corporation (Midland, MI, USA). This material is modeled after silicone pressure-sensitive adhesives (PSAs) and is available as an emulsion with a solid content of about 35 wt%. BDP was purchased from Fagron (Rotterdam, The Netherlands).

The commercial benchmark was an oil-in-water preparation indicated for the treatment of itchy skin disorders such as eczema and psoriasis. It contains 0.064 wt% BDP and has the following ingredients: white petrolatum, liquid paraffin, cetostearyl alcohol, macrogol cetostearylic ether, monohydrated sodium dihydrogenphosphate, phosphoric acid concentrated, chlorocresol, and water.

**Film occlusivity**
Film occlusivity was measured via standard water vapor permeability testing, using standard stainless steel Payne cups (Elcometer, Hermalle-S.-Argenteau, Belgium) with a diffusion area of 10 cm². Formulations of interest were manually coated at 0.5 mil (12.7 μm) on the rough surface of a collagen membrane (Naturin Coffi, Viscofan, Spain). After solvent evaporation, the coated collagen sheets were mounted on Payne cups partially filled with water. Uncoated collagen served as a control. Payne cups were placed in a temperature-controlled oven at 31 ± 1°C and 10% RH. The water loss by evaporation through the coatings was measured gravimetrically over a period of 8 hours.

**In vitro permeability testing**
The percutaneous penetration of BDP delivered from the silicone-based film-forming emulsion was studied using Franz-type diffusion cells with a diffusion area of 1.77 cm² and dermatomed pig skin tissues (n=6). The receptor medium was made of a mixture of acetate buffer pH 5.5/ isopropanol (w/w 70/30) and thermostated at 32°C. An infinite dose of 50 mg·cm⁻² was used in the testing. Experiments were done over a duration of 20 hours, and diffusion cells were sampled every four hours via a Logan 912 auto-sampler system with volume replacement (Logan Instruments Corp., Somerset, NJ, USA). At the end of the diffusion period, the different layers (stratum corneum, epidermis, and dermis) of the skin tissues were separated for recovery analysis. The drug was quantified via a UPLC system (Waters Corporation, Milford, MA, USA), coupled to UV/VIS detection with a high sensitivity cell.

**Rub-off resistance**
The substantivity benefits of the silicone-based film-forming emulsion were compared to both the commercial benchmark and a pure trimethylsiloxyisilicate resin polymer technology (Dow Corning Corporation, Midland, MI, USA) using an internally developed test method. Test products were coated at 12.5 μm on the rough surface of an artificial membrane, Vitro-Skin® (IMS Inc., Portland, ME, USA), which mimics the surface properties of the skin. After complete solvent evaporation, coated samples of 22
mm diameter were punched out and exposed to friction cycles on a polyester felt (Ideal Felt N.V., Belgium) using a washability tester equipment (Braive Instruments S.A., Belgium). The actual amount of Si element remaining on the coated sample was determined by X-ray fluorescence analysis (Oxford Instruments plc, United Kingdom).

**Results and Discussion**

The new silicone-based film-forming technology, modeled after silicone pressure-sensitive adhesives (PSAs) of the type used in transdermal patches, displayed a semi-occlusive behavior with a moisture vapor transmission rate (MVTR) of 60% compared to the untreated collagen membrane set at 100%. For comparative purposes, the behavior of an occlusive material such as petrolatum typically ranges between 0% to 5%.

The performance of the silicone-based film-forming emulsion to deliver BDP to the skin was compared to a commercial benchmark, an oil-in-water preparation indicated for the treatment of itchy skin disorders such as eczema and psoriasis. As illustrated in Figure 7, the penetration of BDP into the skin was initiated earlier from the silicone-based film-forming emulsion than from the commercial benchmark, indicating better bioavailability of the drug in the silicone-based formulation. Both the cumulative penetrated amount and absorption rate of BDP remained higher from the silicone-based film-forming emulsion from 8 hours until 20 hours compared to commercial benchmark (Figures 7A and 7B). At the end of the 20-hour experiment, the total amount of BDP that penetrated into the skin was approximately twice for the silicone-based film-forming emulsion than for the commercial benchmark (5.9% and 3.0%, respectively). In addition, BDP was more abundant in the various skin layers when delivered from the silicone-based film-forming emulsion (67.5% versus 55.8% for the commercial benchmark after 20 hours).

As mentioned above, the substantivity properties of a topical preparation aiming at treating skin disorders such as psoriasis and eczema should be improved in order to increase its overall efficacy and patient compliance. Indeed, the poor aesthetic attributes (heavy, greasy feel) of common formulations found in the market are often responsible for product discontinuation, which prevents an efficient treatment of the skin diseases. It is then very crucial...
to provide patients with a topical preparation that exhibits improved sensorial properties but most of all lasts longer on the skin compared to traditional formulations.

Using an internally developed methodology it was shown that the silicone-based film-forming emulsion was highly resistant to friction insults with 95% of the initial coating remaining on the artificial membrane after 50 friction cycles, whereas both a pure trimethylsiloxy silicate resin and a commercial barrier cream fell below 5% (Figure 8).

This third study highlighted that the silicone-based film-forming emulsion forms a semi-occlusive film on the skin that provides significantly higher durability properties than a commercial benchmark based on an oil-in-water emulsion, without impacting the delivery of BDP to the skin.

Summary and Conclusions for the Three Studies

Overall, the three study components presented here demonstrated that silicone-based excipients should be considered by formulators at consumer health care companies to develop innovative formulation systems that can improve the delivery of drugs to skin:

- They offer an approach to formulating anti-inflammatory drugs such as ibuprofen that require a fast and strong release into the skin.
- They can maximize the efficacy of drugs such as ascorbic acid that are sensitive to oxidation.
- They can provide sustained delivery of actives by enhancing the substantive properties of a formulation on the skin surface.
References


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