

Silicones as Excipients for Topical Pharmaceutical Applications

The *Silky Touch* Product Family from Dow Corning

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Abstract

Over the last five decades, silicones have been used extensively in skin care products, and in numerous pharmaceutical and medical applications; however, the use of silicones in pharmaceutical topical formulations has been low. The introduction of a range of silicones, *Dow Corning® Silky Touch*, designed to improve topical formulations in terms of bioavailability of the active and aesthetics (sensory profile), may change this situation. Formulating with silicones could lead to improved treatment compliance and the overall efficacy of topical products. The flexibility of formulating with silicones allows ointments, emulsions, gels, sprays or sticks to benefit from such technology. For example, ointments that are less tacky or greasy and gels or emulsions that are easier to spread and provide a silky-smooth feel. The superior substantivity of silicone-containing formulations and the effect of silicone gum on the release kinetics of several actives are also discussed. In addition, the regulatory requirements and status of *Silky Touch* products, including acknowledgment that pharmaceutical-grade silicone excipients from Dow Corning are supplied from in a dedicated FDA-inspected site, and toxicology of silicone excipients are reviewed and summarized.

1. Introduction

Treatment compliance and bioavailability are highly valued in the pharmaceutical industry. Less treatment compliance can be traced to the poor aesthetics of pharmaceutical topical formulations that reduces patient comfort. The medical community would, therefore, benefit from more patient-friendly formulations. Bioavailability is another major industry need. Silicones, because of their unique physico-chemical properties, can help achieve higher bioavailability and thus provide an efficient vehicle for drug delivery in topical formulations.

Silicones have been used in the medical and pharmaceutical industry since as early as the 1950s. While their use as topical excipients has been rare, this should change as pharmaceutical-grade silicones become available. The name “silicone” includes a large number of compounds based on polydialkylsiloxanes, with dimethicone and simethicone being the better known in the pharmaceutical world as they are defined by the European Pharmacopoeia (Eur. Ph.), the United States Pharmacopoeia (USP) or the United States National Formulary (NF). Silicone technology, however, reaches far beyond polydimethylsiloxane. Silicone polymers such as silicone gums, silicone elastomers, silicone waxes or silicone emulsifiers bring additional and complementary benefits as excipients for topical pharmaceutical applications.

2. Silicones as excipients for topical formulations

Silicones were introduced for use in skin care applications in the 1950s, and have since become so widely used that now more than half the consumer skin care products contain some silicone [1]. Silicones are also not new to the pharmaceutical and medical world – they are used as transdermal delivery systems, as process aid antifoams in the production of vaccines, and as raw material in catheters and specialized medical devices like pacemakers [2, 3]. What is new to the pharmaceutical world, however, is the commercialization of a broad range of silicones for topical pharmaceutical applications.

Dow Corning® Silky Touch products include a line of unique silicone excipients designed specifically for the pharmaceutical market (see Table 1). This means our *Silky Touch* products are supplied from an FDA-inspected site that uses appropriate current Good Manufacturing Practices (cGMP), and are sold to customers with appropriate regulatory and toxicological documentation. In addition to dimethicone, a well-established silicone pharmaceutical material, Dow Corning has added to its *Silky Touch* offering two volatile silicones, three special silicone blends, a more hydrophilic silicone fluid, two silicone waxes and one emulsifier. This broad range enables formulators to deliver a variety of topical forms and actives; and better suits the unique, individual needs of each formulator.

Table 1: Range of products in the Dow Corning® Silky Touch product line

<i>Silky Touch</i> Material	Chemical Name
Q7-9180 Silicone Fluids (0.65 cSt, 1.0 cSt)	Hexamethyldisiloxane (0.65 cSt), Octamethyltrisiloxane (1.0 cSt)
ST-Cyclomethicone 5-NF	Decamethylcyclopentasiloxane
Q7-9120 Silicone Fluids (20 cSt to 12,500 cSt)	Polydimethylsiloxane
ST-Dimethiconol 40	Hydroxy-terminated polydimethylsiloxane
Dimethiconol Blend 20	Hydroxy-terminated polydimethylsiloxane in Polydimethylsiloxane
Silmogen Carrier	Polydimethylsiloxane in hexamethyldisiloxane
ST-Elastomer 10	Silicone elastomer gel
Silky Wax 10	Stearoxytrimethylsilane and stearyl alcohol
ST-Wax 30	Alkylmethyl siloxane
Emulsifier 10	Alkylmethyl siloxane copolyol

3. Aesthetic benefits of silicone excipients

Study:

The sensory evaluation is designed to compare whether two products present any differences on individual sensory properties. Wetness, spreadability and speed of absorbance (absorbancy) are evaluated before absorption whereas gloss, film residue, greasiness, silkiness and slippery are evaluated after absorption. In the sensory evaluation testing, “absorption” means the perception of absorption felt by the panelists. It does not mean that the product is biologically absorbed by the skin. Please refer to the toxicology section of this paper for information on biological (skin) absorption. Tackiness is evaluated before and after absorption.

This evaluation is conducted on the forearm of 18 untrained panelists. On the spider graph (Figure 1), the confidence level is indicated next to each parameter: when there is no figure, it means that the difference is not statistically significant (i.e. confidence level below 95.0 %).

Each parameter is assessed individually and rated from 1 (low) to 10 (high) by the panelist based on his/her perception. For example, in Figure 2, the silkiness of formulation (a) is higher (7.5 i.e. very silky) than that of formulation (b) (3.6 i.e. quite rough/not very silky). The spreadability of formulation (a) is lower than that of formulation (b) but they are both highly spreadable (7.0 against 8.0). The ratings are relative: for example, formulation (a) of Figure 1 cannot be compared with formulation (a) or (b) of Figure 2 since testing was conducted on different materials at different times looking for different comparisons.

Depending on the application, the customer can choose which properties are desirable: for example, in some applications (e.g. protective lipstick), a high gloss might be

desired whereas in others (e.g. eczema cream) a low gloss might be preferred. The sensory evaluation (e.g. Figure 1 – 3 spider graphs) can be used to help identify which formulation might be the most appropriate.

Results:

Silicone polymers can provide unique aesthetic benefits in liquid and semi-solid topical formulations and positively impact treatment compliance and product differentiation.

In topical formulations, silicone polymers provide attributes such as improved spreadability, emolliency, and lubrication, while also imparting a silky, non-oily, and tack-free feel. *Dow Corning®* brand *Silky Touch* products (Table 1), are essentially odorless and colorless (transparent or translucent) - with the exception of silicone waxes (white flakes). Emulsions usually have a white, rich-looking appearance while gels are either translucent or white.

Figures 1 - 2 show results from two different types of formulations: ointment and hydrogel. In each case, silicone was shown to help improve the sensory feel. This improvement was particularly interesting in the case of ointments, which traditionally have very poor patient compliance due to their tacky and greasy feel, and their lack of spreadability.

In Figure 1, the silicone-containing ointment is easier to spread and is clearly less tacky before and after absorption than petrolatum. After absorption, a perceptible film was present on the skin for both formulations (no significant difference) but the silicone-containing ointment was less greasy, silkier and more slippery (better lubrication) than petrolatum. The panelist's perception of higher wetness for the silicone-containing formulation was attributed to its lower oiliness. In conclusion, the addition of silicones in petrolatum can result in a net improvement in the sensory profile of the ointment.

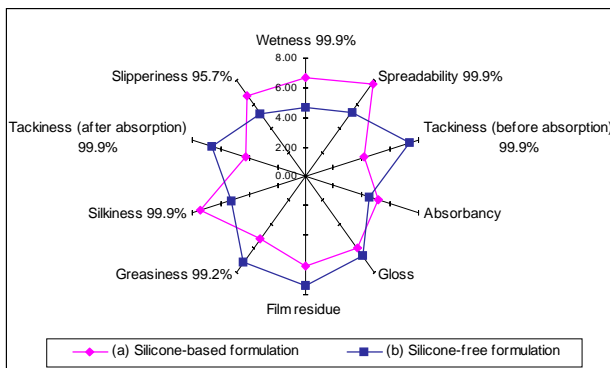


Figure 1: Sensory evaluation (paired comparison) of (a) an ointment containing petrolatum (70%), ST-Cyclomethicone 5-NF (15%) and ST-Elastomer 10 (15%) versus (b) petrolatum (100%).

As shown in Figure 2, upon application, the film of the silicone-free hydrogel was more difficult to spread and is tackier. After absorption, the film formed on the skin by the silicone-containing hydrogel was clearly much silkier, less tacky and more slippery. It is worth noting that the greasiness of the film was not increased by the addition of silicones and that no significant difference was observed on speed of absorbancy, gloss or film residue.

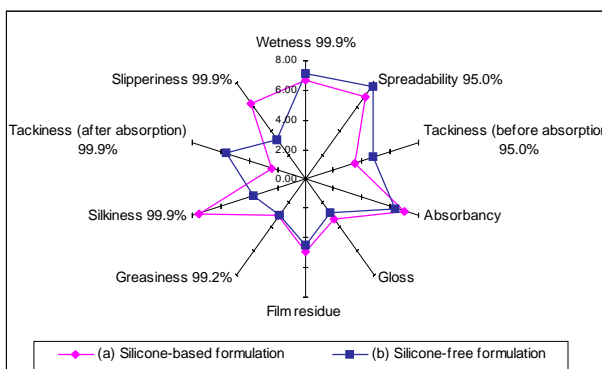


Figure 2: Sensory evaluation (paired comparison) of (a) the hydrogel with Dimethiconol Blend 20 (5%) and ST-Elastomer 10 (10%) versus (b) the same hydrogel with no silicone.

Figure 3 shows the versatility of silicone formulations by highlighting differences in aesthetic property responses obtained for the different silicone containing formulations. The silicone-containing formulation was clearly less tacky before absorption, which was believed to be due to the detackifying effect of Silky Wax 10. However, no significant differences were observed after absorption between formulations (a) and (b). The introduction of Dimethiconol Blend 20 and ST-Cyclomethicone 5-NF in place of mineral oil and petrolatum brought a decrease in gloss, film residue and greasiness but an increase in spreadability and wetness. Depending on the application, the sensory profile of one emulsion might be better than another.

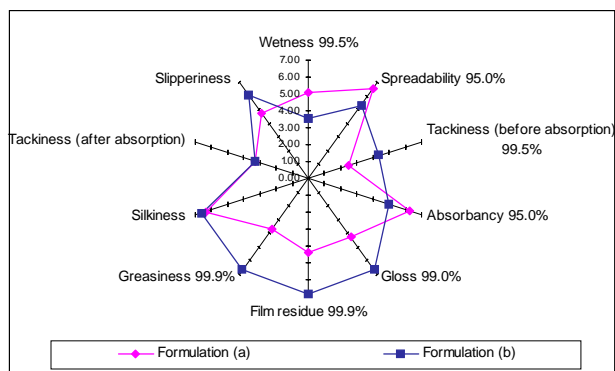


Figure 3: Sensory evaluation (paired comparison) of (a) water-in-oil emulsion based on mineral oil (20%), petrolatum (5%) and Silky Wax 10 (5%) versus (b) water-in-oil emulsion based on mineral oil (10%), ST-Cyclomethicone 5-NF (10%) and Dimethiconol Blend 20 (5%). The same silicone surfactant (2% of Emulsifier 10) has been used in both formulations.

4. Pharmacokinetic benefits of silicone excipients

Substantivity:

Silicone gums are highly substantive on the skin and can significantly improve the substantivity of an active [4]. The film formed, after applying a topical formulation to the skin and removing the volatile, helps to maintain the active in close contact with the skin and prevent loss of the active by abrasion. The substantivity of the silicone was conferred to the active. Figure 4 and Figure 5 show the effect with silicone gum alone and formulations containing ketoprofen with and without gum, respectively. As shown in Figure 4, 25% of the silicone gum remains on the skin after 8 hours of daily activities.

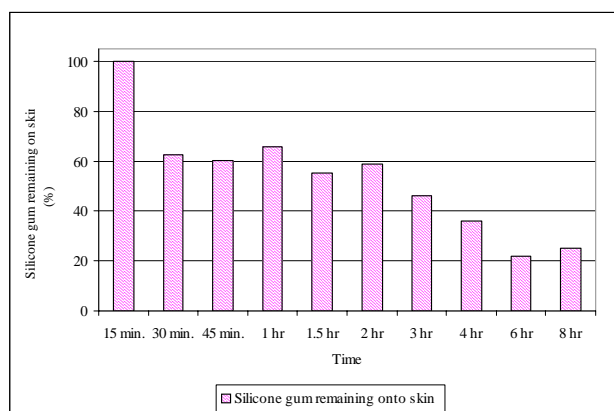


Figure 4: Substantivity of silicone gum on skin over time. Formulation: silicone gum (3%) and hexamethyldisiloxane (97%). Test done on the forearm of 5 panelists. The silicone remaining on the skin of the panelists is analyzed by ATR-FTIR spectroscopy.

Figure 5 shows that the substantivity of silicone gum helps to increase the substantivity of ketoprofen: after 40 minutes, only traces of ketoprofen is detectable in the formulation without the silicone gum whereas after 6 hours ketoprofen was still detectable in the formulation containing the silicone gum. While the substantivity of the silicone gum was believed to be a factor in this effect, the behavior of silicone (acting as a reservoir) in the release of ketoprofen may have also helped delay the release.

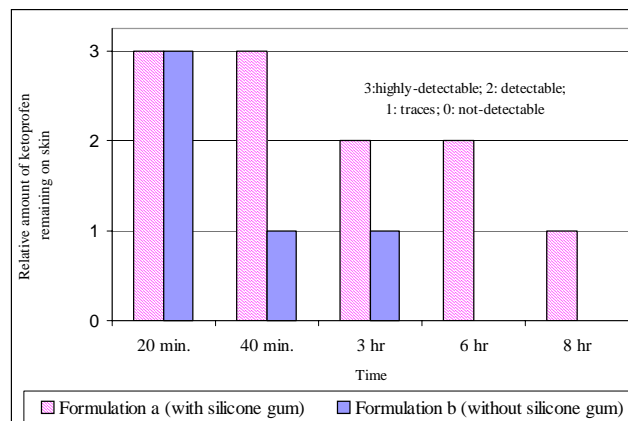


Figure 5: Substantivity of ketoprofen on skin over time. Formulation (a): ketoprofen (2.5%), hexamethyldisiloxane (94.5%) and silicone gum (3%). Formulation (b): ketoprofen (2.5%) and hexamethyldisiloxane (97.5%). Test done on the forearm of 5 panelists. Semi-quantitative analysis of ketoprofen remaining on the skin of the panelists done by ATR-FTIR spectroscopy.

Rub-off and wash-off resistance:

The ability of silicones to form hydrophobic films, which are spreadable and substantive, helps explain their high resistance to wash-off and rub-off (Figure 6) [4].

Figure 6 shows that silicone gums exhibit a high resistance to abrasion. In addition to being tack-free and invisible, silicone gum increases the resistance of ketoprofen to rub-off. Thus, after 3 tape-strips, 66.2% of the ketoprofen was still present on the skin treated with a formulation containing 2%-silicone gum. Only 13.8% of the ketoprofen was still present on the skin treated with a silicone-free formulation. In addition, higher concentrations of silicone provided more resistance to abrasion.

In addition to rub-off resistance, silicone gums and dimethicone of medium or high viscosity can provide wash-off resistance to the film deposited onto the skin. This is due to their hydrophobicity and good film-forming properties. This benefit has been exploited in sun-creams.

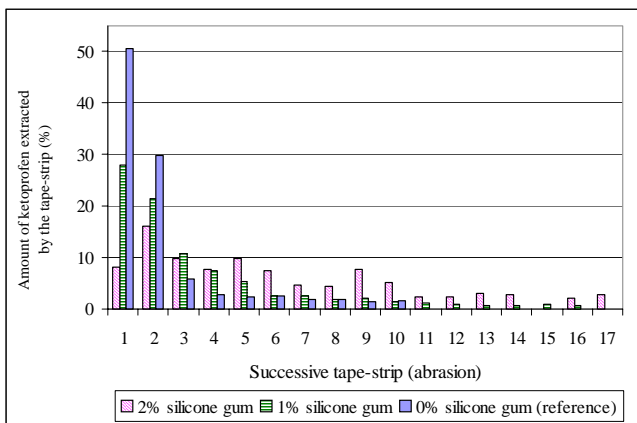


Figure 6: Abrasion resistance of ketoprofen on skin with silicone gum. Three formulations have been tested on the forearm of panelists in 17 successive tape-stripping tests. Formulations: ketoprofen (8%), silicone gum (0%, 1% and 2%), hexamethyldisiloxane (to 100%). Results based on UV analysis of strips after extraction.

Increased bio-availability and managed release:

Penetration of three different actives (ibuprofen, econazole nitrate and hydrocortisone) through a hairless rat skin was monitored over a 24 hour period. The experiment was carried out in a static diffusion cell (Franz cell) at 32°C with a NaCl 0.9% receptor medium. The results are shown in Figures 7-9 and Tables 2 and 3.

Figure 7 shows that the permeation flux of ibuprofen is much higher in the silicone-based formulations (whatever silicone gum loading) than in the silicone-free hydrogel. No increase in dermal storage has been observed (Table 2). These two points mean an improved bioavailability of ibuprofen on site of action (i.e. muscle) with the silicone formulation.

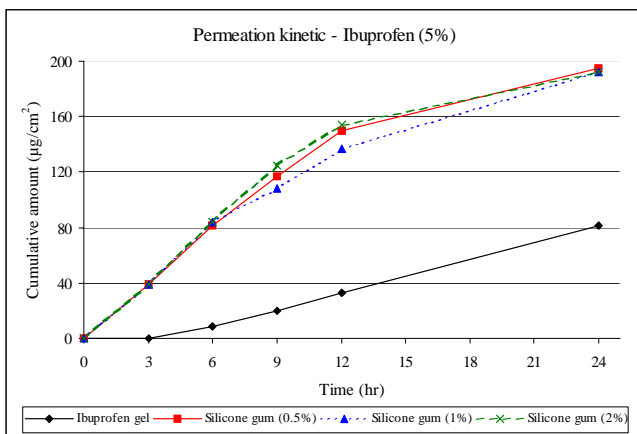


Figure 7: Comparison of the penetration rate of ibuprofen (5%) through hairless rat skin in static diffusion cells silicone-based formulations (silicone gum in hexamethyldisiloxane) versus a silicone-free hydrogel [5].

Figure 8 shows the opposite behavior – less penetration of econazole nitrate through the skin using silicone gum formulations. The compartmental distribution of econazole nitrate was the same in all formulations (Table 2). This meant that a higher bioavailability of econazole nitrate (antifungal agent) was achieved on the site of action (surface of the skin). It also indicated that a lower systemic effect occurred with the silicone-based formulations. This was particularly noticeable in the case of antifungal agents, which exhibited significant adverse systemic effects.

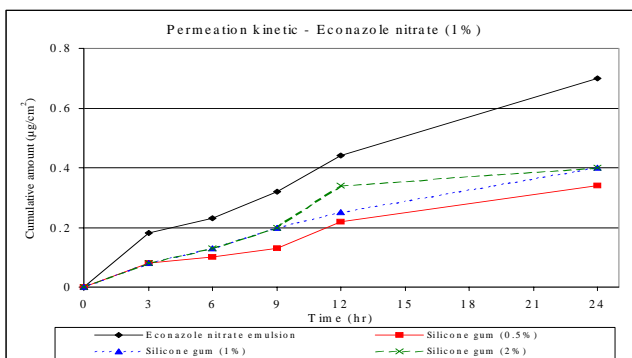


Figure 8: Comparison of the penetration rate of econazole nitrate (1%) through hairless rat skin in static diffusion cells silicone-based formulations (silicone gum in hexamethyldisiloxane) versus a silicone-free emulsion [5].

As shown in Figure 9, the permeation flux of hydrocortisone was the same in all four formulations. However, the compartmental distribution revealed that, with the silicone-containing formulations, hydrocortisone accumulated in the stratum corneum (Figure 10) and less hydrocortisone was present at the surface of the skin (Table 2). This was interpreted to mean that the silicone gum induced the formation of a reservoir of hydrocortisone in the stratum corneum (this effect was not observed with ibuprofen or econazole nitrate). This phenomenon could be interesting for the design of a prolonged-filmogen spray, gel or cream.

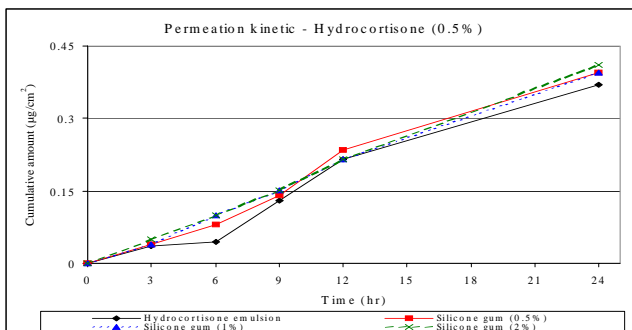


Figure 9: Comparison of the penetration rate of hydrocortisone (0.5%) through hairless rat skin in static diffusion cells of silicone-based formulations (silicone gum in hexamethyldisiloxane) versus a silicone-free emulsion [5].

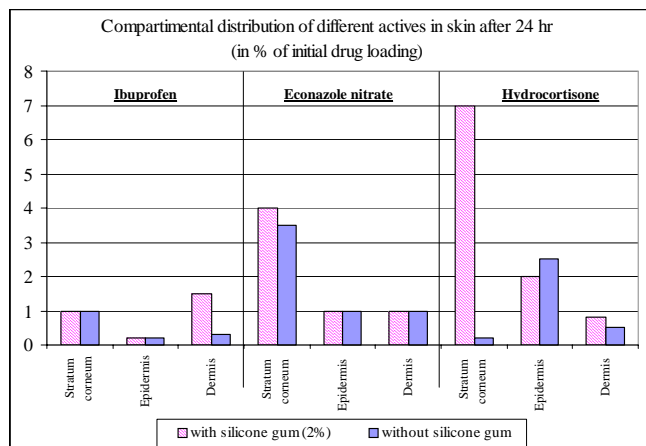


Figure 10: Compartmental distribution of different actives after 24 hr through hairless rat skin in static cells with silicone gum (2%) in hexamethyldisiloxane vs. silicone-free products (same formulations as in Figures 7, 8 and 9) [5].

Table 2: Hydrocortisone remaining at the surface of the skin after 24 hr (same conditions as Figure 10). [5].

Formulation	Silicone-free formulation (emulsion)	Silicone-based formulation (2% silicone gum)
Hydrocortisone on skin (in % of initial loading)	83	65

In conclusion, dermokinetic experiments have shown that silicone gum had an effect on the release of actives through the skin. Figures 7-9 show that this effect was dependent on the active. Thus, depending on the active, the skin penetration could be increased, decreased or unchanged. The film forming properties of silicone and the solubility of the drug in silicone gum relative to the drug's solubility in the skin was thought to play a part in the drug release mechanism.

Occlusivity:

Although most silicones (e.g. polydimethylsiloxane) are non-occlusive, organic-modified silicones, such as silicone waxes, have lower moisture permeability. Thus, the same level of occlusivity was achieved with petrolatum (50% in solvent) and ST-Wax 30 (10% in solvent) as shown in Table 3. Because of its chemical structure, Silky Wax 10 was shown to be less occlusive than ST-Wax 30.

The use of silicone waxes in place of petrolatum might improve treatment compliance of ointments since silicones do not exhibit the negative aesthetics of petrolatum (see section 7).

Table 3: Occlusive index of untreated skin, and skin treated with formulation (a) and (b) over time. The occlusivity was measured by trans-epidermal water loss (TEWL). Formulation (a): ST-Wax 30 (10%), isopar G (90%). Formulation (b): Petrolatum (50%), isopar G (50%).

Time	Untreated skin	Formulation (a)	Formulation (b)
2 hr	0.6	1.2	1.15
4 hr	0.4	1.15	1.1
6 hr	0.4	0.6	0.5

5. Regulatory status of silicone excipients

Today most countries worldwide either have regulations for reviewing and approving pharmaceutical products, or are currently working to establish them. Most pharmaceutical drug approval regulations are targeted at assuring product quality, safety and efficacy. Unfortunately accidents still occur. According to the World Health Organization (WHO), over the last sixty years worldwide, contaminated starting materials cause more than 500 deaths and more than 80 of these deaths resulted from cough syrup contaminated with diethylene glycol, which was distributed to children in Haiti in 1995 and 1996 [6]. Often, the root cause for these accidents can be traced back to a deficient supply chain. These trends reinforce the need for an integrated, total quality system that manages for material origin, tracking, traceability, labeling, change control, manufacturing, distribution, audits and supplier qualification.

Current legislation regulates compliance for Active Pharmaceutical Ingredients (API) and finished pharmaceutical products: however, pharmaceutical excipients are not as highly regulated, even in the most advanced countries.

For example, in the United States the Food & Drug Administration (FDA) more strictly enforces compliance for manufacturers of APIs and finished drugs (FDA 21 CFR 210 & 211) and many other countries are currently implementing regulations based on the International Conference on Harmonization (ICH) Good Manufacturing Practices guidelines for APIs (ICH Q7A) [7]. On the other hand, although excipients typically make up the bulk of a pharmaceutical formulation, their manufacturing, testing, packaging, handling and distribution are not as highly regulated.

In an effort to assist excipient and drug manufacturers establish Good Manufacturing Practices for excipients, both the International Pharmaceutical Excipients Council (IPEC) [8] and the World Health Organization (WHO) [9] have published cGMP guides for Bulk Pharmaceutical Excipients.

Based on emerging trends to more highly regulate all raw materials and components in a pharmaceutical formulation (not just the APIs) the Dow Corning *Silky Touch* products

were specifically designed to be used in topical pharmaceutical formulations. The materials are produced utilizing key principles of starting materials for pharmaceutical cGMPs in order to assure their safe use in pharmaceutical formulations. At Dow Corning, these principles are fully integrated into the supply chain processes with special attention to:

- Inspection/testing/documentation & traceability of all raw materials, intermediates and finished products;
- Change-control and customer notification processes;
- Control of manufacturing, packaging, labeling, holding (storage) and distribution;
- Control for potential contamination throughout the supply chain (raw materials, manufacturing, packaging, storage and distribution) including cleaning agents, lubricants, environmental particulates, and cross contamination from other products.

In addition to the incoming inspection and approval process for raw materials, Dow Corning works with raw material suppliers to ensure that the raw material source is appropriately managed for TSE and GMO. The full traceability, batch documentation, material tracking, testing program, change control/notification and contamination prevention processes that were established at Dow Corning are considered essential practices to assuring identity/purity control and quality consistency for *Silky Touch* products.

Silky Touch products have been extensively and successfully used in Personal Care topical products (skincare and sun care) for their aesthetic benefits described previously. Dimethicone (Q7-9120 Silicone Fluids) is recognized by the FDA as an active skin protectant [10] for use in Over-The-Counter products (FDA 21 CFR Part 347). In addition, some *Silky Touch* products have a long history of use as excipients in both cosmetic [11-15] (e.g. in hand or facial creams, antiperspirant/deodorants [16] or sunscreens) and pharmaceutical formulations [2, 17]. Examples include: use of hexamethyldisiloxane (Q7-9180 Silicone Fluid 0.65 cSt) as a volatile carrier in pump systems for topical applications; stearyltrimethylsilane (*Silky Wax 10*) and cyclomethicone (ST-Cyclomethicone 5-NF) use in topical cream formulations. Some *Silky Touch* products are tested to comply with established monographs (e.g. United States Pharmacopoeia USP or National Formulary (NF) and/or European Pharmacopoeia (Eur. Ph.)). In addition, technical files have been created to provide (under secrecy agreement) technical information such as formulation/composition, manufacturing process description, impurity profiles,

quality control description, stability and toxicological information. These files are intended to help support new regulatory filings in Europe.

Currently, the Q7-9120 Silicone Fluids are certified by the European Pharmacopoeia to conform to the monographs “Dimeticone” and “Silicone Oil used as a Lubricant” depending upon the product viscosity. These Certificates of Suitability (CEP) [18] guarantee that Q7-9120 Silicone Fluids conform to the Eur. Ph. requirements and that regular inspection by the Eur. Ph. can occur. Copies of relevant certificate can be provided by Dow Corning and subsequently included into filing dossier. In conclusion, *Silky Touch* products are silicone-based pharmaceutical excipients designed to deliver consistent quality, purity and safety by utilizing appropriate principles of cGMPs throughout their entire supply chain. These attributes make these materials ideal for use in innovative, topical pharmaceutical formulations.

6. Biocompatibility

As mentioned, silicones are widely used for consumer skin care applications. One reason for this use is that they have typically shown little or no biological effects on their own. The *Silky Touch* products discussed above have been selected, among other reasons, for their highly biocompatible nature.

The Q7-9180 Silicone Fluids, Q7-9120 Silicone Fluids and ST-Cyclomethicone 5-NF have received extensive testing. One of the few effects noted was a transient liver weight increase due to adaptation of the animals to Q7-9180 0.65 cSt. [19]. An additional effect for Q7-9180 Silicone Fluid, 0.65 cSt is an early onset of testicular tumors in rats; this effect is not applicable to humans [20]. Q7-9180, 0.65 cSt applied to skin did not elicit effects if it was allowed to evaporate, however occlusive conditions can produce irritation. Both Q7-9180, 0.65 cSt and ST-Cyclomethicone 5 have been tested for dermal absorption; *in vitro* testing indicates 0.297% and 1.31% absorbed by rat skin. ST-Cyclomethicone 5 showed only 0.04% absorbed by human skin *in vitro*, and 1.38% in rats, *in vivo*. Larger linear siloxanes have not been tested as absorption was expected to be below that seen with Q7-9180, 0.65 cSt and would be at the limits of detection [19, 21].

ST-Dimethiconol 40 has been shown to be nonirritating, nonsensitizing, is not toxic upon repeated ingestion, nor genetically active in a bacterial reverse mutation assay [22]. This data also supports the longer polymer found in Dimethiconol Blend 20, as well as a human repeat insult patch (HRIPT) study that showed no effects from the Blend when tested on 102 volunteers [23].

Since Silmogen Carrier is predominantly made of Q7-9180 Silicone Fluid, 0.65 cSt, that data applies to this product as well. In the same volunteers who participated in the HRIPT study for Dimethiconol Blend 20, the Silmogen Carrier also showed no effects [24].

In tests similar to those conducted on ST-Dimethiconol 40, ST-Elastomer 10, Silky Wax 10, and Emulsifier 10 have been tested in independent assays. None of the materials were toxic if ingested or placed on the skin. Nor were the materials irritating or sensitizing, though as is true with most silicones, slight eye redness was produced for a short time after instillation. None of the materials were genetically active in a bacterial reverse mutation assay [25-27].

In the same volunteers who participated in the HRIPT study for Dimethiconol Blend 20 and Silmogen Carrier, ST-Wax 30 showed no effects [28].

7. Formulation with silicone excipients

It is interesting to note that topical products containing silicone already exist on the market in several different forms; these are mainly cosmetic products but also some pharmaceutical products such as *Retinova*[®] (Roc – Johnson and Johnson) or *Retin-A Micro*[®] (Ortho Dermatological – Johnson and Johnson). The numerous silicone-containing personal care products are proof of the flexibility and the easy processing of formulating with silicones. Thus, ointments, emulsions, dermatological milks, gels (anhydrous or water-based) as well as sprays or sticks can be formulated with silicones. As described earlier in this paper, silicones can be used in pharmaceutical topical formulations either to improve the aesthetics or the efficacy of a formulation: depending on the goal, different silicone materials should be used.

The main points to consider when formulating with silicone are listed below. Table 4 gives more specific information about each *Silky Touch* product.

- Most silicones are hydrophobic materials and are soluble in apolar solvents.
- With the exception of silicone waxes, silicones are liquid at room temperature and heating is not necessary for formulation.
- Silicone waxes need to be melted or softened before being introduced into the formulation.
- No particular safety requirement is necessary when formulating with silicones – with the exception of volatile silicones, which are flammable.

Table 4: Properties of Dow Corning[®] Silky Touch materials.

Dow Corning names (<i>Silky Touch</i>)	Properties
Q7-9180 Silicone Fluids (0.65 cSt and 1.0 cSt)	Apolar, highly-volatile, flammable. Room-temperature formulation. Low flash point: -3.3°C (0.65 cSt) and 34°C (1.0 cSt)
ST-Cyclomethicone 5-NF	Apolar, highly-volatile, flammable. Room-temperature formulation.
Q7-9120 Silicone Fluids (20 cSt, 100 cSt, 350 cSt, 1000 cSt and 12500 cSt)	Apolar, incompatible with hydrophilic materials. Room-temperature formulation.
Dimethiconol Blend 20	Apolar, incompatible with hydrophilic materials. Room-temperature formulation.
Silmogen Carrier	Apolar, highly-volatile, flammable. Non-volatile content: 1%. Room temperature formulation.
ST-Elastomer 10	Apolar, incompatible with hydrophilic materials. Room-temperature formulation.
Silky Wax 10	Heating at 55°C for formulation.
ST-Wax 30	Heating at 75°C for formulation.
Emulsifier 10	Surfactant (HLB 2.2), room temperature emulsification, liquid at room temperature (typically 2500 cSt).

Emulsions:

Water-in-oil and oil-in-water emulsions can be formulated with silicone. Emulsifier 10 is very efficient in stabilizing water-in-oil emulsions – even in those with a high water content (up to 80%) [29]. All *Silky Touch* materials can be used in water-in-oil and oil-in-water emulsions. Q7-9180 Silicone Fluid (0.65 cSt) and Silmogen Carrier, which are very volatile provide a quick evaporation/breakage of the emulsion on application. Several *Silky Touch* materials can be introduced into an emulsion to achieve synergetic effects (formulations 1 and 2 in Table 5).

Gels:

Water-free gels can accept most *Silky Touch* materials. Large amounts of silicone (up to 99%) can be used in such gels. Gels based on ST-Elastomer 10 exhibit unique aesthetics such as smooth-silky feel, no tackiness, superior spreadability, matifying effect and non-greasiness (*data not shown here*). ST-Dimethiconol 40 can be used as a vehicle for actives which are too hydrophilic for ST-Elastomer 10, Dimethiconol Blend 20 and Q7-9120 Silicone Fluids (formulation 3 in Table 5).

Unlike water-free gels, hydrogels can accept a limited amount of silicone – usually up to 10%. The formulation containing Dimethiconol Blend 20 exhibits superior aesthetics and enables the formation of a substantive film on the skin (formulation 4 in Table 5).

Ointments:

Ointments are common pharmaceutical topical products, but exhibit very poor aesthetics. Most silicones are soluble in petrolatum and therefore ointments can be formulated with silicone to improve the aesthetics. An example of this is an ointment based on petrolatum and ST-Cyclomethicone 5-NF (75:25) – which shows remarkable improvement in aesthetics during application without compromising the occlusivity of the formulation. The addition of Dimethiconol Blend 20 or ST-Elastomer 10 can further improve the after-feel of the ointment after application onto the skin. See formulations 5 and 6 in Table 5.

Sprays:

Sprays can be formulated with silicone volatiles such as Q7-9120 Silicone Fluids or ST-Cyclomethicone 5-NF. These vehicles are non-oily, non-cooling and non-stinging. The substantivity of the spray can be improved by adding Dimethiconol Blend 20 or Silmogen Carrier (formulation 7 in Table 5).

Pharmaceutical sticks can be formulated with ST-Wax 30 which is a good structural agent. Q7-9120 Silicone Fluids and Dimethiconol Blend 20 could also be added to improve spreadability (*data not shown here*).

8. Conclusion

Because of their unique physico-chemical properties, silicones can bring topical formulations benefits in terms of aesthetics and bioavailability of the active. Silicones help

establish better sensory profiles in topical formulations; thus, the resulting material is more comfortable for the patients. Silicones can also improve the bioavailability of the active by impacting the penetration of the active through the skin or the compartmental distribution of the active in the skin.

It is worthwhile noting that various types of topical formulation including emulsions, gels, ointments, sprays and sticks can be formulated with silicones. Silicones are quite easy to process.

As part of our Healthcare portfolio, the *Dow Corning* brand *Silky Touch* silicones include the necessary regulatory and toxicological information to support their registration as topical pharmaceuticals. In addition, to assure high quality, change control, consistency, traceability, and full documentation, the *Silky Touch* products are supplied from a dedicated, FDA-registered and inspected facility that applies active Pharmaceutical Ingredients cGMPs.

9. Literature

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Table 5: Examples of silicone-containing topical formulations.

Formulation	Type	Ingredients (%w/w)
1	water-in-oil emulsion	<u>Phase A:</u> Cyclomethicone 5-NF (10%), light mineral oil (10%), Dimethiconol blend 20 (5%), Silky Wax 10 (2%), Emulsifier 10 (2%), <u>Phase B:</u> NaCl (1%), Glycerin (3%), Water (67%)
2	water-in-oil emulsion	<u>Phase A:</u> Dimethiconol Blend 20 (5%), ST-Elastomer 10 (5%), ST-Cyclomethicone 5-NF (8%), Mineral oil (5%), Emulsifier 10 (2%), <u>Phase B:</u> NaCl (1%), Glycerin (3%), Water (71%)
3	water-free gel	ST-Elastomer 10 (80%), ST-Cyclomethicone 5-NF (19%), Isopropyl myristate (1%)
4	hydrogel	<u>Phase A:</u> Water (74.8%), <i>Carbopol</i> [®] 980 NF (0.3%), Anhydrous sorbitol (2.5%), Sodium methylparaben (0.1%), Sodium propylparaben (0.1%), Disodium EDTA (0.1%), <u>Phase B:</u> Ethanol 96.5% (10%), Water (7%), Dimethiconol Blend 20 (5%)
5	ointment	Petrolatum (75%), ST-Cyclomethicone 5-NF (25%)
6	ointment	Petrolatum (50%), Silky Wax (10%), ST-Cyclomethicone 5-NF (15%), ST Elastomer 10 (25%)
7	spray	Silmogen Carrier (96%), talc (4%)

**Carbopol*[®] is a registered trademark of Noveon Inc.

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