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Silicone elastomer blends: A novel topical drug delivery platform

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INTRODUCTION

Silicone elastomers are well known for their use in skin care for their unique, silky, powdery sensory benefits, but are also capable of helping the delivery of active ingredients. The specific materials included in this study are cross-linked silicone elastomer (Dimethicone Crosspolymer) and cross-linked polyglycol-modified silicone organic elastomer (Dimethicone/Bis-isobutyl PPG 20 Crosspolymer) particles swollen in a carrier fluid. These are clear to slightly translucent with paste-like consistency and provide smooth, silky, powdery, and nongreasy aesthetics recognized in high-end beauty care applications.

The capability of efficiently delivering a broad range of active ingredients in silicone-based topical formulations including ibuprofen and vitamins C and E has been previously demonstrated (1–3). The purpose of this investigation was to assess the capability of efficient delivery of the following drugs by silicone-based topical semisolid formulations.

Clobetasol propionate (CLP) is a very high potency corticosteroid and is used to treat a variety of skin conditions (e.g., eczema, dermatitis, allergies) and reduces the swelling, itching, and redness that occurs in these conditions (4,5).

Diclofenac sodium (DCF) is known as a nonsteroidal anti-inflammatory drug (NSAID) and is used to relieve pain, swelling, and joint stiffness (6).

Lidocaine (LDC) is an anesthetic that works to decrease pain by temporarily numbing the area and is used to treat irritation, soreness, and itchiness from certain skin conditions (e.g., scrapes, minor burns, eczema, insect bites) (7).

The capability of silicone elastomer blend–based topical pharmaceutical formulations to deliver CLP, DCF, and LDC efficiently across human cadaver epidermis was investigated using *in vitro* permeability experiments and compared with commercial benchmark products.

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MATERIALS AND METHODS

MATERIALS

Excipients. A polyglycol-modified cross-linked silicone elastomer in isododecane (IDD) [INCI: IDD (and) Dimethicone/Bis-isobutyl PPG 20 Crosspolymer (SiE1)] and another cross-linked silicone elastomer in cyclopentasiloxane [INCI: Cyclopentasiloxane (and) Dimethicone Crosspolymer (SiE2)] were used in the formulation preparation. The products are dispersions of high molecular weight silicone gels particles swollen in respective carrier solvents with a solids content ranging from 12% to 15.75%. Other excipients used in the formulations include propylene glycol, oleic acid, and isopropyl alcohol.

Actives. CLP, DCF, and LDC were used in the experimental formulations at 0.05%, 1%, and 5%, respectively.

Benchmarks. Representative commercially available products containing the same drugs and at the same concentration were used in permeability experiments.

TEST METHODS

In vitro *drug permeability.* The *in vitro* permeability of drug through heat-separated human cadaver epidermis was performed at 32°C using a manual Franz diffusion cell console unit. The permeation area of the cell was 0.63 cm^2 and the cell volume was 5 ml. The receptor chamber of the cell was initially filled with ~3 ml of phosphate-buffered saline (PBS, pH 7.4) and a small magnetic stir bar was added. A 15.5 ± 0.5 mg of the formulation was applied as homogeneously as possible on top of the skin. The experiment was carried out for 8 h for DCF- and LDC-containing formulations and 26 h for CLP-containing formulations. Respective benchmark product was included along with the silicone formulations at the same time in the permeability experiment. Samples were collected from the receptor chamber at several intervals throughout the permeability study duration (8 or 26 h) and replaced with fresh PBS solution. All samples were collected in amber high-performance liquid chromatography vials and taken for drug assay.

Drug assay. Waters® ultra-performance liquid chromatography (UPLC) coupled with Acquity® UPLC BEH column were utilized to determine the drug concentration in the samples from permeability study. An appropriate assay method for each drug was used accordingly.

Formulations. The silicone elastomer–based formulations were prepared and compared versus commercial benchmarks. In a typical formulation preparation, the required amount of drug was weighed into a SpeedMixer™ cup and dissolved by the addition of liquid components of the formulation with mixing. This was followed by weighing the required amount of silicone material and mixing it in the SpeedMixer (Hauschild, AM 501T, Hamm, Germany) at 3000 rpm until a homogeneous formulation was obtained (Table I).

RESULTS

The *in vitro* drug delivery profiles obtained from the permeability study for the silicone elastomer blend formulations versus respective commercial benchmark products are

Table I
Composition of the Silicone Elastomer Blend Formulations

	SiE1-CLP gel	SiE2-CLP gel	SiE1-DCF-gel	SiE1-LDC gel
Ingredient	% (w/w)			
SiE1	60.47[a]	-	69.3	66.5
SiE2	-	74.90[a]	-	-
Propylene glycol	9.57	6.73	7.1	6.8
Oleic acid	1.06	0.75	0.8	0.8
Isopropyl alcohol	28.85	17.57	21.8	20.9
CLP	0.05	0.05	-	-
DCF	-	-	1.0	-
LDC	-	-	-	5.0

[a]Elastomer blends with 26% solids were utilized.

provided in Figures 1–3. These figures show the amount of drug delivered with respect to time and area (flux) across the cadaver epidermis.

On comparing with drug delivered by the commercial products, the silicone elastomer–based prototype formulations delivered either equal and in most cases higher amount of the drug across the skin epidermis. The silicone formulation (SiE1) released about 3× DCF (5.92 ± 0.5 μg vs 2.01 ± 0.7 μg) cumulatively in an 8-h period while showing comparable release profile. Irrespective of very low concentration of the drug CLP, the SiE2-based silicone formulation delivered over double the amount (5181 ± 1457 ng vs 2128 ± 218 ng) delivered by commercial product cumulatively in a 26-h period. The SiE1-based silicone formulation delivered a similar amount (2431 ± 591 ng vs 2128 ± 218 ng) to that of benchmark cumulatively at the same 26-h period. The SiE1-based LDC formulation delivered about 2× (146.4 μg vs 60.6 μg) amount compared with the benchmark.

DISCUSSION AND CONCLUSION

The active-loaded formulations based on silicone elastomer blend technologies delivered drugs effectively across the skin *in vitro*. The study data support the concept that topical

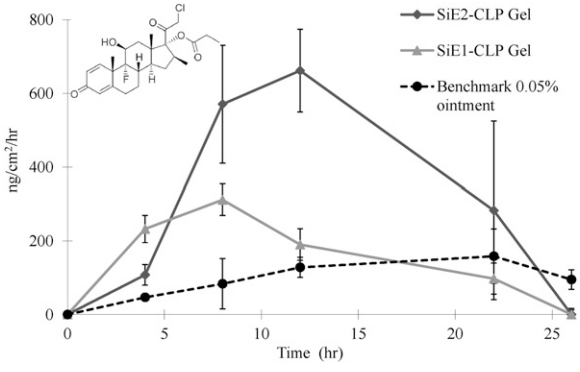

Figure 1. Flux profiles of Si formulation containing 0.05% w/w CLP compared with commercial benchmark.

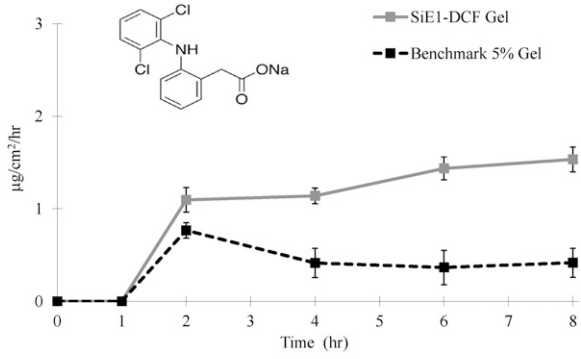

Figure 2. Flux profiles of Si formulation containing 1% w/w DCF compared with commercial benchmark.

formulations using silicone elastomer as excipients can deliver different types of drugs including NSAIDs or steroids efficiently.

As silicone elastomer-based formulations provide improved aesthetics for beauty care applications, similar formulations may enhance patience compliance in topically applied over-the-counter medicated or pharmaceutical drug products. While historically used in skin care because of their sensory benefits, different cross-link chemistries, and a range of carrier solvents, silicone elastomer technologies have allowed for broader compatibility with a range of excipients and drug classes including NSAIDs, potent corticosteroids, and topical anesthetics. Beyond their aesthetics, the silicone elastomer family should be recognized as a novel topical drug delivery platform and provides the ability to formulate a variety of drugs in physically stable formulations.

In general, the silicone-based formulations delivered about 2–3× of drugs compared with respective commercial product. These prototype formulations were not fully optimized toward any product development; however, we believe that there may still be room to improve the drug delivery. It is to be noted that silicone formulation which contained CLP at 0.05% delivered more than twice drug compared with the commercial product. The results indicate that silicone elastomer blend formulations have the capability to show efficient drug delivery even when the formulations had very low drug concentrations.

We have introduced a novel silicone topical drug delivery platform that builds on historical sensory advantages of silicones, but combines the advantages of both silicone and

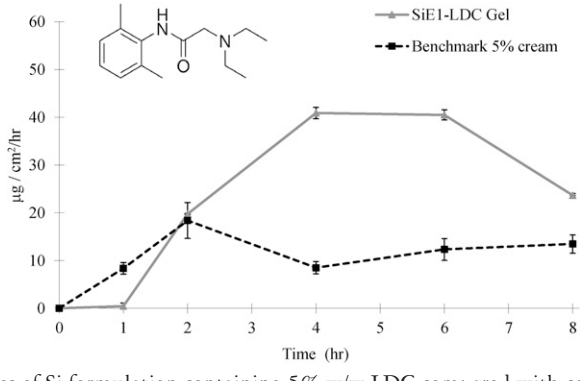

Figure 3. Flux profiles of Si formulation containing 5% w/w LDC compared with commercial benchmark.

organic chemistries. The silicone elastomer blends provide the ability to formulate a variety of drugs in physically stable formulations using different cross-link chemistries, and a range of swelling carrier solvents provide compatibility with a range of other excipients and drugs classes including NSAIDs, potent corticosteroids, and topical anesthetics.

The above-referenced test results have demonstrated an ability of silicone elastomer blends to help deliver drugs efficiently *in vitro* and modulate delivery profile using different solvents or penetration enhancers. Preliminary *in vivo* results of ibuprofen formulations also support *in vitro* results.

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