Impact of Silicone Polymers on Pain Management Drug Delivery

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Purpose

Silicones are widely used in various medical and pharmaceutical applications such as wound and scar management devices, topical and transdermal therapeutic systems. Silicones have been successfully used as pharmaceutical excipients in dermatological and topical drug delivery forms to improve Active Pharmaceutical Ingredient efficacy and patient compliance, which is critical for a pain management treatment plan. The aim of this study was to assess the benefits of selected silicones on key parameters of topical forms e.g. substantivity and skin permeation, using lidocaine as the model drug.

Material & Methodology

Formulation development

The selected silicone excipients are dimethicone 20 cSt (Silicone Fluid) and silicone gum blend (Silicone Gum Blend). Formulation of the same were accomplished in different forms i.e. Water-in-oil emulsions (W/O) and anhydrous gels with lidocaine as the model drug candidate.

W/O Emulsions	Silicone Fluid	Silicone Gum Blend
Ingredients	% w/w	% w/w
DuPont™ Liveo™ Q7-9120 Silicone Fluid, 20 cSt	5.0	–
Liveo™ Dimethiconol Blend 20	–	5.0
W/O Silicone Emulsifier	2.0	2.0
Lidocaine	2.5	2.5
Isopropyl myristate	17.5	17.5
Water	72.0	72.0
Sodium chloride	1.0	1.0

Gels	Silicone Fluid	Silicone Gum Blend
Ingredients	% w/w	% w/w
Liveo™ Q7-9120 Silicone Fluid, 20 cSt	20.0	–
Liveo™ Dimethiconol Blend 20	–	20.0
Ethylcellulose	4.0	4.0
Octlydodedanol	49.5	49.5
Caprylic/Capric triglyceride	24.0	24.0
Lidocaine	2.5	2.5

In vitro drug delivery

The dermal permeation of lidocaine was studied on the dermatomed piglet skin at 32°C using PBS buffer pH 7.4 as receptor fluid. The evaluation was carried out with a static, vertical Franz diffusion cell set-up (n=6) with a penetration surface of 1.77 cm^2. Samples were taken by a Logan 912 auto-sampler system with volume replacement. The drug is quantified by UPLC, coupled to UV/VIS detection with a high sensitivity cell. A qualitative compartment analysis of skin layers were also performed.

Substantivity versus time

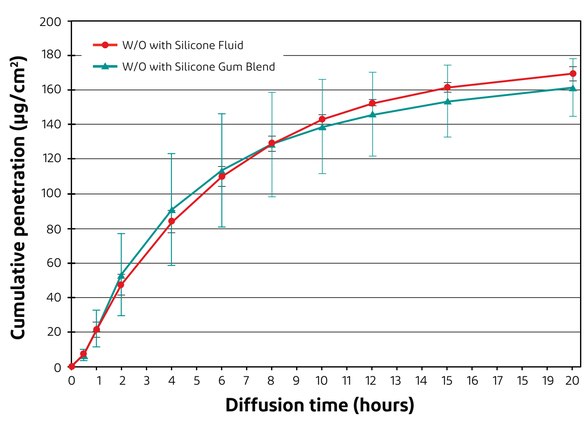
The skin substantivity versus time of silicone-based formulation was evaluated by an Attenuated Total Reflection Fourier Transform Infrared spectrometer (ATR-FTIR) equipped with a skin analyzer device allowing direct measurement on panelist's forearm. This methodology was used to demonstrate the long-lasting properties of topical formulations.

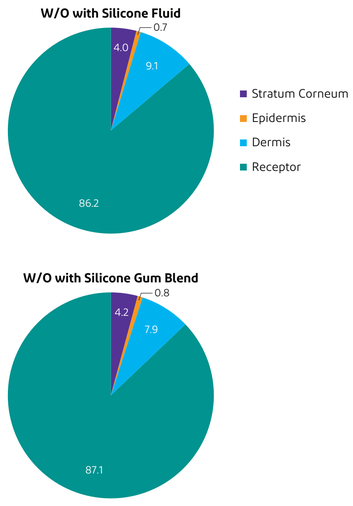
Results & Discussion

In vitro drug delivery – Water-in-oil (W/O) emulsion

The two W/O emulsions deliver the lidocaine with the same profiles:

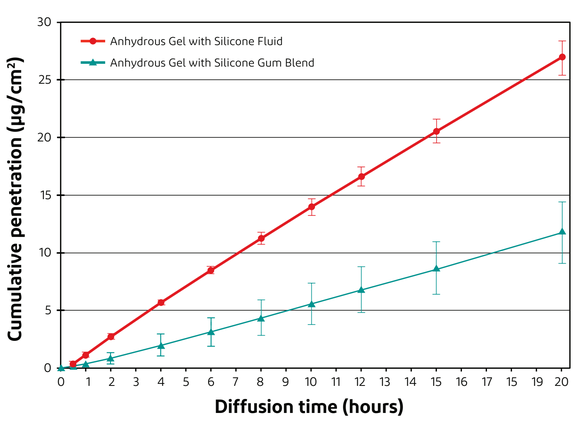
- 100% lidocaine was recovered from both the skin and receptor chamber after 20 h.
- No significant difference in skin penetration was observed.
- Similar concentration (~15%) and distribution in the skin after 20 h was noted.

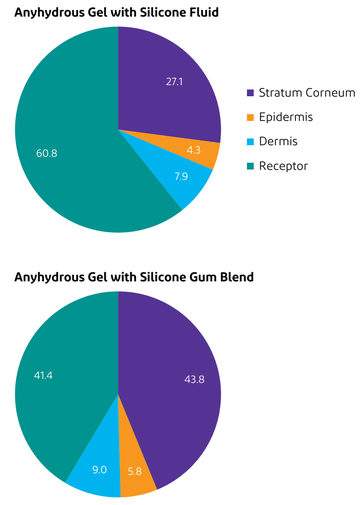




In vitro drug delivery – anhydrous gel

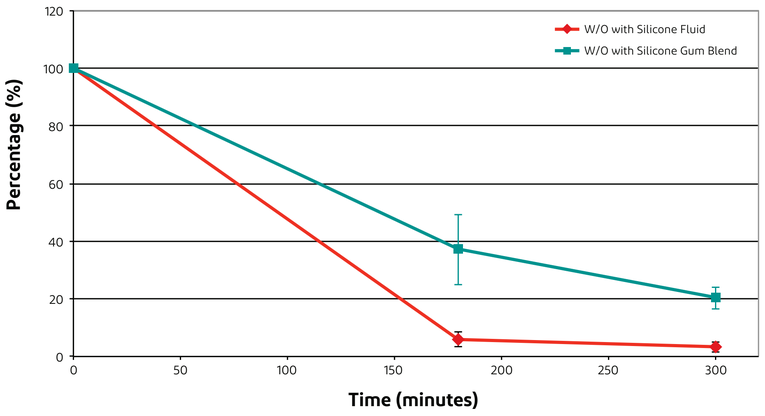
- Faster penetration rate is evident when lidocaine delivered from anhydrous gel formulation with silicone fluid.
- The total amount of lidocaine in skin is similar (~ 10%) for both gels.
- Higher lidocaine concentration is observed in the stratum corneum for the anhydrous gel formulation with silicone gum blend.





Substantivity versus time – water-in-oil emulsion

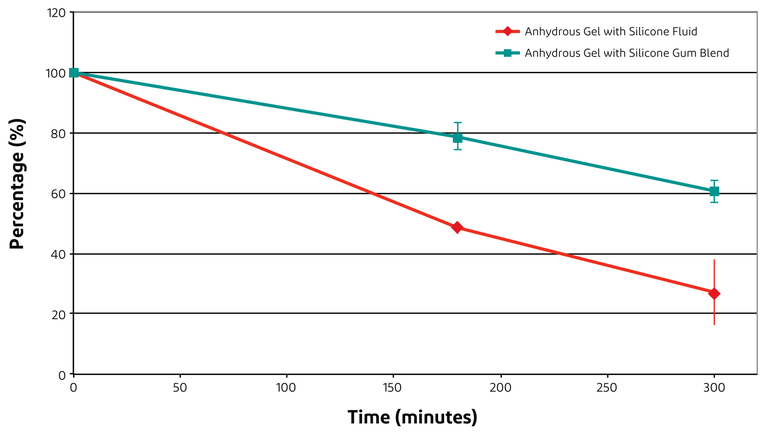
The nature of the silicone excipient in the emulsion impacts the substantivity of the film after application of the emulsion: the W/O Silicone Gum Blend shows a higher substantivity than W/O Silicone Fluid, with about 40% of silicone remaining on skin after 3 h.



Substantivity versus time – anhydrous gel

The nature of the silicone polymer in the anhydrous gel influences the substantivity of the film resulting from the gel application:

- Anhydrous gel Silicone Gum Blend resulted an excellent substantivity with 60% of silicone remaining on skin after 5 h.
- Anhydrous gel Silicone Fluid shows good substantivity with about 30% of silicone remaining on skin after 5 h.



Conclusion

This study demonstrates that silicone excipients enable the formulation of forms with efficient sustained drug delivery combined with a long-lasting substantivity of the film after application of the topical formulation. This offers the formulator and/or end users a product that can help achieve patient compliance.