Soft Skin Adhesive Gels and Liners: New Formulating Options for Tailored Solutions

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Soft skin adhesive (SSA) technology based on silicone adhesive gels has revolutionized advanced wound care treatment. At the same time, the increasing availability of new drugs and the objective of extended wear times have signaled the need for additional high performance properties and a broader array of adhesive solutions. To meet this growth and change in the health care marketplace, silicone technology continues to progress toward the next generation of SSAs.

This article provides an overview of SSAs, their relevant properties for health care applications and recent developments leading to a new generation of silicone adhesive gels. It summarizes the results of several studies that help characterize both SSAs and release liners for use in combination with a range of common therapeutic agents. This information can provide valuable background for screening various adhesive and drug compositions early in the product development process, the result being cost and time efficiencies as well as better performance and greater efficacy for products in use.

**Novel Adhesives for Health Care**

Dow Corning first identified silicone adhesive gels as having properties conducive to health care applications in 1989.¹ Because of their biocompatibility and ability to conform to stringent regulatory requirements for health care, these materials have been adapted to the medical and pharmaceutical industries. The gels are described as having utility in wound dressing and scar management applications² due to their tackiness and a semi-cohesive, gel-like texture.

Designated by Dow Corning as soft skin adhesives, the gels have in recent years become the adhesive of choice in many advanced wound care applications. Among the most important properties of the wound care dressings that use these adhesives is the ability to adhere to human skin, while being easier to remove and causing less pain than dressings with other adhesives.³

Unfortunately, incompatibility of the curing mechanism with some functional molecules has limited the use of first-generation SSAs as delivery vehicles in some drug delivery systems. The relatively short wear time on mobile body areas (e.g., knuckles) that traditional SSAs can sustain compared to other adhesive types can also limit their use in some applications.

**A Versatile Gel Structure**

Expanding opportunities for SSAs exist in innovative developments for topical and transdermal therapeutic systems where the open, three-dimensional structure of the cured SSA may provide advantages in drug delivery applications.

SSAs are fillerless silicone elastomer compositions in which polydimethylsiloxane (PDMS) materials of various functionalities are cross-linked into a tacky structural matrix. Although condensation or reaction with radicals can be used to cross-link the system, platinum-catalyzed hydrosilylation is the most common approach.⁴ Softness and other sensory characteristics of the SSA may be enhanced through the addition of functional and nonfunctional (permethyl) silicone fluid. Molecular weight, relative reactivity and functional locus of the polymers as well as cross-link density of the gel can also be modified to achieve a range of textures, softness, cure profiles and adhesion levels.⁵,⁶

SSAs are two-part systems that when mixed and fully cured possess the tack properties associated with pressure sensitive adhesive behavior and the resiliency of a soft elastomeric matrix.⁴ They differ from silicone pressure sensitive adhesives (PSAs) because they are thermoset elastomers, whereas PSAs are thermoplastic materials. In addition, SSAs are solventless, do not exhibit cold flow and are not sensitive to plasticizing effects but instead remain tacky and soft.⁴ Dow Corning’s SSAs are characterized by a platinum-catalyzed cure mechanism. Their flexible cure temperatures range from ambient to 140 °C
(284 °F) and offer versatility for use in a range of applications and with various active ingredients. Cure rate profiles of Dow Corning 7-9800 Soft Skin Adhesive at various temperatures were attained using a Brookfield RVT viscometer equipped with spindle 3 (Figure 1).

![Figure 1. Cure rate profiles of Dow Corning 7-9800 Soft Skin Adhesive.](image)

Although the SSAs are not aggressive to the skin, they do adhere well. The adhesives are transparent before and after curing and are designed to have moderate skin adhesion. In contrast to many other adhesive types, dressings prepared using silicone adhesive gels retain a low peel release force that does not strip skin, making them safe for fragile or compromised skin. Their property of easy removal and high tack makes them easy to reposition if necessary.

Texture analyses of the adhesives were performed on approximately 200 g/m² (8 mil) coatings of the adhesives on polyester film using a TA-XT Plus texture analyzer with a 7 mm stainless steel probe (TA-57R). Pre-test speed was 0.5 mm/s, test and post-test speed were 0.2 mm/s, and return distance was 3.0 mm.

![Figure 2. Texture analysis comparing a silicone SSA and PSA.](image)

Figure 2 is an example of output from the texture analyzer showing curves for Dow Corning 7-9800 Soft Skin Adhesive and Dow Corning BIO-PSA 7-4502 Silicone Pressure Sensitive Adhesive, a medium-tack PSA designed for transdermal delivery systems. The peak heights correlate to the relative peel force of the two adhesives. The slopes on the right side of the curve indicate softness or compressibility of the

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1 Brookfield Engineering Laboratories, Inc., Middleboro, Massachusetts, USA
2 Texture Technologies Corp., Scarsdale, NY, USA
adhesive. A steeper slope indicates a more rigid material. These data demonstrate the lower peel force and higher compressibility of the SSA compared to the PSA.

Formulating therapeutic patches that combine SSAs with active ingredients presents a number of challenges. Platinum-catalyzed silicones are susceptible to cure inhibition as a result of contact with many chemical categories. Amines, amides, azo compounds, imidazoles, phosphites, thio compounds, and alcohols, as well as many metal compounds, may impact the cure of an SSA. Depending on the functionality of the specific active of interest, the drugs and other active ingredients may affect the cure rate of the adhesive or its ability to achieve a full cure. Therefore, the effects of the active ingredients on the cure rate must be ascertained early in the evaluation and screening phase of development.

Substrate selection is another important consideration when deciding if an SSA is appropriate for a specific application. Traditional SSAs have a general inability to adhere to plastic substrates including polyurethane and other materials preferred as backing. Improved anchorage to substrates has been demonstrated through the use of chemical primers or corona treatment. Since most chemical primers are fairly reactive, if the adhesive is being loaded with a drug, compatibility of the active with the priming system represents another system component that must be considered for its compatibility. A second consideration for substrate selection is its heat tolerance, since the SSA will most likely be coated and cured directly to the substrate. Compatibility of the substrate with the SSA must also be considered. Some substrates have been shown to play a role in the final cured and adhesive properties of the SSA.

Once a full cure is attained, the addition of a release liner is another factor that can affect system stability. Most adhesive coating applications require the use of a release liner to protect the adhesive. The liner must also be easily removed from the adhesive prior to use. The most common release liners in the adhesives industry use silicone functionality to provide low surface energy, which keeps many adhesives from adhering. Silicone release coatings are similar in chemistry to SSA technology. Therefore, it is likely that the release coating and the SSA will react by bonding very tightly over time.

Many alternative films have been screened for the ability to release from the SSA over time. Unlike the more familiar silicone PSA, a fluoropolymer release liner is not a preferred option due to both its high cost and relatively poor performance. It was discovered through this screening that uncoated low density polyethylene (LDPE) films provide an acceptably low and reasonably consistent release force from the SSA. Other polyolefin films evaluated include high density polyethylene (HDPE), polypropylene (PP) polyester (PET) and biaxially-oriented polypropylene (BOPP). Typically, adhesion to common substrates follows this relative ranking order from lowest peel force to highest:

\[
LDPE < HDPE < PP < PET < BOPP < Silicone
\]

The release forces observed initially may not be indicative of the final release force. Upon storage, the release forces of many liners increase to an unacceptable level. Evaluation of release liner properties should be conducted over time to ensure the release force does not build.

Not all polyolefin films of a particular chemistry perform identically. The polymer formulation and the presence or absence of processing aids during the manufacturing process can greatly impact the release properties of the SSA from the release liner, making performance more or less acceptable. However, another key factor is the surface texture of the release liner. Figure 3 compares the release forces of four LDPE films from a single manufacturer. This graph shows the actual peel forces can more than double by changing the texture of the release liner surface, with highly embossed patterns giving lower peel forces than less dramatic finishes. Release liner 1 has a diamond pattern, release liner 2 a less highly
embossed diamond pattern, release liner 3 a matte finish and release liner 4 a taffeta pattern. For this comparison, one batch of new-generation SSA was cast and cured onto polyurethane (PU) at a typical SSA coat weight of approximately 250 g/m² (10 mil).

![Figure 3. Peel forces of developmental SSA from LDPE with different surface textures.](image)

Dow Corning’s Soft Skin Adhesives
Dow Corning’s product line of “traditional” SSAs currently includes:

- **Dow Corning® 7-9800 Soft Skin Adhesive Parts A and B**
  This silicone elastomer is a cohesive and self-adhesive material designed and tested for biomedical applications that include repetitive contact with compromised skin. It is compatible with a polyethylene release liner, and can be washed and reused if required by the application. Typical applications are in wound dressings that can be removed easily and without pain. Other uses might include adhering lightweight medical devices (e.g., drains) to the skin, and as adhesives in topical and transdermal therapeutic systems, where they may be loaded with various drugs. A Drug Master File (DMF) exists for this product; Dow Corning can provide DMF references upon request.

- **Dow Corning® 7-9700 Soft Skin Adhesive Parts A and B**
  This SSA has chemical and adhesion properties similar to Dow Corning 7-9800 Soft Skin Adhesive, but it is tested for short-term contact including scar therapies, over-the-counter bandages and applications that do not involve active ingredients or drugs.

Users are responsible for determining the appropriate SSA for their intended application.

Dow Corning’s future product offering includes:

- **New-generation SSAs**
  To answer new market trends in terms of adhesives for medical devices and wound care applications, Dow Corning has developed and patented new SSA technology that can be adapted and customized to achieve higher adhesion and longer wear times.\textsuperscript{5,6} It is also possible to adjust cure rate based on the requirements of specific applications.

Dow Corning’s SSAs and other silicone health care materials are manufactured in a dedicated, FDA-registered and inspected facility. Production adheres to appropriate current good manufacturing practices (cGMPs) and specifications, US Drug Master Files, European Technical files and ISO 9001:2000 standards. In addition, manufacturing and testing is conducted to comply with regulatory requirements in different geographies.
Dow Corning also provides support services for current products or custom-formulated materials. This support includes a worldwide network of technical assistance centers, toxicological testing and analysis, material analysis and chemical engineering services.

**Evaluations of Release Rates of Actives from SSA Matrices**

Given the utility silicone elastomers and PSAs have found as delivery matrices for transdermal and topical drug delivery systems, evaluations were performed to assess the suitability of the new elastomeric adhesive with several actives either already present in commercial patches or that might capitalize on the physical and chemical properties of the adhesive. Several studies were conducted to evaluate the compatibility of various drugs and their release from SSA matrices. The evaluation included cure profiles of the drug-loaded adhesive matrices and drug diffusion kinetics testing.

In one series of studies, Dow Corning 7-9800 Soft Skin Adhesive was evaluated as the carrier matrix for topically-applied drug delivery systems using ketoprofen, dapsone and lidocaine HCl. Evaluations were conducted using static Franz diffusion cells with a receptor solution of 40% polyethylene glycol (PEG) 400 and a 0.9% sodium chloride isotonic injection. A 50-µm thick polyester film was used as a substrate/backing material.

The formulations were prepared by high speed blending of the pharmaceutical ingredients with the SSA formulations. Each was cast onto the polyester substrate and cured in a forced-draft oven at 120 ºC for 5 minutes. Disks measuring 4 cm in diameter were cut to create a cohesive patch of adhesive and active.

Determination of in vitro drug dissolution rates of the described formulations were conducted in triplicate using Franz static diffusion cells. Each Franz cell had a defined receiving volume, and sampling was performed with complete replacement of receptor solution at specified intervals up to 48 hours. Estimation of the amount of active released into the receptor fluid was performed via UV spectrophotometer or HPLC. Plots of the amount of drug released per unit of membrane area versus the square root of time were prepared for each formulation. Cure conditions of the various patches varied with the heat tolerance of the selected active. Patches containing ketoprofen were cured at room temperature; those containing dapsone and lidocaine HCl were cured at 60 ºC.

All the drug release results reported were from patches prepared as straightforward drug dispersions in polymer matrices, comprised of the active and silicone. The patches studied had no other rate controlling layers. In this type of delivery system, drug diffusion and release from the formulation limits the release rate, and drug release is theoretically proportional to the square root of time once steady state is achieved. This theory is exemplified by the ketoprofen results depicted in Figure 4, which display a correlation coefficient greater than 0.999 for the median concentration and nearly linear release rates over a 48-hour time period when release rates are plotted against the square root of time.

Ketoprofen is indicated for pain relief and has been used in traditional topical formulations for many years. In Figure 4, release rates from the SSA matrix into a 40% PEG 400 receptor fluid show a controlled release at all drug concentrations.
Dapsone is indicated as a topical formulation for treatment and reduction of *acne vulgaris*, and as an oral dosage form for other indications. Figure 5 illustrates release rates from a non-optimized patch formulation using a 40% polyethylene glycol 400 (PEG 400) receptor fluid. The data show a burst effect for the first four hours and a slow delivery throughout the remaining sampling time. The burst effect provides antibiotic concentration above the minimum inhibitory concentration of *Propionibacterium acnes*, while the subsequent steady state release may inhibit *P. acnes* growth.

Lidocaine HCl has a long history of use as a topical anesthetic in tinctures and sprays. In Figure 6, release rates of this drug from the SSA matrix into a 0.9% sodium chloride in water receptor fluid show a controlled, zero to first order release at all drug concentrations, indicating a sustained and steady delivery over time. Because of the generally steady drug release, these data may be applicable to a sustained release lidocaine HCl device.
In another series of evaluations, the “traditional” SSA, Dow Corning 7-9800 Soft Skin Adhesive was compared with a new-generation SSA. The new-generation adhesive combines the soft texture, compressibility and ease of removal from skin of traditional SSAs with the adhesive characteristics and relatively longer wear times associated with PSAs. Materials, sample preparation and evaluations for these studies were the same as for the previous studies. Methods of in vitro drug dissolution testing and active analysis also were the same. Each mixture was cast onto the polyester substrate and cured in a forced-draft oven at 120 °C for five minutes.

Figure 7 compares the release of clindamycin phosphate from two elastomeric silicone matrices, a traditional SSA (Dow Corning 7-9800 Soft Skin Adhesive) and the new-generation SSA. The release rates after 48 hours from both SSA matrices are comparable when 0.9% saline solution is used as the receptor fluid. However, the release profiles differ greatly in that the traditional SSA displays a burst effect with regard to release kinetics, while release kinetics of the resin-reinforced SSA display a more linear release in the 48-hour test period.

Figure 7. Release kinetics of clindamycin phosphate 5% w/w from traditional and new generation SSA.

Figure 8 illustrates the release kinetics of two patches prepared with new-generation SSA as the patch matrix. Both were formulated to contain 2% (w/w) of the selected active, either the hydrophilic vitamin niacinamide or the lipophilic corticosteroid clobetasol propionate. Both sets of patches were prepared as neat formulations of active and adhesive. As such, no solubilizers or release modulators that would increase the release rates of the actives from the matrix were added to the patch formulations. A different receptor fluid was used for the drug delivery of each active. The receptor fluid for the clobetasol propionate release was a solution of 5% PEG 400, 25% ethanol, and 70% water, while the receptor fluid for the niacinamide study was 0.9% sodium chloride in water. Still, controlled release kinetics were observed from both non-optimized formulations within the 24-hour test period.

Figure 8. Release kinetics of new-generation SSA with niacinamide and clobetasol propionate.
When niacinamide was added to the new-generation SSA, a cohesive film resulted. However, at a similar loading level of niacinamide into the traditional SSA, no cure was observed. A study was then instituted using a vibrating needle curemeter to evaluate the cure of the two SSA classes in the presence of actives. The vibrating needle curemeter (VNC) measures the frequency at which a needle vibrates in a given medium at a defined temperature, over a specified time. The frequency at which the needle moves is directly proportional to the viscosity of the test medium at that moment. Measurements of high viscosity materials at elevated temperature are routinely made with a VNC. This makes the VNC an ideal tool for measuring cure rates of elastomeric materials such as the SSA.

When measured using a vibrating needle curemeter, the cure profiles of the traditional SSA (Dow Corning 7-9800 Soft Skin Adhesive) and a new-generation SSA are relatively comparable. However, when lidocaine is solvated in mineral oil and added to uncured traditional and new-generation SSA at a concentration of 4 % (w/w), the new-generation SSA has a more definitive cure curve, indicating a more complete cure in the new-generation SSA than the traditional SSA. VNC data did indicate that the maximum frequency attained by the new-generation SSA in the presence of lidocaine is lower than that attained in the control. Some weakening of the gel is most likely caused by the presence of lidocaine, but the mineral oil also acts to soften the gel matrix. Lidocaine 4% (w/w) laminates prepared with the new-generation SSA form a cohesive film, while those prepared with the traditional SSA showed no signs of achieving cure.

Other actives were screened as neat mixtures of drug in SSA to evaluate their impact on the traditional and new-generation SSA to achieve a full cure. Laminates of both adhesives were prepared at approximately 250 μm thickness on a polyester substrate. The completion of the cure was evaluated via visual inspection of the films and a subjective comparison of each SSA with a control that did not have any actives incorporated. Table 1 shows the results of these evaluations.

<table>
<thead>
<tr>
<th>Pharmaceutical Active</th>
<th>Active Conc. (% w/w)</th>
<th>Traditional SSA</th>
<th>New-Generation SSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocortisone Acetate</td>
<td>5</td>
<td>Full cure</td>
<td>Full cure</td>
</tr>
<tr>
<td>Hydrocortisone</td>
<td>1, 2, 5</td>
<td>Full cure</td>
<td>Full cure</td>
</tr>
<tr>
<td>Hydrocortisone</td>
<td>2</td>
<td>Full cure</td>
<td>Full cure</td>
</tr>
<tr>
<td>Hydrocortisone</td>
<td>5</td>
<td>Slightly more tacky than control</td>
<td>Full cure</td>
</tr>
<tr>
<td>L-Menthol</td>
<td>5</td>
<td>Full cure</td>
<td>Full cure</td>
</tr>
<tr>
<td>Urea salt</td>
<td>5</td>
<td>Full cure</td>
<td>Full cure</td>
</tr>
<tr>
<td>Salicylic Acid</td>
<td>2, 5, 10</td>
<td>No cure</td>
<td>No cure</td>
</tr>
<tr>
<td>Ketoprofen</td>
<td>6.25, 12.5, 25</td>
<td>Full cure</td>
<td>Incomplete cure</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>5</td>
<td>No cure</td>
<td>Cured, but slightly more tacky than control</td>
</tr>
<tr>
<td>Econozole Nitrate</td>
<td>5</td>
<td>No cure</td>
<td>Partial cure; slight gumminess</td>
</tr>
</tbody>
</table>
When allowed to remain at room temperature, ketoprofen slowed the cure of the traditional adhesive, with several hours required for the SSA to attain a full cure. After two months, the traditional SSA patches prepared with ketoprofen still appeared homogenous and cohesive. The new-generation material did not achieve a fully-cured state even after resting overnight. When samples were placed in an oven at various constant temperatures from 60 °C to 140 °C, for all ketoprofen concentrations no cure was observed in either SSA matrix. The melting point of ketoprofen is reported in the literature as 92 °C. It is likely that the cure inhibition is amplified in the presence of melted ketoprofen. Elevated temperatures seem to have played a significant role in ketoprofen cure inhibition, likely exacerbated by the degradation of ketoprofen at elevated temperatures.

Results of this study indicate the physical characteristics of Dow Corning 7-9800 Soft Skin Adhesive (e.g., low peel release force and compressibility) combine to create a unique drug delivery vehicle characterized by painless removal from the skin.

**Conclusions**

The drug release profiles of the selected actives from all the studied SSA matrices may be applicable for clinical indications of the actives. The adhesive tolerates variable cure profiles to accommodate the temperature tolerance of the selected drug.

Using the same drug at similar concentrations allows for adjusting the release rate from both new-generation SSAs and traditional SSAs, suggesting the chemistry set may have wider utility and be conducive to fine tuning of application-specific release rate profiles. Although the release rates of the actives from most SSA matrices were not high, the patches were neat formulations of adhesive and active. As such, no release enhancing species that could increase the release statistics were added to the patches. Optimization of an SSA-based patch would certainly include the addition of release enhancers to refine and align the diffusion rates to the therapeutic and pharmacological requirements.

Additional conclusions may be made as a result of this series of studies. Foremost among these is that the selection of active is integral to deciding if the SSA may be used as the delivery matrix. Compatibility of the active with the SSA must be confirmed early in the process, as some drugs slowed cure, while others completely prevented the cure.

VNC data and subjective cure evaluations suggest that the new SSA may be compatible with a wider range of actives than traditional SSAs. The new-generation SSA has improved resistance to cure inhibition over the traditional SSA, not only with respect to the number of compounds, but also with regard to drug concentration. The improved resistance to cure inhibition may allow SSAs to be a matrix of choice for a greater number of indications than previously thought possible.

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References