Pressure-Sensitive Adhesives versus Tacky Gels

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By definition, transdermal, drug-delivery applications mandate the use of adequate adhesive systems to not only keep the pharmaceutical agent in contact with the intended surface, but to facilitate sustained, controlled delivery. Engineers who must determine which silicone chemistry is optimal for their device have a few options. While pressure-sensitive silicone adhesives (PSAs) have typically been considered optimal for transdermal applications, silicone gel technology has emerged as an excellent option.

To make an educated decision regarding chemistry choices, it's vital to understand the differences between silicone PSAs and gels in both composition and physical performance. After extensive testing, NuSil Technology, LLC, compared these factors, as well as peel and tack data, to illustrate the strengths, advantages and disadvantages of each technology.

Historic Perspective

Since 1979, PSAs have been a mainstay in transdermal, drug delivery. PSAs, provide pharmaceutical companies the means to supply a range of active agents in a non-invasive, controlled-release system and reduce the healthcare industry's dependence on gastrointestinal and needle-based administrations. The overriding benefits of these systems include improved patient compliance and steady drug levels within the bloodstream.

Estradiol, testosterone, and nitroglycerin are just a few of the compounds currently found in prescribed, transdermal, drug-delivery systems. Over-the-counter (OTC) products — such as Dr. Scholl's Clear Away Wart Remover, Neutrogena's On-the-Spot Acne Treatment, and several brands of the nicotine patch — are examples of how this technology has moved readily into direct consumer applications. Estimates for growth in this area are 12 percent annually[(1)]. Some of the usual adhesives incorporated in transdermal, drug-delivery systems are polyisobutylenes (PIBs), silicones and acrylic-based PSAs. For this article, silicone-based PSAs are used for comparative purposes.

Silicones are good candidates for transdermal, drug-delivery systems because they offer two major benefits to drug-device developers. First, silicones have a more than 50-year history in biomedical applications and, in that time, a considerable body of work has been assembled that characterizes silicones as biologically inert[(2)]. In addition, silicones are ubiquitous in the medical device industry in both long-term, implantable devices and external devices. Second is the compatibility/permeability of silicones with many pharmaceutical agents, not just hormones. Other compatible drugs include antidepressants; anxiolytics; vitamins B6, D, and E; antifungals; opioid and non-opioid analgesics; and antiviral compounds [(3)].

Siloxane Chemistry

Silcones' compatibility and permeability with pharmaceutical agents is a function of the siloxane-based polymers and resins used to formulate these systems, and the siloxane polymer backbone of repeating silicon and oxygen atoms creates an interaction potential. The two free pairs of electrons associated with each oxygen atom can form hydrogen bonds with proton donors, often resulting in different degrees of hydrogen bonding with reinforcing fillers. Despite its ability to form hydrogen bonds, silicone is considered hydrophobic in nature. The methyl constituency on the siloxane polymer backbone creates this effect. A vinyl-terminated, dimethyl polysiloxane can be seen in Figure 1.

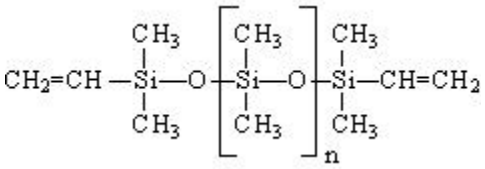

Figure 1. A vinyl-terminated, dimethyl polysiloxane's hydrophobicity is ideal for the solubility of pharmaceutical agents.

This hydrophobicity is ideal for the solubility of pharmaceutical agents having mostly non-polar structures. Another characteristic of silicone systems is the large atomic volume of the silicon atom itself, which — along with the size and position of constituent groups — explains the virtually complete freedom of rotation around the Si-O-Si bond. Silicone polymers form helixes, and the bond angles of the silicon-oxygen bonds create large amounts of free volume in silicone elastomers. This free volume, and the high compressibility found in silicones, is associated with their permeability to certain gases and liquids. The gas permeability of silicone rubber is up to 100 times greater than natural or butyl rubber.

In the specific case of drugs or active pharmaceutical molecules, release rates in silicones are determined by the drug's solubility in a silicone and the diffusion coefficients of those drugs in silicones through the Higuchi equation[4,5](equation 1 corresponds to a matrix device, and equation 2 corresponds to a reservoir device):

Equation 1 : $Q = (D_{sil} (2A - C_{sil}) C_{sil} t)^{1/2}$

Equation 2 : $Q = ((D_{sil} C_{sil})/ h_{sheth})*t.$

"Q" is the cumulative amount of drug released per device-unit area, "A" is the drug loading, "C_{sil}" is the drug solubility in the silicone, "D_{sil}" is the diffusivity of the drug in the elastomer, and "t" is the time in days. Additional research in this area relates the molecular weight and melting point of the drugs to release rates[4], as well as demonstrates that the addition of fatty acid esters improve release rates of certain drugs[6].

Silicone polymer chemistry can be modified to include different groups on the backbone. For example, trifluoropropyl methyl dimethyl siloxane copolymers are used in applications in which solvent resistance is required, while diphenyl silicone polymers are used in elastomeric formulations, when a high-refractive index is necessary (intraocular

lenses or UV and heat protection). The diphenyl and trifluoropropylmethyl functionality may also affect drug solubility and, in turn, affect release rates. The concentration of these groups on the backbone can be easily altered and optimized for specific compounds. A diphenyl polysiloxane structure is seen in Figure 2.

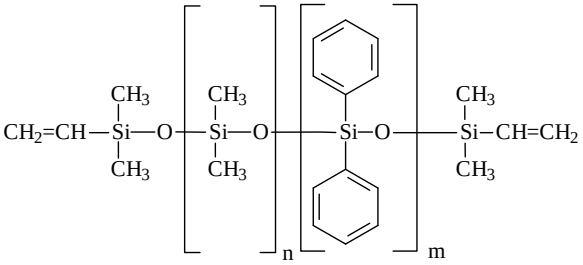

Figure 2. A diphenyl polysiloxane structure can be easily altered and optimized for specific compounds.

Silicone PSAs

Silicone PSAs incorporate a high-molecular-weight polydimethylsiloxane polymer and a tackifying silicone resin dispersed in a solvent system. The solvent provides the system with viscosity control, as silicone components are virtually impossible to process at room temperature with standard coating equipment. Two systems are currently available: platinum-catalyzed and peroxide-catalyzed. The platinum catalyzed system is less common in PSA systems.

The more-common, peroxide-cure system employs benzoyl peroxide, or 2,4-dichlorobenzoyl peroxide, as a catalyst to drive a free-radical reaction and achieve cure. Curing is normally performed in a multi-zoned oven. Solvent removal is achieved through a gradual increase in temperature, starting at 60°C to 90°C to ensure that the peroxide catalyst does not cure while solvent is present. The temperature is then increased to 130°C to 200°C, eliminating the peroxide through decomposition. A high-crosslink-density PSA can be better achieved through peroxide curing due to the ability to increase peroxide levels up to 4 percent.

Tape and adhesive-backed component fabricators take the liquid PSA and either wet coat in sheet form, for small applications, or in roll form (pilot coaters and full-width production coaters), when large quantities are required. The PSA may be applied on one or both sides of a substrate — such as Kapton®, Mylar®, Nomex®, foils, foams, and rubbers — or it can be coated directly onto a release film. Coat weights on supported film range from 0.0003” to more than 0.010” thick. When the adhesive is coated directly onto a release film, this is called an unsupported PSA transfer film. Common post-production processes include die cutting and laser cutting for later use in component assembly, and automated pick-and-place solutions for difficult-to-apply parts and materials[(7)].

Silicone PSAs are not without their drawbacks. As stated above, most PSAs are dispersed in a solvent system to provide viscosity control. The solvent can be problematic and limiting to transdermal, drug-delivery systems. Environmental concerns regarding Volatile Organic Compounds (VOCs) and plant-safety initiatives are costly factors that

must be considered. In addition, solvent systems are dynamic, and evaporating solvent can impact viscosity, leading to process variations. PSAs can also limit the transdermal system design, as these materials are typically used in multilaminate, reservoir designs. PSAs that utilize peroxide systems, as mentioned above, require an elevated temperature and may negatively impact active agents. This limitation may require that the PSA is processed in a separate step.

Silicone Gel Technology

Silicone gels share the same basic siloxane polymer chemistry as silicone PSAs but lack the silicone resin credited with supplying adhesive strength to the system. Silicone gels are typically composed of two types of siloxane polymers: vinyl-functional polysiloxanes and hydride-functional polysiloxanes. Silicone gels are low-viscosity materials that are not dispersed in solvent systems. These materials do not contain reinforcing fillers, such as silica or silicone resins, found in silicone elastomer systems. As a result, they offer little tensile or tear strength. Typically, gels used in thin-film applications use reinforcing fabrics to add strength.

The tack and adhesion of silicone gels have proven sufficient in transdermal, adhesive-type applications. The testing discussed later in this article illustrates the superior tack properties of silicone gels compared to silicone PSAs. Pfizer's Scar Solution and Smith & Nephew's Cica Care are OTC examples of silicone gels used in transdermal applications to treat hypertrophic and keliod scarring.

Silicone gels cure in the presence of platinum catalysts to solid forms that do not flow. Gels can be formulated to cure completely at low temperatures, which may be ideal for pharmaceutical agents that are unstable a higher temperatures. These materials can be utilized in mulitlaminate, reservoir or monolayer, drug-in-adhesive delivery systems.

Comparative Adhesive Properties

The discussion above provides some basic differences between silicone PSAs and gels — from chemistry to supplied forms. The following data was compiled to determine the key property differences between silicone PSAs and gels (and differences in silicone gels with dissimilar compositions). The two properties tested in this study were 90-degree peel strength (NuSil Technology Test Method TM087 Reference ASTM D1876) and tack testing (NuSil Technology Test Method TM103 Reference ASTM D429 Method D)[8]. Because pressure-sensitive system properties are influenced by the thickness or amount of adhesive, care was taken to ensure identical amounts of silicone were used. The materials were prepared per the applicable test method and specific material cure recommendations. Four materials were tested; Table 1 describes the material and characteristics:

Material Name	**Material Composition**	**Cure Schedule**
MED-1356	Dimethylpolysiloxane PSA, 35% Solids in Ethyl Acetate	37ºC for 30 minutes, 150ºC for 90 minutes
MED-1356 (peroxide catalyzed)*	Dimethylpolysiloxane PSA, 35% Solids in Ethyl Acetate,	37ºC for 30 minutes, 150ºC for 90 minutes

	0.5 pph PD-50S Based on Solids	
MED-6340	Dimethylpolysilixane Gel, 100% solids	100ºC for 30 minutes
GEL-9502-30	Diphenyldimethylpolysiloxane Gel, 100% solids	100ºC for 30 minutes

Table 1. The tested materials, as well as their material composition and cure schedule.

The testing was performed in triplicate for each material, results appear in Table 2:

Material Name	**Peel Strength Mean (lbf/in)**	**Peel Strength Standard Deviation (lbf/in)**	**Surface Tack Mean (psi)**	**Surface Tack Standard Deviation (psi)**
MED-1356	14.7	0.1	2.5	0.8
MED-1356 (peroxide-catalyzed)*	4.4	0.3	3.4	1.1
MED-6340	1.3	0.0	5.0	2.1
GEL-9502-30	1.4	0.2	8.2	2.5

* MED-1356 product is not supplied as a peroxide-cured product

Table 2. Test results.

Conclusions and Observations

The discussion and data presented above provide transdermal, drug-delivery system designers with another choice in pressure-sensitive-type, silicone-based adhesives. Silicones' historic healthcare use and drug solubility make both silicone PSAs and tacky gels good candidates for certain drug-delivery applications. From the data, it is apparent silicone gels offer higher tack, but lower peel strength, than PSAs. It can also be concluded that gels containing phenyl functionality gave higher tack and peel results than the dimethyl gel. When considering these results — alongside factors such as drug-release rates, VOC elimination and reservoir/matrix delivery designs — it is clear that, no matter which chemistry you choose, tradeoffs must be expected.

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(8) NuSil Technology's Test Methods are available by request at www.nusil.com

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