

# **Silicone Adhesives in Healthcare Applications**

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The history of silicones as biomaterials finds its origin in the 1940s, with the silicization of glass vials containing pharmaceutical preparations. Since then, they have been used in many medical applications for life improvement and health restoration, such as lubricants for syringes, elastomer tubing for blood transfusion and antifoams for antiflatulent medicines<sup>1</sup>. Today, silicones have a 50 year history of safety and efficiency in their applications: polydimethylsiloxanes are recognized for their biocompatibility and are one of the most tested materials for their safety. With the emerging trend toward pain management in wound care and the revitalized interest for transdermal drug delivery forms, silicone skin adhesives are experiencing a renewed popularity, partly because they can provide gentle adhesion to skin as well as providing formulation options to deliver hydrophilic molecules.

Silicones are macromolecular structures that are comprised of siloxane backbones with alkyl, aryl or organo-functional substitutions. In the medical and pharmaceutical industries, the term “*silicone*” typically encompasses materials based on the dimethylsiloxane structure. The physico-chemical properties of polydimethylsiloxanes (PDMS) are directly dependent on the molecular characteristics of the permethylsiloxane chains. This is especially evident at the interface with other fluids and materials. These interface properties contribute to the ever-increasing use as silicone adhesives for temporarily attaching therapeutic patches, wound dressings, and medical devices to skin.

## Silicone Chemistry

In medical applications, silicone materials are available in many physical forms: from volatile to high molecular weight fluids (viscosity ranges from 0.65 mm<sup>2</sup>/s to 20 x 10<sup>6</sup> mm<sup>2</sup>/s), visco-elastic compounds and cross-linked elastomers. However, these materials mainly refer to the same dimethylsiloxane structure that has been recognized for its biocompatibility in polymeric states. The excellent biocompatibility is due in part to the low chemical reactivity, the low surface energy and the hydrophobicity of polydimethylsiloxanes<sup>2</sup>. Indeed, they have a semi-organic molecular structure in which an inorganic silica-like backbone supports a regular arrangement of pendant methyl groups (Figure 1).

Characterized by a high bond energy (about 106 kcal/mol) and polarity, polysiloxanes

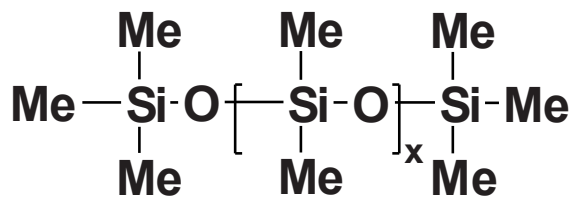


Figure 1—Polydimethylsiloxane (PDMS)

are not easily broken by homolytic scission. Only strong acids or bases are capable of depolymerizing the siloxane chain. As a result, polydimethylsiloxanes are not very susceptible to oxidation or thermal degradation. These materials are relatively inert towards non-aqueous ingredients and active molecules used in pharmaceutical formulations. In addition, PDMS hot-melt materials can be formulated.

There are some unique atomic characteristics as well. Siloxane bonds have nearly zero energy of rotation about Si-O bond. As such, the rotation is virtually free. The Si-O bond length is exceptionally long (about 0.16 nm) and the Si-O-Si angles are extremely large (130° for Si-O-Si in hexamethyldisiloxane), which contribute to the ease of interconversion of configurations. These unique atomic characteristics are further enhanced by the divalency of the oxygen, thus yielding silicon-oxygen chains with highly flexible and very open macromolecular structures.

An inherent consequence of this flexibility is the ability of the siloxane backbone to spread out the methyl substitutions at an interface. These methyl groups shield the polar siloxane backbone and form a hydrophobic sheath with very low intermolecular interactions. As a result, the PDMS molecule coils in a mobile spiral configuration onto its inorganic axis surrounded by a non polar organic cloud. This dense methyl array at interfaces, results in polydimethylsiloxanes with reduced surface tension and reduced surface energy. Consequently, PDMS-based materials have truly unique properties directly driven by the mobility of the open siloxane mesh and the low intermolecular interactions. These unique properties are demonstrated in several ways:

- Polydimethylsiloxanes are liquid at room temperature, even at high molecular weight, with glass transition temperatures below -80°C. As a result, based on their degree of cross-linking and the type of reinforcement (e.g. silica, resin), silicones have suitable visco-elastic behavior and consequently elastomeric and pressure sensitive properties.

- Polydimethylsiloxanes have low surface tension, with a critical surface tension around 24 mN/m and a liquid surface tension around 20.4 mN/m at 20°C. As a result, PDMS polymers not only spread easily and form thin films over substrates such as skin and other organic substrates, but they are also able to spread over their own absorbed film. This allows silicones to wet, spread and subsequently adhere to skin. Coupled with visco-elastic behavior, this property reinforces the silicone ability for adhering to skin and subsequently releasing from skin, thus performing as expected as true pressure sensitive adhesives.
- Compared to other hydrophobic polymers, PDMS is very permeable to the diffusion of various substances including gases, water vapor and active drugs. These are appropriate properties for transdermal and topical drug delivery applications.

Finally, some methyl groups can be substituted by other organic groups or atoms (e.g. hydrogen, hydroxyl, vinyl, polyethylene oxide, methoxy, fluoride group), when specific chemical and physical properties are desired, such as adhesion to a certain substrate, higher or lower polarity, better thermostability, enhanced hydrophilicity, compatibility with other organic materials or targeted reactivity. This capability to functionalize the polydimethylsiloxanes is critical for transforming liquid or highly flowable materials into thermoplastic or thermoset materials that are represented respectively by visco-elastic silicone pressure sensitive adhesives (PSA) and by elastomeric silicone soft skin adhesives (SSA).

The broad spectrum of physico-chemical properties of the siloxane chemistry translates to multi-functional performances, flexibility in choice of silicone solutions and versatility in formulations, as shown in Figure 2. This is particularly useful to an adhesive formulator in designing the silicone adhesive composition to meet unique application needs.

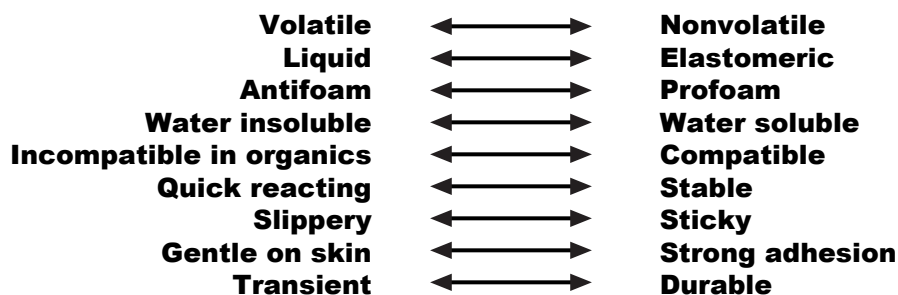


Figure 2 - Versatility of siloxane chemistry

### Skin adhesion

Pressure sensitive adhesives (PSAs), unlike structural adhesives or sealants, differ in that the adhesive-substrate interface does not resist separation when the adhesive is peeled off. In other words, PSAs are intended to show adhesive failure, especially when skin is the substrate, whereas this would be a major fatal flaw for cement and glue.

Developing a suitable PSA for a targeted adherend, should include considerations for the critical adhesive attributes: surface activity and visco-elastic properties. They are directly associated to the three steps of adhesion process:

- The first step involves contact between the adhesive and the surface. This dynamic step is known as “bonding” and is dependent on wetting behavior and quick spreadability of the adhesive.
- The second step “adhering” relies on the capacity of the adhesive to remain in contact with surface. Flowability and creep resistance are the physical characteristics that contribute to maintain the established bond. During this more static phase, the adhesion will build up if the adhesive-to-surface interactions increase (e.g. interpenetration).
- The third step “debonding” is also dynamic. It consists in separating the adhesive from the surface by means of a peel release process. The peel adhesion property of the adhesive will direct the force required to break the bond in an adhesive failure mode.

In the case of a medical adhesive device or a transdermal patch, these attributes are essential for the device to be positioned and fixed, to remain in place for the duration of the treatment, and then to be removed without leaving residue or damaging the skin. Identification of suitable materials requires a good understanding of the interfacial surface activity and a suitable knowledge of rheological characteristics necessary for the application. When skin is the adherend, silicone adhesive technology is one

of the definitive choices because silicone adhesives have:

- Lower surface tension than skin, thus allowing for wetting to occur quickly and extensively.
- Fast spreadability under low deformation rate, enhanced by light pressure and mild heat.
- Tunable visco-elastic profile with adjustment of the rheological parameters for delivery of the appropriate level of adhesion in terms of intensity and duration.

At Dow Corning, silicone adhesive technology currently translates into two options for adhesion to skin: silicone pressure sensitive adhesives (PSA) and the silicone soft skin adhesives (SSA)<sup>3</sup>.

### Medical silicone pressure sensitive adhesives

Medical silicone pressure sensitive adhesives are truly visco-elastic compounds based on the resin-in-polymer concept. Unlike organic PSAs, they do not need additives such as antioxidants, stabilizers, plasticizers, catalysts or other potentially extractable ingredients. Silicone PSAs are produced by condensing dimethiconol to MQ resin in the presence of ammonia, as shown in the Figure

3. The dimethiconol is a medium to low viscosity silanol end-blocked polydimethylsiloxanes. The MQ resin is a soluble 3-dimensional silicate network comprised of SiO<sub>4/2</sub> units (Q) and R<sup>1</sup>R<sup>2</sup>R<sup>3</sup>SiO<sub>1/2</sub> units (M), where R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> are mainly methyl or hydroxy groups.

The dimethiconol, as a fluid, contributes to the viscous component of the visco-elastic behavior, and impacts the wetting and spreadability properties of the adhesive. The resin acts as a tackifying and reinforcing agent, and participates in the elastic component. The resin content is the major factor for enhancing the cohesion to the required level in order to obtain the optimum balance of tack, adhesion and peel release<sup>4</sup>.

For dynamic rheological testing, the viscous or loss modulus, G<sup>''</sup>, is one indicator of the fluid phase. It indicates how much energy is lost as heat per cycle of deformation. The elastic or storage modulus, G', accounts for the elasticity of the adhesive and translates to energy stored under strain such as shear or peeling off (Figure 4). Optimum wetting, and consequently optimum bonding, occurs at low deformation rate when the elastic modulus is low. Subsequently, debonding occurs at high deformation rate when the adhesive strip is removed. Sufficient elasticity is required to transfer the energy and break the adhesive interface, and in fact remove the device<sup>5,6,7</sup>. Increasing the silicone fluid content yields PSAs with higher tack (quick bonding) and less shear strength, whilst increasing resin content leads to lower tack and higher cohesiveness (cold flow resistance).

A simple blend of silicone fluid and resin can provide initial bonding; however, unless polymer and resin are covalently tied together, low cohesive properties result, thus

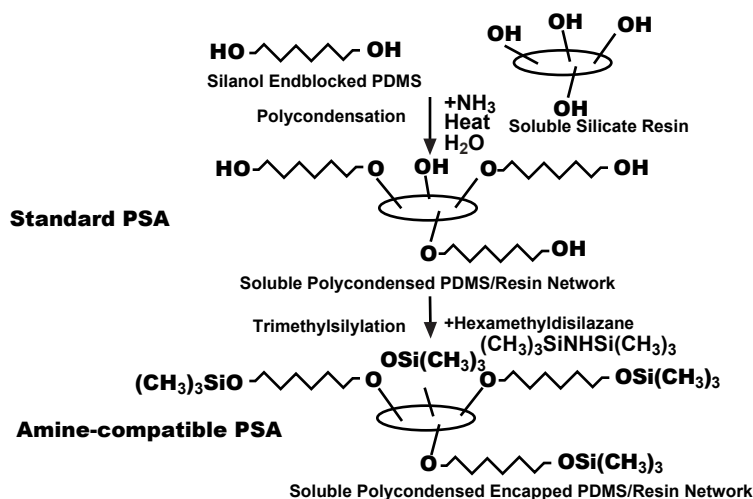


Figure 3– Synthesis of silicone PSAs

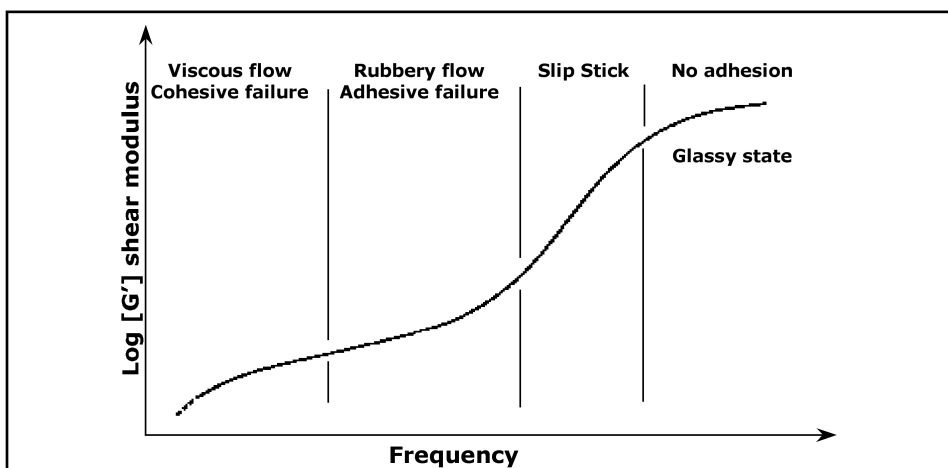


Figure 4 – Rheological profile of pressure sensitive adhesives<sup>7</sup>

leading to cold flow effect and cohesive failure when debonding. Both cohesive and shear strength are improved by coupling the dimethiconol and resin together. The hydroxy groups present on both the silicone fluid and resin are condensed in the presence of ammonia and heat, to produce the standard version of medical silicone PSA. Subsequently heat treatment at reduced pressure removes ammonia and the processing solvent. Small amounts of reactive hydroxy groups remain in the standard adhesive and can be significantly reduced by subsequently reacting them with a trimethylsilyl endcapping agent (e.g. hexamethyldisilazane in Figure 3). This end-capped version is labeled “amine- compatible” because it exhibits enhanced chemical stability in the presence of amines<sup>8,9,10</sup>. Independent of the degree of silylation, the medical silicone PSAs are high molecular weight PDMS networks with optimum adhesive properties for a ratio resin/polymer in the range of 40/60 to 65/35. Despite their high molecular weight and tri-dimensional structure, silicone PSAs remain in several organic solvents and silicone fluids.

Dow Corning medical silicone PSAs are non-reactive systems that flow under light pressure at skin temperature to conform to the stratum corneum surface<sup>11</sup>. Silicone PSAs are recognized as suitable adhesives for use in medical adhesive devices, tapes and bandages, wound dressings and transdermal drug delivery system (TDDS) applications. They can provide the following benefits:

- Suitable tack for quick bonding to various skin types, including wet skin
- Suitable adhesive and cohesive qualities
- Long-lasting adhesion to skin (up to seven days)

- High degree of flexibility
- Permeability to moisture
- Compatibility with many therapeutic molecules
- Compatibility with most of the film substrates (e.g. polyurethane substrate)
- Co-formulation with pharmaceutical excipients to adjust the kinetics of drug release

Dow Corning medical silicone PSAs are supplied in solvents such as heptane, ethyl acetate or volatile silicone fluids<sup>3,12,13</sup>. They can be processed by coating onto a suitable release liner (e.g. fluorinated/fluorosilicone coated polyester film), removing the solvent followed by transferring the dry film to the final substrate. Direct coating is possible if the substrate is compatible with the solvent and the drying temperature condition. Hot-melt versions can be prepared by incorporating high molecular weight plasticizers such as silicone PDMS or organic waxes (e.g. ceresin wax) into a solventless silicone

PSA formulation<sup>3</sup>. Hot-melt silicone adhesives can be softened to viscosities suitable for coating at temperatures between 180°C and 200°C; they return to a flowless state upon cooling.

## Soft Skin Adhesive Silicone Elastomers

A second class of solventless silicone adhesives is based on cross-linked silicone elastomer technology. Labeled as SSA for “soft skin adhesive”, these materials are often referred to as “tacky gel” or “silicone gel”. They differ from analogous silicone elastomers by the absence of reinforcing silica filler. As a result, they have the consistency of a gel but they are not truly polymeric gel because they are not based on an insoluble polymer network swollen with low molecular weight fluids. SSAs are cross-linked polydimethylsiloxanes with low amounts of free extractable molecules.

The elastic behavior of SSAs also differs from silicone PSAs. Despite low consistency and some compressibility, SSAs show resilience and quick recovery under cyclic deformation<sup>7</sup>. The pressure sensitive adhesive property of SSA is mainly based on the capacity of the surface to quickly wet the substrate and conform to its relief without excessive flow. Because the viscous component is minimal, the material does not flow, and only small dissipation of the energy occurs when deformation pressure is applied (Figure 5). The result is an immediate debonding, which happens at low peel or shear force. The advantage in skin adhesion is the atraumatic removal obtained with SSA: no skin stripping and no painful skin or hair pulling. Another advantage lies in the fact that SSAs, unlike PSAs, have a low viscous component that limits their flow and consequently the readiness to

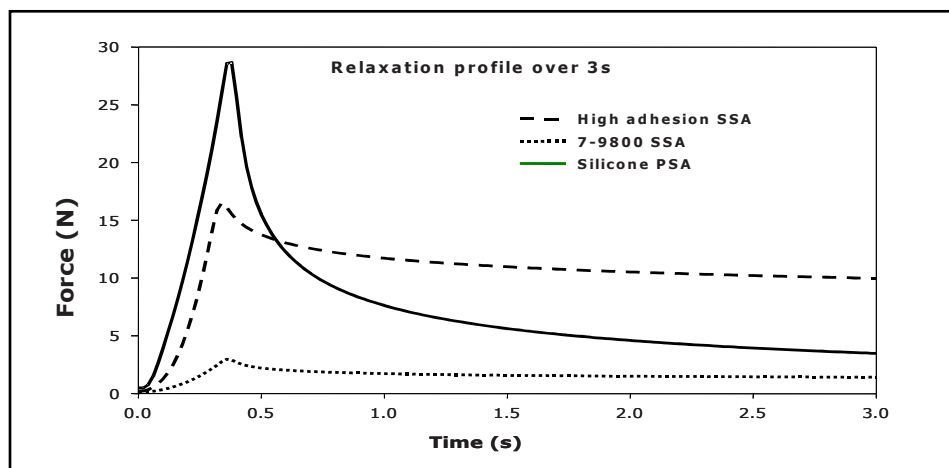


Figure 5– Comparison of relaxation of silicone adhesives<sup>7</sup>

absorb materials at the surface of the skin such as stratum corneum cells and lipids. The adhesive surface of SSAs remains relatively clean. It can be removed and re-adhered easily to the same location.

Cross-linking of SSAs is based on an addition reaction (hydrosilylation), between vinyl functional PDMS and hydrogen functional siloxanes (e.g. dimethyl, methylhydrogen siloxane copolymers, hydrogen dimethylsiloxy terminated PDMS) as shown in the Figure 6. The cure reaction is catalyzed by a platinum complex. It can occur at room temperature or be accelerated at elevated temperature (80°C to 145°C), without the formation of by-products.

Silicone SSAs are cross-linked elastomers that are not susceptible to plasticizing effects. They quickly adhere to skin under light pressure and provide an immediate cushioning protection. This adhesive technology has been extensively used in scar treatment for more than 20 years, demonstrating safety and efficacy recognized by wound care professionals<sup>14,15</sup>. SSAs can be used in medical adhesive devices, tapes and bandages, wound dressings and topical drug and active delivery applications when the following benefits are desired:

- Suitable tack for quick bonding to various skin types, including wet skin
- Suitable adhesiveness and cohesiveness
- Gentle adhesion to fragile and compromised skin
- No skin stripping (painless at removal)
- Repositioning capability
- High degree of flexibility
- Permeability to moisture
- Compatibility with many therapeutic molecules
- Co-formulation with pharmaceutical excipients to adjust the kinetics of drug release

Silicone SSAs are supplied as two-part systems: part A contains at least the vinyl polymer and the catalyst while part B contains the vinyl polymer and the SiH siloxane cross-linker<sup>16</sup>. SSAs can be processed by coating them onto a suitable release liner (e.g. polyethylene film) followed by transferring them to the final substrate; or by directly coating them onto the substrate, if this latter is impermeable enough to prevent the liquid SSA from wicking through.



Figure 6 – Hydrosilylation reaction

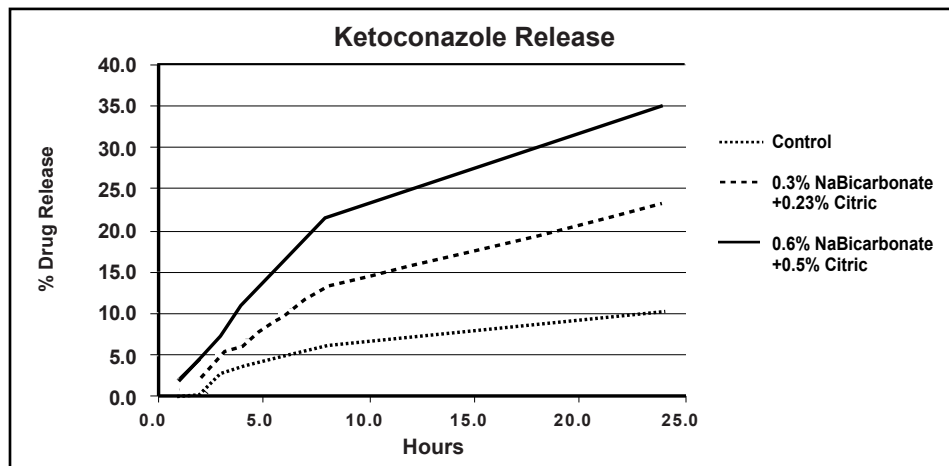


Figure 7 – Release of ketoconazole from silicone PSA

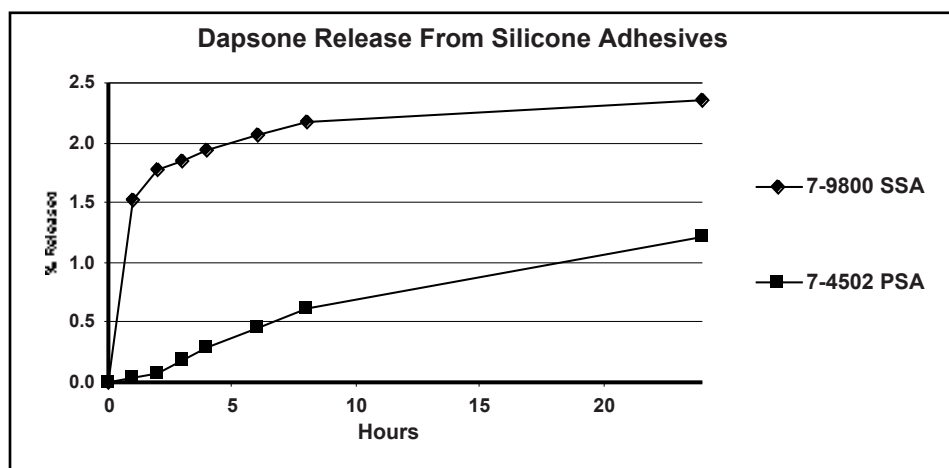


Figure 8 – Release of dapsone from silicone PSA and SSA

### Comparative Data On Drug Loading

Transdermal and topical drug delivery devices benefit from the versatility of silicone adhesives. As described in the previous paragraphs, the adhesion to skin can be adjusted to last from a few hours to several days. Due to their hydrophobic, highly open and mobile dimethylsiloxane network, silicone adhesives allow for the preparation of adhesive matrices permeable to many molecules. An abundant amount of prior art has demonstrated the sustained release of actives from silicone pressure sensitive adhesive matrices. Examples include the following: nitroglycerin (arterial & vasodilator), hydrocortisone (anti-inflammatory), salicylic acid (keratolytic agent), estradiol (hormone replacement), niacinamide (skin regeneration), dapsone (anti-acne agent), ketoconazole (anti-fungal), and enzymes.

To prevent re-crystallization of the drugs and to enhance their release, other excipients such as silicone polyethers, cellulose derivatives, polyvinyl alcohols, carbomers, glycerol, and bicarbonates are often formulated into the device<sup>17,18,19,20,21</sup>. This is illustrated in Figure 7, with the release of ketoconazole from silicone PSAs<sup>22</sup>. Ketoconazole has limited release from a silicone PSA matrix due to a certain affinity to the polydimethylsiloxane environment. Dispersion of the ketoconazole in a more hydrophilic matrix (e.g. addition of 0.3% to 0.6% of sodium bicarbonate-citric acid) increases its dissolution in an aqueous medium<sup>22</sup>. This less lipophilic matrix is more favorable to a partitioning of the drug into the dissolution receptor medium.

The choice between the two silicone adhesive technologies: PSAs and SSAs, allows

one to produce different release profiles and burst effects in order to address specific therapeutic needs. As reported earlier<sup>23</sup>, this is demonstrated by the release of dapsone from silicone PSA and SSA in Figure 8.

## Conclusions

Silicones benefit from 50 years of safety and efficiency in a variety of health care applications. They have been extensively tested to ensure their biocompatibility and possess a number of unique attributes that are conducive for new product development.

The relative simplicity of the silicone adhesive chemistry provides a low barrier for customization, and the more recent discovery of controlled release of biologicals will undoubtedly extend their use into new biotechnology health care applications.

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