Low Trauma but High Adhesion Silicone Adhesive

for Medical Applications

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Abstract:

Silicone adhesives have seen increased uses as medical adhesives for drug delivery, for medical tapes, for wound dressings, and for scar management. Great biocompatibility and excellent kind removal without skin trauma are two inherent benefits silicone adhesive brings to the table.

In this paper, authors will discuss the technology advancement of silicone adhesives with enhancement of skin adhesion to provide reliable securement for the medical devices while maintaining the low Medical Adhesive Related Skin Injuries (MARSI) by leveraging the unique combination properties silicone adhesives provide.

Introduction:

Medical Pressure Sensitive Products are important in the medical device industry and are extensively used in hospitals. Those medical products include adhesive transfer tapes, single side coated products, and double side coated tapes. Adhesive transfer tapes and double coated tapes are usually used by Medical Device OEMs to adhere medical devices, strips, and pouches for medical diagnosis and management of waste discharges. Single side coated products serve as bandages, medical tapes, wound dressings, surgical drapes, wound closure tapes, and skin attachments for electrodes, IV dressings, and medical sensors (Figure 1). Fueled by population demographics, product innovation, and increased market needs within and outside the United States, the global market of Medical Pressure Sensitive Products reached $7 billion in 2016.

Figure 1. Medical Pressure Sensitive Products

Skin Characteristics:

Medical Pressure Sensitive Products require skin adhesion, however adhering to skin reliably and safely is very challenging, not only because skin is a very complicated adherent [(1)] and varies a lot person to person, time to time, skin location to skin location, and physical condition to physical condition, but also because skin is a delicate and bio-reactive adherent with relatively low cohesive strength [(2)] and with possible sensitive reactions [(3)] to many chemicals, especially those with low molecular weights.

Skin is the largest organ in the body averaging 3000 square inches and 7 pounds in an adult, which provides primary function as a two-way barrier between the body and environment. On one side, skin prevents inward penetration of destructive chemicals, infective microorganisms, and damaging radiation from sun. On the other side, skin prevents outward passage of water and electrolytes. Such barrier function of the skin is largely situated in the epidermis [(4)].

Dermis and hypodermis, layers underneath epidermis is the most part of skin and is also the layers containing nerves and sensatory receptors, which detect incoming stimuli of touch, vibration, pressure, temperature, pain, and itch.

The characteristics of skin, especially epidermis, make the adhesion to skin very challenging:

1. Skin is a surface renewable and replenishable:
   The outermost surface of epidermis, called stratum corneum, is made of cells migrated from the base of epidermis and is sloughed off in about 14 days, while the entire epidermis renews itself on a cycle of 45 ~ 75 days [(5)].
   Therefore, a medical pressure sensitive adhesive must stick to the layer that is being shed off every couple week.

2. Skin is a surface highly contaminated:
   Skin is loaded with skin perspiration or exudate (water, mineral, lactate, and urea), skin cosmetic and skin care chemicals (oil, glycerol, petroleum jelly, silicone, fragrance, dye, preservative, protein or peptide), and loose debris (dust, dead skin cells).
   Therefore, a medical pressure sensitive adhesive must be tolerant to variety surface contaminates in order to stick to the skin layer.

3. Skin is surface with low surface energy (LSE):
   Being composed of lipidic components, especially the sebum, skin surface is primarily hydrophobic and has low surface tension of 25~29 dyne/cm [(6)].
   Therefore, a medical pressure sensitive adhesive must have equivalent or lower surface tension to achieve sufficient skin-wet out and ultimate skin adhesion (Table 1).

Material	Surface Tension (dyne/cm)
PTFE	18
Silicone	21
Skin	25~29
PP / PE	31
Acrylic	38
Water	72

Table 1. Skin as Low Energy Surface

4. Skin is a surface with high roughness resulted from hair, folds, wrinkles, crevasses, and pores for sweat and oil glands:
   For example, the mean depth of skin crevasses (measured by profilometry) is 91 micron for an old man and 36 micron for a young man [(7)].
   Therefore, a medical pressure sensitive adhesive must be soft enough and be able to flow to achieve ultimate surface contact.

5. Skin is a surface with high elasticity:
   The mechanical properties of skin depend mainly on the dermis, which is elastic to a degree and can be stretched reversibly by 10~50%.
   Therefore, a medical pressure sensitive adhesive must have resistance to constant elastic stretch to achieve robust skin adhesion.

6. Skin is a live surface sensitive to many chemicals:
   Being a live surface, skin is highly sensitive and prone to allergic reaction when in contact with certain substance (allergen) that the immune system believes is dangerous and reacts to it. The longer the skin is in contact with the allergen, or the stronger the allergen is, the more severe the skin allergic reaction will be.
   Therefore, a medical pressure sensitive adhesive must have as low concentration as possible of sensitive chemicals, especially those low molecular weight monomers, oligomers, and additives, so to be hypoallergenic, low irritation, and low sensitivity.

7. Skin is a surface highly variable in its physical constructions and properties described above:
   Skin is highly variable with gender, age, ethnicity, location on the body, and ambient conditions. For example, one of the skin barrier properties against water loss is referred as TransEpidermal Water Loss (TEWL). A typical value of TEWL for an intact skin of a forearm is 9.7 $g/m^2/h$ in contrast to a typical value of intact skin of a palm is 101.4 $g/m^2/h$. In another example the tensile strength of human stratum corneum could change from 3 MPa at 100% relative humidity to 370 MPa at 30% relative humidity [(8)].

Skin Adhesion Test

Due to what described above, evaluating medical tape performances becomes a huge challenge. Since no artificial adherent substrates can represent all skin characteristics, including high degree of variations, the best way to assess medical adhesive is to measure adhesion on human skin in randomized experiments.

In our work, twelve healthy human subjects were selected for each experiment. The back of each subject was washed with a dilute solution of soap and water (approximately 1% suspension), rinsed with tepid water, and gently dried with a soft paper towel. For a given subject, a tape test specimen measuring 1 inch wide by 3 inche long was placed on the subject back so that the long axis of the tape test specimen was oriented perpendicular to the subject's spine. The order of application of the tape test specimens was randomized (i.e., rotational placement) on each subject. The tapes were secured to the skin using a 4.5 pound roller, rolling the tapes once in each direction. After a given dwell time, the tape test specimens were removed at 180° with an imass peel tester at a constant rate of 6 inches / minute and the results recorded in grams / inch. The average peel force required to remove the tape test specimen was calculated based on twelve tests across the twelve randomized subjects. Results are reported as "Skin Adhesion" The following dwell times were used in the paper:

T0 peel adhesion: tapes were removed within 5 to 15 minutes after initial application;

T02: T0 peel adhesion of the same tape when repositioned and applied to a different skin location a second time;

T03: T0 peel adhesion of the same tape when repositioned and applied to a different skin location a third time;

T24 peel adhesion: tapes were removed after 24 hours after initial application;

T48 peel adhesion: tapes were removed after 48 hours after initial application;

Low Trauma Silicone Adhesive to Prevent MARSI

Besides testing challenges, adhering to skin reliably also remains as a huge task. However silicone adhesive seems to tailor made for skin adhesion, due to its low surface tension (21 dyne/cm) – be able to substantially wet-out on LSE skin surface (1^{st} step to achieve robust adhesion); low glass transition temperature (-128^{o}C) – be able to sufficiently flow on highly textured skin surface; high permeability especially for O_2 and CO_2 – be able to allow skin breath and thus enable cell growth; high hydrophobicity – be able to tolerate skin perspirant and skin care chemicals; and great biocompatibility; resulting in robust skin adhesion to deliver reliable device securement on skin, as well as kind removal of adhesive from skin to minimize MARSI.

MARSI is a prevalent but underrecognized complication that occurs across all care settings and among all age patient groups [(9)], when superficial layers of skin are removed by medical adhesive, in which erythema and/or other manifestation of skin trauma or reaction including formation of

vesicles, bulla, skin erosion, and skin tears, persist longer than 30 minutes after removal of the adhesive. MARSI, as shown in Figure 2, not only affects skin integrity, but also causes pain, increases risk of infection, potentially increases wound size, and delays healing. Besides skin trauma / stripping caused by adhesive removal. Another category of MARSI is dermatitis reactions such as irritant contact dermatitis, and allergic dermatitis. Complete differentiation between an irritant and an allergic response is somewhat difficult. Other types of MARSI include maceration and folliculitis.

Figure 2. Photo Images of MARSI Examples

Soft silicone gel adhesives have been developed as low trauma or gentle to skin adhesives, followed by some gentle acrylate and urethane adhesives, most of which demonstrated low skin trauma or low skin stripping to certain degree partially because low skin adhesion. While low skin stripping or gentle removal is greatly appreciated by patients and health givers, low skin adhesion compromises securement of medical devices, which remains to be enhanced.

Low Trauma but High Adhesion Silicone Adhesive

The work we have been doing in past few years have proved that the skin adhesion of low trauma silicone gel adhesive could be significantly improved.

Comparison of Skin Adhesion & Skin Stripping T0 (g/in)

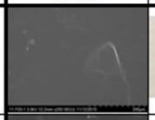
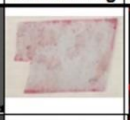
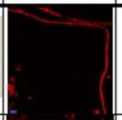
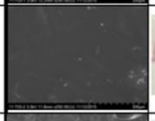
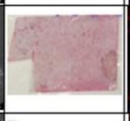
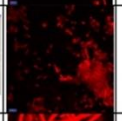
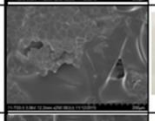
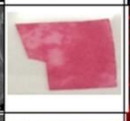
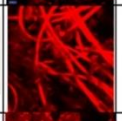
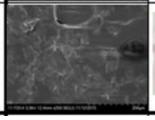
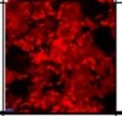
	Skin Adhesion			Measurement of Skin Stripping			
	T0	T02	T03	SEM	Cell Staining	Confocal MS	BCA
Silicone Tape (high adhesion)	198	114	108				2.1
Silicone Tape (low Adhesion 1)	72	68	56				3.9
Acrylate Tape (general purpose)	35	17	10				5.5
Acrylate Tape (securement)	87	30	26				8.1

Figure 3 Comparison of Instant Skin Adhesion (g/in) and Skin Stripping at T0

In Figure 3, high adhesion silicone gel adhesive is compared to low adhesion silicone gel adhesive, general purpose acrylate adhesive, and securement acrylate adhesive.

The instant skin adhesions (g/in) were measured as T0 - instant skin adhesion from 1st application (unwound tape from a roll, teared 4 inch long, applied to skin, and measured peel adhesion immediately), T02 - instant skin adhesion when reapplied to skin after removal from 1st application (re-applied the same piece of the tape removed from T0 test to skin and measured peel adhesion immediately), and T03 - instant skin adhesion when reapplied to skin after removal from 2nd application (re-applied the same piece of the tape removed from T0 and T02 tests to skin and measured peel adhesion immediately).

The skin stripping was measured by detection of skin cells from the tape stripes peeled off from skin, such as visual detection by SEM, cell staining, confocal microscope, and BCA (μg/mL) test (bicinchoninic acid assay – a quantitation of total protein in a sample resulted from skin cells peeled off by an adhesive).

As shown in Figure 3, high adhesion silicone gel adhesive has the highest instant skin adhesion (T0) comparing to low adhesion silicone gel adhesive, general purpose acrylate adhesive, and securement acrylate adhesive. 2nd time readhesion (T03) of high adhesion silicone gel adhesive remains high, indicating a great re-positionability for high adhesion silicone gel adhesive since there are very little skin cells peeled off by the silicone tape (low skin stripping). In comparison, T03 of both acrylate tapes fall below 30g/in, indicating a poor repositionability for acrylate tapes due to skin cell removal, which coverages on the adhesive surfaces (high skin stripping). The skin stripping is further evidenced in SEM, cell staining, confocal microscope, and BCA test, while both silicone adhesive tapes have significantly lower skin stripping than acrylate tapes.

Skin stripping by tape removal was also measured by Trans Epidermal Water Loss (TEWL).

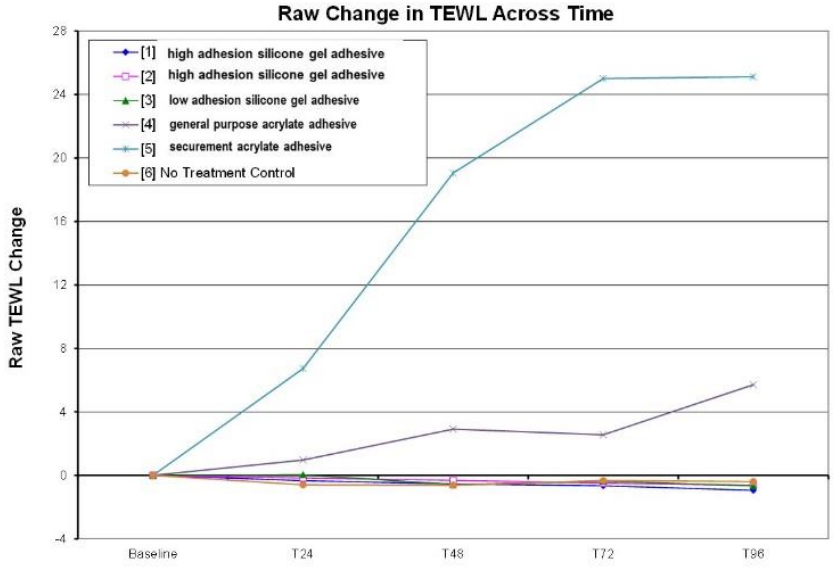


Figure 4. Trans Epidermal Water Loss upon Repeated Tape Removal

During the TEWL study, tapes were applied, removed, and re-applied with a fresh piece every 24 hours up to 98 hours on the backs of 12 human subjects. Subject visits to the test laboratory for the applications/removals were prescheduled so that tape dwell time was approximately 24 hours. Transepidermal water loss measurements and grader assessments were conducted from where tapes were removed and reapplied on assessment days.

When skin stripping occurs, skin cell would be shed away and skin becomes more transmissive to water, resulting in higher TEWL. As shown in Figure 4, acrylate tapes would give higher TEWL after repeated adhering and removing from skin, indicating high skin stripping upon removal. In comparison, silicone tapes did not cause any increase in TEWL, indicating a very low skin stripping upon removal.

Similar trends were observed when the testing tapes were peeled off after one day wear as shown in Figure 5 and after two day wear as shown in Figure 6. Once again, high adhesion silicone gel adhesive demonstrates significantly higher adhesion than low adhesion silicone gel adhesive and equivalent high adhesion to acrylate securement tape, while maintaining low skin stripping, as low as low adhesion silicone gel adhesive.

Comparison of Skin Adhesion (g/in) & Skin Stripping T24

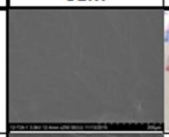
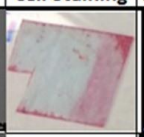
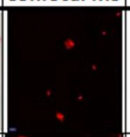
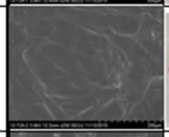
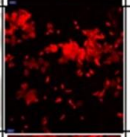
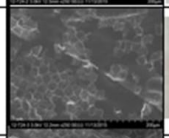
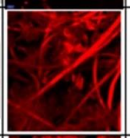
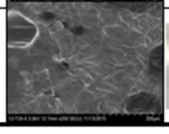
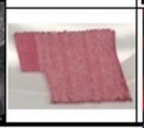
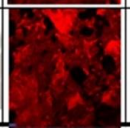
	Skin Adhesion	Measurement of Skin Stripping			
	T24	SEM	Cell Staining	Confocal MS	BCA
Silicone Tape (high adhesion)	255				4.7
Silicone Tape (low Adhesion 1)	84				6.4
Acrylate Tape (general purpose)	136				9.8
Acrylate Tape (securement)	271				12.2

Figure 5 Comparison of Skin Adhesion (g/in) and Skin Stripping at T24

	Skin Adhesion (T48) g/in	BCA µg/ml
acrylate adhesive	167	15.3
low adhesion silicone	54	5.9
high adhesion silicone	189	4.5

Figure 6 Comparison of Skin Adhesion and Skin Stripping at T48

High adhesion silicone tapes were also compared to many acrylate medical tapes in a proprietary test, when the acrylate adhesive tapes can only achieve the surface adhesion at about the strength of the adherent substrate, no matter how high the peel adhesion of those acrylate adhesive tapes have on stainless steel (SS) surfaces. This is what have been learnt from common sense and fundamental adhesion science: surface adhesion could not be higher than the cohesive strength of adherent substrate, otherwise adherent substrate would be tore.

However, when silicone gel adhesive is used, significantly higher surface adhesion than the cohesive strength of the adherent substrate could be achieved without damaging the substrates, which is exactly what is needed for the medical applications - **high skin adhesion** for device securement, but **low (or no) skin trauma** upon removal (sometimes maybe even higher than the strength of fragile skins).

When such low trauma but high adhesion silicone adhesive is used in the medical products, the wear time would be greatly improved from shorter than a week to longer than a week, as shown in Figure 7.

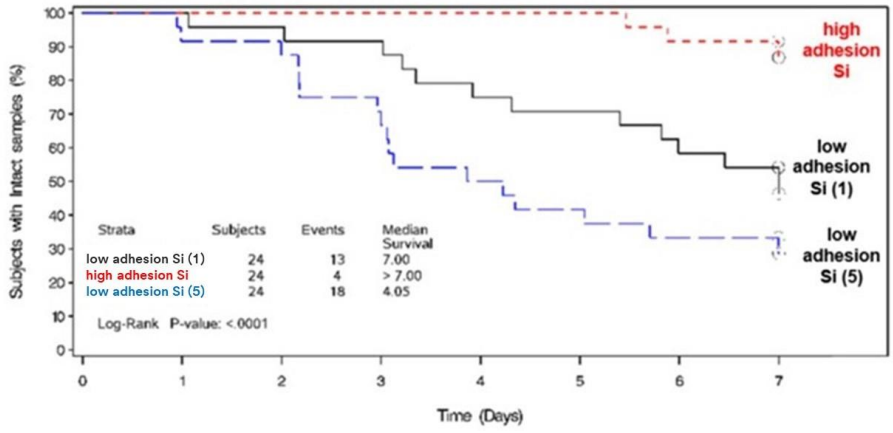


Figure 7. Comparison of Wear Time

Besides high skin adhesion, high adhesion silicone adhesive also demonstrated high peel and high shear adhesion on substrates other than skins, as shown in Figure 8 and 9.

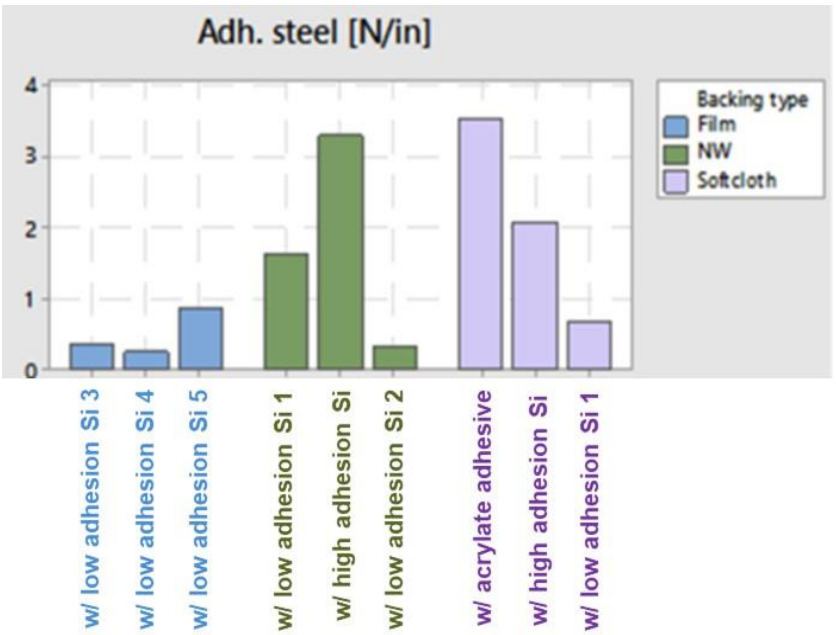


Figure 8. Comparison of Peel Adhesion on SS Surface of Silicone Gel Adhesive Tapes with Various Backings

	Instant Peel Adhesion (oz/in)			Shear Adhesion on SS (min)	Cardboard Grid
	SS	PVC	PP		
high adhsion silicone gel adhesive	23.47	19.40	19.03	>10,000	0
low adhsion silicone gel adhesive	6.85	5.51	9.20	20	0
securement acrylate adhesive	7.71	19.49	13.33	646	100

Figure 9. Comparison of Peel and Share Adhesion

In addition to high peel adhesion on skin; high peel adhesion on device surfaces, including: SS, PVC, and PP; high shear adhesion; high repositionability; but low skin stripping or low skin trauma, high adhesion silicone gel adhesive also demonstrated extremely low residuals, such as low MW silicone cyclics, organic solvents, or heavy metals.

Conclusion

Low trauma but high adhesion silicone gel adhesive was developed, which not only delivers high peel adhesion on skins, but also high peel adhesion on device surfaces, high shear adhesion, and low residual silicone cyclics or heavy metals, enabling reliable and safe securement of medical device with extended wear time, while maintaining low skin trauma and great repositionability.

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