

ADHESIVE FOR GENTLE REMOVAL FROM SKIN

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Abstract

A novel medical pressure sensitive adhesive (PSA) and tape have been developed to reduce pain upon removal from a variety of skin types¹. The new technology provides a solution for medical device manufacturers who require PSA tape to hold a medical device securely in place, while being able to remove it gently after any given skin wear time with minimal patient discomfort or skin trauma.

Introduction

In order to hold a medical device in place or to provide long term skin wear, PSA tapes usually have to be aggressive enough to adhere to skin without lifting or falling off for extended time periods, sometimes in conditions of active wear including exercise, daily shower, sauna, swim, and other activities. Such adhesive tapes have high adhesion to skin values making them difficult and painful to remove, especially, if premature removal is required after just a few minutes or hours of wear instead of after days or weeks. Reduced pain upon adhesive removal from skin is a desirable adhesive property, but typically it can only be achieved if adhesion to skin is decreased, leading to quick loss of adhesion to skin over longer wear time and, as a result, the adhesive tape falling off the skin. Weak adhesion allows gentle removal, but results in a loss of holding power to skin, which could be detrimental if the adhesive is used to hold a medical device in place.

In some medical device applications, the adhesive is applied to the same area of skin multiple times over time periods ranging from days to months. The pain of removal and damage to skin adds to the discomfort of the patient. Essentially, there are two scenarios of PSA tape failure on skin: either the PSA holds the medical device in place, but causes significant pain upon removal, or it removes gently, but lifts or falls off prematurely. Finding the optimal solution for such applications means creating a PSA tape that holds a medical device securely in place over extended time periods, but removes gently at any stage of skin wear.

Research and development of new PSA technologies to provide gentle removal PSA products with application performance matching that of more aggressive adhesives for the medical device industry has a long history. The search is further complicated by the high variability of skin types, skin preparation techniques, and skin conditions, which can vary with the patient's age, diet, health, environmental, and genetic factors. Thus, PSA tape that works for one person will not necessarily work for another. In addition, pain level is a highly subjective characteristic. Statistical analysis performed on data for multiple patients in clinical trials allows selecting the best candidate in terms of pain removal.

The way to overcome the intrinsic ambiguity of pain measurement is to consistently obtain positive feedback from a variety of patients. Interestingly, the new technology that is the subject of this paper received consistent positive feedback from a variety of skin test volunteers. Specifically, it was found that the new PSA tape was removed with lower pain rating for all participants, while the commercially available "gentle removal" adhesives tested differently. For example, for younger participants, less difference was observed between the levels of pain removal for the new adhesive compared to commercially available adhesives. However, for older people the new technology stood out as substantially more gentle. It was not expected that the new adhesive tape would also hold a medical device in place for weeks without detaching from the skin, and yet the testing showed that the new adhesive has excellent long term skin wear properties.

Defining Gentle Removal from Skin

Pressure sensitive adhesive is a viscoelastic material that adheres instantaneously to most substrates with the application of very light pressure and which remains permanently tacky. The novel PSA adhesive may be removed from skin without substantial pain to the wearer. In many instances, there was no significant pain upon removal of the novel adhesive tape after any stage of wear. Furthermore, the novel adhesive was found to not leave residue upon removal at any stage of wear, *i.e.*, after either long term (weeks) or short term (minutes or hours) use.

One of the useful features of the novel adhesive is the ability to be applied multiple times to the same skin site, as might be required by design of a specific medical device, and to be removed gently after each of the consecutive applications. In such instances, the adhesive tape is applied to the skin for fixed time period, then removed and a new piece of the tape is applied to the same skin site. After multiple applications of the tape in such manner the adhesive removes gently, does not cause skin irritation and does not leave residue on skin.

One other useful property of the novel adhesive is the ability to re-bond to skin in moist environment, such as during a shower. If the tape edge was accidentally pulled and lifted during the shower, the tape is able to adhere back securely to wet skin under light hand pressure and will not lift again or fall off.

The composition of the novel adhesive is associated with a noticeably low adhesion to both hydrophilic and hydrophobic substrates in combination with noticeably low level of pressure-sensitive tack. The above-mentioned features lead to significant reduction in the level of pain experienced upon removal of the adhesive from skin. Since “pain” is a subjective property, it was rated on the scale from 0 = *No Noticeable Pain* to 5 = *Notable Pain*, and statistical data were collected in multiple wear tests showing overall lower pain level when removing the novel adhesive from skin compared to commercially available adhesives, which have higher pain rating (see below section data on pain removal, Table 4 and Figures 9 and 10).

Designing Adhesive for Gentle Removal

Variations of the novel adhesive were prepared by modification of conventional acrylic adhesives by incorporating the functional additives that include water-soluble polymer Polyvinylpyrrolidone (PVP), also commonly called polyvidone or povidone and low molecular weight acrylic resin with functional groups that include polyacrylamide and long chain alkyl functionality. It was found that the combination of the above-mentioned functional groups provides the best bond to skin under variety of skin conditions, due to each of the functional groups promoting bonding in different conditions. Specifically, the PVP and polyacrylamide hydrophilic functional groups promote bonding and re-bonding in wet environments (skin perspiration or shower), while the long chain alkyl group, hydrophobic in nature, will increase the bond to hydrophobic skin types such as oily skin.

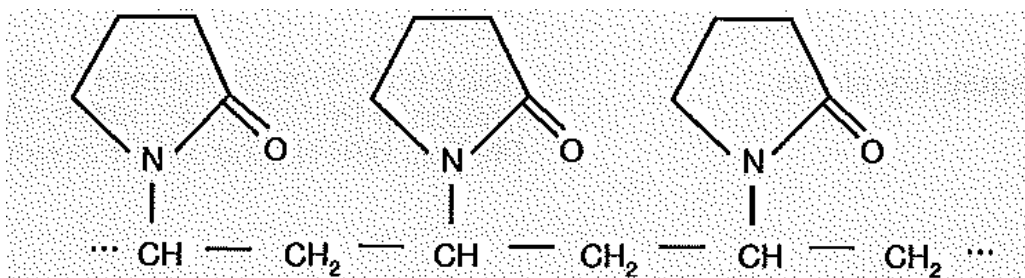
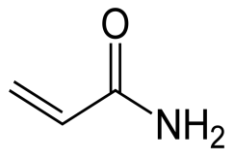
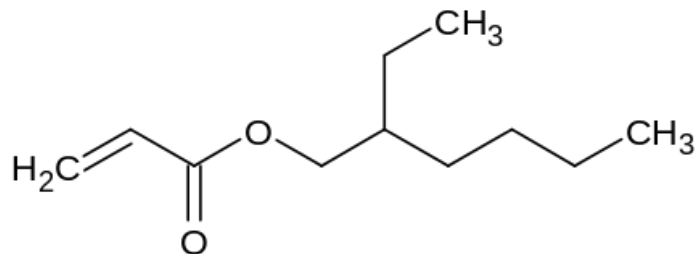


Fig. 1: Polyvinylpyrrolidone (PVP) structure (hydrophilic)



Acrylamide



2-ethylhexyl acrylate

Fig. 2: Acrylamide (hydrophilic) and 2-ethylhexyl acrylate (hydrophobic long chain) components of low softening point copolymer.

Medical adhesives comprising acrylic co-polymers such as a copolymer of 2-ethylhexyl acrylate, ethyl acrylate and acrylic acid or copolymers of similar composition are well known in the PSA industry ². Commercially available acrylic adhesives used as a polymer base to prepare the novel adhesive of present study include polyacrylates prepared from monomers of acrylic acid and acrylic or meth(acrylic) esters. PVP or mixtures of polyvinylpyrrolidones (PVPs) include a water-soluble polymer prepared from monomers of N-vinylpyrrolidone ^{3, 4} with the structure presented on Fig.1. Weight average molecular weight (M_w) of PVP as determined by light scattering is between about 2,000 and about 1,500,000 g/mol, and K-values are ranging from about 10 to about 96.

A comprehensive review of synthesis, properties, available grades and applications of PVP was published by Buhler ⁴. K-value, which is used to characterize PVP, is a function of the average molecular weight, the degree of polymerization, and the intrinsic viscosity. For example, a correlation was found that relates solution viscosity to the K value and weight percent of PVP ⁵.

The amount of PVP added to the base acrylic adhesive is between 3% and 20% by weight. The molecular weight of PVP(s) in the adhesive exerts noticeable effects on the adhesive properties of a polyacrylate mixed therewith. PVP(s) can be dissolved by mixing with solvents, such as ethyl alcohol, after which they may be mixed into a polyacrylate adhesive solution.

Another essential component of the novel adhesive is a low softening point acrylic resin that increases the bond of the adhesive to skin. Such resins may be low-molecular weight compounds that do not substantially change the glass transition temperature (T_g) of a base polymer. The content of such resins in the adhesive is about 5% to 20% by weight. Useful resins include copolymers of acrylamide and ethylhexyl acrylate, a relatively low molecular weight product from polymerization of a mixture of

20%-80% acrylamide and 20%-80% ethylhexyl acrylate. The aforementioned resins have a number-average molecular weight (M_n) range between 15,400 and 31,800 g/mol, a weight-average molecular weight (M_w) between 80,300 and 96,500 g/mol, and a degree of polydispersity in the range of 2.9 – 6.0 as determined by gel permeation chromatography (GPC) using polystyrene standards.

The low softening point of such resins provides cold flow at room temperature, which rheologically enhances the final formulation by improving flow properties of the adhesive when applied to skin at body temperature and thereby enabling improved wettability of skin.

The adhesive is directly coated or transfer coated onto a device, such as a pad, film, foam or other suitable carrier (substrate) that is approved for medical application. The thickness of the adhesive typically is between 1 and 5 mils. The adhesive is dried in an oven to remove solvent and then exposed to higher temperatures to cure the base acrylic adhesive providing the desired degree of cohesive strength. For all testing of the present study, the 2.0 mil of adhesive was directly coated on a silicone release liner, dried, and laminated to 2 mil PET film.

In the present study, three groups of adhesives were tested side by side for direct comparison:

- (1) Three base adhesives identified as A, B and C, which are conventional commercially available adhesives for long term skin wear applications, used as polymer base for modification with functional additives to prepare novel adhesives.
- (2) Novel adhesives identified as E1 through E6 prepared using base adhesives A, B and C with functional additives consisting of PVP and low softening point acrylic resin, which is a copolymer of 40 wt. % of acrylamide and 60 wt. % of 2-ethylhexyl acrylate.
- (3) Comparative Adhesives identified as C1 through C5 used as a reference when only one of the functional additives, either PVP or low softening point acrylic resin, is included in the formulation, demonstrating that both functional additives are required to achieve desirable gentle removal properties combined with long term skin wear properties.

The summary of adhesive formulations is presented in Table 1.

Table 1. Adhesive Compositions

Component description	<u>Base Adhesives</u>			<u>Novel Adhesives</u>					<u>Comparative Adhesives</u>				
	A	B	C	E-1	E-2	E-3	E-5	E-6	C-1	C-2	C-3	C-4	C-5
Acrylic adhesive 1	-	-	100	-	-	-	82	-	-	-	-	-	-
Acrylic adhesive 2	-	100	-	82	-	-	-	-	-	-	-	-	-
Acrylic adhesive 3	100	-	-	-	82	82	-	82	82	82	82	82	82
PVP (K value 12, $M_w = 2 - 3K$)	-	-	-	-	-	-	-	-	-	-	8	-	-
PVP (K value 25, $M_w = 28 - 34K$)	-	-	-	8	8	8	8	4	-	-	-	-	8
PVP (K value 90, $M_w = 1.0 - 1.5M$)	-	-	-	5	5	-	5	2.5	-	-	-	5	-
Copolymer of acrylamide and 2-EHA	-	-	-	5	5	5	5	5	5	15	-	-	-

Note: for complete list of tested adhesive formulations refer to US Patent Application 20130260134 (2013).

Testing of Gentle Removal Adhesive

Texture Analyzer Test

The Texture Analyzer test using a high surface energy stainless steel probe is intended to simulate re-bonding to the hydrophilic part of a substrate, for example, skin areas with moisture or perspiration.

The stainless steel probe is brought into contact with the adhesive tape under a fixed load of 150 g for 1 second and then removed from the adhesive at 0.1 mm/sec. A graph of the separation force of adhesive from the probe surface vs. time is plotted forming TA curve. Peak Force is the maximum force achieved in the TA test. It corresponds to the part of the test when the adhesive is still attached to the whole area of the probe, as it moves away from the adhesive. As adhesive starts detaching from the probe, the force is reduced. Total area under the TA curve represents the energy required to break the adhesive bond with the probe surface. A greater area under TA curve is typical of more aggressive adhesives.

Peak force and total area under TA curve were recorded for initial probe application to the adhesive and for every consecutive repeated application. The test was performed in two modes: (1) without cleaning the probe between measurements on the same adhesive area to simulate repeat application to the same surface; (2) with cleaning the probe before each measurement to simulate re-application to a new surface. It was found that the percent of retained force is considerably higher for novel adhesive compared to conventional long term wear adhesive (Table 2).

Table 2: Percent TA Peak Force Retention after 10 Consecutive Applications.

Test Mode	Description of Adhesive	% Force Retention
Probe cleaned with MEK before each reapplication	Novel Adhesive E-2	71
	Base Adhesive A	23
Probe not cleaned before each reapplication	Novel Adhesive E-2	95
	Base Adhesive A	33

To illustrate further, the peak force for the novel adhesive did not change over ten repeated applications, while it was significantly decreased for conventional adhesives (Figure 3). Total area under TA curve was also stable for the novel adhesive (Figure 4), while it decreased for the conventional adhesive. Note, that the absolute value of the total TA curve area was much lower for the novel adhesive platform indicating that it is less aggressive. Typically, adhesives with such low area under TA curve are not sufficiently aggressive to be suitable for long-term wear.

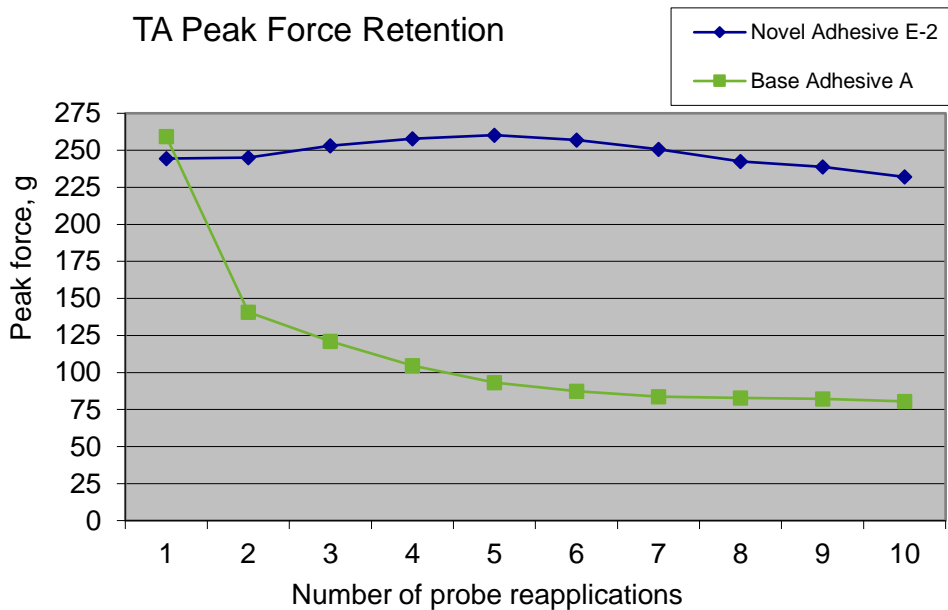


Figure 3: Peak Force retention for repeated applications of the probe to the same area of adhesive surface.

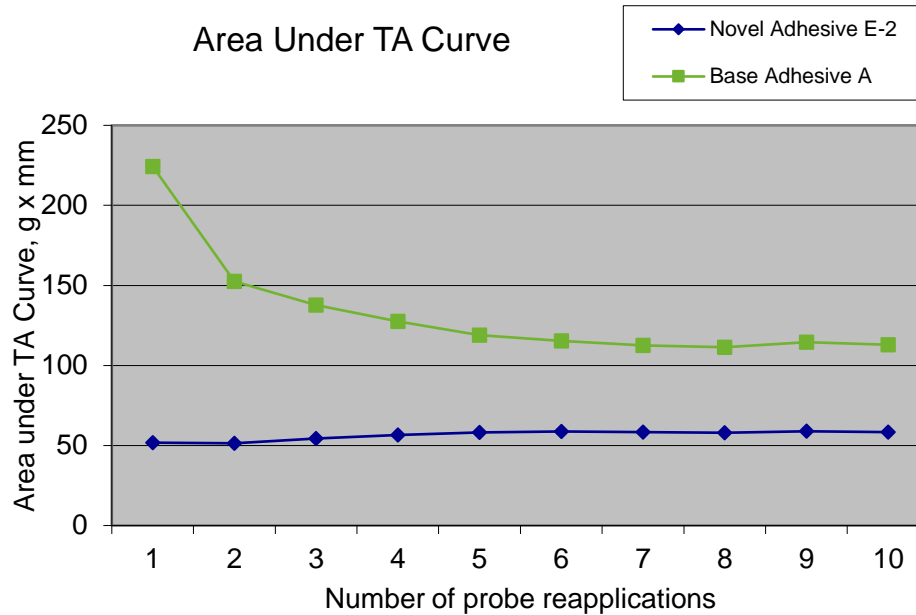


Figure 4: Total area under TA curve after probe re-applications to the same area of adhesive surface.

Adhesion test

Adhesion to steel and to HDPE was tested per ASTM D3330/D3330M at 180 degree peel angle and 12 in/min jaw separation speed with no dwell time: samples were tested immediately after adhesive application to the panel ⁶. Adhesive mode of failure was observed for all tested samples, which were re-applied at the same place on the panel as tested initially to simulate re-positionability to the same surface. The test was repeated multiple times using the same strip of adhesive tape and the panel. Adhesion retention test results after multiple re-applications are presented on Figures 5 and 6.

Adhesion testing on steel or plastic substrates does not directly simulate repositionability on skin. It shows that adhesion as tested on steel or HDPE is much lower for the novel adhesive compared to conventional base adhesive. In fact, low adhesion values to both hydrophilic and hydrophobic surfaces can be beneficial in the application where gentle removal is required, since lower adhesion would result in less pain during removal of the patch from the skin, as confirmed by skin wear test results shown in the Table 4 and Figures 9 and 10.

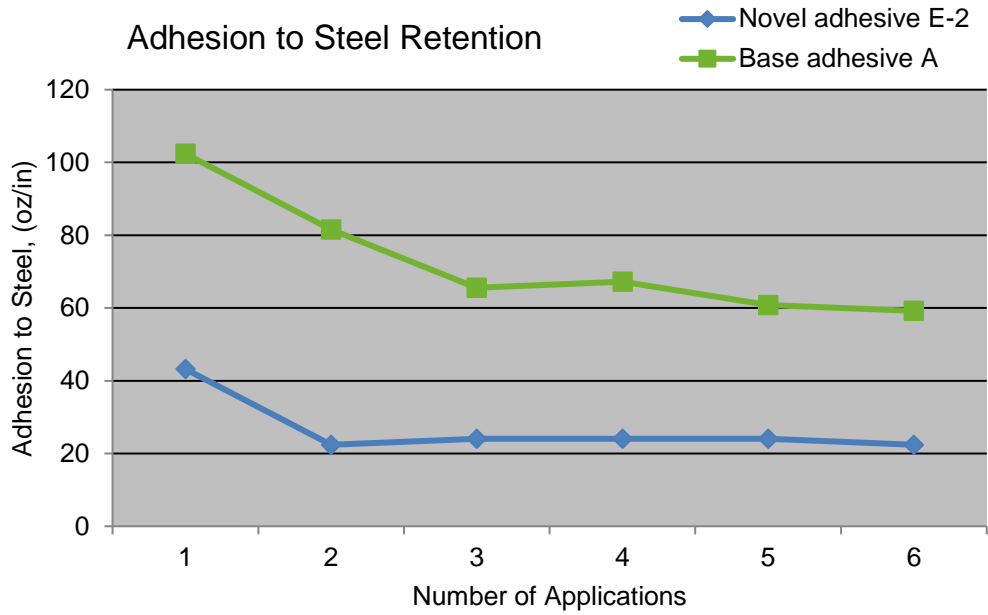


Figure 5: Adhesion to steel retention after multiple re-application of adhesive to steel panel.

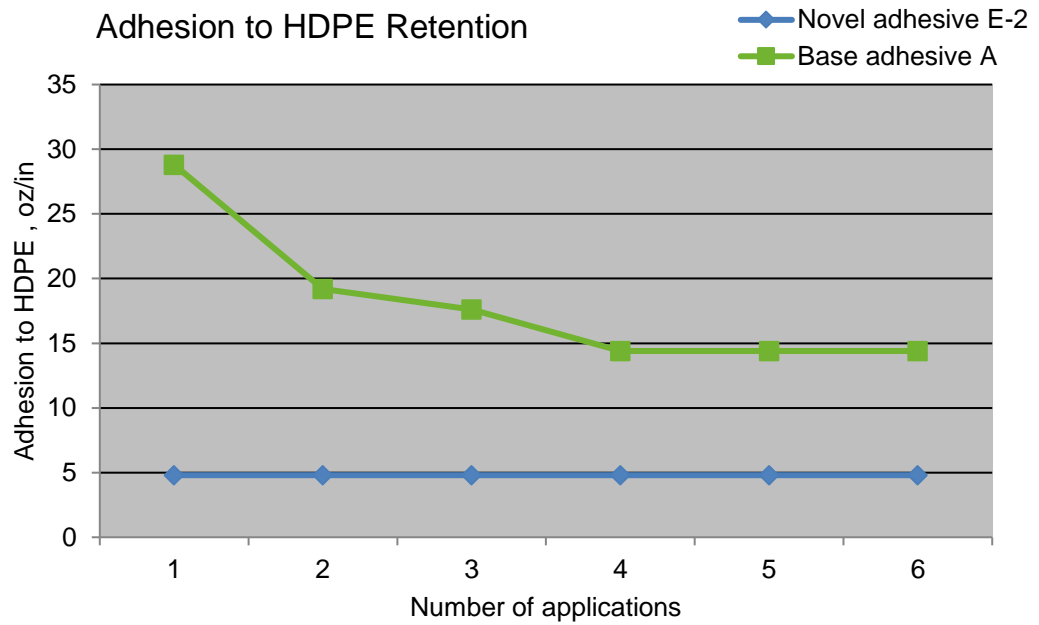


Figure 6: Adhesion to HDPE retention after multiple re-applications of adhesive to steel panel.

Typically, long term wear adhesives are more aggressive (have high adhesion values) to be suitable for long term wear applications. The novel adhesive has significantly lower adhesion to steel and HDPE. Unexpectedly, it can hold on skin for extended time periods (7+ days). The initial adhesive strength might not be as high for the novel adhesive as for commercially available adhesives, however, the adhesion level retains after re-bonding.

Probe Tack

Probe Tack was determined using ASTM D 2979-01 standard test method for measuring pressure-sensitive tack of adhesives ⁷. An inverted probe machine with 5.0 mm diameter Type 304 stainless steel probe was operated at 10 mm/s, contact time of 1.0 s, and a contact pressure of 9.79 kPa. The results of these tests are shown in Table 3.

Table 3. Adhesive Properties: Adhesion and Tack

	<i>Base Adhesives</i>			<i>Exemplary (Novel) Adhesives</i>					<i>Comparative Adhesives</i>				
Property	A	B	C	E-1	E-2	E-3	E-5	E-6	C-1	C-2	C-3	C-4	C-5
Adhesion to steel, lb/in	8.6	5.0	4.8	3.8	2.3	2.8	2.9	3.1	7.5	6.0	6.6	3.0	4.0
Adhesion to PP, lb/in	3.0	3.0	2.8	2.3	1.0	0.8	1.3	0.87	2.4	1.1	0.5	2.9	1.5
Probe tack, g	1878	1246	1169	677	528	550	544	625	1682	1381	961	1000	700

As evident from Table 3 and Figures 7 and 8, the novel adhesives have low adhesion to steel and to PP in combination with low Probe tack.

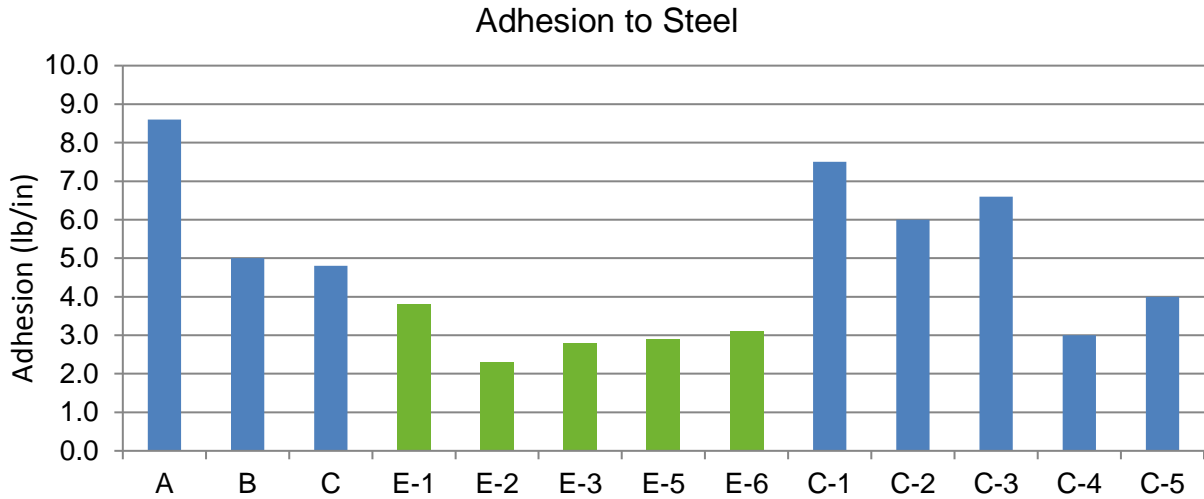


Figure 7: Adhesion to steel for a variety of medical adhesives showing low adhesion level for gentle removal formulations E1-6.

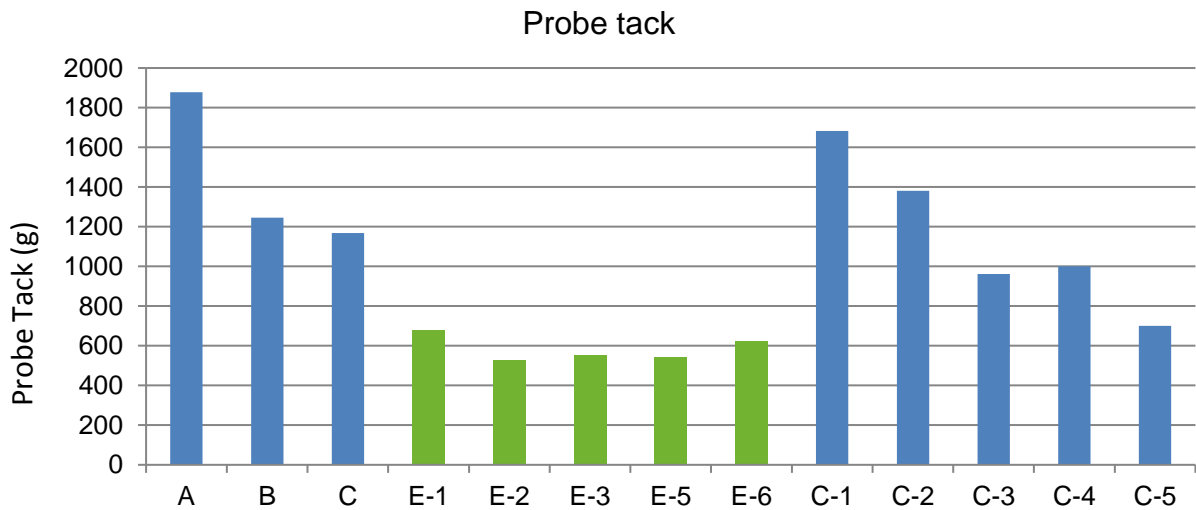


Figure 8: Probe Tack for a variety of medical adhesives showing lower Probe Tack level for gentle removal formulations E1-6.

Static Shear Test

Cohesive strength was determined using ASTM D6463/D6463M-06 standard test method for measuring the time to failure of pressure-sensitive articles under sustained shear loads. Each adhesive coated on a 2 mil PET film was bonded to a stainless steel panel by rolling the 1 in² sample twice with a 4.5-lb roller, and then allowed a dwell time of 30 minutes before a 500-g load was applied parallel to

the bonding surface. The sample was placed in the oven at 70 °C. Slippage of the sample was measured in mm. Adhesives with lower slippage have higher cohesive strength. The results of these tests, which are shown in Table 4, indicate that the novel adhesives have a range of cohesive strengths. Higher cohesive strength formulations may be useful for long term skin wear because such formulations have more resistance to skin oils and perspiration.

Table 4: Cohesive Strength at 70 °C on Steel as Slippage (in mm) after 1 hour and Scaled Pain Level upon Adhesive Removal: 0 = No Noticeable Pain, 5 = Notable Pain

<u>Base Adhesives</u>			<u>Exemplary (Novel) Adhesives</u>					<u>Comparative Adhesives</u>				
A	B	C	E-1	E-2	E-3	E-5	E-6	C-1	C-2	C-3	C-4	C-5
2 mm	0 mm	0mm	fell off	1mm	1mm	0 mm	2 mm	2 mm	fell off	fell off	0.5 mm	0.8 mm
5	4	4	1	0	1	1	2	5	5	4	3	3

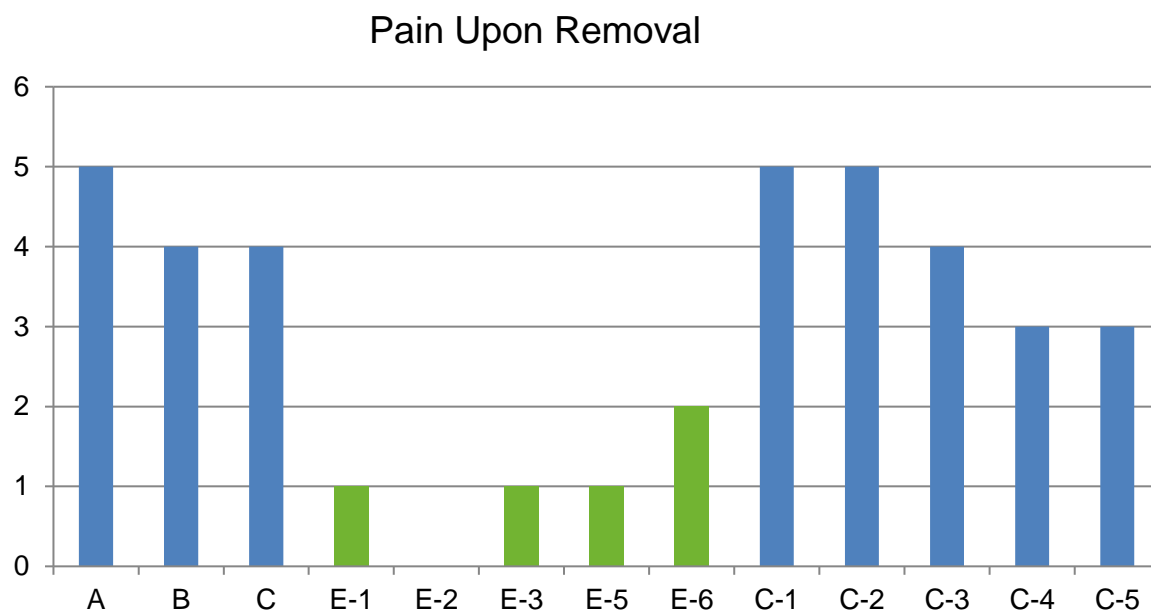


Figure 9: Scaled Pain Level upon Adhesive Removal (0 = No Noticeable Pain, 5 = Notable Pain) showing lower pain level for gentle removal E-formulations.

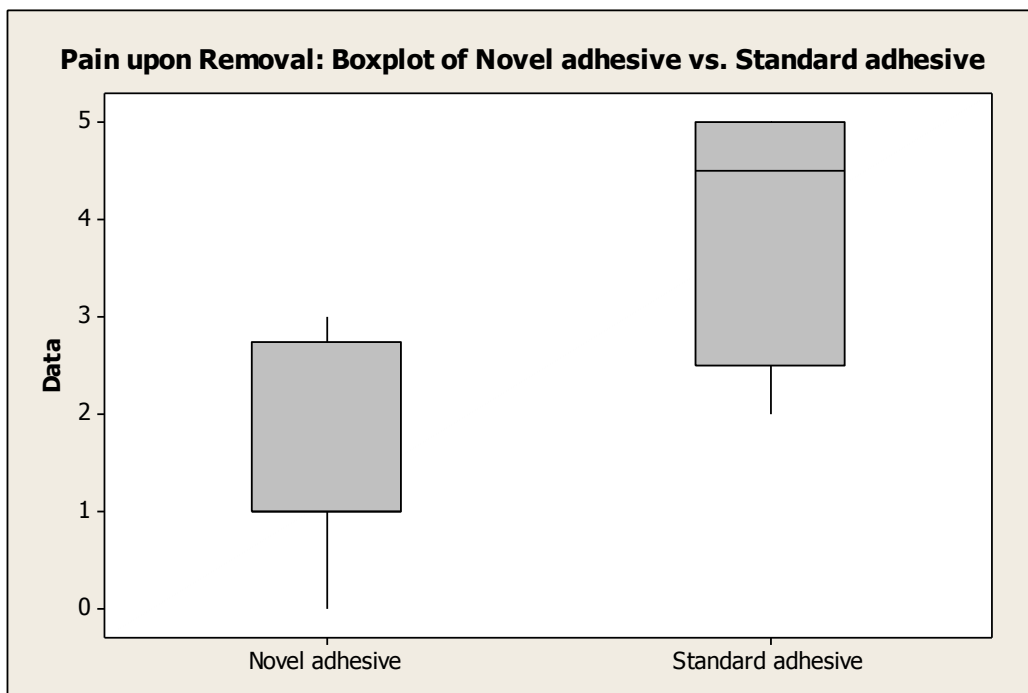


Figure 10: Scaled Pain Level upon Adhesive Removal after 24 hours skin wear time (0 = No Noticeable Pain, 5 = Notable Pain) showing lower pain level for gentle removal formulations.

Rheology test

Rheological properties of the adhesives were tested in a TA Instrument ARES rheometer, RDA-3, using parallel plate geometry. Temperature-frequency sweeps were performed at an angular frequency of 1 rad/s and at a heating rate of 4 °C/min.

Table 5 shows rheological data for the novel adhesive E2, commercially available base adhesive A and some of the comparative formulations, providing quantitative information about the rheological properties of the adhesives.

According to the test results, novel adhesive E-2 has a higher complex modulus, G^* , and a slightly higher glass transition temperature, T_g , compared to the base adhesive A. Individual components exert different effects on the rheological properties of base adhesive. Addition of PVP results in a harder adhesive, as evident from an increase in G^* , a decrease in tan delta, and an increase in T_g . However, addition of a low softening point resin resulted in a slight shift in T_g to a lower temperature and an increase in tan delta with a slight decrease in G^* .

Table 5: Rheological Data for Novel, Base and Comparative Adhesives

Adhesive	T _g (°C)	G* (kPa) @ 50 °C	tan delta @ 50 °C
Base adhesive A	-22.4	12.5	0.61
Novel adhesive E-2	-20.5	35.4	0.61
C-1	-24.1	10.5	0.76
C-2	-24.8	12.8	0.77
C-4	-22.3	39.2	0.43
C-5	-16.6	52.4	0.61

As Fig. 11 demonstrates, the novel adhesive E-2 is overall harder compared to the conventional acrylic adhesive A used as its base polymer, which is consistent with a decreased level of adhesion and corresponds to reduced pain upon removal from skin. Both elastic modulus G' and viscous modulus G'' are higher for novel adhesive E-2 compared to the base adhesive A (Fig. 12).

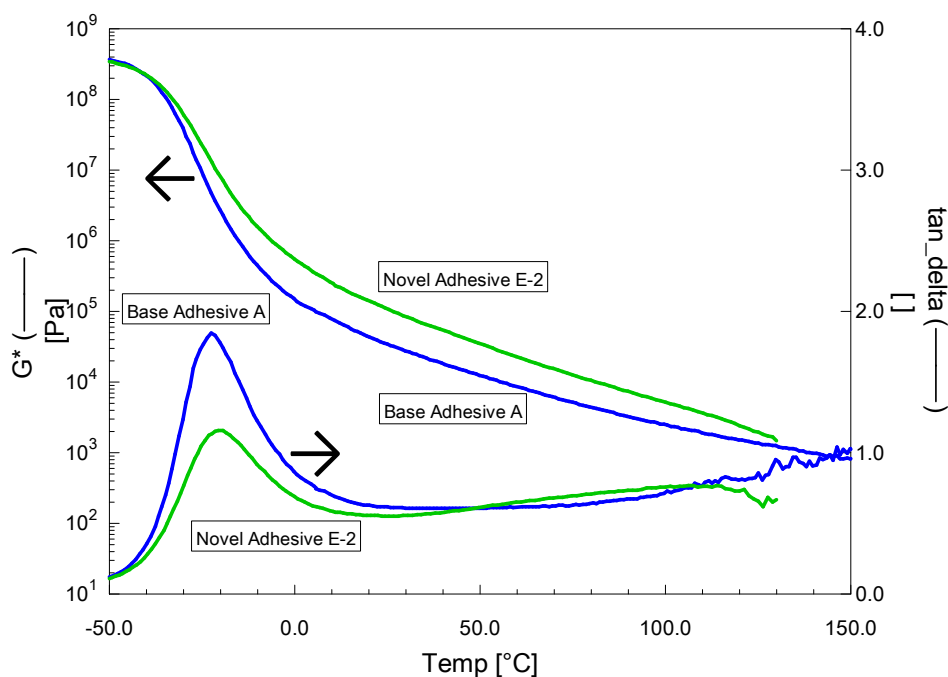


Figure 11: Complex Modulus (G^*) and tan delta for novel and base adhesives.

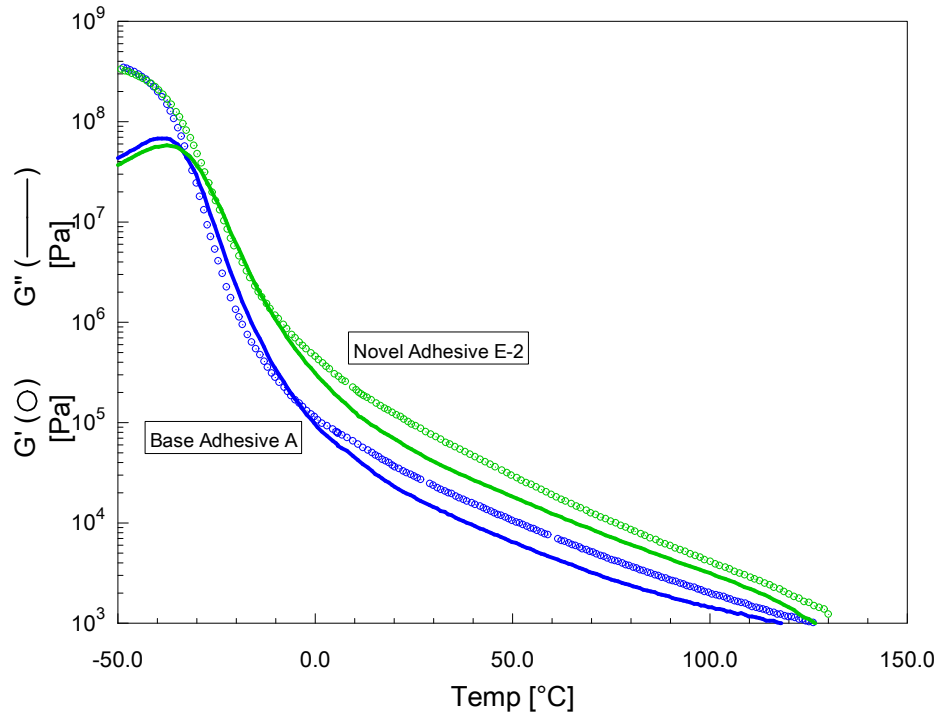


Figure 12: Elastic Modulus (G') and Viscous Modulus (G'') for novel and base adhesives.

Analytical Identification

FT-IR spectra of the adhesives were obtained using Fourier Transform Infrared Spectrometry per ASTM E168 and ASTM E1252 utilizing the Spectrum Two FT-IR spectrometer with ATR Diamond accessory manufactured by Perkin Elmer.

Analytical identification of the novel gentle removal adhesives of the present study and their differentiation from typical commercially available acrylic adhesives by FT-IR test is feasible due to presence of PVP in the formulation. For example, the FT-IR spectra are nearly identical for the novel adhesive E-1 and the base adhesive B, except for a prominent PVP peak at 1661 cm^{-1} , as shown on Fig. 13. This peak is clearly discernible in the spectra of the novel adhesives. The conventional commercially available acrylic adhesives do not absorb energy at that wavenumber.

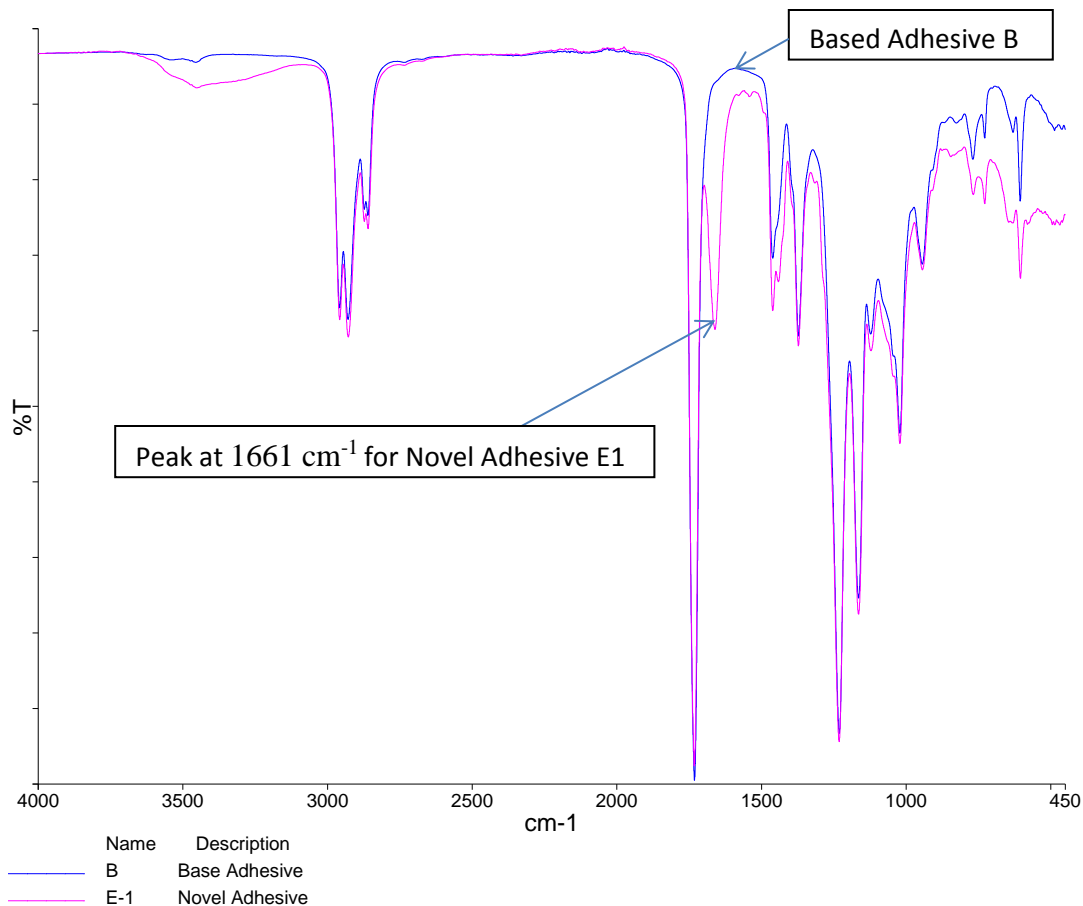


Figure 13: FT-IR spectra of the novel adhesive and the base adhesive.

Conclusion

New gentle removal adhesive technology allows reduced pain upon removal of long term skin wear acrylic adhesives. The effect is achieved by modification of initially aggressive long term wear adhesives by functional additives resulting in low adhesion and tack values and a desirable degree of cohesive strength without sacrificing the duration of skin wear time. The gentle adhesive is intended to help with pain management of adhesive removal from skin for a variety of direct-skin contact medical articles requiring use of pressure-sensitive adhesives and tapes. The new approach to formulating of gentle removal adhesives presented in this paper could be used to design medical PSA tapes with properties tailored to specific customer applications and requirements.

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