Transdermal Excipients Effect on Adhesion Strength of a Pressure Sensitive Adhesive

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ABSTRACT

Different amounts of two skin permeation enhancers, oleic acid (OA) and propylene glycol (PG), were mixed thoroughly with solution of an acrylic copolymer pressure sensitive adhesive (PSA). Films with different adhesive layer thicknesses (30 and 60 μ) were prepared by casting of the mixed solutions with a film applicator on PET 80 μ films followed by drying of solvents. The results of peel test were explained on the basis of changing of entanglement molecular weight ($\overline{M}_e$) of the copolymer and its miscibility with the enhancers. PG concentration had no significant effect on the peel strength. This is related to a constant amount of $\overline{M}_e$, resulting from hydrogen bonding between PG and the copolymer. The presence of OA decreased the peel strength, specially when concentration exceeded 5(w/w%). This decrease can be related to the formation of a weaker surface layer in addition to the diminution of the adhesive effective thickness. A two fold increase in the thickness had no effect on the peel strength of OA samples. This shows that at least one half of the thickness of 60 μ samples is ineffective in viscoelastic energy dissipations in the copolymer. Cohesive failure for 30 μ samples occurred, when OA concentration exceeded 15 (w/w%). However, this failure was observed above 10 (w/w%) for 60 μ samples, because the applied force is not transferred through the ineffective thickness to the backing layer.

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Key Words:
pressure sensitive adhesive;
enhancer;
peel; T_g;
surface energy.

INTRODUCTION

Pressure sensitive adhesives (PSAs) are polymers that can adhere strongly onto solid surfaces upon application of light contact pressure and short contact time. PSAs have numerous health care applications; one innovative use is in transdermal drug delivery systems (TDDS)[1,2]. The transdermal route offer many advantages over conventional routes of drug administration (i.e., oral, injection, etc.), the most important are avoidance of the first pass effect, ease of use and withdrawal (in case of side effects) and better patient compliance, which means patients

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can notice whether they remembered to take their medication[3]. PSAs Are important components of TDDS, because they insure intimate contact between the drug-releasing area of a TDDS and the skin surface, which is critical for controlled-drug delivery.

The major classes of medical PSAs are acrylics, silicones and polyisobutylenes[4]. The acrylic PSAs have several desirable features, such as resistance to oxidation and sunlight. They are inherently tacky without any additional compounding. The properties of acrylic adhesive copolymers can be easily changed by combining different kinds of monomers [5].

Mechanical performance of the PSA layer in a TDDS for a particular drug depends on the type and concentration of excipients, the type of PSA, and the coating thickness. Three important performance tests of PSAs are peel strength, tack and creep resistance. Peel strength data can give more information about the adhesive character and its expected performance[6]. Peel energy is related to thermodynamic work of adhesion (WA) and viscoelastic energy dissipations (VED). The relationship can be expressed as in ref. [7] :

$$\text{Peel energy} \propto W_A [1 + VED] \quad (1)$$

W_A, is the change in free energy when the materials are brought into contact and it is determined by the following equation :

$$W_A = \gamma_A + \gamma_S - \gamma_{AS} \quad (2)$$

where, γ_A is the adhesive's surface energy, γ_S is the substrate s surface energy and γ_{AS} is the substrate-adhesive s interfacial surface energy. Zosel, examining substrates with various surface energies, has shown that for long contact times (about 100 s), there is a weak dependence between peel and surface energy. W_A, resulting from the rupture of the Van der Waals bonds at the interface, can be several orders of magnitude smaller than VED [7]. Then the effect of W_A on peel strength can be neglected.

The enhancers are the most common and necessary excipients of any transdermal formulation. Lin and his coworkers have examined the effect of several enhancers on the peel strength of a water-borne crystallizable acrylic resin[8]. However, adhesive properties of the water-borne acrylic PSAs are much inferior to those of solvent-borne PSAs[7]. It is expected that a PSA tape will strip cleanly from the adherend (e.g., its protective liner or the skin), leaving no visually noticeable residue. This type of failure is called adhesive failure, and it occurs at or near the adhesive-adherend interface. Some adhesives may fail cohesively, leaving adhesive residue on the adherend surface. Typically, adding enhancers to PSAs will plasticize the PSAs and lowers their shear strength. This may lead to cohesive failure and usually decreases the peel strength[9]. Also the enhancer may migrate to the adhesive surface. This should be investigated using miscibility and surface energy studies.

In this research work, the effect of two enhancers, oleic acid (OA) and propylene glycol (PG), and adhesive thickness on peel strength of a commercial solvent-borne acrylic copolymer (DuroTak 87-2196) is investigated. The results are explained on the basis of the copolymer viscoelastic properties and its miscibility with the enhancers.

EXPERIMENTAL

Materials and Methods

Duro-Tak 87-2196 (National Starch and Chemical Co., USA), 1,2-propylene glycol USP (Merck), oleic acid USP (Merck) and PET film with 80 μ thickness (kindly prepared by Daroupat Shargh Co., I.R. Iran) were used.

Duro-Tak was thoroughly mixed with OA and PG to prepare formulations containing 0 to 25 (w/w%) of the mentioned enhancers in dry adhesive. The mixed solutions were cast on PET films by a film applicator (BYK-Gardner, USA). After staying at room temperature for 10 min, drying was completed in a 65 C oven throughout 20 min.

Peel Test

Peel tests were carried out according to the ASTMD3330 on adhesive coated tapes with 25 mm width. After preparation of PSA tape/stainless steel joints, they were stored at room temperature for 24 h. Peel force in 180 direction was measured at a peel rate of 300 mm/min at room temperature using an Instron machine (Model 6025, USA). The test was accomplished at least three times for each sample.

Thermal Analysis

Glass transition temperature (T_g) of various formulations is measured with a differential scanning calorimeter (PL, UK) with a heating rate of 10 C/min. In all

Table 1. Contact angles and surface energies of the samples.

Sample	A0	OA5	OA10	OA15	OA20	OA25	PG5	PG10	PG15	PG20	PG20
Water	109.3	104.4	106.3	105.7	111.3	113.1	105.9	100.3	100.2	101.3	98.27
Contact angle (°)											
Diiodomethane	58.5	68.9	72.4	82.5	86.7	95.7	56.0	60.1	58.2	58.0	57.9
γ (mJ/m^2)	33.0	23.9	22.0	16.2	14.2	10.4	33.6	29.1	30.4	30.8	30.3

(*) A_0: acrylic adhesive with no excipient.

cases T_g is taken as the midpoint of the heat flow curve.

Contact-angle Measurement

In order to evaluate the surface energies, equilibrium contact angles were measured at room temperature for distilled water and diiodomethane on the surfaces of the different samples. The measurements were done using a contact angle measuring system G10 (Kruss, Germany). Dispersion and polar components of the surface energy, γ_A^d and γ_A^p were determined according to improved Owens method[10].

RESULTS AND DISCUSSION

Peel strength versus concentration curves for different thicknesses of the adhesive are shown in Figure 1 for PG containing samples. It is obvious that increasing concentration of PG from 0 to 25 weight percentage has no significant effect on peel force. It is observed in Figure 2 that addition of OA causes the peel strength to decrease, specially when the concentration exceeds 5(w/w%). In contrast with PG, the peel strength does not change when the thickness is doubled. The cohesive failure (region B) for 30 μ samples occurs when OA concentration exceeds 15(w/w%). However, this failure is observed above 10 (w/w%) for 60 μ OA samples.

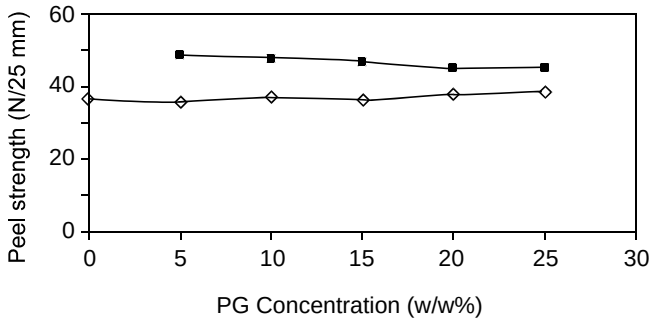

Figure 1. Plot of peel strength against PG concentration for 30μ (◇) and 60μ (■) adhesive layer thickness.

Miscibility

Dealing with blended materials, it is necessary to examine the miscibility between components, because it must be effective on physical properties and also performance of the materials. Examining on some miscible tackifier resin/acrylic PSA systems, Hayashi has resulted that the dynamic mechanical properties of the PSA bulk and also its performance are systematically modified. However, in the immiscible systems the mechanical properties of the PSA are not modified [11]. The simple rule of mixing, indicated by the following equation, can be used for investigating the miscibility.

$$W_1/T_{g1} + W_2/T_{g2} = W / T_g \quad \text{(Fox equation)} \qquad (3)$$

where, W_1 and W_2 are weight percentages of the mixture components. Equal amounts of measured and calculated T_g, by eqn (3), is indicative of the complete miscibility. Deviations of the measured from the calculated amounts, can be explained on the basis of some interactions between the mixture components. Usually, low molecular weight materials have a plasticizing effect on the macromolecules and decrease their T_g. Measured and calculated amounts of T_g for the different samples are shown in Table 2. The positive deviations observed for PG samples, mean that the effect of

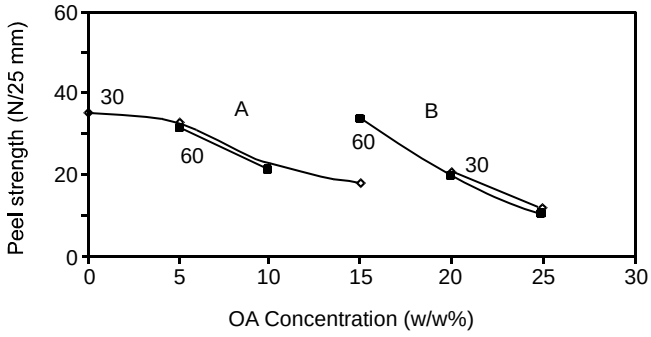

Figure 2. Plot of peel strength against OA concentration for 30μ (◇) and 60μ (■) adhesive layer thickness in adhesive failure (A) and cohesive failure (B) regions.

Table 2. Measured and calculated T_g of the samples and their deviations.

Sample	A0	OA5	OA10	OA15	OA20	OA25	PG5	PG10	PG15	PG20	PG20
$T_g$exp(°C)	-24.7	-36.9	-43.9	-60.3	-66.3	-71.7	-28.5	-30.7	-32.0	-32.0	-30.3
cal.T_g* (°C)	-	-26.1	-27.5	-28.8	-30.2	-31.5	-29.9	-35.0	-39.8	-44.5	-48.9
Deviation	-	-10.8	-16.4	-31.5	-36.1	-40.2	+1.4	+4.3	+7.8	+12.5	+18.6

(*) Calculated on the basis of the Fox equation.

PG on decreasing of T_g has been limited by another factor. Duro-Tak (87-2196) adhesive copolymer contains acrylate and vinyl acetate comonomers. Both acrylate and vinyl acetate have carbonyl groups in their structure. It can be concluded that many hydrogen bonds can be formed between two OH groups of PG and CO groups of the copolymer. These hydrogen bonds act as cross-linking agents which offset the expected plasticizing effect of PG. The negative deviations are observed in Table 2 for OA samples. OA has a large molar volume, which is more than four times of that for PG (Table 3). It is expected that OA large molecules cause not only more entanglements between the copolymer chains to be dissociated, but also the remaining ones to become significantly weaker than a low molar volume plasticizer. This causes T_g to be lower than calculated values.

In a polymer/plasticizer system, the plasticizer may migrate to the surface and forms a mechanically weak surface layer. In respect to a large difference between solubility parameter (δ) of PG (Table 3) and reported δ for the adhesive (16 $(cal/cm^3)^{1/2}$), an incompatible system and migration to the surface can be expected. However, there is approximately no difference between surface energies of PG samples and the adhesive (Table 1). This is indicative of no migration to the surface, which can be related to a chemical interaction (the hydrogen bonds) between PG and the copolymer. The sharp drop observed in the surface energy with addition of a low amount 5 w/w% of OA (Table 1) is indicative of an immiscibility between the mixture components and OA migration to the surface. As OA solubility parameter (Table 3) is very close to the copolymer, the immiscibility is related to large molar volume of OA.

DSC Curves for PG and OA samples are shown in Figures 3 and 4, respectively. A broad T_g region for concentrations below 15 w/w% of OA, in contrast with PG samples, signifies a micro-hetereogenous microstructure. However, exothermic peaks for 15 w/w% and higher concentrations is indicative of OA crystallization and macroscopic immiscibility. This immiscibility is accompanied with a large drop in the surface energy amount from about 22 to 16 (mJ/m^2).

Viscoelastic Properties

Adhesive Failure

As mentioned before, the effect of interfacial work of adhesion on peel strength is negligible. Then peel strength results can be explained on the basis of viscoelastic energy dissipations in the copolymer. Generally, hydrogen bonding, like cross-linking, increases both T_g and the storage modulus of the polymer. Then it is concluded that the amount of G' for the different PG samples with approximately constant T_g, is equal. It has been shown that the debonding energy, in a peel or tack test, is proportional to the average mass between polymer chain entanglements ($\overline{M}e$). This has been explained on the basis of formation and growth of fibrils (fibrilation) in the polymer [12]. $\overline{M}e$ can be estimated from rubbery plateau modulus (G^0_n) as follows:

$$M_e = \rho RT / G^0_n \qquad (4)$$

where, ρ is density of the polymer or blend, R is 8.31 J/mol.K and T is absolute temperature. As densities of PG and the copolymer (0.91 g/mL) are close to each other, there are negligible differences between the amount of ρ for the different samples. G^0_n is determined from G' at the onset of rubbery region. Then an approximately constant amount for G' leads to a constant amount for $\overline{M}e$. This explains the insignificant change in the peel strength of PG samples. OA has a plasticizing effect and plasticizers usually increase $\overline{M}e$ value. Then it is expected that peel strength may be improved by increasing the OA concentration. However, it is observed in Figure 2 that the peel strength not only is not increased, it shows a very small decrease when 5 w/w% of OA is added. As it was shown before, migration to the surface is occurred even at this low concentration which leads to formation of a mechanically weak surface layer. On the other hand, a large increase in $\overline{M}e$ is expected because of a significant

Table 3. Physical properties of the excipients.

Excipient	Formula	$\bar{M}_w$ (g/mol)	Molar volume V (cm^3/mol)	T_g (°C)	bp_{100} (°C)	δ (cal/cm^3)$^{1/2}$	ρ(g/mL)
PG	$C_3H_8O_2$	76.10	73.6	-100	132	25.8	1.03
OA	$C_{18}H_{34}O_2$	282.47	320	-50	286	17.38	0.89

decrease in the copolymer T_g (Table 2). It seems that the effect of $\bar{M}e$ increase is overcome by the effect of the weak surface layer. When the concentration changes from 5 to 10 (w/w%), a large drop in the peel strength is observed which can be explained by the following description:

OA Molecules not only cause many entanglements to be dissociated, but also weaken the remained entanglements significantly. Then, the copolymer chains move under very low limitations. This causes the average realxation rate of the chains to decrease and becomes slower than the rate of the applied force. Then, there is not enough time for the force to transfer in total thickness of the adhesive. In the other words, the effective thickness of the adhesive, entering in the dissipation process, is decreased. Usually, increasing of thickness improves peel strength, because energy dissipation occurs in a larger volume of the adhesive[13,14]. However, it is observed in Figure 2 that doubling of the thickness has no effect on the peel strength. This shows that the peel force does not transfer in at least one half of the adhesive thickness. It has been shown that PSA thickness has an important effect on peel strength at low (up to 20 μ) thicknesses. For example, 5 μ decrease in the thickness causes 40% decrease in the peel strength[6]. On the other hand, a weaker surface layer is formed with increasing of OA concentration. Then the large drop in the peel strength, can be related to diminution of the effective thickness in addition with more weakening of the surface layer. However, it is logical to suppose that these factors do not change significantly in all higher concentrations.

Cohesive Failure

The peel strength curves in Figure 2 are divided into two different parts. The adhesive failure occurs in the left hand (region A) and the cohesive failure in the right hand (region B) of the Figure. The large OA molecules weaken the copolymer physical structure. This effect is reinforced severely, above 10(w/w%), by formation of OA crystals which leads to the cohesive failure. However, transition from adhesive to cohesive failure for 60 μ samples occurs above a lower concentration (10w/w%) because :

The applied peel energy is supported by both of the adhesive and backing layer. When the thickness is doubled, transferring of the peel force from the adhesive surface to the backing layer is not accomplished.

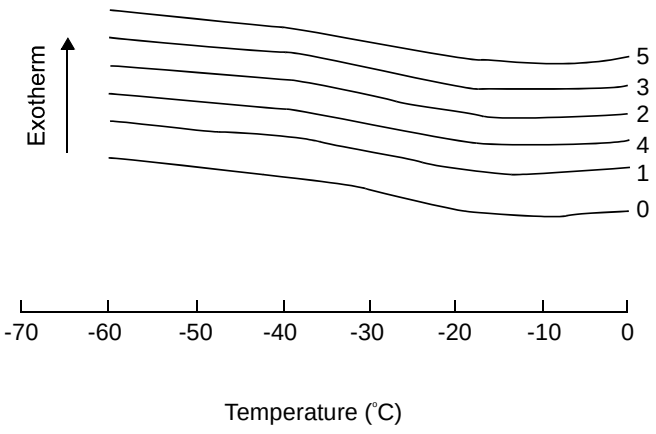

Figure 3. DSC Thermograms of the copolymer containing: (0) 0 (1) 5 (2) 10 (3) 15 (4) 20 and (5) 25 wt % of PG.

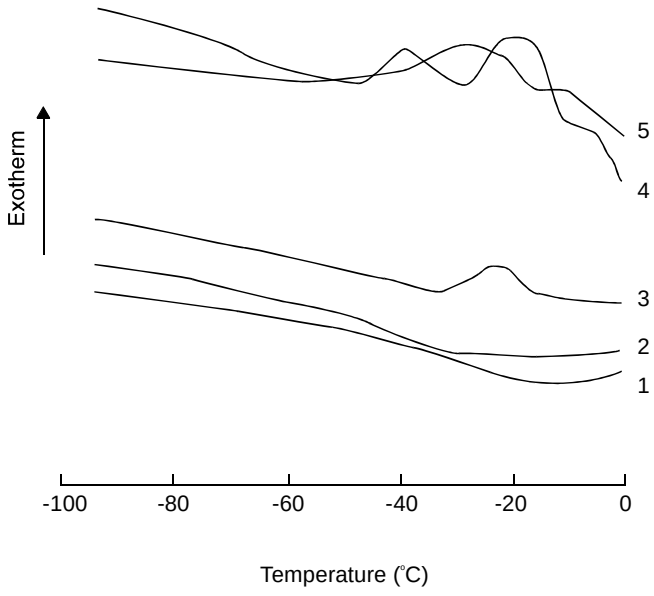

Figure 4. DSC Thermograms of the copolymer containing: (1) 5 (2) 10 (3) 15 (4) 20 and (5) 25 wt % of OA.

Then, the part of force which is not being transferred is applied on the 30 μ surface layer which reinforces the effect of OA crystals.

CONCLUSION

Effect of PG and OA on peel strength of an acrylic adhesive copolymer was investigated. PG had no significant effect on the peel strength. This was explained on the basis of a constant $\overline{M}_e$, resulting from formation of hydrogen bonds between PG and the copolymer.

Whereas, OA, with a plasticizing effect, it is expected to increase $\overline{M}_e$ and consequently the peel strength. However, OA with strong effect on the decrease of T_g, it has no significant effect on the peel strength at low concentration (5% (w/w)). This is explained with respect to the effect of migrated OA to the surface. Double fold increase in adhesive thickness had no effect on the peel strength of OA samples. This indicated that, at least, one half of the thickness was ineffective in the viscoelastic energy dissipations. A sharp drop in peel force was observed, when OA concentration changed from 5 to 10 (w/w%). This can be related to diminution of the adhesive effective thickness in addition with formation of a weaker surface layer. Cohesive failure for 30 μ samples occurred, when OA concentration exceeded 15(w/w%). However, this failure was observed above 10 w/w% for 60 μ samples, because the applied force is not transferred from the adhesive surface to the backing layer.

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