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RESEARCH PAPER

Evaluation of Adhesive Properties of Patches Based on Acrylic Matrices

P. Minghetti,* F. Cilurzo, and L. Montanari

Istituto di Chimica Farmaceutica, Università degli Studi di Milano viale Abruzzi 42, 20029 Milano, Italy

ABSTRACT

Adhesion is an essential property of the dermal and transdermal therapeutic systems (TS). It is influenced by the composition and the thickness of the matrix and also by the characteristics of the backing layer. Our aim was to evaluate the usefulness of the ''thumb tack test,'' the ''tack rolling ball test,'' and the ''peel adhesion 180° test'' in the development studies and quality control of TS. These tests were performed on two series of placebo patches in which the backing layer was made of artificial silk (series 1) and polyurethane film (series 2). The patches of both series were prepared using five different mixtures of a hydrophilic adhesive copolymer and a hydrophobic nonadhesive copolymer as matrices. Plastoid® E 35 L, a copolymer of dimethylaminoethyl methacrylate and neutral methacrylic esters, was used as the adhesive polymer. Eudragit® NE 40 D, a copolymer of ethylacrylate and methylmethacrylate, was used as the nonadhesive copolymer. In the standard procedure for the peel adhesion 180° test, used in the tape industries, the adherent is made of stainless steel. Because the latter has a high surface energy, it was not suitable for the analysis of the patches with a polyurethane backing layer. Therefore, the critical surface tension of five alternative materials (rubber, polysiloxane, polyethylene, nylon, polyvinyl chloride) was evaluated. Polyethylene was selected for the modified peel adhesion 180° test, and better results were obtained in terms of feasibility of the test and ability to discriminate between the different patches prepared.

Key Words: *Patch; Adhesive properties; Evaluation of adhesion.*

INTRODUCTION

The adhesive properties of transdermal and dermal therapeutic systems (TS) are fundamental to transdermal or dermal treatment. The entire delivery surface of the patch has to maintain complete skin contact for the required period to ensure an efficient drug delivery. It has been demonstrated that when the patch fails to adhere,

* To whom correspondence should be addressed.

the ratio cost-effectiveness increases (1). The adhesive properties can be influenced by the composition and the thickness of the matrix and also by the characteristics of the backing layer. Indeed, flexibility, surface free energy, and roughness, as well as the chemicophysical properties of the backing layer, influence the adhesion of the final patch significantly.

The adhesive polymers used in TS formulations are classified as pressure-sensitive adhesive and are defined as adhesives capable of bonding to surfaces with the application of light pressure (2). The most widely used approach to explain the adhesive properties of these materials is based on the belief that the pressure-sensitive adhesive will adhere to the substrate because of interatomic and intermolecular forces established at the interface, provided that intimate contact is effected. Generally, the formation of an assembly is achieved by means of a liquid–solid contact step, and thus the criteria for effective adhesion becomes the criteria of good wetting (3,4). The magnitude of these forces can be related to fundamental thermodynamic quantities, such as surface free energies of both adhesive and adherent. For a solid, the critical surface tension provides a basis for estimating the surface energy.

The adhesive properties can be evaluated in term of ''tack'' and ''peel.'' Tack could be defined as the property that enables an adhesive to form a bond with the surface of another material upon brief contact under light pressure (4). Peel adhesion is the force required to peel away a strip of tape from a rigid surface (5). Many tests have been developed in the adhesive tape industries to measure peel adhesion, generally using stainless steel as the adherent plate. In the case of TS the adherent is human skin, and therefore it would be useful to have tests that are able to predict the adhesion of the patch to the skin.

In the present work, the ''thumb tack test,'' ''tack rolling ball test,'' and ''peel adhesion 180° test,'' adhesion tests used in the adhesive tape industries, were evaluated to verify their fitness in the development studies and in the quality control of TS made of methacrylic adhesive copolymers, widely used in transdermal formulations.

These tests were performed in two series (S1 and S2) of placebo patches in which the backing layer was made of artificial silk (S1) and polyurethane film (S2). The patches of both series were prepared using five different mixtures of a hydrophilic adhesive copolymer and a hydrophobic nonadhesive copolymer as matrices. Plastoid® E 35 L (PL L), a copolymer of dimethylaminoethyl methacrylate and neutral methacrylic esters, was used as the adhesive polymer. Eudragit® NE 40 D (EU NE), a copolymer of ethylacrylate and methylmethacrylate, was used as the nonadhesive copolymer. All polymers were kindly donated by Rofarma-Röhm (Milan, Italy).

In the case of peel adhesion 180° test, the standard procedure in the tape industries uses the stainless steel plate as the adherent. This material was not suitable to perform the test with the prepared patches, and therefore five alternative materials (rubber, polysiloxane, polyethylene, nylon, polyvinyl chloride [PVC]) were selected with the aim of finding a more suitable adherent for the quality control of the prepared TS. Patches, with the same composition (Table 1, no. 2) but different thicknesses, were prepared and tested to verify the ability of the method to discriminate the different formulations.

MATERIALS AND METHODS

Constituents and Preparation of TS

Backing Layers

Artificial silk, based on fibers of rayon acetate (Bouty, Milan, Italy), was used, with the following specifications: thickness 130 μm; weight 70 g × m^2; warp/weft 42/26 yarns/cm. Polyurethane BPU film (Rexham, Charlotte, NC) was also used, with the following specifications: thickness 15 μm; weight 14 g × m^2.

Polymers

PL L is a copolymer of dimethylaminoethyl methacrylate and neutral methacrylic esters neutralized by fatty acids. It is supplied as an aqueous solution that has a dry weight of 34% w/w. EU NE is a neutral copolymer of ethylacrylate and methylmethacrylate. It is supplied as an aqueous dispersion at 40% w/w. The composition of the suspending medium was not given by the producer.

Preparation of Polymeric Matrices

Polymeric mixtures of PL L and EU NE were prepared to obtain patches with defined composition of the dry matrices as reported in Table 1. The weighed amounts of PL L and EU NE were mixed using a mechanic stirrer (RW20DZM, IKA, Staufen, Germany) at 50 rpm for 1 hr and used after 24 hr of rest.

Preparation of TS

The TS were prepared using a laboratory coating unit (Mathis LTE-S(M), Switzerland). The polymeric mix-

Table 1

Composition of the Therapeutic Systems

	Formulation No.	Matrix PL L: EU NE (%w/w)	Backing Layer
Series 1	1	55:45	AS
	2	65:35	AS
	3	75:25	AS
	4	85:15	AS
	5	100:0	AS
Series 2	6	55:45	PU
	7	65:35	PU
	8	75:25	PU
	9	85:15	PU
	10	100:0	PU

AS, artificial silk; PU, polyurethane film.

tures were spread on the backing layer at the constant rate of 2.2 m/min and at the thickness of 500 μm. The systems were dried at 60°C for 12 min and covered with a protective foil. For the preparation of the thicker TS, two or more additional coatings were applied on the first one by the method described above. The thickness of the various TS were expressed in mg of polymeric matrix per cm^2.

Adhesion Evaluation

Thumb Tack Test

The thumb was lightly put into contact for a short time with a sample and then quickly withdrawn (4). By varying the pressure and time of contact and noting the difficulty of pulling the thumb from the adhesive, it is possible to perceive how easily, quickly, and strongly the adhesive can form a bond with the skin. Some major drawbacks of the thumb tack test are its subjectivity and the fact that the data are poorly quantifiable. However, it is the most simple and straightforward test for the evaluation of the adhesive skin bonding. All tests were simultaneously performed, blind, on five samples. The adhesive properties of the TS were expressed by the following value range: good adhesion, poor adhesion, and no adhesion.

Tack Rolling Ball Test

In this procedure (6), an 11-mm-diameter stainless steel ball weighing 5.6 mg was rolled down an inclined track (21°,30′) to come into contact at the bottom with horizontal upward-facing adhesive. Adhesive patches were cut in strips and conditioned for 24 hr at 23 ± 2°C and 50 ± 5% relative humidity (R.H.). The running of the ball on the track was of 5.5 mm. The distance the ball traveled out along the tape is taken as the measure of tack. The distance the ball rolled gave an inverse compressed scale of tack; the greater the distance, the less tacky the adhesive, but not in proportion to the ratio of distance (4). In this work, the reciprocal of roll out distance was taken as the tack value. When the rolling of the ball on the adhesive tape was superior to 25 cm, the tack value was considered zero.

The results were the average of five determinations and were expressed as the reciprocal of running of the ball on the adhesive tape.

Peel Adhesion 180° Test

Adhesive patches were cut into strips 2.5 cm wide and conditioned for 24 hr at 23 ± 2°C and 50 ± 5% R.H. (7,8). The tests were performed in the same environmental conditions with an Instron Corporation Series IX Automated Material Testing System 1.26. The samples were applied to an adherent plate made of stainless steel, smoothed with a 4.5 pound roller, and pulled from the substrate at a 180° angle at a rate of 300 mm/min. The matrix had to strip cleanly from the plate, leaving no visually noticeable residue.

The force was expressed in centiNewton per centimeter (cN/cm) width of adhesive tape under test. Peel adhesion values represented the mean of three samples.

Selection of Material for Adherent Plate in the Peel Adhesion 180° Test

Materials

The following materials were used:

1. Stainless steel of a Brinell hardness, ranging from 130 to 200 and comprising the following constituents: carbon $< 0.12\%$, nickel $> 8\%$, chromium $> 17\%$;
2. Natural rubber (ATAG, Italy), density 0.96 g/cm^3;
3. Rau Sik polysiloxane with high molecular weight (ATAG, Italy), density 1.38 g/cm^3;
4. Polyethylene processed at low pressure (SARGOM, Italy), density 0.95 g/cm^3;
5. Nylon (ATAG, Italy), density 1.38 g/cm^3;
6. PVC (ATAG, Italy), density 1.18 g/cm^3.

Table 2

Composition and Surface Tension of the Mixtures Used in the Determination of the Critical Surface Tension

Method A			Method B		
Formamid (% v/v)	Ethylenglycol (% v/v)	Surface Tension (dine/cm)	Methanol (% v/v)	Water (% v/v)	Surface Tension (dine/cm)
0	100	30	67	33	30
10.5	89.5	32	59.8	40.2	32
26.5	73.5	34	53.5	46.5	34
42.5	57.5	36	47.9	52.1	36
54	46	38	42.8	57.2	38
63.5	36.5	40	38.3	61.7	40
71.5	28.5	42	34.2	65.8	42
78	22	44	30.5	69.5	44
83	17	46	27.1	72.9	46
87	13	48	24	76	48
90.7	9.3	50	21.1	78.9	50
93.7	6.3	52	18.5	81.5	52
96.5	3.5	54	16	84	54
99	1	56	13.7	86.3	56
–	–	–	11.6	88.4	58

Determination of the Critical Surface Tension (DIN 53364)

A sample of material to be tested was moistened with a brush soaked with the different solutions with known surface tension. Two different series of mixtures were used (method A and method B); the compositions and the related surface tensions are reported in Table 2. The critical surface tension (dine/cm) of the material was considered equal to the surface tension of the mixture when the film formed by the solution remained uniform and unbroken on the surface of the material for 2 sec. The results obtained were the average of three determinations.

RESULTS AND DISCUSSION

The tack properties of the different patches, analyzed with either the thumb tack test (Table 3) or the tack rolling ball test (Fig. 1), increased with the percentage of adhesive polymer in the matrix; adhesion was higher when the backing layer was polyurethane. Only formulation 1, containing the lowest percentage of adhesive polymer (55% w/w) and having as backing the artificial silk, did not show good tack properties.

The tack rolling ball test is very sensitive to small variations in operative conditions (temperature, relative humidity, sample preparation, ball push), and for the tested patches, significant differences were obtained only for values ranging from 0.1 to 0.4 cm^{-1} (Fig. 1).

The values of the peel forces, obtained using the stainless steel as adherent and reported in Table 4, confirmed that all TS of series 1 had good adhesive properties, except for formulation 1.

The peel adhesion values of the TS of series 2 could not be evaluated because the patches warped and broke during the test; this was because the strength of the bonds established between the patches and the stainless steel plate was greater than the tensile strength of the polyure-

Table 3

Thumb Tack Test Determination

Formulation No.	Evaluation
1	No adhesion
2	Good adhesion
3	Good adhesion
4	Good adhesion
5	Good adhesion
6	Poor adhesion
7	Good adhesion
8	Good adhesion
9	Good adhesion
10	Good adhesion

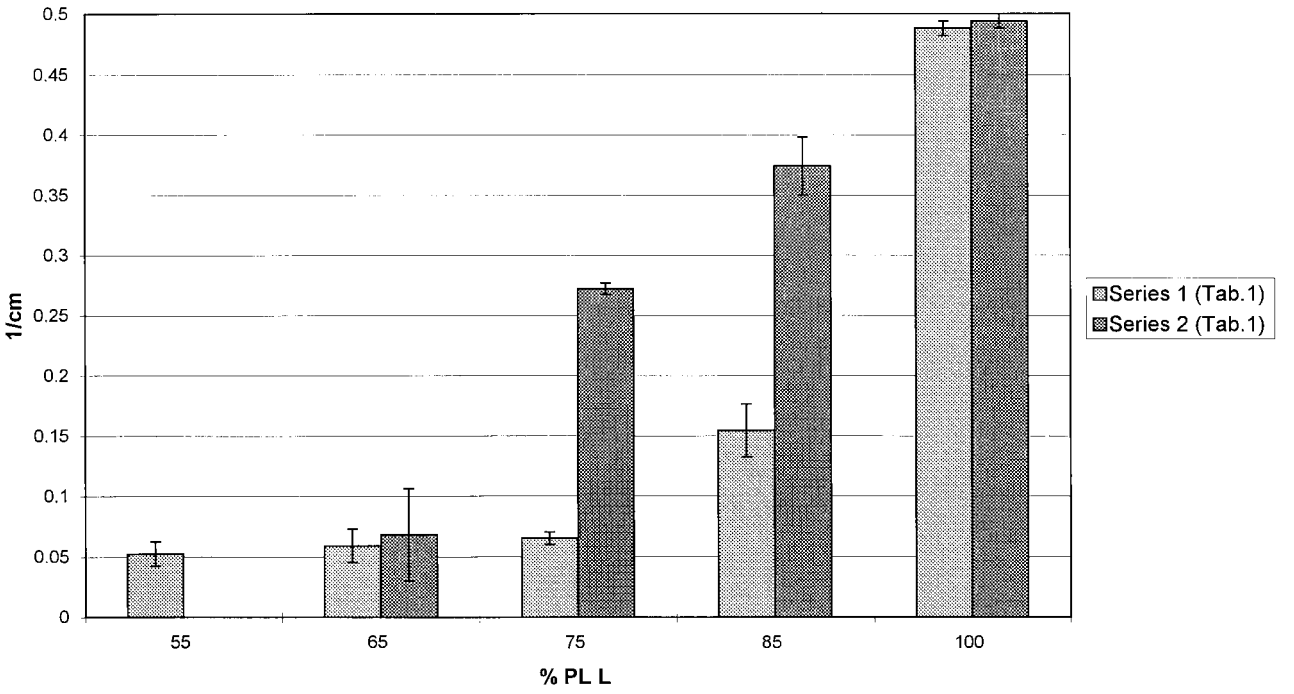

Figure 1. Tack rolling ball test values of the different patches.

thane film. The patches were reinforced with adhesive tape on their backing layer to avoid this problem. However, the problem was not overcome because of differences in elongation of traction of the polyurethane and adhesive tape and because the adhesive force between the two was not sufficient to avoid detachment. This problem could be solved using a material with a critical surface tension lower than that of the stainless steel as a plate.

The critical surface tension of other selected materials was therefore evaluated with the aim of finding an adherent plate suitable to analyze patches with polyurethane film as the backing layer. The critical surface tensions of the materials tested are reported in Table 5. The materials with the lowest critical surface tensions were Rau Sik polysiloxane, polyethylene, and PVC. Because the polyethylene was more rigid, it was chosen as the alternative material to the stainless steel for further evaluations.

The peel adhesion 180° test was performed with the same method for all prepared TS using polyethylene as the adherent plate. The results are reported in Table 6. The peel adhesion values were determinable for all patches with the exclusion of formulation 10. The values were lower than those obtained with the stainless steel plate because the adhesion bonds were weaker due to the

Table 4

Peel Adhesion 180° Test Values with Stainless Steel Plate

Formulation No.	Peel Force (cN/cm)
1	75
2	432
3	507
4	541
5	598

SD was less than 15%.

Table 5

Critical Surface Tension of the Different Materials

Material	Method A (dine/cm)	Method B (dine/cm)
Stainless steel	36	40
Natural rubber	34	40
Nylon	38	38
Polyethylene	30	<30
PVC	<30	<30
Rau Sik polysiloxane	30	<30

Table 6

Peel Adhesion 180° Test Values with Polyethylene Plate

Formulation No.	Peel Force (cN/cm)
1	1
2	40
3	118
4	184
5	282
6	16
7	379
8	417
9	487
10	n.d.

SD was less than 15%. n.d., not determinable.

inferior free energy of the surface of the polyethylene. The data obtained permitted a satisfactory differentiation between the adhesion of the different formulations.

Patches having the same composition (Table 1, no. 2) but different thicknesses were tested to verify the performance of the method in differentiating these TS. The results reported in Table 7 confirmed that the proposed method also had sufficient sensibility in this case. Moreover, all patches were stripped cleanly from the plate, leaving no visually noticeable residue, showing good behavior.

CONCLUSIONS

The tack rolling ball test does not seem suitable for patches made of acrylic copolymer because the results are influenced by very small variations in the operative conditions and its sensitivity is not satisfactory in the range of adhesion measured for the patches considered. Despite the fact that the thumb tack test is subjective and nonquantifiable, it is useful in development studies because it is the only one indicative of the adhesive skin bonding.

The peel adhesion 180° test was the most reliable among those considered; the storage and preparation of the samples are critical, and relative procedures should be carefully standardized.

The stainless steel plate used in the tape industries was not suitable for the quality control of patches made of methacrylic matrices and polyurethane backing layers, but good results were obtained using the polyethylene plate as an adherent.

The peel adhesion test was modified by substituting the stainless steel plate with a polyethylene plate, which permitted the measurement of the adhesion of the prepared TS and also the verification of the cohesion properties and the anchorage of the matrix to the backing layer. The proposed modification of the standard method PSTC-1 (7) can be applied in development studies and quality control of patches made of acrylic matrices and flexible backing layers. This indication could be useful, especially because the USP XXIII monograph concerning adhesive tape does not indicate the specific plastic material used to apply the sample to analyze (9).

Table 7

Peel Adhesion Test Values of TS (Formulation No. 2) with Different Thicknesses

Thickness of the Matrix (mg/cm^2)	Peel Force (cN/cm)
10	40
20	100
30	230

SD was less than 15%.

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