Preparation and evaluation of cosmetic patches containing lactic and glycolic acids

H. Mahdavi, Z. Kermani, G. Faghihi*, A. Asilian*, H. Hamishehkar, A. Jamshidi**

Department of Novel Drug Delivery Systems, Science Faculty, Iran Polymer and Petrochemical Institute, Tehran, Iran, *Department of Dermatology, Isfahan University of Medical Sciences, Isfahan, **Department of Pharmaceutical Technology, Drug Applied Research Center, Tabriz university of Medical Sciences, Tabrize, Iran

Address for correspondence: H. Mahdavi, Novel Drug Delivery Systems Department, Science Faculty, Iran Polymer and Petrochemical Institute, Tehran, Iran. E-mail: H.Mahdavi@ippi.ac.ir

ABSTRACT

Background: Alpha-hydroxy acids such as glycolic acid (GA) and lactic acid (LA), are used in cosmetic patches. The important fact in cosmetic patches is its suitable adhesion and peel properties. **Aim:** The objective of this study was to prepare LA- and GA-containing cosmetic patches and evaluate in-vitro/in-vivo correlation of adhesion properties. **Methods:** Pressure-sensitive adhesives with different concentrations of GA and LA were cast on a polyethylene terephthalate film. The patches were evaluated for peel adhesive strength. On the basis of in vitro adhesion properties the patches were selected for wear performance tests and skin irritation potential. **Results:** The adhesion properties (adhesion to steel plate and skin) and cohesive strength tests indicated the substantial influence of GA and LA concentrations. Based on in vitro adhesion studies the patches containing 3% (w/w) GA were selected for in vivo studies. In vivo studies show that a formulation containing 3% GA displays good adhesion on the skin, but it leaves little residues on the skin. Skin Irritation studies on healthy human volunteers showed negligible erythema at the site of application after 48h. **Conclusion:** The noninvasive patch test model was found useful for detecting irritant skin reactions to the cosmetic patch containing GA. Our results demonstrated a strong correlation between the adhesion to steel plate and adhesion to skin. But a weak correlation between the degree of adhesive residue on the skin in in vitro and in vivo tests was observed for the formulation containing 3% (w/w) GA.

Key Words: Cosmetic patch, Glycolic acid, Lactic acid, Peel adhesive strength, Pressure-sensitive adhesive, Tack

INTRODUCTION

Cosmetic patches are unique dermal delivery systems that quench the body's need for important vitamins, alpha hydroxy acids, other ingredients and allow active compounds to be administered transdermally.[1] Such conventional patches contain several successive layers. The first layer is a backing layer (protects the patch from the environment) enclosing the inside layer of adhesive (contacts the skin during treatment) that is fastened to the support layer and often contains one or more active compounds. Pressure-sensitive adhesives (PSAs) are materials that adhere to a substrate by application of light force and leave no residue when removed. Pressure-sensitive adhesives are also important components of transdermal drug delivery systems (TDDS), because they ensure intimate contact between the drug-releasing area of a TDDS and the skin surface, which is critical for controlled release

How to cite this article: Mahdavi H, Kermani Z, Faghihi G, Asilian A, Hamishehkar H, Jamshidi A. Preparation and evaluation of cosmetic patches containing lactic and glycolic acids. Indian J Dermatol Venereol Leprol 2006;72:432-6.

Received: January, 2006. **Accepted:** April, 2006. **Source of Support:** See acknowledgement. **Conflict of interest:** None declared.

of the drug.[2] Pressure-sensitive adhesives are also important components of cosmetic patches and include at least one cosmetically active compound. The last layer is a release liner. Release liner protects the patch but it is removed prior to use.[1] Keratolytic agents such as glycolic acid and lactic acid, have recently been used in cosmetic and dermatological formulations. However, the mechanisms of action of these substances have not been well documented.[3,4]

Our previous studies have shown that alpha-hydroxy acids (AHAs) can have an effect on one of the important adhesion properties such as tackiness of the PSAs used in cosmetic patches.[5] Another typical test for measuring adhesive bond strength is the peel adhesion. This test measures the force required to peel away a strip of adhesives from a rigid steel surface and might be a good predictor of the difficulty of removing a pressure sensitive patch at the end of its application time from the skin.[3,6]

We studied the effect of two cosmetic patch active ingredients: lactic acid (LA) and glycolic acid (GA), on the peel adhesive strength of the cosmetic patches.

METHODS

Poly (acrylate-co-vinyl acetate) as commercial adhesive (Duro-tak 87-2196), was purchased from National Starch and Chemical Company, Bridgewater, NJ. Glycolic acid 99% (Aldrich), L-lactic acid 85% (Aldrich) and poly (ethylene terephthalate) film with 80 mm thickness were used. Ethical Committee approval was obtained prior to conducting the study.

Cosmetic patch preparation

Duro-Tak was thoroughly mixed with GA and LA to prepare formulations containing 0-6 (w/w %) of the mentioned additives in the adhesive. PSAs containing AHAs films for the peel adhesive strength tests were prepared by coating these solutions on polyethylene terephthalate. Cosmetic patches using a commercial PSAs were evaluated for peel adhesive strength (adhesion to steel and skin) and primary skin irritation.

Adhesion to steel (peel adhesion)

The measure of bond strength between an adhesive and a substrate is defined as adhesion. The peel test is one of the standard tests used to evaluate the strength of adhesive bonds when at least one bonded member is relatively thin.[7] These properties are typically measured using the 180° or 90° peel adhesion test method. One week after preparation, the cosmetic patches were cut into strips with a width of 2.5 cm and applied to an adherent plate, smoothed three times with a 4.5-kg roller and pulled from the plate at a 180° angle at 300 mm/min rate. The 300 mm/min rate is recommended by the standard procedure.[8] The test was performed with a tensile testing machine (MTS 10/M, USA), according to the ASTM D3330. The reported adhesion to steel value (N/25 mm) is the average force required to peel away the adhesive divided by the adhesive width perpendicular to the peel direction. Peel adhesion values were the average of three replicates.

Wear performance test

Wear performance test, i.e., physical activity and moist environment are important factors influencing the failure of a PSAs. Therefore this test was conducted utilizing a panel of 46 human subjects under temperature of 35±2°C and humidity 50±4%. Cosmetic patches with dimension of 2×2 cm^2 were applied to the upper back area of the volunteers. After 8h, the adhesion to skin and adhesive residue on the skin were evaluated. Adhesion was ranked from 0 to 4 according to Hill Top Research Inc [Table 1]. The adhesive transfer was rated from 0 (no residue), 1 (little residue) and 2 (heavy residue).[9]

Skin irritation study

Irritant skin reactions to alpha hydroxy acids are,

Table 1: Adhesion scoring the cosmetic patches according to Hill Top Researches, Inc

Adhesion score	Evaluation value
0	90% adhered (essentially no lift off of the skin)
1	75% to < 90% adhered (some edges only lifting off of the skin)
2	50% to < 75% adhered (less than half of the system lifting off of the skin)
3	< 50% adhered but not detached (more than half the system lifting off of the skin without failing off)
4	Patch detached (patch completely off the skin)

however, known to occur. In order to prevent such irritant reactions reliable test methods for irritancy testing of AHA are needed. This study was undertaken to evaluate a noninvasive patch test model for the detection of irritant skin reactions to cosmetic patch containing AHAs.[10] In the patch test, two patches (patch without AHAs (formulation A) and patch containing 3% glycolic acid (formulation B)) were placed on the body back area of 46 female and male human volunteers in the age group of 20 to 65 years for 48h. Readings were made at 1h and 48h after removal, according to the Guidance for Industry Skin Irritation and Sensitization Testing of Generic Transdermal Products protocol [Table 2].

Statistical analysis

The results were analyzed by Student's t-test using Graph Pad Instat Software (Version: 1.13). A difference under the probability level of 0.05 was considered statistically significant.

RESULTS

Adhesion to steel (peel adhesion)

Figures 1 and 2 show that the peel adhesive strength of PSA initially increased with the addition of lactic acid up to 1% (w/w), but then decreased to a minimum value when the lactic acid was added from 1 to 6% (w/w). Also, the peel value increased with addition of glycolic acid up to 1% (w/w). However, the peel adhesive strength of patches containing glycolic acid decreased with glycolic acid concentrations of 1-3%, then increased again above 3% (w/w).

Wear performance test

After the peel tests of different formulations containing lactic acid, adhesive residue was observed on the test plates [Figure 3, Plates C, D and E]. As a result, the *in vivo* tests were not performed for patches containing lactic acid. However, no residue on the test panels was observed for patches with different glycolic acid concentrations [Figure 3, plates A and B].

On the basis of the results obtained, it can be predicted that the patches containing 3% (w/w) of glycolic acid with better tack properties[6] and lower peel adhesive strength [Figures 2, 4] adhered and peeled off more easily from the skin. Therefore, the patches with 3% (w/w) of glycolic acid were selected for *in vivo* tests. Forty-six volunteers, ages ranging from 20 to 65, applied the patches on their back area for 48h. The evaluation ranking graded the patches on ease of removal of patch, adhesive residue on the skin and irritation observed upon the patch removals.

Table 2: Typical skin reaction scoring used in patch test method for skin irritation studies

Skin reaction	Evaluation value
0	No evidence of irritation
1	Minimal erythema, barely perceptible
2	Definite erythema, readily visible; minimal edema or minimal popular response
3	Erythema and papules
4	Definite edema
5	Erythema, edema and papules
6	Vesicular eruption
7	Strong reaction spreading beyond test site

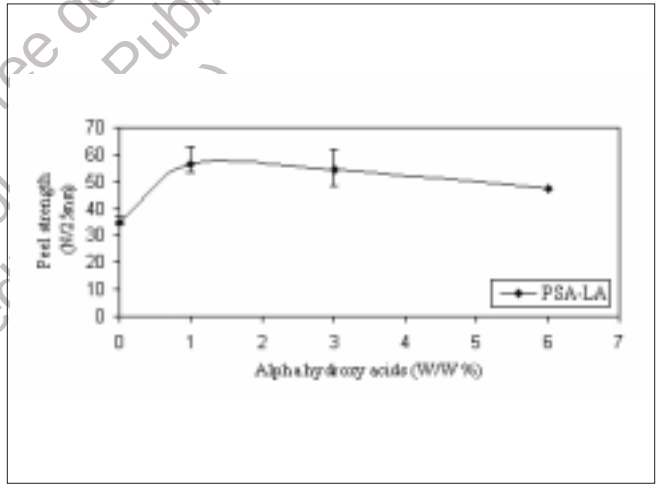

Figure 1: A plot of peel force versus LA concentration for 30 µm adhesive layer thickness (n=3)

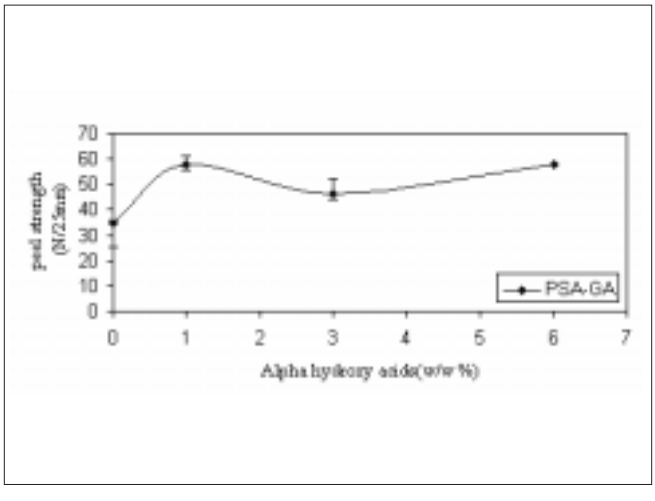

Figure 2: A plot of peel force versus GA concentration for 30 µm adhesive layer thickness (n=3)

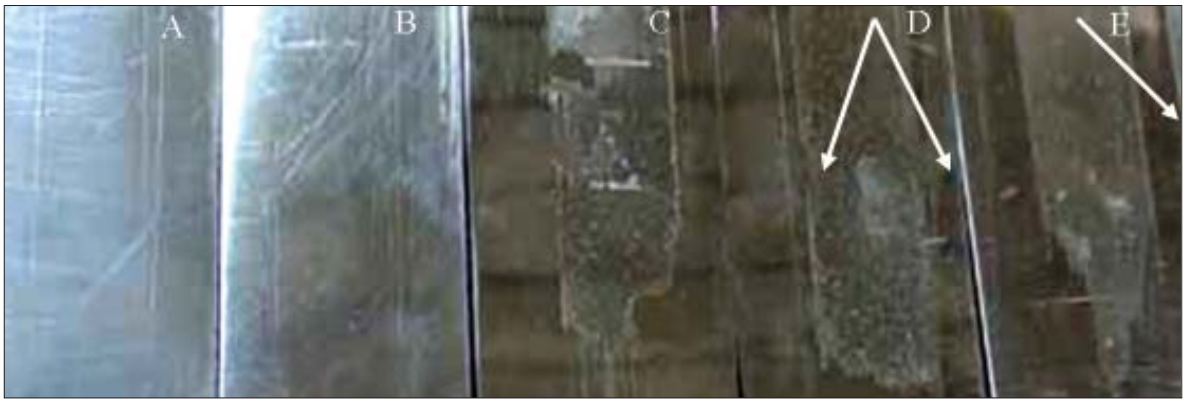

Figure 3: Peel test plates of PSA containing 3 and 6 (w/w %) of GA (A and B respectively) and 1, 3 and 6 (w/w %) of LA (C, D and E respectively)

The scoring was made 1h and 24h after patch removal. The patches containing 3% (w/w) of glycolic acid showed 90% adhesion as there was 'essentially no lift off of the skin' of the patches from the steel and skin. The corresponding adhesion score was '0' as per the US FDA document (http://www.fda.gov/ cder/guidance/ 2887fnl.htm) on 'Guidance for Industry: Skin Irritation and Sensitization Testing of Generic Transdermal Drug Products'. This emphasized the ability of the cosmetic patch to adhere to the steel and skin during the intended time of application.

It was observed that both formulations (A and B) had good adhesion to the steel and then could be removed without leaving substantial adhesive residue on the steel (adhesive transfer = 0). Wear performance test indicated good adhesion of the formulations (A and B) with the skin throughout the application period of 48h and then could be removed from the skin with an adhesive transfer rate of one (little residues on the skin) [Table 3].

Skin irritation study

Skin irritation studies on healthy human volunteers showed negligible erythema at the site of application after 48h, indicating minimal irritation on the skin during its contact time with the skin. It was also observed that after 72h all signs of irritation disappeared in 45 of the 46 volunteers.

DISCUSSION

Cosmetic patches containing AHAs are designed to adhere to the skin for a period of time sufficient for the treatment of wrinkles, acne and pigmentations. However, the adhesion and tackiness properties of dermal and transdermal devices, particularly the cosmetic patches are very important factors that can be altered by adding additives. Our previous studies have shown that alpha hydroxy acid concentration can change tack properties of PSAs used in cosmetic patches.[6] where a tack test measures the strength of adhesive bond formed after brief contact, a peel adhesion test is a measure of the bond strength after long contact. Therefore, peel adhesion might be a better predictor of the difficulty of removing a PSA at the end of its application time from the skin.[7] Effect of GA and LA concentrations on the adhesion properties of a cosmetic patch were investigated. The adhesion properties and cohesive strength tests indicated the substantial influence of GA and LA concentrations. The results showed that the formulation containing 3% (w/w) GA had good adhesive property and could be peeled off from the surface steel without leaving significant residue on the adherent. *In vivo* studies also showed a good adhesion property with little residue on the skin from this formulation. Our results demonstrated

Table 3: Results of wear performance test

Volunteers	Formulation	Adhesion to steel	Adhesion to skin	Residual on the steel	Residual on the skin
46	A	0	0	0	1
46	B	0	0	0	1

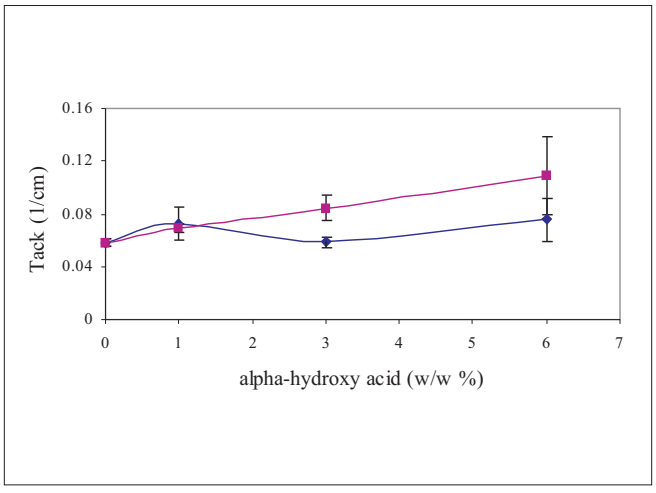

Figure 4: A plot of Tack versus concentration of (◆) GA and (■) LA for 30 µm adhesive layer thickness (3) (n=3)

strong correlation between the adhesion to steel plate and adhesion to skin. But a weak correlation between the degree of adhesive residue on the skin in *in vitro* and *in vivo* tests was observed for the formulation containing 3% (w/w) glycolic acid.

Studies have shown that several AHAs in low concentration (5%) have the potential to irritate the skin. This activity is closely linked to acidic pH as neutralized acids lose their ability to exfoliate the skin.[11,12] The results of the irritation study showed that both systems (formulations A and B) exhibited a minimal response (1 and 2) after the 48h. Since skin irritations were equal for both the systems (formulations A and B), the observed minimal skin irritation may be due to the applied mechanical force of the cosmetic patch removing from the skin not to ingredients of patches. It was also observed that after 72h all signs of irritation disappeared. These studies demonstrate that these cosmetic patches containing glycolic acid do not cause irritation.

ACKNOWLEDGMENT

We are grateful to Daroupat Shargh Com. for supplying backing layer. This work was supported by a grant from the Iran Polymer and Petrochemical Institute.

REFERENCES

1. Spiros AF. Cosmetic patches. *In*: Barel A, Marc P, Maibach HI, editors. Handbook of Cosmetic Science and Technology. 3rd ed. New York: Marcel Dekker; 2001. p. 237-40.
2. Dimas DA, Dallas PP, Rekkas DM, Choulis NH. Effect of several factors on the mechanical properties of pressure- sensitive adhesives used in transdermal therapeutic systems. AAPS Pharma Sci Tech 2000:1: E16.
3. Quan D, Venkateshwaran S, Ebert CD. Transdermal delivery devices containing polydiorganosiloxane polymers to regulate adhesive properties. US Patent 2004;6, 730, 318.
4. Vidt DG, Bergfeld WF. Cosmetic use of alpha-hydroxy acids. Cleve Clin J Med 1997;64:327-9.
5. Mahdavi H, Taghizadeh M. The effect of alpha hydroxy acids on the tack of pressure sensitive adhesive. Iran Polymer J 2005;14:379-85.
6. Minghetti P, Cilurzo F, Tosi L, Casiraghi A, Montanari L. Design of a new water-soluble pressure-sensitive adhesive for patch preparation. AAPS Pharma Sci Tech 2000:4: E8.
7. Chivers RA. Easy removal of pressure sensitive adhesive for skin applications. Int J Adhesion Adhesives 2001;21:381-8.
8. Satas SD. Peel. In: Satas D, editor. Handbook of pressure sensitive adhesives technology. 2th ed. Van Nostrand Reinhold: New York;1986. p. 61-97.
9. Mare VS, Bharti PV, Vavia PR. Acrylate terpolymer in fabrication of medicated skin patches. Polym Adv Technol 2001;12:466-71.
10. Tardiff RG, Hubner RP, Graves CG. Harmonization of thresholds for primary skin irritation from results of human repeated insult patch tests and laboratory animal skin irritation tests. J Appl Toxicol 2003;23:279-81.
11. Fartasch M, Teal J, Menon GK. Mode of action of glycolic acid on human stratum corneum: Ultrastructural and functional evaluation of the epidermal barrier. Arch Dermatol Res 1997;289:404-9.
12. Quan D, Venkateshwaran S, Ebert CD. Antioxidant composition for topical/transdermal prevention and treatment of wrinkles. US Patent 2001;6,180,133.