Arab International University[1], Damascus, Syria; Otto Bock Kunststoff Holding GmbH[2], Duderstadt, Germany

Adhesion testing of polyurethane matrix patches for transdermal delivery of testosterone

M. DITTGEN[1], P. GANSEN[2]

Received September 15, 2011, accepted October 25, 2011

Dr. Peter Gansen, Otto Bock PUR Life Science GmbH, Max-Näder-Strasse 15, D-37115 Duderstadt
gansen@ottobock.de

Pharmazie 67: 567–568 (2012)
doi: 10.1691/ph.2012.1138

The 180° peel test was applied to measure adhesion of three experimental polyurethane (PU) matrix patches and one commercial patch, Testopatch®, on human volunteers skin. Comparing the results with those measurements on stainless steel or leather, a significant correlation between the leather data and the skin measurements was found. In contrary to results from stainless steel tests, all of the PU patches achieved better adhesion on skin than the commercial patch.

A new technology to manufacture transdermal active patches without solvents or increased temperatures based on polyol and isocyanate reacting to polyurethane (PU) in the presence of the drug was established (Gansen et al. 2010). The technology was recently applied using testosterone (T) and two enhancers to improve skin permeation (Gansen and Dittgen 2011) at which adhesion was tested using the 180° peel test and stainless steel (St) or leather (Le) as substrates. The results differed and the question remains which of these substrates are more realistic when predicting adhesion on human skin (Sk).
Besides peel adhesion, probe tack test and shear strength measurement have been used to determine adhesive performance of patches. However, all of these tests do not reflect true material properties since they depend on a substrate, backing material and test parameters (Wokovich et al. 2006). Also, a recent evaluation of a probe tack test to measure adhesion of transdermal matrix patches came to the conclusion that the methods predictability is limited (Gutschke et al. 2010). The primary objective of this study was to apply the 180° peel test to measure adhesion of the patches on Sk. The resulting peel strength (F_S) was compared with that of a parallel investigation of 180° peel tests on two laboratory substrates, St or Le.
The theory of peeling adhesives from reversible flexible substrates like skin was elucidated a few years ago (Steven-Fountain et al. 2002). Furthermore, the peel test was applied to investigate the removal of a range of adhesive wounds (Dykes and Heggie 2003). Peeling tests on various human subjects were performed presenting a better representation of the interactions occurring at the skin/adhesive interface than conventional substrates used for peel test i.e. steel (Renvoise et al. 2009). The method used there was adapted for this investigation.
F_S was found highest on St, lower on Le and lowest on Sk (Table). The influence of enhancers on F_S followed different trends as earlier observed using St or Le as substrate only (Gansen and Dittgen 2011). That means the reduction of the enhancer limonene in the PU patches decreased F_S. This was also observed on Sk as one can see comparing P1 and P2. Comparing P1 and P3, the patches with the highest concentration of the second enhancer, *N,N*-diethyl-*m*-toluamide, F_S on skin was not significantly different whilst F_S on St and Le was dramatically decreased by reduction of limonene within the patch.
When comparing the F_S of P0, the reference, with F_S of the experimental PU patches P1, P2, P3, it can be seen that all of the PU patches have better adhesion on skin than P0. On St the reference P0 was found more adhesive than P3, but the adhesion of P3 on Le and Sk was found to be the highest.
The average standard deviation of the measurements was 33% for Le, 37% for Sk and 48% for St. Plotting F_S resulting from measurements on St and Le versus F_S measured on Sk, the upward trend follows the order P0, P3, P2, P1 (Fig.). The adhesion on skin did correlate significantly ($r = 0.96 > r_{krit} = 0.9587$, $\alpha = 0.01$) with F_S on Le while adhesion on St did not. The limited predictability of the peel test on St was found in accordance with investigations of the Wokovich group (Wokovich et al. 2009, 2006) as well our own earlier work (Fauth et al. 2002).

Table: Peel strength (F_S) on stainless steel, leather or skin measured by 180° peel test, standard deviation (STD), n = 4, n* = 3

Patch:		P0	P1	P2	P3
Stainless steel	F_S [mN/mm]	114.2	384.9	232.3	110.7
	STD [mN/mm]	72.02	46.24	187.13	41.18
	STD [%]	63.1	12.0	80.6	37.2
Leather	F_S [mN/mm]	18.8	169.1	151.9	59.2
	STD [mN/mm]	11.83	19.2	56.22	7.32
	STD [%]	70.4	11.4	37.0	12.4
Human skin	F_S [mN/mm]	3.0	31.1	20.3	10.7*
	STD [mN/mm]	1.90	5.02	1.09	6.61
	STD [%]	63.4	16.2	5.4	61.6

Experimental

Regarding the materials, patch manufacture and design, and peel adhesion test on laboratory substrates (St, Le) see Gansen and Dittgen (2011).
To determine F_S on Sk, the method of Renvoise et al. (2009) was adapted as follows: stripes were prepared by fitting and gluing the patches on the laminate Epurex Platilon® U4200 T 025 (Epurex Films GmbH & Co.KG, Bayershofer Weg 21, Bomlitz, Germany) providing a free contact area of

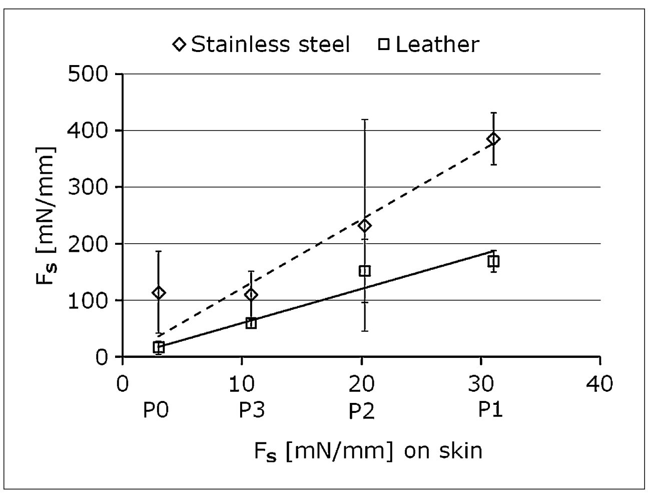

Fig.: Relationship between peel adhesion on stainless steel or leather with that on human skin, bars represent standard deviation

50 mm width/length. This was applied to the forearm of a volunteer, and left for a dwell time of 1 min. The stripe was peeled off afterwards under the conditions mentioned above. The volunteers (average age: 61 years) gave their prior consent and subsequent skin cleaning with alcohol avoided noticeable absorption of T.
For all peeling experiments, the standard rubber roller (weight 2.25 kg) was applied.

Acknowledgment, declaration of interest: The authors wish to thank F. Köpps for his support within the lab. The work was granted by Otto Bock Kunststoff Holding GmbH, Duderstadt, Germany.
The authors are consultants[1] or employees[2] of Otto Bock Kunststoff Holding GmbH, Duderstadt, Germany, and the work published here was financed by this company. However, the authors alone are responsible for the content and writing of this paper.

References

Dykes PJ, Heggie R (2003) The link between the peel force of adhesive dressings and subjective discomfort in volunteer subjects. J Wound Care 12: 260–262.

Fauth C, Wiedersberg S, Neubert RHH, Dittgen M (2002) Adhesive backing foil interactions affecting the elasticity, adhesion strength of laminates, and how to interpret these properties of branded transdermal patches. Drug Dev Ind Pharm 28: 1251–1259.

Gansen P, Dittgen M (2011) Polyurethanes as self adhesive matrix for the transdermal drug delivery of testosterone. Drug Dev Ind Pharm, 2011, 1–6 □ Early Online.

Gansen P, Dittgen M, Steinfatt-Hoffmann I, Schulte C, Henze J (2010) Polyurethane plaster for the transdermal application of active substances, and method for the production thereof. WO 2010060621(A1).

Gutschke E, Bracht S, Nagel S, Weitschies W (2010) Adhesion testing of transdermal matrix patches with a probe tack test - *in vitro* and *in vivo* evaluation. Eur J Pharm Biopharm 75: 399–404.

Renvoise J, Burlot D, Marin G, Derail C (2009) Adherence performances of pressure sensitive adhesives on a model viscoelastic synthetic film: A tool for the understanding of adhesion on the human skin. Int J Pharm 368: 83–88.

Steven-Fountain AJ, Atkins AG, Jeronimidis G, Vincent JFV, Farrar DF, Chivers RA (2002) The effect of flexible substrates on pressure-sensitive adhesive performance. Int J Adhesion Adhesives 22: 423–430.

Wokovich AM, Brown SA, Shen M, Doub WH, Cai B, Sadrieh N, Chen ML, Machatha S, Buhse LF (2009) Evaluation of substrates for 90 peel adhesion – a collaborative study. II. Transdermal drug delivery systems. J Biomed Mater Res 88B: 61–65.

Wokovich AM, Prodduturi S, Doub WH, Hussain AS, Buhse LF (2006) Transdermal drug delivery system (TDDS) adhesion as a critical safety, efficacy and quality attribute. Eur J Pharm Biopharm 64: 1–8.