The effect of adhesive dressing edges on cutaneous irritancy and skin barrier function

Objective: To assess the effect of repeated application and removal of adhesive edges from wound-care products on cutaneous irritancy and barrier function in normal volunteer subjects.

Method: This was a study using a 'repeat-insult patch test'. Adhesive edges from six commonly used wound-care products were applied continuously to the same site (six applications over a 14-day period) in 30 normal volunteer subjects. The test sites were assessed clinically before product reapplication using established ranking scales for cutaneous erythema. The cumulative irritancy score (CIS) for each test site was determined by adding the erythema scores at days 3, 5, 8, 10, 12 and 15. At the study end the barrier function of each test site was assessed by measuring transepidermal water loss (TEWL).

Results: The CIS showed that the products fall into two distinct groups, with Mepilex, Tielle and Allevyn giving low scores and Biatain, Comfeel and DuoDERM higher scores. Statistical analysis indicated significant differences (p<0.05) between Mepilex and Biatain, Mepilex and Comfeel, Mepilex and DuoDERM, Tielle and Biatain, Allevyn and Biatain. The mean TEWL values also indicated that the products fall into two distinct groups: Mepilex, Tielle and Allevyn with low mean values close to that of normal adjacent back skin and Biatain, Comfeel and DuoDERM with much higher mean values. Statistical analysis indicated that Mepilex, Tielle and Allevyn were not significantly different from normal skin (p<0.05), whereas Biatain, Comfeel and DuoDERM were significantly higher than normal skin and the other products tested.

Conclusion: The results show clear differences between products; the clinical scores and TEWL measurements indicate that the products fall into two distinct groups. This novel approach seems able to discriminate between adhesive borders and may be useful during product development and in selecting products for clinical trials.

Declaration of interest: This study was supported by a research grant from Mölnlycke Health Care AB, Göteborg, Sweden.

Method

Subjects

This study was conducted using healthy volunteers and was undertaken at Cutest Systems, Cardiff. Ethical approval was obtained from the Cardiff Independent Research Ethics Review Committee.

Thirty normal, healthy volunteer subjects — 12 male and 18 female, mean age 58 years (range 43–74) — were recruited from the test panel of Cutest. The written, informed consent of each volunteer was obtained.

References


P.J. Dykes, BSc, PhD, Director, Cutest Systems, Cardiff, UK.
Email: peter.dykes@cutest.co.uk
obtained and a medical history and examination were undertaken to ensure each subject was in good health before participation. Subjects using concomitant medications likely to interfere with the study, those with any history or presence of allergy or skin disease, females who were pregnant or lactating or likely to become pregnant, and those known to be intolerant to adhesive tapes were excluded.

**Study design**

The study design was that of a 'repeat-insult patch test', which maximises the cutaneous insult and is designed to reveal low orders of irritancy.

The test site was the lower part of the back between the iliac crest and the lower costal margin, avoiding the area over the vertebral column. This was an open study and the six test products were randomly allocated to the test sites. Each of the products was removed and reapplied every two to three days. Fresh applications of the test products and tape were made at each of these time points. The test sites were assessed clinically before reapplication using established ranking scales for cutaneous erythema. Cumulative irritancy scores (CIS) for each test site were determined by adding the erythema scores on days 3, 5, 8, 10, 12 and 15.

At the end of the study, the barrier function of each test site was assessed by measuring TEWL. This was to provide objective data to support the subjective clinical assessment.

From day 5 of the study the test products were covered with non-occlusive Scanpor tape (Alpharma AS, Norway) because, in a minority of subjects, accidental removal of some products was occurring. The Scanpor tape was 5 x 5cm and completely covered the test product.

**Test products — application and removal**

The adhesive edges from six adhesive dressings were tested. The test products chosen represent different types of products and are currently in use clinically. The products were:

- Mepilex Border Lite (MÖlnlycke)
- Allevyn Adhesive (Smith & Nephew)
- Biatain Adhesive (Coloplast)
- Tielle Plus (Johnson & Johnson)
- DuoDERM ET (Convatec)
- Comfeel Plus Transparent (Coloplast).

The adhesive borders were applied directly to the skin surface. Approximately 2.5 x 2.5cm areas of adhesive edge were applied to the test sites. Where the adhesive border was less than 2.5cm wide, two parallel strips of adhesive border were used to cover an equivalent area.

The materials were applied, removed and reapplied repeatedly under occlusion to the same site over a 14-day period, with removal and reapplication every two to three days.

All test products were removed carefully using the same peeling motion and not necessarily according to the manufacturer's instructions for use in a clinical situation (in order to standardise the procedures for all products). The sites were assessed after a minimum of 10 minutes to allow any skin reactions resulting from the removal process to subside.

**Clinical assessment of erythema**

The test sites were assessed clinically for cutaneous irritation at product re-application by trained study nurses who routinely carry out repeat-insult patch tests on a day-to-day basis.

The primary sign of cutaneous irritancy was taken to be erythema, and this was assessed using an established 0-6 ranking scale for cutaneous erythema. In this scale a grade 2 reaction (moderate, uniform erythema) is considered a noteworthy indication of cutaneous irritancy. The assessment was observer-blinded in that the study nurse carrying out the assessments was unaware of the product allocation. If a grade 2 or greater reaction was recorded and application of study material stopped, a score of grade 2 or higher was used at subsequent time points in the data analysis.

**Transdermal water loss measurement**

Transdermal water loss was measured using a Tewameter (Courage & Khazaka, GmbH) in accordance with the manufacturer's instructions and published guidelines on TEWL measurement. Measurements were taken at the end of the study one hour after removal of the test products. Control measurements were made at adjacent normal skin sites that were untreated. The delay in measurement was to enable evaporative loss of any surface moisture present due to the covering of the skin surface.

**Statistical analysis**

The study design was a within-subject comparison of six adhesive edges. The main variables were the CIS and TEWL measurements.

To avoid assumptions about the normality of the data, analysis was carried out using a non-parametric Friedman two-way ANOVA procedure, followed by a multiple comparison procedure based on the Tukey HSD test. All statistical analyses were done using Unistat for Windows version 5.5. Differences were considered significantly different if p<0.05.

**Results**

The median CIS values and 75% quartiles are illustrated in Fig 1. There was a high number of zero values for the CIS and the median values were low or even zero in some cases. Nonetheless, differences were apparent in the clinical scores, with products
Table 1. Mean TEWL plus standard deviation

<table>
<thead>
<tr>
<th>Subject</th>
<th>Mepilex</th>
<th>Tielle</th>
<th>Allevyn</th>
<th>Biatain</th>
<th>Comfeel</th>
<th>DuoDERM</th>
<th>Normal adjacent skin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>7.78</td>
<td>10.87</td>
<td>14.92</td>
<td>60.78</td>
<td>56.68</td>
<td>49.88</td>
<td>9.10</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>2.97</td>
<td>10.20</td>
<td>10.98</td>
<td>21.71</td>
<td>24.11</td>
<td>22.82</td>
<td>2.63</td>
</tr>
</tbody>
</table>

falling into two distinct groups (Mepilex, Tielle and Allevyn in one group and Biatain, Comfeel and DuoDERM in the other). Statistical analysis indicated significant differences between treatments at \( p < 0.05 \). The following pairs are significantly different \( (p < 0.05) \): Mepilex versus DuoDERM; Mepilex versus Comfeel; Mepilex versus Biatain; Tielle versus Biatain; Allevyn versus Biatain.

An alternative way of expressing the results of a repeat-insult patch test is to determine the number of subjects with a CIS score of 1 or more. When analysed in this way, the result is very similar, with the products again falling into two distinct groups (Fig 2). The mean TEWL values plus standard deviation are given in Table 1. The results indicate the products fall into two distinct groups. Mepilex, Tielle and Allevyn have low mean values close to that of normal adjacent back skin, while Biatain, Comfeel and DuoDERM have much higher mean values. Statistical analysis indicated that Mepilex, Tielle and Allevyn were not significantly different from normal skin \( (p < 0.05) \), whereas Biatain, Comfeel and DuoDERM were significantly higher than normal skin and higher than the other products tested.

Discussion

The results clearly show there are differences between adhesive borders in terms of their potential for skin damage following repeated application to normal skin. Both markers of skin damage (CIS and TEWL) showed similar differences between products, which appeared to fall into two distinct groups, with Mepilex, Tielle and Allevyn causing less damage to the skin than Biatain, Comfeel and DuoDERM.

The reasons for the differences observed are by no means certain, and there are several possible explanations. There may be differences in the chemistry of the adhesives used and thus in the release of potentially irritant molecules. Information on the chemistry of the adhesive used is not in the public domain as it is commercially sensitive.

Alternatively, bacterial overgrowth may occur with long-term occlusion, resulting in the release of toxins that may damage the skin surface. Although the test sites were not totally occluded, they were covered for a 14-day period and changes in the skin microflora may have taken place.

However, the most likely explanation is that the adhesive edges used were removing part of the stratum corneum, so-called skin stripping.

Removing and replacing the test products two to three times a week is probably more frequent than occurs in clinical practice and may well magnify the effect of stratum corneum removal. Previous studies have shown that variable amounts of stratum corneum are removed after one or three application-and-removal cycles of wound-care adhesive products.9
Furthermore, skin stripping leads to functional loss of the skin barrier, as shown by increased TEWL..

The relevance of normal volunteer studies to the clinical situation has to be considered. Although the two- to three-day schedule of a repeat-insult patch test may be similar to that in clinical use, the peri-wound skin may be abnormal, both structurally and in the way it responds to external stimuli. In addition, the way the dressings are removed in a clinical situation may be different from that used here.

Nevertheless, volunteer studies may have some relevance, as shown by a recent publication comparing the effects of adhesive dressings on normal forearm skin and peri-ulcer skin. Four adhesive dressings were applied to peri-ulcer skin and normal forearm skin over a 14-day period in patients with open or healed venous leg ulcers. Transepidermal water loss measurement showed very similar responses on the forearm and peri-ulcer skin, with hydrocolloid adhesives showing much greater changes than soft silicone or polyurethane adhesives.

**Conclusion**

These results show clear differences between products. The CIS and TEWL measurements indicate that the products fall into two distinct groups, with Mepilex, Tielde and Allevyn causing less damage to the skin surface than Biatain, Comfeel and DuoDERM. The novel approach of using a repeat-insult patch test seems to be able to discriminate between adhesive borders and may be useful during product development and in selecting products for clinical trials.

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**Bulletin board**

**Joint approach to cost-effective medicines**

The UK government and the pharmaceutical industry have launched a joint strategy to support the better use of cost-effective medicines.

The Long-term Leadership Strategy is led by a group comprising government ministers, officials and key figures in the pharmaceutical industry. Its focus is on three areas:

- The Partnership Working Group aims to improve relations between the NHS and industry to support the better use of cost-effective innovation, particularly in relation to medicines. It will be developing tools to support this.
- The European Working Group provides a mechanism for government and industry to develop proposals to assist the aims of the European Commission’s Pharmaceutical Forum to improve European effectiveness.
- Key areas include pricing, relative effectiveness and patient information.

- The Regulatory Working Group is considering what is needed to improve the effectiveness of the regulation of medicines.

Its recommendations relate to all stages of the regulatory process, starting with the way new drugs are developed, developing new opportunities for industry and the regulator to debate the way new drugs are developed, and improving mechanisms for monitoring safety of medicines.


**New clinic opens in Rochester**

A wound care clinic has been opened by local MP, Robert Marshall-Andrews, in Rochester, North Kent.

The clinic will provide specialist holistic wound assessment and care for patients who were previously seen by GPs and practice nurses, community nurses, minor injury unit staff and podiatrists.

Benefits to patients include appointment times to suit their lifestyle and commitments, prompt and efficient referrals, and earlier discharge.

It is anticipated that this will result in fewer hospital re-admissions.

Claudia Parnell, Lead Nurse Tissue Viability at Medway Primary Care Trust, helped to set up the clinic.

Speaking at the opening, she said, 'All the time and effort involved in consulting and creating the new clinic has been worthwhile.'

'We have seen a complete transformation of the way we assess our patients’ needs and they now get better care much faster and hospital visits or stays have been considerably reduced.'

'The whole project is vital not just to the local community of Medway, but to the wider population as a whole.'