An evaluation of five different dressing materials on split-thickness skin graft donor site and full-thickness cutaneous wounds: an experimental study

Muhammet Uraloğlu¹, Murat Livaoğlu¹, Özgür Agdoğan¹, Sevdeğül Mungan², Etem Alhan³ & Naci Karaçal¹

¹ Department of Plastic and Reconstructive Surgery, Faculty of Medicine, Karadeniz Technical University, Trabzon, Turkey
² Department of Pathology, Faculty of Medicine, Karadeniz Technical University, Trabzon, Turkey
³ Department of General Surgery, Faculty of Medicine, Karadeniz Technical University, Trabzon, Turkey

Key words
Dressing; Full-thickness cutaneous wounds; Split-thickness skin graft donor site

Correspondence to
M Uraloğlu, MD, Karadeniz Teknik Üniversitesi Tip Fakültesi, Farabi Hastanesi Plastik Cerrahi Anabilim Dali, Trabzon 61080, Turkey
E-mail: uraloglu@hotmail.com
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Abstract
The objective of this study was to investigate the healing effect of five different products on split-thickness skin graft (STSG) donor sites and full-thickness cutaneous wounds (FTCWs) using an occlusive dressing model. Six groups were included: 1 control and 5 experimental groups, with a total of 24 rats, using an occlusive dressing model. STSG donor sites and FTCWs were established in two separate areas, to the right and left on the animals’ backs. Wound sites were dressed with one of the following materials: fine mesh gauze, microporous polysaccharide hemosphere (MPH), clinoptilolite, alginate, hydrogel or biosynthetic wound dressing (Biobran®). These materials were compared in terms of healing rate, healing quality and histopathological findings. Occlusive dressings were applied to each wound on days 0, 3, 5, 7, 10 and 14. Area measurements were taken using images of each dressing. The alginate and clinoptilolite groups gave the best healing rate results for both STSG donor sites ($P = 0.003$) and FTCWs ($P = 0.003$). MPH came third in each group. The alginate group produced better results in terms of healing quality criteria, followed by hydrogel, MPH, clinoptilolite and Biobran®, in that order. Statistically significant results were obtained in all groups compared to the control group ($P < 0.0007$). Rapid and good healing quality for both the STSG donor sites and FTCWs were obtained with alginate. Healing with clinoptilolite and MPH was rapid, but poor quality, while slower but good healing quality was obtained with hydrogel. Slower and worse quality healing was obtained with Biobran®.

Introduction
As the donor site represents a new defect following the harvesting of a thin skin graft, it leads to morbidity and therefore requires good wound care (1). Dressings must protect the wound and accelerate healing, extend changing intervals, reduce the risk of local and systemic infection and pain and also be cost-effective and non-allergic (1–4).

Wound dressings may be non-occlusive, semi-occlusive or occlusive (3). Semi-occlusive and occlusive dressings support re-epithelialisation, reduce pain and healing time and absorb blood and tissue fluids, and prevent fluid loss and mechanical trauma and exogenous contamination (4). The main semi-occlusive and occlusive dressing materials are...
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paraffin gauze, alginites and hydrocolloid, foam and hydrofiber dressings (4,5).

We selected products with different properties from different groups capable of use in split-thickness skin graft (STSG) donor sites and full-thickness cutaneous wounds (FTCWs). Microporous polysaccharide hemispheres (MPH), clinoptilolite and alginate are used as hemostatic dressing materials in vascular surgery in the literature (1,6,7), but their effects on wound healing have not been comprehensively studied before.

This experimental study was designed in order to evaluate MPH, clinoptilolite, alginate, hydrogel and Biobrane® in STSG donor sites and FTCWs.

Materials and methods

The study was approved by the local Ethics Committee. Twenty-four female Sprague-Dawley rats weighing 250–300 g were used. These were housed in rooms maintained at 21 ± 1°C and in a 12:12 light : dark cycle. Animals were fasted overnight before the experiment, but had free access to water. Care was provided in accordance with Ethics Committee guidance. One control group and five experimental groups were planned. Four rats with two wound sites each were examined for STSG donor sites and FTCW groups for each product:

1. fine mesh gauze (control group);
2. MPH (Traumadex®, Medafor, Inc., Minneapolis, MN);
3. clinoptilolite (Froximun®, Froximun AG, Schlanstedt, Germany);
4. alginate (Kaltostat®, ConvaTec, Princeton, NJ);
5. hydrogel (Elastogel®, Southwest Technologies Inc., N. Kansas City, Kansas);
6. biosynthetic wound dressing (Biobrane®, Bertek Pharmaceuticals Inc., Morgantown, WV).

General anaesthesia was administered with intraperitoneal 50 mg/kg ketamine and 10 mg/kg xylazine. Areas of 2 cm × 6 cm in size were shaved on the right and left of the back. The central, healthy area was left untouched, the two areas to the right and left being investigated. The dorsum was disinfected, and STSG sites 4 cm × 2 cm in size were obtained from the two sites using a hand dermatome and had the same thickness (0.2 mm) (8) (Hand Dermatome, Aesculap, Germany). A bilateral 1.0-cm² area of skin and panniculus carnosus was excised in the caudal direction, creating a full-thickness dorsal excisional wound (9) (Figure 1).

Isotonic-saline-embedded tie-over dressings were applied to the control and experimental groups using wound-care products on days 0, 3, 5, 7, 10 and 14 for each group and all bilateral dorsal wound areas. New closed dressings with the appropriate group materials were applied on each specified day to the eight STSG donor sites and eight FTCW sites. Images of every dressing, taken from the same distances (Figures 2 and 3), were loaded onto the Image J (1.42q, Wayne Rasband National Institutes of Health, Bethesda, Maryland) program, and donor and FTCW sites were measured. All rats were euthanised by cervical dislocation.

The dressing materials were compared according to the following criteria:

Figure 1 Sites for dressing were established. Split-thickness skin graft (STSG) donor site and full-thickness cutaneous wound (FTCW) extending to the cephalic area from the cranial on the right and the left.

Figure 2 Appearance on the third day after dressing.
Figure 3 Appearance on the tenth day.

1. Healing rate: Level of sites with no epithelialisation over time.
2. Healing quality: Vascularity (10), clinical findings of infection, erythema, induration, purulent discharge or unpleasant odour and fibrinous wound appearance (5,11).
3. Histopathological findings: Masson Trichrome and haematoxylin-eosin stains were applied in each group.

Vascularity was evaluated using orthogonal polarisation spectral (OPS) imaging (12–14). Donor sites and FTCWs were examined on dressing day 10. The OPS video microscope (Cytoscan A/R, Cytometrics, Philadelphia, PA) was attached to a moveable shaft and microcirculation was recorded over at least 20 seconds (Figure 4). Images were stored in AVI format on the computer (Sony VGN-FW 230J/H). Video sequences were performed for each and transferred from the OPS imaging device to computer software (CapiScope®, Lekam Medical Ltd., Devon, UK) for further evaluation. The required measurements (functional capillary density) were performed using this software (12). Functional capillary density (FCD) was defined as the length of red blood cell-perfused capillaries (cm) per observation area (cm²). We thus selected FCD as the parameter for measuring the microcirculation.

Macroscopic appearance of wounds was scored by six blinded members of the staff (four assistant professors and two residents) from the plastic surgery unit that participated in the application of the five materials studied (from 0, an infected, fibrinous wound, to 10, a clean wound appearance).

Statistical analysis

Group comparisons for each time point were performed using Kruskal–Wallis analysis of variance (post hoc Bonferroni corrected Mann–Whitney U-test).

Results

MPH, a material with a granular structure, was statistically significantly better in donor site and FTCW healing rate compared to the control group, the best result after the alginate and clinoptilolite groups. FCD values were at the highest level in FTCW dressings and were statistically significant. Histopathologically, there were greater inflammation, collagen formation and fibroblast proliferation. Foreign body reaction and giant cells were also observed (Figure 5). Macroscopically, it was one of the three groups with the highest wound appearance scores.

Clinoptilolite, with a granular structure, gave statistically significant good results in donor site healing. It exhibited the best performance in the FTCW site, and the defect dimension was significantly better compared to the control group on day 14. It represented the group with the best macroscopic wound appearance. Microscopically, inflammation was low.
but collagen formation and fibroblast proliferation were high (Figure 6). Multinuclear giant cells were more pronounced compared to those of MPH group. It was one of the groups with the lowest FCD values.

Microscopically, inflammation, collagen formation and fibroblast proliferation were low (Figure 7) with alginate, which represented one of the best groups, especially for re-epithelialisation. Macroscopically, it provided a clean wound appearance. FCD values were lower than those of the clinoptilolite group, one of the best performing groups.

The result of hydrogel in donor site dressing was significant on day 10, but it did not exhibit a good performance in FTCW. No expansion in FTCW was observed on the first day. Macroscopically, the wound had a fibrous, moist appearance. Microscopically, inflammation, collagen formation and fibrosis were lower compared to the other groups (Figure 8).

Biobrane® exhibited the worst performance in terms of healing rate. At donor site FCD investigation, the lowest value was obtained in this group and this was statistically significant, despite a fibrinous wound appearance. Infection was observed in two sites in the Biobrane® group. *Staphylococcus aureus* grew in the wound cultures taken for microbiological examination. Microscopically, collagen tissue and inflammation were higher in this group (Figure 9).

**Healing rate**

At investigation of the STSG donor site, statistically significant faster healing compared to the control group was observed on the fifth day in the alginate and clinoptilolite groups ($P < 0.0005$) and on the seventh and tenth days in the alginate, clinoptilolite and MPH groups ($P < 0.0005$, $P = 0.003$) (Table 1, Figure 10).
Figure 9 Biobran®: Mild hyperkeratosis in the epidermis, rete elongation, increased fibrosis in the dermis and severe chronic inflammatory cell infiltration [Haematoxylin-Eosin (H&E) ×100].

In the FTCW site, statistically significantly rapid healing was observed on the 7th day in the alginate group \( (P = 0.001) \) and on the 14th day in the alginate and clinoptilolite groups \( (P = 0.003) \) (Table 2, Figure 11). Statistically significant healing was obtained in all groups compared to the control group \( (P < 0.0007) \).

Healing quality

FCD measurements in the donor site using OPS imaging were statistically significantly low in the Biobran® group \( (P = 0.011) \). In the FTCWs, significantly high FCD values were determined in the MPH group \( (P = 0.041) \) (Table 3).

Macroscopically, wounds had a cleaner and better healing appearance in the alginate, clinoptilolite and MPH groups compared to the control group. Wounds in the Biobran® and hydrogel groups were worse, more fibrinous and had an unclean appearance. The differences were not statistically significant (Table 3).

Table 1 STSG donor site area measurements (mm²): results of comparison between groups*

<table>
<thead>
<tr>
<th></th>
<th>Day 0</th>
<th>Day 3</th>
<th>Day 5</th>
<th>Day 7</th>
<th>Day 10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fine mesh gauze</td>
<td>274.7 ± 83.8</td>
<td>179 ± 70.5</td>
<td>121.5 ± 23</td>
<td>72.6 ± 17.5</td>
<td>12.2 ± 14.3</td>
</tr>
<tr>
<td>MPH</td>
<td>316.8 ± 90.1</td>
<td>224.8 ± 71.5</td>
<td>84.5 ± 24.6</td>
<td>21.8 ± 25.2</td>
<td>0</td>
</tr>
<tr>
<td>Clinoptilolite</td>
<td>300.8 ± 110</td>
<td>173.4 ± 84.5</td>
<td>58.2 ± 22.4</td>
<td>8.6 ± 18</td>
<td>0</td>
</tr>
<tr>
<td>Alginite</td>
<td>346.9 ± 57.2</td>
<td>126.4 ± 26.4</td>
<td>9 ± 11</td>
<td>3.4 ± 6.1</td>
<td>0</td>
</tr>
<tr>
<td>Hydrogel</td>
<td>331.4 ± 151</td>
<td>282 ± 155.9</td>
<td>175.2 ± 55.5</td>
<td>89.3 ± 47.4</td>
<td>11.3 ± 3.2</td>
</tr>
<tr>
<td>Biobran®</td>
<td>289.2 ± 59.4</td>
<td>188.5 ± 60.5</td>
<td>128.5 ± 40.1</td>
<td>85.5 ± 61.5</td>
<td>53.5 ± 53</td>
</tr>
</tbody>
</table>

\( P = 0.443 \) \( P < 0.0005 \) \( P < 0.0005 \) \( P = 0.003 \)

*Statistical significance was obtained for eight measures, and the values are expressed in bold.

Table 2 Full-thickness cutaneous wound (mm²) measurements by day*

<table>
<thead>
<tr>
<th></th>
<th>Day 0</th>
<th>Day 3</th>
<th>Day 5</th>
<th>Day 7</th>
<th>Day 10</th>
<th>Day 14</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fine mesh gauze</td>
<td>97.1 ± 15.1</td>
<td>97 ± 23</td>
<td>86.1 ± 26.2</td>
<td>103.5 ± 18.4</td>
<td>73.3 ± 45.4</td>
<td>35.8 ± 35.3</td>
</tr>
<tr>
<td>MPH</td>
<td>107.4 ± 19.3</td>
<td>95.6 ± 15.5</td>
<td>85.4 ± 14.3</td>
<td>78.5 ± 9.7</td>
<td>42.6 ± 12.1</td>
<td>18.1 ± 7.7</td>
</tr>
<tr>
<td>Clinoptilolite</td>
<td>106.7 ± 14.9</td>
<td>88.7 ± 25</td>
<td>81.9 ± 28.6</td>
<td>78.6 ± 30.5</td>
<td>42 ± 23.1</td>
<td>56 ± 6.2</td>
</tr>
<tr>
<td>Alginite</td>
<td>111 ± 12.6</td>
<td>-</td>
<td>82.4 ± 12.5</td>
<td>70 ± 10.8</td>
<td>33.9 ± 7.8</td>
<td>12.8 ± 10.6</td>
</tr>
<tr>
<td>Hydrogel</td>
<td>106.3 ± 12</td>
<td>147.6 ± 45.1</td>
<td>140.7 ± 39.8</td>
<td>137 ± 25.1</td>
<td>84.5 ± 90</td>
<td>36.1 ± 54.7</td>
</tr>
<tr>
<td>Biobran®</td>
<td>93.5 ± 5.9</td>
<td>97.8 ± 30.2</td>
<td>76.8 ± 21.8</td>
<td>53.1 ± 19.7</td>
<td>39.1 ± 11.4</td>
<td>26.5 ± 12.1</td>
</tr>
</tbody>
</table>

\( P = 0.146 \) \( P = 0.088 \) \( P = 0.001 \) \( P = 0.325 \) \( P = 0.003 \)

*Statistical significance was obtained for three measures, and the values are expressed in bold.
Inflammation was lower in the alginate, clinoptilolite and hydrogel groups in particular and higher in the MPH and Biobran® groups.

Fibroblast proliferation, collagen formation and granulation tissue were greater in the MPH, clinoptilolite and Biobran® groups. Foreign body reaction and multinuclear giant cells were observed in the clinoptilolite group compared to the MPH group. Fibrotic parameters were particularly lower in the alginate group.

Re-epithelialisation was better in the alginate, MPH and hydrogel groups. Neovascularisation was at similar levels in all groups.

Discussion

Dressing materials are mainly classified as occlusive, semi-occlusive or non-occlusive and include a broad spectrum of chemical and physical structures (3). The first two provide the best protection against dehydration, contamination and mechanical trauma, which therefore facilitates healing. The use of occlusive or semi-occlusive dressings, which provide a moist environment, is known to lead to earlier completion of epithelialisation (15–18). Wound healing is a complex process in which inflammation, formation of granulation tissue, production of new structures and tissue remodelling all play a part. Inadequate angiogenesis, epithelial migration and wound contraction can all make wound healing problematic (16).

Inflammation in these groups was lower than in the hydrogel groups, particularly in the alginate and clinoptilolite groups. Foreign body reaction and multinuclear giant cells were also lower in the alginate and clinoptilolite groups. Histopathological examination showed the presence of multinuclear giant cells in the hydrogel group in particular, because of phagocytosis by macrophages. Although MPH can absorb excess fluid, it still maintains a moist wound environment. It has also been reported that MPH acts as a haemostatic agent following release of calcium ions essential for clotting cascade, and that it establishes a gel–fibre matrix that facilitates clotting and permits the dressing to be removed in a trauma-free manner (22). Among its advantages are ease of application, maintenance of a moist wound environment, potential haemostatic properties, and excess wound fluid absorption. Alginate is not an antimicrobial dressing, although it may assist with reducing the possibility of infection because it contains considerable quantities of exudate and traps micro-organisms and cell debris in the gel–fibre matrix (23,24).

Hydrogel consists of 95% water, meaning that it cannot absorb excess water and is therefore suitable for dry wounds or those with minimal drainage. It does not adhere to the wound, and cools the skin surface to 5°C, subsequently maintaining that low temperature. These effects reduce inflammatory response (25). Hydrogel is suitable for first- and second-degree burns, grade 1 and 2 bed sores, superficial epithelium defects, skin abrasions and fine-thickness graft donor sites (1,26).

Biobran® is a biosynthetic wound dressing that consists of a silicone film with a nylon mesh embedded into the film (27). This mesh is covered by a layer of porcine collagen which attaches to the dressing to maintain a moist wound environment.

Histopathological findings

Histopathological examination showed the presence of multinuclear giant cells in the hydrogel group in particular, because of phagocytosis by macrophages. Although MPH can absorb excess fluid, it still maintains a moist wound environment. It has also been reported that MPH acts as a haemostatic agent following release of calcium ions essential for clotting cascade, and that it establishes a gel–fibre matrix that facilitates clotting and permits the dressing to be removed in a trauma-free manner (22). Among its advantages are ease of application, maintenance of a moist wound environment, potential haemostatic properties, and excess wound fluid absorption. Alginate is not an antimicrobial dressing, although it may assist with reducing the possibility of infection because it contains considerable quantities of exudate and traps micro-organisms and cell debris in the gel–fibre matrix (23,24).

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Biobran® is a biosynthetic wound dressing that consists of a silicone film with a nylon mesh embedded into the film (27). This mesh is covered by a layer of porcine collagen which attaches to the dressing to maintain a moist wound environment.
Studies have shown that Biobrane® is an effective and low-trauma dressing for children with superficial partial-thickness burns, and that it does involve increased outpatient burn-care costs (28). Infection rates as high as 10.7% have been reported; however, levels of scarring for infected areas were not significantly worse than the levels for non-infected burns (29). Other studies have reported no rises in infection in partial-thickness burns dressed with Biobrane in children of all ages (30). In our study, no infection was observed in any site or group, although infection was seen in two FTCW sites in the Biobrane® group.

The use of orthogonal polarisation imaging has been recommended for recording and quantifying changes in the microcirculation (12). OPS (11–13) imaging has been used for non-invasive real-time observation of functional microvascular networks. Arterioles, venules and capillaries can be directly visualised, and the movement of individual blood cells through them can be observed. The technique uses optical filtration of polarised light that is absorbed by haemoglobin so that red blood cells appear dark. FCD, identified as the best parameter for the measurement of the microcirculation, was defined by Messner (12). Elevated FCD in the early period may be regarded as a positive characteristic in terms of healing speed, but negative in terms of healing quality in the late stage.

We examined wound closure in rats after the application of six different dressing materials. Our aim was to investigate the effect of an occlusive dressing model, frequently employed in plastic surgery departments, on STSG donor site and FTCW site healing.

The alginate and clinoptilolite groups gave the best results for both donor site and FTCW. MPH followed in third place for both groups. There are no previous studies regarding the effect of MPH, clinoptilolite and alginate on wound healing. This study evaluated their effects on wound healing. Alginate provided rapid and good-quality healing. Rapid but lower-quality healing was obtained with clinoptilolite and MPH, while healing with hydrogel was slower, but of better quality. Slower and lower-quality healing was obtained with Biobran®. However, healing in both wound types was evaluated as successful in all groups compared to the control group.

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### References

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