

## A Randomized Trial of Two Occlusive Dressings in the Treatment of Leg Ulcers

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Two occlusive dressings – one zinc oxide medicated (Mezinc®) and one hydrocolloid (Duoderm®) – were compared in a prospective, randomized trial over a period of 8 weeks to determine their healing ability and effect on pain for venous and arterial leg ulcers. All patients were patch-tested before the study and colophony allergy was an exclusion criterion. Of the 43 outpatients included, 31 completed the trial and 6 patients randomized to each treatment group were withdrawn. The initial ulcer areas decreased after 8 weeks of treatment with Mezinc® by 64% and by 48% after treatment with Duoderm®. Ulcer pain was relieved in 50% of the patients – with a similar analgesic effect for the two dressings. Mezinc® treatment was discontinued in 2 cases due to sensitization to colophony (one ingredient of Mezinc®) which indicated a risk of contact allergy to colophony due to Mezinc® treatment. 1103 consecutive eczema patients were patch-tested on the back with Mezinc® and colophony 20% in petrolatum simultaneously. It was found that 42 (4%) of the patients showed allergic skin reactions to colophony and 19 (2%) to Mezinc®. Both dressings were well tolerated by leg ulcer patients and there appeared to be no major differences in the efficacy of the two occlusive dressings. *Key words:* Contact dermatitis; Colophony; Gum rosin.

(Accepted November 13, 1989.)

Acta Derm Venereol (Stockh) 1990; 70: 231-235.

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Animal experiments have demonstrated that occlusive dressings are superior to air exposure for the healing of both superficial and deep skin wounds (1,2,3). Although all occlusive dressings act as protective membranes and prevent the desiccation of wounds, some have additional properties. For example, substances dissolved from the occlusive hydrocolloid dressing Duoderm® are incorporated in the granulation tissue of rats (3). Duoderm® was compared with a wet-to-dry gauze dressing on full-thick-

ness wounds in rats. In accordance with previous findings, Duoderm® increased wound contraction compared with the gauze dressing (3).

In contrast to the affirmative investigations on laboratory animals, results from clinical evaluations of Duoderm® are inconclusive. In a randomized trial conducted under strictly standardized conditions on 56 patients with venous leg ulcers, the authors found no significant difference between Duoderm® and a plain non-adherent dressing for the healing frequency or healing rate after 12 weeks of treatment (4). Furthermore, Handfield-Jones et al. (5) compared Duoderm® with a plain paraffin gauze dressing in a cross-over trial on 10 venous leg ulcer patients. They too reported a non-significant difference in the healing rate. Although a beneficial therapeutic effect of zinc oxide over placebo has been demonstrated (6), both Eriksson (7) and Robinson (8) failed to show such a beneficial effect of zinc oxide in paraffin bandages compared with Duoderm® in the treatment of leg ulcers. The frequency at which the ulcers were dressed, however, varied (5,7,8). Zinc oxide in another occlusive vehicle, Mezinc®, was found to enhance the healing of leprosy leg ulcers, compared with gauze (9). Pain reduction in leg ulcers has been observed with Duoderm® treatment (10). Hence, this controlled clinical trial was undertaken to compare the effects of Duoderm® and Mezinc® on the healing and on the local pain caused by leg ulcers.

### MATERIALS AND METHODS

#### *Leg ulcer study*

The trial took place from September 1985 to May 1988. The study protocol was approved by the local medical ethics committees of the Universities of Odense and Lund.

Only new outpatients were considered for inclusion. Ulcers were limited to areas measuring between 1 and 100 cm<sup>2</sup>. The ulcers' lowest edges were located in the lower



Table I. Comparability of the two treatment groups for the patients who completed the trial ( $n =$  no. of patients)

	Mezinc ( $n = 16$ )	Duoderm ( $n = 15$ )
Age (years)	73±14	77±9
Sex (F : M)	11 : 5	13 : 2
Systolic blood pressure (mmHg)	149±25	163±29
Etiology (venous:arterial)	14 : 2	14 : 1
Duration of present ulcer (months)		
Median	8	5
Range	2-24	1-68
Initial ulcer status		
Area (cm <sup>2</sup> )	13.7±15.9	11.1±9.1
Granulations	12/12	12/13
Necrosis	3/12	5/13

Variability is given as mean ± SD.

two-thirds of the lower leg and their upper edges were above the malleoli. Multiple ulcers were treated uniformly, but only the largest was monitored. No patient received chemotherapy, glucocorticosteroids or antibiotics systemically at entry. Only patients with negative patch-tests to the two dressings, colophony 20% pet. (Hermal, Reinbek, W. Germany) and polymerized 2,2,4-trimethyl-1,2-dihydroquinoline 0.5% pet. (antioxidant in Mezinc®) were included. Colophony 20% pet. contains a mixture of four types of gum rosin (two types of Portuguese, one Chinese and one American) in equal portions. Each patient's informed consent was obtained before randomization.

According to the clinical evaluation, patients were classified as having either venous or arterial ulcers. In order to avoid influences of time-associated variables and of the type of ulcer (venous/arterial), patients were consecutively matched in pairs within these two groups. The presence of granulations and necrotic material were quantified blindly by one of the investigators (F.B.) from colour slides taken on admission. From sealed envelopes, each member of the pair was randomly allocated to either treatment with Duoderm® or Mezinc®. The occlusive zinc dressing Mezinc® (Mölnlycke AB, Mölnlycke, Sweden; water vapour permeability: 2.5 g/m<sup>2</sup>/h) consists of a PVC-coated cotton fabric and an adhesive compound composed of natural rubber, white mineral oil, Portuguese gum rosin and zinc oxide (25% w/w). The occlusive hydrocolloid dressing Duoderm® (Squibb Inc., Princeton, New Jersey, USA; water vapour permeability: 2.2 g/m<sup>2</sup>/h) is composed of a polyurethane membrane and a polyurethane foam. The foam is laminated with a mixture of polyisobutylene, pectin, gelatin and sodium carboxymethylcellulose. Duoderm® and Mezinc® were applied to the ulcer and to 5 cm and 0.5 cm of surrounding skin, respectively. Absorbent material was laid on top of the dressings in the case of heavily discharging ulcers. A compression bandage (Dauerbinde®, Lohmann, Neuwied, W. Germany) was applied with a standardized technique on venous ulcers. Dressing of the ulcers and bandaging was carried out between clinic visits once

daily during the first 14 days of treatment and thereafter every third day by the district nurses according to written instructions. Loosely attached necrotic material was removed, and ulcers were cleaned with 0.9% (w/v) NaCl at each change of dressing.

'Ulcer healing ability' was assessed at the initial stage and during clinic visits after 2, 4 and 8 weeks of treatment. Ulcerated areas were measured planimetrically on tracings drawn on plastic foil. The relative initial ulcer area change after the entire treatment period was then compared for each patient pair, and the patient showing the highest ulcer area reduction was considered as having the best 'ulcer healing ability'. When both ulcers were completely healed in the same patient pair, a shorter healing time was regarded as superior 'ulcer healing ability'. If the treatment was discontinued due to an unacceptable dressing-related sideeffect, e.g. unfavorable skin reactions, infection, or a 50% increase in ulcer area, the result was considered extremely poor.

At presentation the patients were asked to rate the type of pain as either constant, intermittent, or absent, and the change in pain after the complete treatment period on a 5-grade scale as: marked relief, moderate relief, unchanged, moderate impairment or marked impairment.

#### Patch-testing

In an additional study, with reference to the risk of contact dermatitis in colophony-sensitive patients treated with Mezinc®, a total of 1103 consecutive eczema patients were patch-tested at Odense Hospital from December 1986 to August 1988 and at Gentofte Hospital from December 1986 to May 1987 with the ICDRG (The International Contact Dermatitis Research Group) standard series (Hermal), supplemented with a patch (1×1 cm) of Mezinc®, Finn Chambers® (Epitest Ltd, Helsinki, Finland) on Scanpor® tape (Norgesplaster A/S, Oslo, Norway) were applied on the back for 48 h and read at 72 h according to the ICDRG recommendations (11). Intensity of the test reaction + to +++ was interpreted as a positive reaction.

## RESULTS

### Leg ulcer study

Forty-three outpatients (35 women and 8 men), aged 75±11 years (mean±SD), entered the trial. Thirty-six patients had ulcers due to venous insufficiency and 7 ulcers were of arterial origin. Twenty-two patients were assigned to Mezinc treatment and 21 patients to the Duoderm treatment. Six patients randomized to each treatment group were withdrawn from the study. The characteristics of the remaining 31 patients who completed the 8-week trial period are shown in Table I.

Mezinc treatment had to be interrupted in 2 patients due to positive patch tests to Mezinc and colophony after 6 and 2 weeks of treatment, respectively, despite percentage ulcer area reductions of 30 and 26%, respectively. However, it was revealed



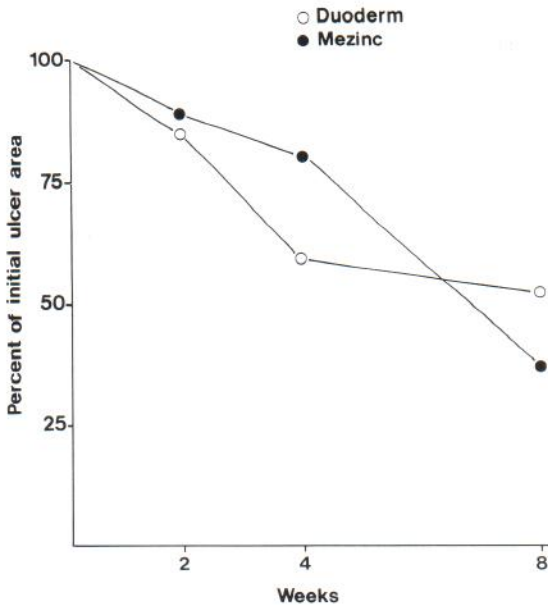


Fig. 1. The course of healing of the ulcers in the 31 patients (16 Mezinc-treated and 15 Duoderm-treated) fulfilling the trial period (median values).

after the termination of this study that Mezinc was incorrectly applied covering >10 cm of intact surrounding non-ulcerated skin as opposed to the recommended <0.5 cm in the patient whose treatment was interrupted after 2 weeks. Another Mezinc-treated patient became bedridden due to a recurring erysipelas and that ulcer increased in size by 12% after 2 weeks. Two Mezinc patients were lost to follow-up because one patient was transferred to another hospital and the other patient died. Severe ulcer pain was the cause of discontinuance of Mezinc treatment in one arterial ulcer patient. Two patients treated with Duoderm were withdrawn from the study after 1 and 4 weeks because of skin irritation of surrounding skin. The ulcer area was reduced by 2% during the 4-week period. One Duoderm patient developed erysipelas requiring oral antibiotic treatment and had a 3% increase in ulcer area in 2 weeks. One venous ulcer treated with Duoderm became gradually necrotic, and the patient was excluded after 4 weeks. An arterial Duoderm treated ulcer was heavily colonized with *Pseudomonas aeruginosa* and increased by 12% after 4 weeks and treatment was changed to an aluminum subacetate solution. Another arterial ulcer treated with Duoderm deteriorated and was covered with fibrin after 1 week.

Four venous ulcers healed completely in each

Table II. Results of pain assessments after the 8-week treatment period (n = no. of patients)

Change of pain	Mezinc (n = 13)	Duoderm (n = 13)
Marked relief	5	3
Moderate relief	1	4
Unchanged	7	5
Moderate impairment		1

group. Overall, the Duoderm ulcers were reduced by 48% in area and the Mezinc ulcers by 64% after the trial period (Fig. 1). The effect of important background variables on healing was evaluated by calculating the Spearman correlation coefficient ( $r_s$ ) between these and the healing rate (= relative reduction of the initial ulcer area expressed as %/week). A statistically significant correlation ( $r_s = -0.63$ ) was found between the systolic blood pressure and the healing rate, whereas there was no significant correlation between the patients age ( $r_s = -0.19$ ), duration of the ulcer ( $r_s = -0.30$ ), or initial ulcer area ( $r_s = -0.14$ ). The two groups were essentially similar regarding these variables (Table I).

At the first examination 82% (33/39) of the patients complained of pain, 82% (27/33) of intermittent pain. Fifty% (13/26) stated that the pain had been relieved partially or totally after the treatment period (Table II).

#### Patch testing

The results of the patch tests for 1103 consecutive eczema patients showed a positive reaction to colophony in 42 patients (4%) and a positive reaction

Table III. Results of patch-testing of 1103 eczema patients expressed as the number of patients with positive and/or negative skin reaction to colophony 20% pet. and/or Mezinc

		Colophony		Total
		Positive	Negative	
Mezinc	Positive	19	6	25
	Negative	23	1055	1078
Total		42	1061	1103

for the simultaneous testing of Mezinc in 25 patients. In 6 of the 25 positive Mezinc patients a selective, weaker positive reaction seemed to be an irritant reaction. Significantly ( $p < 0.01$ ; McNemar's test) fewer positive reactions were found for Mezinc than for colophony (Table III).

## DISCUSSION

The leg ulcer study had originally been designed to result in a test with a high probability (power) for detecting important differences in the patients' 'ulcer healing ability' with the two occlusive dressings. However, the recruitment rate of patients was far below our predictions and therefore the study had to be prematurely terminated. Thus, the number of patients was insufficient to conclude whether there was a significant difference between the two treatments.

The pain reduction achieved by occlusive dressings has been observed earlier (10); however, the mechanism by which occlusive dressings alleviate the pain remains unknown.

Development of exuberant granulation tissue has been reported after Duoderm treatment (10). In rats it was found that Duoderm increased the thickness of granulation tissue twice as much as a gauze treatment did (3). We found hypertrophic granulation tissue in one of our patients, however, this did not seem to impede re-epithelialization. Duoderm treatment was discontinued due to skin irritation caused by leaking exudate in 2 patients.

Mezinc treatment was discontinued due to sensitization to Mezinc and colophony in 2 patients. In a recent Danish series of 2166 eczema patients, 4% showed a positive reaction to colophony 60% pet. (12). Female patients older than 60 years and suffering from leg eczema/leg ulcer showed the highest prevalence (12%) of sensitization to colophony. Thus, application of Mezinc implies a risk of contact dermatitis in leg ulcer patients. Although the total colophony content of Mezinc is 35%, only half of the eczema patients, sensitive to colophony 20% pet., showed positive reactions to simultaneous patch-testing with Mezinc. This finding could be explained by an inactivation and/or inhibited migration to the skin of colophony by the adhesive as Karlberg & Lidén (13) found a concentration-dependent relationship between colophony and the elicitation of positive skin reactions in colophony sensitive patients. However, prolonged application of Mezinc

on eczematous skin, e.g. stasis dermatitis, might possibly elicit an allergic contact dermatitis in a higher percentage of colophony-sensitive patients. Furthermore, the use of Mezinc implies a risk of primary sensitization to colophony. However, a contributing factor in one of the 2 sensitized patients could be that Mezinc extended well over intact surrounding skin, which is against the manufacturer's recommendation.

Our general impression is that the two dressings perform equally well during a period of 8 weeks in the treatment of leg ulcers. However, attention must be paid to signs of skin irritation, ranging from leaking exudate and to colophony sensitization, following Mezinc treatment. In the present study, patients with an established sensitivity to colophony were excluded. However, in ordinary clinical practice, far from all patients are tested, which might involve a risk of more frequent contact allergic reactions to Mezinc, than was found in our study.

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