General & Plastic Surgery Panel of the Medical Device Advisory Committee on Classification of Devices

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Derma Sciences Interest

Of the 417 wound dressing products in the FRO category, 10 are marketed by Derma Sciences Inc. These dressings were cleared, as per FDA's guidance and direction, more than 10 years ago.

Silver containing products	Decision Date	510k #
ALGICELL AG	9/13/2006	K052536
DERMA SCIENCES CALCIUM ALGINATE DRESSING WITH ANTIMICROBIAL SILVER (ALGICELL AG)	6/27/2008	K080497
Honey containing products		
HONEY ALGINATE DRESSING	7/12/2007	K053095
MEDIHONEY WOUND GEL	11/19/2015	K150985
MEDIHONEY WOUND DRESSINGS	6/25/2015	K133279
MEDIHONEY HYDROGEL SHEET DRESSINGS WITH ACTIVE LEPTOSPERMUM HONEY	7/27/2011	K110546
MEDIHONEY GEL DRESSING WITH ACTIVE MANUKA HONEY	2/22/2011	K101793
DERMA SCIENCES OTC MEDIHONEY DRESSINGS WITH ACTIVE MANUKA HONEY	6/19/2008	K081584
DERMA SCIENCES MEDIHONEY DRESSINGS WITH ACTIVE MANUKA HONEY	4/23/2008	K080315
MEDIHONEY PRIMARY DRESSINGS WITH ACTIVE MANUKA HONEY	11/7/2007	K072956

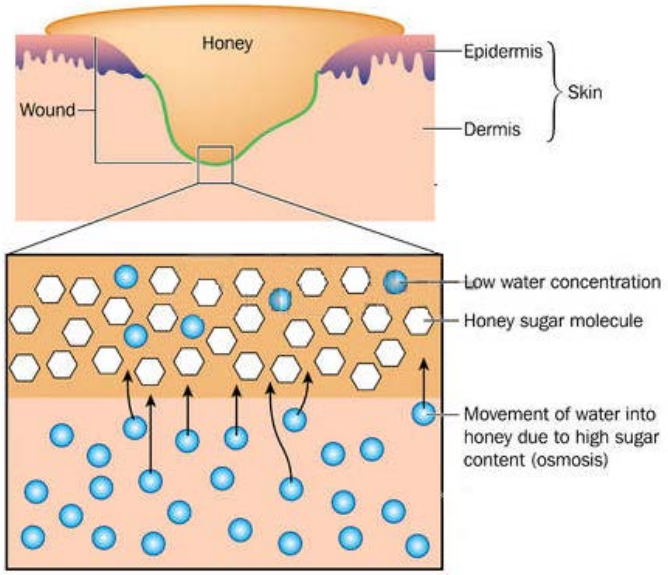
Honey is a naturally occurring food source that has been used for therapeutic benefit for thousands of years. Its clinical use was supplanted as part of everyday wound care practice with the advent of antibiotics until recently.

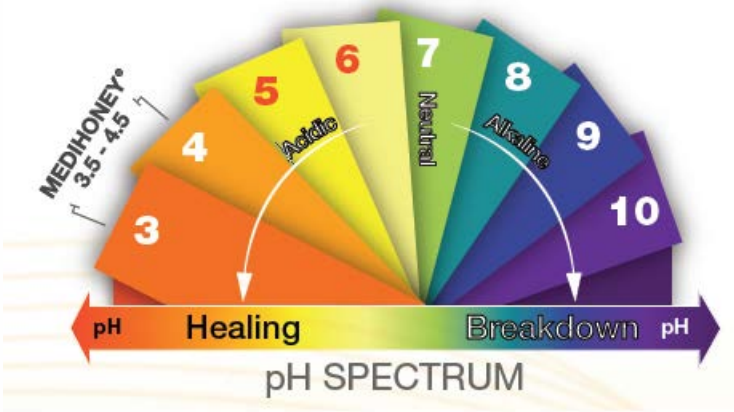
Medical grade, UMF rated, *leptospermum* honey used for the manufacture of various dressing materials, is harvested and prepared under a rigorous set of systems and standards.

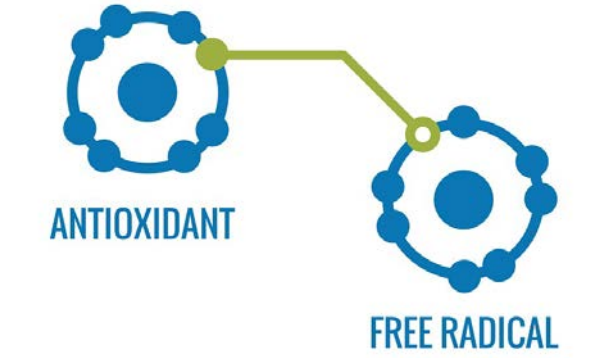
Various physical properties of dressing mechanically cover and protect the wound, help maintain a moisture balance within the wound environment and provide a barrier to environmental contamination.

The addition of honey to dressing substrates however, brings additional positive impact to the wound environment, including:

1. Acidification of the wound
2. Antioxidant effects, and
3. Osmotic potential







The antioxidant donates an electron to the free radical's unpaired electron.

Clinical Evidence - DFU

Kamaratos AV, Tzirogiannis KN, Iraklianou SA, Panoutsopoulos GI, Kanellos IE, Melidonis AI. Manuka honey-impregnated dressings (MHID) in the treatment of neuropathic diabetic foot ulcers. Int Wound J 2014;1(3):259-63.

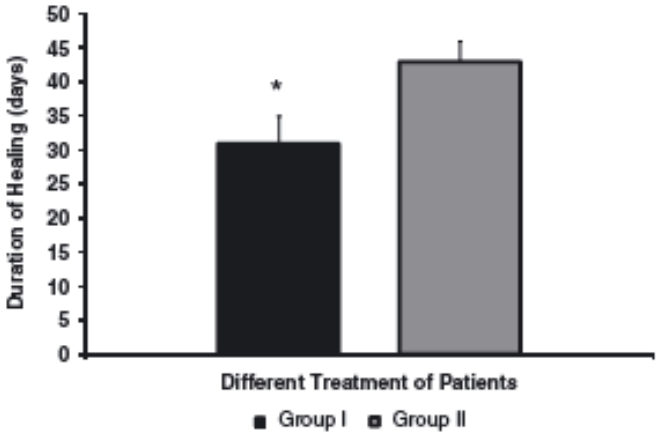
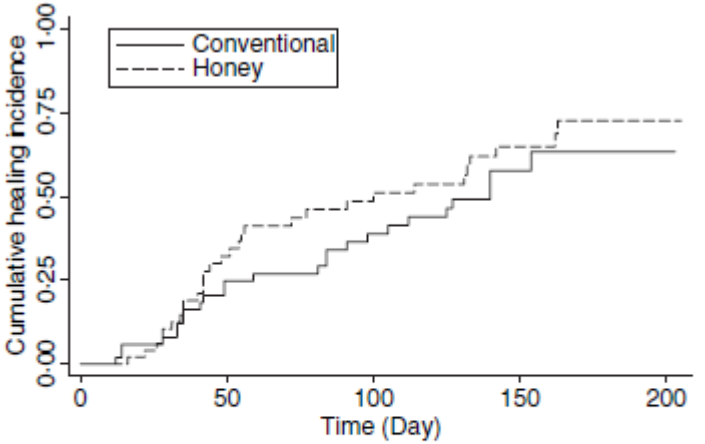


Figure 1. Duration of healing of neuropathic diabetic foot ulcers in diabetic type II patients treated with manuka honey-impregnated dressings (group I) and with conventional dressings (group II). Results represent the findings from 32 patients in group I and 31 patients in group II. Values are expressed as means ± SD. $^{*}P < 0{\cdot}05$ group I versus group II.

- In MHID group of patients, 25 (78%) patients presented with sterile wounds within the 1st week, 5 (15·6%) within the 2nd week and the remaining 2 (6·25%) within 4 weeks. In group II of patients, 11 (35·5%) patients presented with sterile ulcers within the 1st week, 12 (38·7%) patients within 2 weeks, 4 (12·9%) patients within 4 weeks and the remaining 4 (12·9%) patients within 6 weeks.
- None of the patients in group I (honey dressings) needed treatment with antibiotics, while 9 (29%) patients in group II (conventional dressings) needed antibiotic treatment during the follow-up period.

Clinical Evidence – Wounds healing by secondary intent

ROBSON V, DODD S & THOMAS S. Standardized antibacterial honey (Medihoney) with standard therapy in wound care: randomized clinical trial. J Adv Nurs 2009; 65(3), 565–575



Number at risk

Time (Day)	0	50	100	150	200
Conventional	51	36	25	15	1
Honey	50	30	20	12	1

Figure 2 Cumulative healing incidence.

<u>Adverse Events</u>

Of the 105 subjects randomized (52 to honey dressings and 53 to conventional), 1 patient in each group died. Leg ulcers deteriorated in 2 patients in the honey group and 1 patient in the control group.

Safety

Thousands of patients treated over past 10 years without any observed safety issue.

MAUDE and MDR databases demonstrate:

- the most reported issue is stinging upon application
- no infection or superinfection associated with the use of honey impregnated dressings

Acidification of the wound, scavenging of free radicals as well as the osmotic effect of drawing fluids and endogenous enzymes to wound bed from deeper tissues combine to provide an antimicrobial activity at levels of 13-18% phenol (wt/vol)[1].

1. Molan PC. Honey: antimicrobial actions and role in disease management. IN: Ahmad I Aqil, eds. *New Strategies Combating Bacterial Infection*. Wiley-VCH: Weinheim Germany; 2009:229-253.

Resistance to honey is not acquired following continuous exposure to sub-lethal concentrations[2]

Table 2 Induction of resistance to honey and antibiotics

	Initial values		Final values for 'TE resistant' strain		[1]Final values for 'OX/CP resistant' strain	
	MIC[a]	MBC[a]	MIC	MBC	MIC	MBC
S. aureus						
LuBl honey (% w/v)	8.0±0.0	8.0±0.0	8.0±0.0	8.0±0.0	8.0±0.0	8.0±0.0
Active *Leptospermum* honey (% w/v)	5.0±0.0	7.0±0.0	4.8±0.5	6.8±0.5	5.0±0.0	7.0±0.0
Tetracycline (µg)	1.0±0.0	>16*	64±0.0	>64*	[3]32±0.0	>32*
Oxacillin (µg)	0.5±0.0	>16*	[2]16.0±0.0	>32*	32±0.0	>32*
P. aeruginosa						
LuBl honey (% w/v)	13.0±0.0	16.0±0.0	13.0±0.0	15.3±0.5	13.0±0.0	16.0±0.0
Leptospermum honey (% w/v)	14.0±0.0	16.0±0.0	13.5±0.6	16.0±0.0	14.0±0.0	16.0±0.0
Tetracycline (µg)	16.0±0.0	>64*	512±0.0	>1028*	[3]128±0.0	>512*
Ciprofloxacin (µg)	0.5±0.0	4±0.0	[2]16.0±0.0	>32*	32±0.0	>32*

TE = tetracycline; OX = oxacillin; CP = ciprofloxacin

[a,b] MICs and MBCs were determined using the NCCLS broth dilution methods

*Highest concentration tested

[1] OX = oxacillin-induced resistance in *S. aureus*; CP = ciprofloxacin-induced resistance in *P. aeruginosa*

[2] Cross-resistance of the strains with induced tetracycline (TE) resistance to OX (*S. aureus*) or CP (*P. aeruginosa*)

[3] Cross-resistance of the strains with induced OX resistance (*S. aureus*) or CP resistance (*P. aeruginosa*) to TE

2. Blair SE, Cokcetin NN, Harry EJ, Carter DA. The unusual antibacterial activity of medical grade Leptospermum honey: antibacterial spectrum, resistance and transcriptome analysis. Eur J Clin Microbiol Infect Dis 2009;28(10):1199-208

Current Labelling

INDICATIONS

Under the supervision of a healthcare professional, MEDIHONEY (various) dressings provides a moist environment, which is conducive to wound healing, and supports and aids autolytic debridement. These dressings are intended for the management of the following:

- Diabetic foot ulcers
- Leg ulcers (venous stasis ulcers, arterial ulcers and leg ulcers of mixed etiology)
- Pressure ulcers/sores (partial and full thickness)
- 1st and 2nd degree partial thickness burns
- Donor sites, and traumatic and surgical wounds.

CONTRAINDICATIONS

MEDIHONEY (Various) dressing is not indicated for:

- Third degree burns
- Patients with a known hypersensitivity to honey

Conclusion

- Honey containing dressings are safe and effective within their current indications
- Risk of resistance development is low and has not been reported despite years of use in thousands of patients
- Resistance has not been induced, even under laboratory conditions where bacteria do develop resistance to antibiotics.

Honey containing dressings should be considered for the lowest Device Classification possible.