

MANUKAMED

WORLD LEADERS
IN HONEY SCIENCE

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Device Description and Clearance Dates – 510K

ManukaMed wound dressings have been in commercial distribution in the United States for more than 6 years and have an established reputation for safety and effectiveness.

MANUKAtex

Medical Grade Manuka honey impregnated into a knitted viscose gauze. It is provided in gamma sterilized individual pouches in a variety of sizes. K110042. Clearance date: 24 March 2011

MANUKAhd

A sterile Medical Grade Manuka honey impregnated into super absorbent polymer fibers (SAF). It is provided in gamma sterilized individual pouches in a variety of sizes. K102659. Clearance date: 08 Dec 2010

MANUKAhd Rope

Identical to the primary device, but is spirally cut to provide flexibility in packing a wound. K102659. Clearance date: 08 Dec 2010

MANUKAhd Border

Manufactured with an adhesive border. K102659. Clearance date: 08 Dec 2010

MANUKApli

A sterile wound dressing consisting of 100% Medical Grade Manuka honey sealed into tubes before sterilization with gamma irradiation. It is designed for single use, and the tube has a twist and shear off end cap that cannot be replaced. K092689. Clearance date: 20 May 2010



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Safety and Efficacy

The ancient Egyptians, Assyrians, Chinese, Greeks and Romans all used honey

Aristotle (circa 350BC) and Dioscorides (50 AD) wrote about medical use of honey

Modern clinical evidence in support of safety and effectiveness of honey in wound care has been comprehensively reviewed with over 33 randomised controlled trials

Honeys can vary in 100 fold in potency

Medical Grade Manuka Honey is now standardised for anti-bacterial efficacy and sterilised for safety

Specifications for Medical Grade Manuka honey demonstrate controlled manufacturing process



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Efficacy

Non-peroxide activity can be attributed to the antibacterial efficacy of Medical Grade Manuka honey that is not due to hydrogen peroxide. All other honeys are hydrogen peroxide based.

Methylglyoxal (MGO) was identified in 2008 as a dominant non-peroxide active molecule responsible for killing bacteria (Mavric et al., 2008). The correlation between the level of measured MGO and the antibacterial potency of Manuka honey is well defined (Adams et al., 2008; Atrott and Henle, 2009).

The evidence for the antimicrobial efficacy of Manuka honey is significant in the form of log reduction and inhibition zones both from ManukaMed's own studies along with numerous publically available studies.

A study report on the antibacterial activity of ManukaMed's honey using the suspension time kill procedure (E2315) with *Staphylococcus aureus* 6538 and *Escherichia coli* 8739 demonstrate that a 1.5×10^6 cfu concentration of *S. aureus* was reduced 99.9997% after 8 hours. Similarly, a 2.03×10^6 cfu concentration of *E. coli* was reduced 99.9998% after 8 hours.

Additionally, the antimicrobial finishes have been evaluated for these wound dressings using AATCC Test Method 100-2012. The GLP reports the results of the challenge procedure demonstrate > 99.99% reduction of test organisms, including Methicillin resistant *S. aureus* (MRSA), *E. coli*, *P. aeruginosa*, *Enterococcus faecalis* (VRE), and *C. albicans*.



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ManukaMed conducted suspension time kill analysis and modified AATCC 100 to include barrier testing and growth inhibition in the dressings. The testing included the following eight organisms:

- MRSA multiple drug resistant *S. aureus*
- VRE vancomycin resistant Enterococci, *E. faecium*
- *Enterobacter cloacae/aerogenes*, carbapenem resistant
- *Klebsiella pneumoniae* extended spectrum ESBL (extended spectrum beta lactamase resistant)
- Multiple drug resistant *P. aeruginosa*
- *C. albicans*
- *A. baumannii*
- *Proteus mirabilis*



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Microorganism	Challenge Time	Test surface	Percentage Reduction vs Initial numbers	Log reduction Vs Initial Numbers	Percentage Reduction vs Relative control	Log reduction Vs Relative control
P. Aueruginosa BAA – 2114	24hr	Manukahd	>99.99999%	> 5.84	>99.9995%	>5.33
	48hr	Manukahd	>99.99999%	> 5.84	>99.9992%	>7.09
	72hr	Manukahd	>99.99999%	> 5.84	>99.9993%	>7.13
	168hr	Manukahd	>99.99999%	> 5.84	>99.9998%	>7.67
S aureus BAA-42	24hr	Manukahd	>99.9998%	>5.60	>99.98%	>3.75
	48hr	Manukahd	>99.9998%	>5.60	>99.97%	>3.55
	72hr	Manukahd	>99.9998%	>5.60	>99.96%	>3.44
	168hr	Manukahd	>99.9998%	>5.60	>99.99%	>3.90
A.Baumannii 19606	24hr	Manukahd	>99.9999%	>5.94	>99.9995%	>5.31
	48hr	Manukahd	>99.9999%	>5.94	>99.99997%	>6.59
	72hr	Manukahd	>99.9999%	>5.94	>99.999993%	>7.13
	168hr	Manukahd	>99.9999%	>5.94	>99.999998%	>7.67
E.Cloacae BAA-2468	24hr	Manukahd	>99.9999%	>5.97	>99.9993%	>5.59
	48hr	Manukahd	>99.9999%	>5.97	>99.9993%	>6.17
	72hr	Manukahd	>99.9999%	>5.97	>99.99998%	>6.87
	168hr	Manukahd	>99.9999%	>5.97	>99.999994%	>7.24
P.Mirabalis	24hr	Manukahd	>99.9999%	>5.97	>99.9993%	>5.19
	48hr	Manukahd	>99.9999%	>5.84	>99.999992%	>7.09
	72hr	Manukahd	>99.9999%	>5.84	>99.999993%	>7.13
	168hr	Manukahd	>99.9999%	>5.84	>99.999998%	>7.67
K pneumoniae	24hr	Manukahd	>99.9998%	>5.81	>99.9998%	>5.81
	48hr	Manukahd	>99.9998%	>5.81	>99.99998%	>6.73
	72hr	Manukahd	>99.9998%	>5.81	>99.99998%	>6.79
	168hr	Manukahd	>99.9998%	>5.81	>99.99999%	>6.88

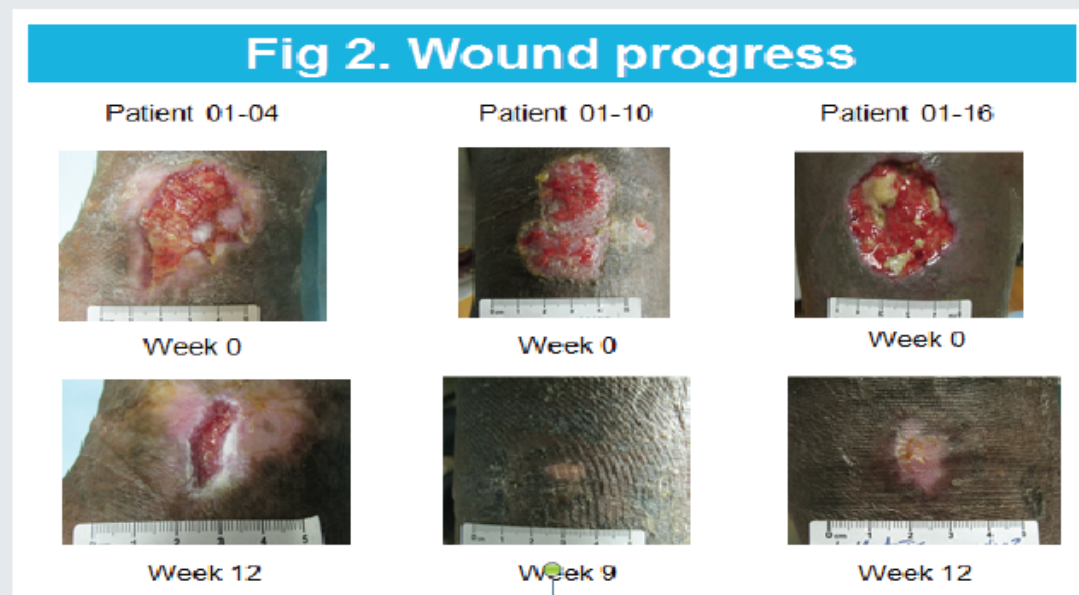
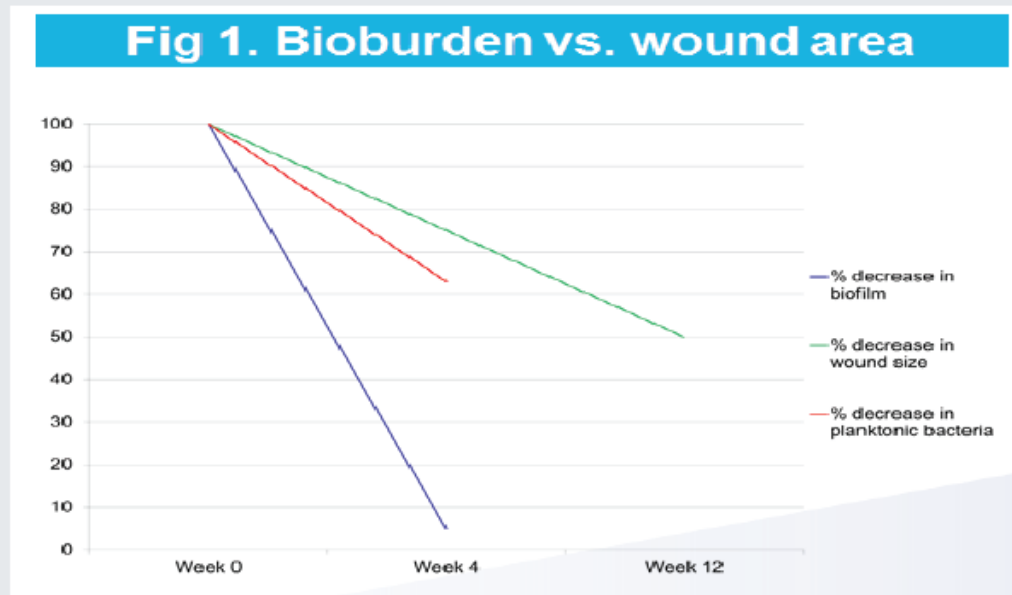
Photos illustrate a diabetic foot ulcer prior to application of MANUKAhd and the healed wound six weeks later, where no infection was observed.



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MANUKAMED STUDY

A recent study conducted by ManukaMed on the relationship between bio burden and wound size in critically colonized Venous leg ulcers has shown a notable reduction in the wound size after just four weeks of treatment with topical honey. This period of time coincided with the reduction in biofilm also.



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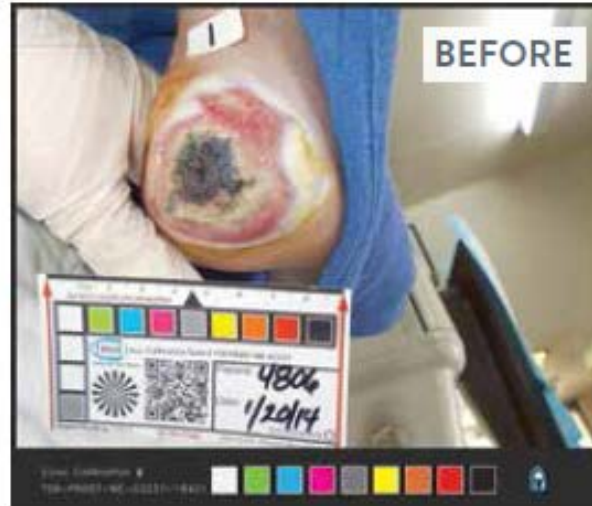
CASE REPORTS

58 YEAR OLD MALE WITH DIABETIC HEEL ULKER

- Open for 3 weeks prior to treatment
- Initial size: 5.2cm x 6.0cm x 0.2cm

Treated with MANUKAhd

- 100 % closure by week 12



Mechanism of Action of Manuka Honey

Studies have shown (Jenkins et al. 2011) through gene expression mechanisms of action for bactericidal behaviour of Medical Grade Manuka honey.

Cell division was affected in *S. aureus* (Henriques et al., 2010), whereas cell integrity was disrupted in *P. aeruginosa* (Henriques et al., 2011).

Also confirmed (Jenkins et al., 2011) that Manuka honey prevented cell division of methicillin-resistant *S. aureus* (MRSA).

Molecular and morphological analysis of effects on *P. aeruginosa* showed that Manuka honey down-regulated cell wall proteins that were key to cell wall stability resulting in cell lysis and death, as illustrated by electron microscopy below (Roberts et al., 2014).

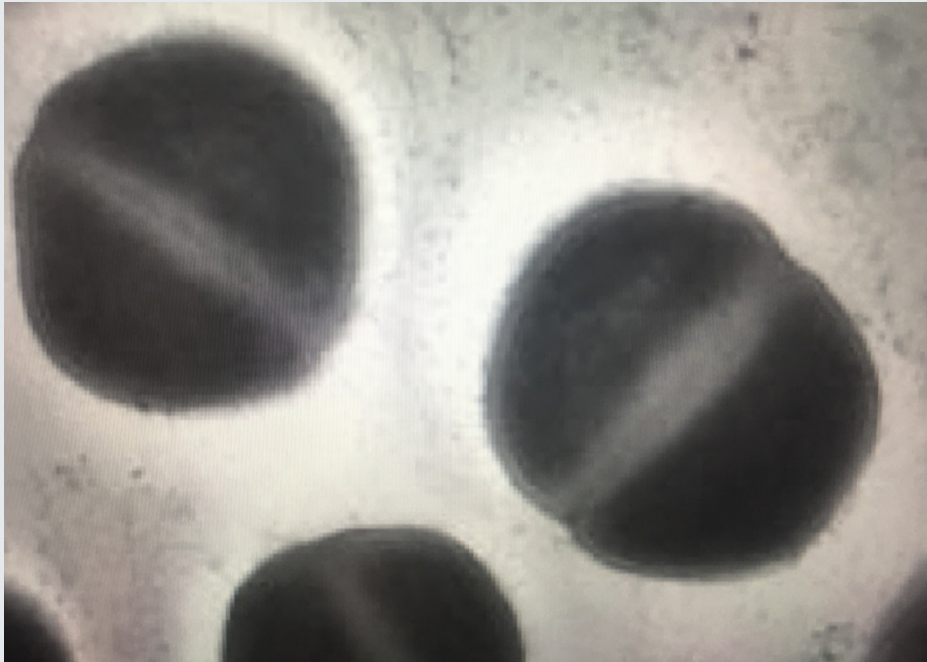
The evidence for mechanism of action through gene expression can be summarized by three key areas: (1) reduction in bacterial virulence; (2) reduction of cell wall integrity; and (3) reduction in quorum sensing. These three mechanisms alone are fatal to bacteria.

Ongoing research into the antimicrobial activities of medical grade Manuka honey continues to identify additional molecular mechanisms of action. For example, a more recent article by Rabie et al. (2016) clearly shows that MGO, the major antibacterial constituent of medical grade Manuka honey directly damages or inhibits the formation of fimbriae and flagella.

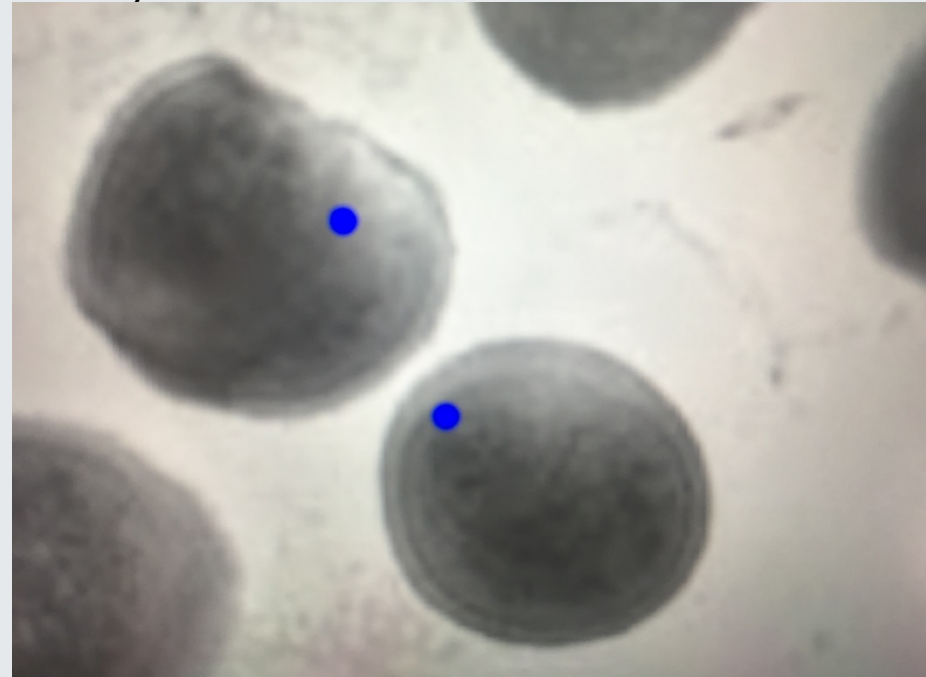


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Normal cell wall structure in dividing cells



Absence of cell wall and lack of cell division in presence of 10% Manuka honey



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Absence of Resistance

The absence of resistance to medical grade Manuka honey has been demonstrated and makes the ManukaMed wound dressings clinically desirable (Cooper et al., 2010).

Repeated exposure of bacteria to sub-lethal concentrations of Manuka honey in “resistance training experiments” in six bacterial species failed to select for bacterial mutants with permanent genotypic changes that conferred resistance to honey (Cooper et al., 2010).



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Conclusion

The anti microbial efficacy of Medical Grade Manuka honey is well established and increases resource available clinicians who are being challenged by MDR pathogens.

The absence of resistance to medical grade Manuka honey is clearly a benefit to clinicians and a health care system burdened with increasing infection rates.

FDA should continue to regulate wound care dressings with medicinal honey as class II devices, because there are no safety or effectiveness issues to support changing the risk/benefit assessments of the devices.



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