

**Utilizzo del miele medicale in un ambulatorio di
wound care:
dalle origini antiche
alla ingegnerizzazione moderna
- *Review della letteratura* -**

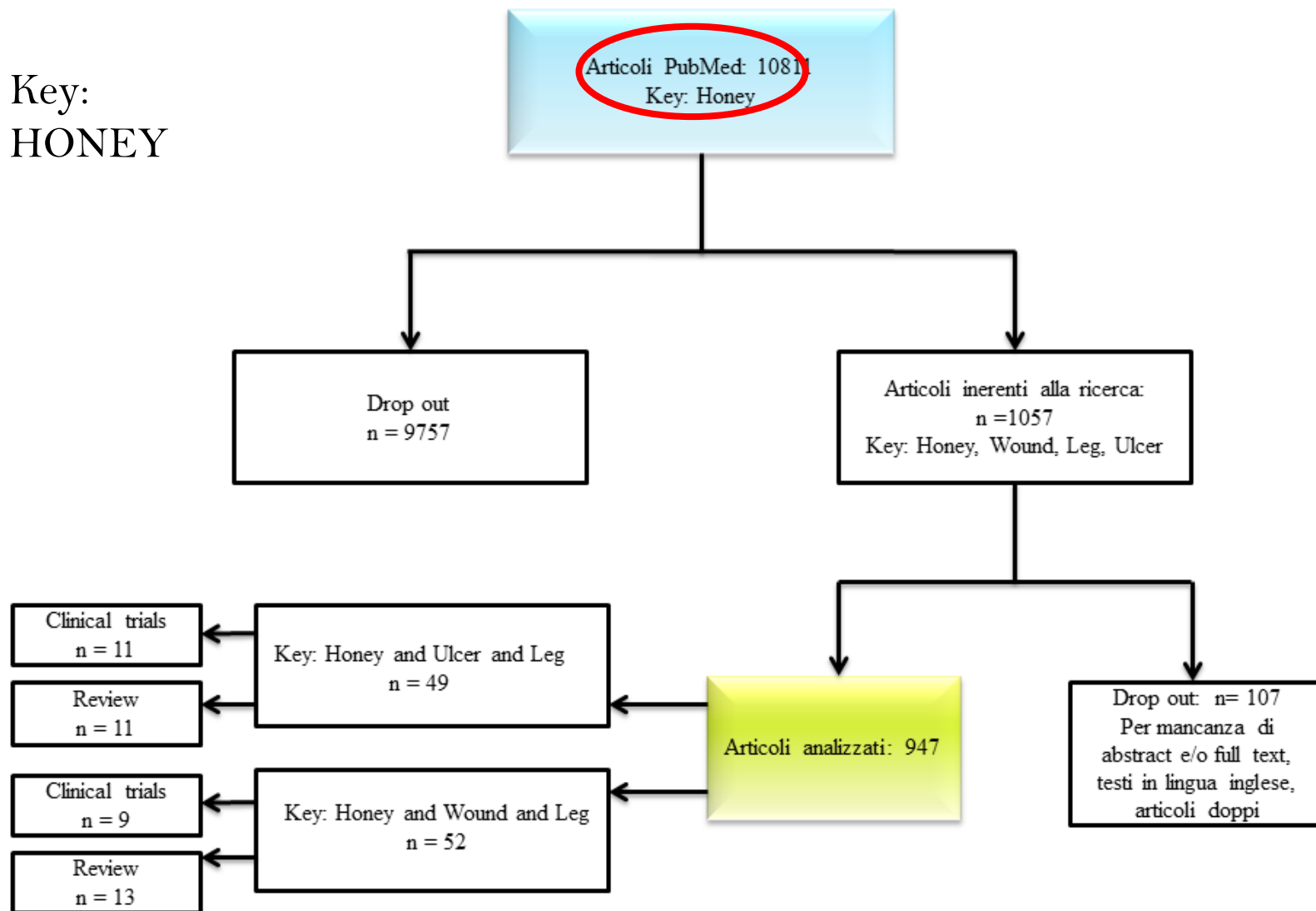
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 [Debridement for venous leg ulcers.](#)

 1. Gethin G, Cowman S, Kolbach DN.
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 PMID: 25742878

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Fin dall'antichità.....



Apicoltore Egizio che coltiva miele. Dipinto proveniente dalla tomba di Pabusa a Luxor (600 a.C.)

Papiro di Ebers (1550 a.C.)
Descrive 147 modi di applicare il miele al corpo

Tra cui: curare ustioni e piaghe



GESTIONE DEL BIOFILM

Il ruolo del biofilm nella guarigione ritardata delle ferite
 La gestione del biofilm nella pratica
 Progressi della ricerca nella conoscenza del biofilm

BIOFILM: insieme di batteri adesi alla superficie della lesione che bloccano la guarigione

Tabella 1: Potenziali agenti anti-biofilm

Meccanismo d'azione	Esempi	Altri dati
Interferenza con l'attacco del biofilm alla superficie	Lactoferrina Acido etilendiamminotetraacetico (EDTA) Xilitolo <u>Miele</u>	La lactoferrina, in base ad un meccanismo di risposta umano innato, si lega alle pareti cellulari causando destabilizzazione, fuoriuscite ed infine morte cellulare ^[17] . L'EDTA è stato usato come agente permeante e sensibilizzante per patologie da biofilm in odontoiatria e in altri campi ^[18] . Inoltre, è stato dimostrato che anche lo xilitolo (un dolcificante artificiale) e il miele sono in grado di bloccare l'attacco ^[17]
Interferenza con il "quorum sensing", un meccanismo di segnalazione chimica o di comunicazione tra le cellule all'interno del biofilm	Farnesolo Iberina Ajoene Miele di Manuka	Vari agenti bloccano o interferiscono con il quorum sensing, tra cui: <ul style="list-style-type: none"> • Farnesolo, • Iberina (ricavata dal rafano), • Ajoene (ricavato dall'aglio). Il miele di Manuka sottoregola 3 dei 4 geni responsabili del processo di "quorum sensing" ^[19]
rottura della sostanza polimerica extracellulare (EPS), una matrice protettiva secreta dal biofilm, che lo circonda.	EDTA	L'EDTA supporta e potenzia gli antimicrobici topici rompendo l'EPS in cui sono incapsulati i microrganismi ^[18] . Esistono anche prodotti registrati che vantano, tra le varie azioni, di poter rompere l'EPS ^[19]
Falsi metaboliti	Gallio, xilitolo	È stato dimostrato che basse dosi di gallio e di xilitolo interferiscono con la formazione del biofilm ^[20]
Rottura del biofilm esistente	Betaina (combinazione di PHMB e betaina)	Le soluzioni attuali preferite per la rottura del biofilm contengono tensioattivi, come la betaina, che abbassano la tensione superficiale del mezzo in cui sono disciolte, permettendo di aspirare sporcizia e detriti e di sospenderli nella soluzione ^[21,22]

Nel biofilm troviamo un'antibiotico-resistenza data dall'utilizzo improprio di antibiotici topici

[IUBMB Life](#), 2012 Jan;64(1):48-55. doi: 10.1002/iub.578. Epub 2011 Nov 17.

Antibacterial components of honey.

[Kwakman PH¹](#), [Zaat SA](#).

[Author information](#)

[Clin Infect Dis](#), 2008 Jun 1;46(11):1677-82. doi: 10.1086/587892.

Medical-grade honey kills antibiotic-resistant bacteria in vitro and eradicates skin colonization.

[Kwakman PH¹](#), [Van den Akker JP](#), [Güçlü A](#), [Aslami H](#), [Binnekade JM](#), [de Boer L](#), [Boszhard L](#), [Paulus F](#), [Middelhoek P](#), [te Velde AA](#), [Vandenbroucke-Grauls CM](#), [Schultz MJ](#), [Zaat SA](#).



Adv Wound Care (New Rochelle). 2014 Apr 1;3(4):324-334.

Dressings and Products in Pediatric Wound Care.

King A¹, Stellar JJ², Blevins A³, Shah KN⁴.

Br J Nurs. 2014 Mar 27-Apr 9;23(6):S30, S32-4.

Medical honey and its role in paediatric patients.

Weissenstein A¹, Luchter E², Bittmann S³.

Honey dressing on a leg ulcer with tendon exposure in a patient with type 2 diabetes

Ilarla Teobaldi¹, Vincenzo Stolco¹, Fabrizia Perrone¹, Massimiliano Bruti², Enzo Bonora¹ and Alessandro Mantovani¹

¹Division of Endocrinology Diabetes and Metabolism, Department of Medicine and ²Division of Plastic Surgery, Department of Surgery, University and Azienda Ospedaliera Universitaria Integrata of Verona, Verona, Italy

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Int J Endocrinol Metab. 2012;10(1): 444-445. DOI:10.5812/ijem.3628



International Journal of
Endocrinology & Metabolism
Journal home page: www.EndoMetabol.com



The Use of Honey in Diabetes Mellitus: Is It Beneficial or Detrimental?

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¹ Department of Pharmacology, School of Medical Sciences, Universiti Sains Malaysia, Kelantan, Malaysia



72% venose



8% arteriose



14% miste





Revamil

Produzione
controllata/standardizzata
in serre
Da miscele floreali

Manuka

Produzione non controllata,
all'aperto
Ricavate da fiori di
Leptospermum Scoparium

OPEN ACCESS Freely available online

PLoS one

Two Major Medicinal Honeys Have Different Mechanisms of Bactericidal Activity

Paulus H. S. Kwakman¹, Anje A. te Velde², Leonie de Boer¹, Christina M. J. E. Vandenbroucke-Grauls^{1,3}, Sebastian A. J. Zaat^{1*}

¹ Department of Medical Microbiology, Center for Infection and Immunity Amsterdam (CINIMA), Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands, ² Tytgat Institute for Liver and Intestinal Research, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands, ³ Department of Medical Microbiology and Infectious Diseases, VU Medical Center, Amsterdam, The Netherlands

	GLUCOSIO OSSIDASI	METILGLOSALE (MGO)	BEE DEFENSIN-1 PEPTIDE
Revamil	si	no	si
Manuka	no	si	no

Revamil

Glucosio-ossidasi

(GOX) trasforma lo zucchero del miele

in

Acido gluconico

Crea un ambiente acido nella ferita tale da inibire la proliferazione batterica

Perossido di idrogeno (H₂O₂)

Concentrazione bassissima al 3‰ che contrasta la crescita batterica

Manuka

Metilgliossale (MGO)

- L'MGO è un prodotto collaterale (secondario) del metabolismo dello zucchero,
- è un composto organico con la formula $\text{CH}_3\text{C}(\text{O})\text{CHO}$

Dagli studi emerge però....

- Che è citotossico ad alte concentrazioni
- Reagisce con le proteine del collagene e danneggia la matrice
- Nei pazienti diabetici il livello di MGO è alto con conseguente ritardo nella guarigione della ferita

[FASEB J. 2010 Jul;24\(7\):2576-82. doi: 10.1096/fj.09-150789. Epub 2010 Mar 12.](#)

How honey kills bacteria.

[Kwakman PH¹, te Velde AA, de Boer L, Speijer D, Vandenbroucke-Grauls CM, Zaat SA.](#)

[Evid Based Complement Alternat Med. 2011;2011:295494. doi: 10.1093/ecam/nejq013. Epub 2010 Oct 14.](#)

Methylglyoxal-a potential risk factor of manuka honey in healing of diabetic ulcers.

[Majtan J¹.](#)



Bee defensin-1 peptide

Prodotto dalle ghiandole ipofaringee della api coinvolte nella produzione di pappa reale e miele antibatterico

[FASEB J.](#) 2010 Jul;24(7):2576-82. doi: 10.1096/fj.09-150789. Epub 2010 Mar 12.

How honey kills bacteria.

[Kwakman PH¹](#), [te Velde AA](#), [de Boer L](#), [Speijer D](#), [Vandenbroucke-Grauls CM](#), [Zaat SA](#).

...la grande maggioranza delle proprietà antibatteriche del miele proviene da questa proteina...



Honey as a topical treatment for wounds.

Jull AB¹, Cullum N, Dumville JC, Westby MJ, Deshpande S, Walker N.

MAIN RESULTS: We identified 26 eligible trials (total of 3011 participants). Three trials evaluated the effects of honey in minor acute wounds, 11 trials evaluated honey in burns, 10 trials recruited people with different chronic wounds including two in people with venous leg ulcers, two trials in people with diabetic foot ulcers and single trials in infected post-operative wounds, pressure injuries, cutaneous Leishmaniasis and Fournier's gangrene. Two trials recruited a mixed population of people with acute and chronic wounds. The quality of the evidence varied between different comparisons and outcomes. We mainly downgraded the quality of evidence for risk of bias, imprecision and, in a few cases, inconsistency. There is high quality evidence (2 trials, n=992) that honey dressings heal partial thickness burns more quickly than conventional dressings (WMD -4.68 days, 95%CI -5.09 to -4.28) but it is unclear if there is a difference in rates of adverse events (very low quality evidence) or infection (low quality evidence). There is very low quality evidence (4 trials, n=332) that burns treated with honey heal more quickly than those treated with silver sulfadiazine (SSD) (WMD -5.12 days, 95%CI -9.51 to -0.73) and high quality evidence from 6 trials (n=462) that there is no difference in overall risk of healing within 6 weeks for honey compared with SSD (RR 1.00, 95% CI 0.98 to 1.02) but a reduction in the overall risk of adverse events with honey relative to SSD. There is low quality evidence (1 trial, n=50) that early excision and grafting heals partial and full thickness burns more quickly than honey followed by grafting as necessary (WMD 13.6 days, 95%CI 9.82 to 17.38). There is low quality evidence (2 trials, different comparators, n=140) that honey heals a mixed population of acute and chronic wounds more quickly than SSD or sugar dressings. Honey healed infected post-operative wounds more quickly than antiseptic washes followed by gauze and was associated with fewer adverse events (1 trial, n=50, moderate quality evidence, RR of healing 1.69, 95%CI 1.10 to 2.61); healed pressure ulcers more quickly than saline soaks (1 trial, n= 40, very low quality evidence, RR 1.41, 95%CI 1.05 to 1.90), and healed Fournier's gangrene more quickly than Eusol soaks (1 trial, n=30, very low quality evidence, WMD -8.00 days, 95%CI -6.08 to -9.92 days). The effects of honey relative to comparators are unclear for: venous leg ulcers (2 trials, n= 476, low quality evidence); minor acute wounds (3 trials, n=213, very low quality evidence); diabetic foot ulcers (2 trials, n=93, low quality evidence); Leishmaniasis (1 trial, n=100, low quality evidence); mixed chronic wounds (2 trials, n=150, low quality evidence).

AUTHORS' CONCLUSIONS: It is difficult to draw overall conclusions regarding the effects of honey as a topical treatment for wounds due to the heterogeneous nature of the patient populations and comparators studied and the mostly low quality of the evidence. The quality of the evidence was mainly downgraded for risk of bias and imprecision. Honey appears to heal partial thickness burns more quickly than conventional treatment (which included polyurethane film, paraffin gauze, soframycin-impregnated gauze, sterile linen and leaving the burns exposed) and infected post-operative wounds more quickly than antiseptics and gauze. Beyond these comparisons any evidence for differences in the effects of honey and comparators is of low or very low quality and does not form a robust basis for decision making.

Update of

Honey as a topical treatment for wounds. [Cochrane Database Syst Rev. 2013]

Debridement for venous leg ulcers.

Gethin G¹, Cowman S, Kolbach DN.

MAIN RESULTS: We identified 10 RCTs involving 715 participants. Eight RCTs evaluated autolytic debridement and included the following agents or dressings: biocellulose wound dressing (BWD), non-adherent dressing, honey gel, hydrogel (gel formula), hydrofibre dressing, hydrocolloid dressings, dextranomer beads, Edinburgh University Solution of Lime (EUSOL) and paraffin gauze. Two RCTs evaluated enzymatic preparations and one evaluated biosurgical debridement. No RCTs evaluated surgical, sharp or mechanical methods of debridement, or debridement versus no debridement. Most trials were at a high risk of bias. Three RCTs assessed the number of wounds completely debrided. All three of these trials compared two different methods of autolytic debridement (234 participants), with two studies reporting statistically significant results: one study (100 participants) reported that 40/50 (80%) ulcers treated with dextranomer beads and 7/50 (14%) treated with EUSOL achieved complete debridement (RR 5.71, 95% CI 2.84 to 11.52); while the other trial (86 participants) reported the number of ulcers completely debrided as 31/46 (76%) for hydrogel versus 18/40 (45%) for paraffin gauze (RR 0.67, 95% CI 0.45 to 0.99). One study (48 participants) reported that by 12 weeks, 15/18 (84%) ulcers treated with BWD had achieved a 75% to 100% clean, granulating wound bed versus 4/15 (26%) treated with non-adherent petrolatum emulsion-impregnated gauze. Four trials assessed the mean time to achieve debridement: one (86 participants) compared two autolytic debridement methods, two compared autolytic methods with enzymatic debridement (71 participants), and the last (12 participants) compared autolytic with biosurgical debridement; none of the results achieved statistical significance. Two trials that assessed autolytic debridement methods reported the number of wounds healed at 12 weeks. One trial (108 participants) reported that 24/54 (44%) ulcers treated with honey healed versus 18/54 (33%) treated with hydrogel (RR (adjusted for baseline wound diameter) 1.38, 95% CI 1.02 to 1.88; P value 0.037). The second trial (48 participants) reported that 7/25 (28%) ulcers treated with BWD healed versus 7/23 (30%) treated with non-adherent dressing. Reduction in wound size was assessed in five trials (444 participants) in which two autolytic methods were compared. Results were statistically significant in one three-armed trial (153 participants) when cadexomer iodine was compared to paraffin gauze (mean difference 24.9 cm², 95% CI 7.27 to 42.53, P value 0.006) and hydrocolloid compared to paraffin gauze (mean difference 23.8 cm², 95% CI 5.48 to 42.12, P value 0.01). A second trial that assessed reduction in wound size based its results on median differences and, at four weeks, produced a statistically significantly result that favoured honey over hydrogel (P value < 0.001). The other three trials reported no statistically significant results for reduction in wound size, although one trial reported that the mean percentage reduction in wound area was greater at six and 12 weeks for BWD versus a non-adherent dressing (44% versus 24% week 6; 74% versus 54% week 12). Pain was assessed in six trials (544 participants) that compared two autolytic debridement methods, but the results were not statistically significant. No serious adverse events were reported in any trial.

AUTHORS' CONCLUSIONS: There is limited evidence to suggest that actively debriding a venous leg ulcer has a clinically significant impact on healing. The overall small number of participants, low number of studies and lack of meta-analysis in this review precludes any strong conclusions of benefit. Comparisons of different autolytic agents (hydrogel versus paraffin gauze; Dextranomer beads versus EUSOL and BWD versus non-adherent dressings) and Larvae versus hydrogel all showed statistically significant results for numbers of wounds debrided. Larger trials with follow up to healing are required.

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J Glob Antimicrob Resist. 2014 Sep;2(3):168-172. doi: 10.1016/j.jgar.2014.03.006. Epub 2014 Apr 26.

Engineered honey: In vitro antimicrobial activity of a novel topical wound care treatment.

Dryden M¹, Lockyer G², Saeed K², Cooke J³.

Author information

Abstract

Surgihoney is a novel engineered organic honey product for wound care. Its antimicrobial activity can be controlled and adjusted by the engineering process, allowing preparation of three different potencies, labelled Surgihoney 1-3. Susceptibility testing of a range of wound and ulcer bacterial isolates to Surgihoney by the disc diffusion method, minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) determination, and time-kill measurements by time suspension tests were performed. Surgihoney demonstrated highly potent inhibitory and cidal activity against a wide range of Gram-positive and Gram-negative bacteria and fungi. MICs/MBCs were significantly lower than concentrations likely to be achieved in topical clinical use. The topical concentration of Surgihoney in wounds was estimated at ca. 500g/L. MICs/MBCs for *Staphylococcus aureus* were 32/125g/L for Surgihoney 1 and 0.12/0.25g/L for Surgihoney 3. Cidal speed depended on potency, being 48h for Surgihoney 1 and 30min for Surgihoney 3. Maintenance of the Surgihoney inoculum preparation for up to a week demonstrated complete cidal activity and no bacterial persistence. Surgihoney has wide potential as a highly active topical treatment combining the effects of the healing properties of honey with the potent antimicrobial activity of the engineered product for skin lesions, wounds, ulcers and cavities. It is highly active against multidrug-resistant bacteria. It is more active than other honeys tested and is comparable with chemical antiseptics in antimicrobial activity.

KEYWORDS: Honey; MBC; MIC; Soft tissue infection; Surgihoney; Tissue viability; Topical therapy

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J Mater Sci Mater Med. 2018 Mar 13;29(3):31. doi: 10.1007/s10856-018-6038-4.

Repositing honey incorporated electrospun nanofiber membranes to provide anti-oxidant, anti-bacterial and anti-inflammatory microenvironment for wound regeneration.

Sarkar R¹, Ghosh A¹, Barui A¹, Datta P².

⊕ Author information

Abstract

Topical application of honey for tissue regeneration, has recently regained attention in clinical practice with controlled studies affirming its efficacy and indicating its role in regeneration over repair. Parallely, to overcome difficulties of applying raw honey, several product development studies like nanofibrous matrices have been reported. However, one approach concentrated on achieving highest possible honey loading in the nanofiber membranes while other studies have found that only specific honey dilutions result in differential cellular responses on wound healing and re-epithelization. From these results, it can be suggested that high honey loading provides optimum external microenvironment, low-loaded membranes could provide a more conducive internal microenvironment for tissue regeneration. With this hypothesis, this paper sought to evaluate ability of low-honey loaded nanofibers to modulate the anti-oxidant, anti-biofilm and anti-inflammatory properties which are important to be maintained in wound micro-environment. A loading-dependent reduction of biofilm formation and anti-oxidant activity was noted in different concentration ranges investigated. After scratch assay, a certain honey loading (0.5%) afforded the maximum re-epithelization. Since there is lack of methods to determine anti-inflammatory properties of nanofiber membranes during epithelial healing process, we performed anti-inflammatory assessment of nano-fibers by evaluating the expressions of pro-inflammatory markers-Cyclooxygenase-2 (COX-2) and Interleukin-6 (IL-6) and to confirm the optimized concentration. Considering the role of COX-2 and IL-6, the novel methodology used in this study can also be developed as an assay for anti-inflammatory matrices for wound healing.



CONCLUDENDO:

- ✓ - Dall'antichità..... Ritorno al passato
- ✓ - Contrasta l'antibiotico resistenza grazie a... proprietà antibatteriche naturali
- ✓ - Utilizzato in vari ambiti
- ✓ - Di facile utilizzo , non istolesiva né citotossica, economico
- ✓ - Debriedment (MIELE OTTIMO ALLEATO)
- ✓ - Aiuto per la bioingegnerizzazione dei tessuti
- ✓ - Ambulatorio a gestione infermieristica

GRAZIE PER L'ATTENZIONE