

## Honey and its Anti-Inflammatory, Anti-Bacterial and Anti-Oxidant Properties

Natalia G Vallianou<sup>1\*</sup>, Penny Gounari<sup>1</sup>, Alexandros Skourtis<sup>1</sup>, John Panagos<sup>1</sup> and Christos Kazazis<sup>2</sup>

<sup>1</sup>Evangelismos General Hospital, Athens, Greece

<sup>2</sup>Island of Samos, Internist, Athens, Greece

### Abstract

Honey mainly consists of sugars and water. Apart from sugars, honey also contains several vitamins, especially B complex and vitamin C, together with a lot of minerals. Some of the vitamins found in honey include ascorbic acid, pantothenic acid, niacin and riboflavin; while minerals such as calcium, copper, iron, magnesium, manganese, phosphorus, potassium and zinc are also present. Honey has been used for its healing, nutritional and therapeutic properties since ancient times. Its antibacterial potentials even against multi-drug resistant bacteria, such as *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Acinetobacterbaumanni* have been proved. Honey is well known for its anti-inflammatory and antioxidant capacities, which may be useful for the prevention of chronic inflammatory process like atherosclerosis, diabetes mellitus and cardiovascular diseases. The antibacterial, anti-inflammatory and antioxidant properties of honey will be reviewed here.

**Keywords:** Honey; Inflammation; Anti-bacterial properties

### Introduction

Honey mainly consists of sugars and water. Sugars in honey comprises predominantly of monosaccharides and oligosaccharides. The most abundant sugar in honey is fructose, while sugars in it are sweeter and give more energy than artificial sweeteners [1-3]. Apart from sugars, honey also contains several vitamins, especially B complex and vitamin C, together with a lot of minerals. Some of the vitamins found in honey include ascorbic acid, pantothenic acid, niacin and riboflavin; while minerals such as calcium, copper, iron, magnesium, manganese, phosphorus, potassium and zinc are also present [4]. Honey contains at least 181 constituents [2,5]. The other constituents of honey are amino acids, antibiotic-rich inhibine, proteins and phenol antioxidants [6]. It also contains other bioactive substances such as phenolic constituents, flavonoids, organic acids, carotenoid-derived compounds, nitric oxide (NO) metabolites, amino acids and proteins [7,8]. Evidence indicates that some varieties of honey contain kynurenic acid (a tryptophan metabolite with neuroactive activity) which may contribute to its antimicrobial properties [9]. The presence of enzymes such as glucose oxidase, diastase, invertase, phosphatase, catalase and peroxidase has also been documented in honey [10].

### Anti-Bacterial and wound Healing Activity

The medicinal importance of honey has been known since ancient times and its antimicrobial property as well as wound-healing activities was well-known long ago. The first written reference for honey was a Sumerian tablet writing dating back to 2100-2000 BC, which mentioned honey's use as a drug and an ointment. Aristotle (384-322 BC), when discussing different honeys, referred to pale honey as being "good as a salve for sore eyes and wounds" [11]. The healing property of honey is due to the fact that it offers anti-bacterial activity, maintains a moist wound condition, and its high viscosity helps to provide a protective barrier to prevent infection. Its immune-modulatory property is relevant to wound repair, too [12].

Nowadays, with the presence of multi-drug or pan-drug-resistant microbes, alternative anti-microbial strategies are urgently needed. This need has led to a re-evaluation of the therapeutic use of ancient remedies, such as plants and plant-based products, including honey [13-15]. The antimicrobial activity in most honeys is due to the enzymatic production of hydrogen peroxide [13]. However, another kind of honey, called non-peroxide honey (e.g. manuka honey), displays significant

anti-bacterial effects even when the hydrogen peroxide activity is blocked. Its mechanism may be related to the low pH level of honey and its high sugar content (high osmolarity) that is enough to hinder the growth of microbes. Honey traditionally has an acidic pH, between 3.2 and 4.5, which is low to be inhibitory for many bacteria [15,16]. The anti-bacterial property of honey is also derived from the osmotic effect of its high sugar content and low moisture content, along with its acidic properties of gluconic acid and the antiseptic properties of its H<sub>2</sub>O<sub>2</sub> [17]. A recent study examining the antimicrobial properties of honey *in vitro* found that H<sub>2</sub>O<sub>2</sub>, methylglyoxal and an antimicrobial peptide, bee defensin-1, are distinct mechanisms involved in the bactericidal activity of honey [18]. The medical grade honeys have potent *in vitro* bactericidal activity against antibiotic-resistant bacteria causing several life-threatening infections to humans. Nevertheless, there is a large variation in the antimicrobial activity of some natural honeys, which is due to temporal variation in sources of nectar. Thus, identification and characterization of the active principles may provide valuable information on the quality and possible therapeutic potential of honeys.

Currently, many researchers have reported the anti-bacterial activity of honey and found that natural unheated honey has some broad-spectrum antibacterial activity when tested against pathogenic bacteria, oral bacteria as well as food spoilage bacteria [12,19]. At present a number of honeys are sold with standardized levels of anti-bacterial activity. The *Leptospermum scoparium* honey, the best known of the honeys, has been reported to have an inhibitory effect on around 60 species of bacteria, including aerobes and anaerobes, gram-positives and gram-negatives [20]. Manuka honey is produced from the manuka bush (*Leptospermum scoparium*) indigenous to New Zealand and Australia. Exceptionally high concentrations of the anti-

**\*Corresponding author:** Natalia G Vallianou, Evangelismos General Hospital, 5 Pyramidonstr, 190 05, Municipality of Marathon, Athens, Greece, Tel: +302294092359; E-mail: [natalia.vallianou@hotmail.com](mailto:natalia.vallianou@hotmail.com)

**Received** January 06, 2014; **Accepted** January 20, 2014; **Published** February 03, 2014

**Citation:** Vallianou NG, Gounari P, Skourtis A, Panagos J, Kazazis C (2014) Honey and its Anti-Inflammatory, Anti-Bacterial and Anti-Oxidant Properties. Gen Med (Los Angel) 2: 132. doi: [10.4172/2327-5146.1000132](https://doi.org/10.4172/2327-5146.1000132)

**Copyright:** © 2014 Vallianou NG, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

bacterial compound methylglyoxal have been found in manuka honey, but the exact contribution of this and possible other compounds to the bactericidal activity of manuka honey remains largely unknown [21,22]. In a report testing anti-bacterial activity of two different honeys, after 24 hours of incubation, both honeys killed all tested bacteria, including methicillin-resistant *Staphylococcus aureus* (MRSA), but manuka honey retained activity up to higher dilutions than RS honey (unprocessed Revamil source usually from the Netherlands honey). Bee defensin-1 and H<sub>2</sub>O<sub>2</sub> were the major factors involved in rapid bactericidal activity of RS honey. These factors were absent in manuka honey, but this honey contained 44-fold higher concentrations of methylglyoxal than RS honey. Methylglyoxal was a major bactericidal factor in manuka honey, but after neutralization of this compound, manuka honey retained bactericidal activity due to several unknown factors. RS and manuka honey have highly distinct compositions of bactericidal factors, resulting in large differences in bactericidal activity [23].

There are several reports that Tualang honey has variable broad-spectrum activities against many different kinds of gram positive and enteric bacteria [24-26]. Unlike glucose oxidase, the antibacterial properties from *Leptospermum* spp. honeys are light- and heat-stable. Natural honey of other sources can vary as much as 100-fold in the potency of their antibacterial activities, which is due to hydrogen peroxide. In addition, honey is hygroscopic, which means that it can draw moisture out of the environment and dehydrate bacteria, and its high sugar content and low level pH can also prevent the microbes from growth.

Most deaths in severely burn-injured patients are due to burn wound sepsis or complications due to inhalation injury. Currently, the emerging antimicrobial resistance trends in burn wound bacterial pathogens are a serious challenge [27]. Thus, honey with effective antimicrobial properties against antibiotic-resistant organisms such as MRSA (methicillin-resistant *Staphylococcus aureus*), vancomycin-resistant *Enterococcus spp* (VRE) and multiple-resistant Gram-negative rods such as *Pseudomonas aeruginosa*, *Acinetobacter spp.* and members of the family *Enterobacteriaceae*, which have been associated with infections of burn wounds and sites of major thermal injury and in nosocomial infections, is much anticipated [28-30].

The honey has been used from ancient times as a method of accelerating wound healing. It's potential to assist with wound healing has been demonstrated repeatedly [31,32]. Honey is gaining acceptance as an agent for the treatment of ulcers, bed sores and other skin infections resulting from burns and wounds [33,34]. The healing properties of honey can be ascribed to the fact that it offers antibacterial activity, maintains a moist wound environment that promotes healing, and has a high viscosity which helps to provide a protective barrier to prevent infection [35]. There are many reports suggesting that honey is very effective as a dressing of wounds, burns, skin ulcers and inflammations; the anti-bacterial properties of honey speed up the growth of new tissue to help healing the wound [36]. The medihoney and manuka honey have been shown to have *in vivo* activity and are suitable for the treatment of ulcers, infected wounds and burns [37,38].

More specifically, the honey, when applied topically, rapidly clears wound infection to facilitate healing of deep surgical wounds with infection [39]. The application of honey can promote the healing in infected wounds that do not respond to the conventional therapy, (*i.e.*, antibiotics and antiseptics), including wounds infected with MRSA or multi-drug resistant *Pseudomonas aeruginosa* [40-43]. Moreover, it has been used on skin grafts and infected skin graft donor sites successfully [44]. The removal of exudate in wounds dressed with honey is of help in managing inflammatory wounds.

The manuka, jelly bush and pasture honeys are capable of stimulating the monocytes, the precursors of macrophages, to secrete TNF- $\alpha$  [29,45]. Also, glycosylated proteins in honey can induce TNF- $\alpha$  secretion by macrophages, and this cytokine is known to induce the mechanisms of inflammation, the formation of granulomatous tissue and of wound repairing [46]. Thus, the immune-modulatory properties of honey, when topically applied, are relevant to wound repair.

The notion for using honey as a treatment regimen for peptic ulcers and gastritis comes from traditional folklore as well as from reports in modern times [11]. Honey may promote the repair of damaged intestinal mucosa, stimulate the growth of new tissues and work as an anti-inflammatory agent [37-39]. Manuka honey has been reported to exhibit antimicrobial activity against pathogenic bacteria *Helicobacter pylori* making this honey a promising functional food for the treatment of wounds or stomach ulcers [47].

### Anti-Inflammatory Effects

As mentioned above, raw honey contains substantial amounts of compounds such as flavonoids and other polyphenols which may function as anti-oxidants [7,8].

In Malaysia, there are several types of honey, including Tualang, Nenas, Coconut, and Gelam. Among these, Tualang and Gelam honeys are well known in Malaysia for their potential health benefits, such as anti-oxidant and anti-inflammatory activities [48,49]. Mohamed et al. have shown that Tualang honey contains highly phenolic compounds that possess relatively good anti-oxidant activity. In an animal model, a topical dressing of Tualang honey showed a positive effect for treating full-thickness burn wounds [41,50,51]. As previously reported, Gelam honey has anti-oxidative and radical scavenging activities, which are mainly attributed to its phenolic content.

In a recent study, it has been reported that honey reduced the activities of cyclooxygenase-1 and cyclooxygenase-2, thus showing anti-inflammatory effects. Furthermore, ingestion of diluted natural honey has produced reductions on concentrations of prostaglandins such as PGE<sub>2</sub> (prostaglandin E<sub>2</sub>), PGF<sub>2 $\alpha$</sub>  (prostaglandin F<sub>2 $\alpha$</sub> ) and thromboxane B<sub>2</sub> in plasma of normal individuals [52]. Interestingly, in an inflammatory model of colitis, honey was as effective as prednisolone treatment [53]. While NSAIDs and corticosteroids may have many serious side effects, honey has an anti-inflammatory action free from major side effects.

Recently, Gelam honey has been demonstrated to decrease inflammatory mediators such as COX-2 and TNF- $\alpha$  via attenuating NF- $\kappa$ B translocation to the nucleus and thus inhibiting the activation of the NF- $\kappa$ B pathway [54]. It is widely known that the activation of NF- $\kappa$ B plays a key role in the pathogenesis of inflammation [55,56]. Therefore, Gelam honey has just been documented to inhibit the inflammatory process by inhibiting NF- $\kappa$ B pathway.

### Anti-Oxidant Activity of Honey

Natural honey contains many flavonoids (such as apigenin, pinocembrin, kaempferol, quercetin, galangin, chrysin and hesperetin), phenolic acids (such as ellagic, caffeic, p-coumaric and ferulic acids), ascorbic acid, tocopherols, catalase, superoxide dismutase, reduced glutathione, Maillard reaction products and peptides, most of which work together to provide a synergistic antioxidant effect [57-59].

It is noteworthy that the botanical origin of honey has the greatest influence on its anti-oxidant activity, while processing, handling and storage affects its anti-oxidant capacity only to a minor degree [60-65]. The anti-oxidant activity has been shown to strongly correlate with the

content of total phenolics [66-70]. In addition, a strong correlation has been found between anti-oxidant activity and the color of honey. Many researchers have reported that dark honey has a higher total phenolic content and consequently a higher anti-oxidant capacity [71]. Blasa et al. have shown that the anti-oxidant activity is located in both the ether and the water fractions, indicating that the flavonoids of honey may be available to various compartments of the human body, where they may exert different physiological effects [67,72].

The presence of free radicals and reactive oxygen species (ROS) is of the outmost importance in the process of cellular dysfunction, pathogenesis of metabolic and cardiovascular diseases as well as aging. The consumption of foods and substances rich in anti-oxidants may protect against these pathological changes and consequently prevent the pathogenesis of chronic inflammatory disorders. Researches have reported that honey contains several important substances and these include mainly anti-oxidants [73,74]. The qualitative and quantitative composition of honey (including the anti-oxidants constituent and the other phytochemical substances) is a reflection of the floral source as well as the variety of the particular honey [75]. In their analysis of the phytochemical composition of mono-floral Cuban honeys, Alvarez-Suarez et al. [71] have concluded that Cuban honeys contain important phenolic, flavonoid and carotenoid concentrations with high substantial anti-oxidant capacity [72,76]. Researchers in California have also advocated the consumption of the anti-oxidants from foods such as honey highly-rich.

A report in which two buckwheat honey treatments were administered to 37 healthy human adults at the rate of 1.5 g/kg body weight, with corn syrup as control, has demonstrated increased ( $p < 0.05$ ) plasma total-phenolic content and plasma anti-oxidant. This study has supported the notion that phenolic anti-oxidants from processed honey are bioavailable and that they increase the anti-oxidant activity of plasma. Therefore, they advocated for the substitution of honey in some foods as traditional sweetener for enhanced anti-oxidant defense system in healthy human adults [77].

It has been shown that honey intake ameliorates risk factors of metabolic and cardiovascular diseases in patients and healthy individuals at risk. Unlike refined sugars, diabetic patients can safely and harmlessly eat this natural and sweetest sugar (fructose)-containing product, natural honey. Recently, researchers have fed male and female rats with honey or sugar (golden syrup) supplemented diet for 12 weeks from 7 days of age to compare their metabolic response, and see if honey is protective against metabolic syndrome. In male rats, golden syrup has significantly increased ( $p < 0.05$ ) blood levels of metabolic substrates (glucose and triglycerides); and caused enhanced ( $p < 0.001$ ) visceral adiposity, hypercholesterolemia, hyperinsulinemia, hepatomegaly and fatty liver. These cardiovascular diseases and metabolic diseases' risk factors were not observed in the honey fed rats in this trial. They concluded that honey is cardio-protective, and its consumption may ameliorate risk factors of metabolic and cardiovascular diseases in patients and healthy individuals at risk. Unlike refined sugars, diabetic patients can safely and harmlessly eat this natural and sweetest sugar (fructose)-containing product, natural honey. These results confirmed the conclusion drawn from earlier study that substituting honey for refined carbohydrates was beneficial [78]. Earlier researches from other laboratories and clinical trials further affirmed the metabolic and cardiovascular health significance of eating honey by recording some health profiles. These were reduction in the plasma levels of risk factors which include total cholesterol, LDL-cholesterol, triglycerides,

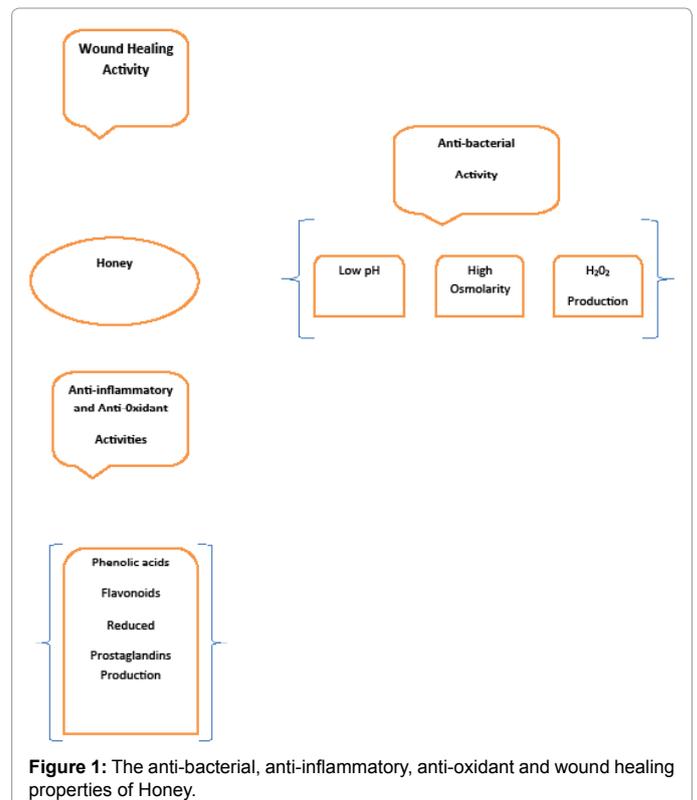


Figure 1: The anti-bacterial, anti-inflammatory, anti-oxidant and wound healing properties of Honey.

glucose in normal and diabetic patients, C-reactive protein, while the health indices elevated in the blood were HDL cholesterol [79-81]. Besides that, other researchers recorded higher plasma anti-oxidants levels in rats nurtured with natural honey relative to fructose-fed rats, and consequently low susceptibility of these subjects to cardiovascular diseases. Another study has demonstrated that the combination of glibenclamide or metformin with honey improves glycemic control, and provides additional metabolic benefits, not achieved with either glibenclamide or metformin alone in streptozocin-induced diabetic rats.

## Conclusion

Honey mainly consists of sugars and water, but also contains several vitamins, especially B complex and vitamin C, together with a lot of minerals. Honey has been used for its healing, nutritional and therapeutic properties since ancient times. It possesses anti-bacterial, anti-inflammatory and anti-oxidant properties that may be beneficial for combating multi-drug resistant bacteria as well as for preventing chronic inflammatory processes, such as atherosclerosis and diabetes mellitus (Figure 1).

## Teaching Points

Honey has antibacterial properties. Honey has wound healing activity. Honey possesses anti-oxidant and anti-inflammatory capacities, which may be useful in chronic inflammation process such as atherosclerosis and diabetes mellitus.

## Conflicts of Interest

There are no conflicts of interest regarding this manuscript. Also, there was no funding. Ethical approval was not required.

## References

- White JW, Doner LW (1980) Honey composition and properties: Beekeeping in the United States. *Agric Handbook* 335: 82-91.
- Bogdanov S, Jurendic T, Sieber R, Gallmann P (2008) Honey for nutrition and health: a review. *J Am Coll Nutr* 27: 677-689.
- Ajibola A, Idowu GO, Amballi AA, Oyefuga OH, Iqot IS (2007) Improvement of some haematological parameters in albino rats with pure natural honey. *J BiolSci Res* 2: 67-69.
- Ajibola A, Chamunorwa JP, Erlwanger KH (2012) Nutraceutical values of natural honey and its contribution to human health and wealth. *Nutr Metab (Lond)* 9: 61.
- Gheldof N, Wang XH, Engeseth NJ (2002) Identification and quantification of antioxidant components of honeys from various floral sources. *J Agric Food Chem* 50: 5870-5877.
- Wang J, Li QX (2011) Chemical composition, characterization, and differentiation of honey botanical and geographical origins. *Adv Food Nutr Res* 62: 89-137.
- Arriaga E, Navarro-Calvo AL, Díaz-Carbajal E (2011) Botanical characterisation of Mexican honeys from a subtropical region (Oaxaca) based on pollen analysis. *Grana* 50: 40-45.
- Beretta G, Gelmini F, Lodi V, Piazzalunga A, MaffeiFacino R (2010) Profile of nitric oxide (NO) metabolites (nitrate, nitrite and N-nitroso groups) in honeys of different botanical origin: nitrate accumulation as index of origin, quality and of therapeutic opportunities. *J Pharm Biomed Anal* 53: 343-349.
- Beretta G, Caneva E, Facino RM (2007) Kynurenic acid in honey from arboreal plants: MS and NMR evidence. *Planta Med* 73: 1592-1595.
- Crane E (1975) History of honey. In: Crane E, editor. *Honey: a comprehensive survey*. London: William Heinemann 439-488.
- Mandal MD, Mandal S (2011) Honey: its medicinal property and antibacterial activity. *Asian Pac J Trop Biomed* 1: 154-160.
- Lusby PE, Coombes AL, Wilkinson JM (2005) Bactericidal activity of different honeys against pathogenic bacteria. *Arch Med Res* 36: 464-467.
- Mandal S, Deb Mandal M, Pal NK (2010) Synergistic anti-Staphylococcus aureus activity of amoxicillin in combination with *Embllicaofficinalis* and *Nymphaeodorata* extracts. *Asian Pac J Trop Med* 3: 711-714.
- Basualdo C, Sgroy V, Finola MS, Marioli JM (2007) Comparison of the antibacterial activity of honey from different provenance against bacteria usually isolated from skin wounds. *Vet Microbiol* 124: 375-381.
- Mandal S, Deb Mandal M, Pal NK, Saha K (2011) Antibacterial activity of honey against clinical isolates of *Escherichia coli*, *Pseudomonas aeruginosa* and *Salmonella entericaserovarTyphi*. *Asian Pac J Trop Med* 1: 154-160.
- Haniyeh K, Seyyed MS, Hussein M (2010) Preliminary study on the antibacterial activity of some medicinal plants of Khuzestan (Iran). *Asian Pac J Trop Med* 3: 180-184.
- O'Grady FW, Lambert HP, Finch RG, Greenwood D (1997) *Antibiotic and Chemotherapy*. (7<sup>th</sup>edn). New York: Churchill Living Stone.
- Khan FR, UI Abadin Z, Rauf N (2007) Honey: nutritional and medicinal value. *Int J Clin Pract* 61: 1705-1707.
- Kwakman PH, te Velde AA, de Boer L, Speijer D, Vandenbroucke-Grauls CM, et al. (2010) How honey kills bacteria. *FASEB J* 24: 2576-2582.
- Mundo MA, Padilla-Zakour OI, Worobo RW (2004) Growth inhibition of foodborne pathogens and food spoilage organisms by select raw honeys. *Int J Food Microbiol* 97: 1-8.
- Molan PC (1992) The antibacterial nature of honey. The nature of the antibacterial activity. *Bee World* 73: 5-28.
- Adams CJ, Boulton CH, Deadman BJ, Farr JM, Grainger MN, et al. (2008) Isolation by HPLC and characterisation of the bioactive fraction of New Zealand manuka (*Leptospermum scoparium*) honey. *Carbohydr Res* 343: 651-659.
- Church D, Elsayed S, Reid O, Winston B, Lindsay R (2006) Burn wound infections. *Clin Microbiol Rev* 19: 403-434.
- Erol S, Altoparlak U, Akcay MN, Celebi F, Parlak M (2004) Changes of microbial flora and wound colonization in burned patients. *Burns* 30: 357-361.
- Mavric E, Wittmann S, Barth G, Henle T (2008) Identification and quantification of methylglyoxal as the dominant antibacterial constituent of Manuka (*Leptospermum scoparium*) honeys from New Zealand. *Mol Nutr Food Res* 52: 483-489.
- Kwakman PH, Te Velde AA, de Boer L, Vandenbroucke-Grauls CM, Zaat SA (2011) Two major medicinal honeys have different mechanisms of bactericidal activity. *PLoS One* 6: e17709.
- Tan HT, Rahman RA, Gan SH, Halim AS, Hassan SA, et al. (2009) The antibacterial properties of Malaysian tualang honey against wound and enteric microorganisms in comparison to manuka honey. *BMC Complement Altern Med* 9: 34.
- AL-Waili N, Al-Ghamdi A, Ansari MJ, Al-Attal Y, Salom K (2012) Synergistic Effects of Honey and Propolis toward Drug Multi-Resistant *Staphylococcus Aureus*, *Escherichia Coli* and *Candida Albicans* Isolates in Single and Polymicrobial Cultures. *Int J Med Sci* 6: 773-780.
- Al-Waili NS (2003) Effects of daily consumption of honey solution on hematological indices and blood levels of minerals and enzymes in normal individuals. *J Med Food* 6: 135-140.
- Hussein SZ, Mohd Yusoff K, Makpol S, Mohd Yusof YA (2012) Gelam Honey Inhibits the Production of Proinflammatory Mediators NO, PGE(2), TNF- $\alpha$ , and IL-6 in Carrageenan-Induced Acute Paw Edema in Rats. *Evid Based Complement Alternat Med* 2012: 109636.
- Molan P (1998) Brief review of honey as a clinical dressing. *Aust J Wound Manage* 6: 148-158.
- Molan PC (1999) The role of honey in the management of wounds. *J Wound Care* 8: 415-418.
- Molan PC (1999) Why honey is effective as a medicine. I. Its use in modern medicine. *Bee World* 80: 80-92.
- Blassa M, Candracci M, Accorsi A, Piacentini MP, Albertini M C, et al (2006) Raw millefiori honey is packed full of antioxidants. *Food Chem* 97: 217-222.
- Bilsel Y, Bugra D, Yamaner S, Bulut T, Cevikbas U, et al. (2002) Could honey have a place in colitis therapy? Effects of honey, prednisolone, and disulfiram on inflammation, nitric oxide, and free radical formation. *Dig Surg* 19: 306-311.
- Medhi B, Prakasha A, Avti K, Saikia UN, Pandhia P, et al. (2008) Khanduja KL. Effect of manuka honey and sulfasalazine in combination to promote antioxidant defense system in experimentally induced ulcerative colitis model in rats. *Indian J Experiment Biol* 46: 583-590.
- Prakash A, Medhi B, Avti PK, Saikia UN, Pandhi P, et al. (2008) Effect of different doses of Manuka honey in experimentally induced inflammatory bowel disease in rats. *Phytother Res* 22: 1511-1519.
- Aljadi AM, Kamaruddin MY (2004) Evaluation of the phenolic contents and antioxidant capacities of two Malaysian floral honeys. *Food Chem* 85: 513-518.
- Kassim M, Achoui M, Mansor M, Yusoff KM (2010) The inhibitory effects of Gelam honey and its extracts on nitric oxide and prostaglandin E(2) in inflammatory tissues. *Fitoterapia* 81: 1196-1201.
- Yao LK, Razak SLA, Ismail N (2011) Malaysian gelam honey reduces oxidative damage and modulates antioxidant enzyme activities in young and middle aged rats. *J Med Plant Res* 5: 5618-5625.
- Mohamed M, Sirajudeen K, Swamy M, Yaacob NS, Sulaiman SA (2009) Studies on the antioxidant properties of Tualang honey of Malaysia. *Afr J Tradit Complement Altern Med* 7: 59-63.
- Khoo YT, Halim AS, Singh KK, Mohamad NA (2010) Wound contraction effects and antibacterial properties of Tualang honey on full-thickness burn wounds in rats in comparison to hydrofibre. *BMC Complement Altern Med* 10: 48.
- Hussein SZ, Yusoff KM, Makpol S, Yusof YA (2011) Antioxidant capacities and total phenolic contents increase with gamma irradiation in two types of Malaysian honey. *Molecules* 16: 6378-6395.
- Zohdi RM, Zakaria ZA, Mustapha NM, Yusof N, Abdullah MNH (2004) The effect of topical application of Malaysian honey on burn wound healing. *J Veterinar Malaysia* 16:47-50, 2004.
- Yun KJ, Kim JY, Kim JB, Lee KW, Jeong SY, et al. (2008) Inhibition of LPS-induced NO and PGE2 production by asiatic acid via NF-kappa B inactivation in RAW 264.7 macrophages: possible involvement of the IKK and MAPK pathways. *Int Immunopharmacol* 8: 431-441.

46. Ndip RN, Malange Takang AE, Echakachi CM, Malongue A, Akoachere JF, et al. (2007) In-vitro antimicrobial activity of selected honeys on clinical isolates of *Helicobacter pylori*. *Afr Health Sci* 7: 228-232.
47. Guerrini A, Bruni R, Maietti S, Poli F, Rossi D, et al. (2009) Ecuadorian stingless bee (*Meliponinae*) honey: A chemical and functional profile of an ancient health product. *Food Chem* 114: 1413-1420.
48. Bansal V, Medhi B, Pandhi P (2005) Honey--a remedy rediscovered and its therapeutic utility. *Kathmandu Univ Med J (KUMJ)* 3: 305-309.
49. Yao LK, Razac SLK, Ismail N (2011) Malaysian gelam honey reduces oxidative damage and modulates antioxidant enzyme activities in young and middle aged rats. *Journal of Medicinal Plant Research* 5: 5618-5625.
50. Al-Waili NS, Boni NS (2003) Natural honey lowers plasma prostaglandin concentrations in normal individuals. *J Med Food* 6: 129-133.
51. Hussein SZ, Mohd Yusoff K, Makpol S, Mohd Yusof YA (2013) Gelam honey attenuates carrageenan-induced rat paw inflammation via NF- $\kappa$ B pathway. *PLoS One* 8: e72365.
52. Reyes-Gordillo K, Segovia J, Shibayama M, Vergara P, Moreno MG, et al. (2007) Curcumin protects against acute liver damage in the rat by inhibiting NF- $\kappa$ B, proinflammatory cytokines production and oxidative stress. *Biochim Biophys Acta* 1770: 989-996.
53. Himaya SW, Ryu B, Qian ZJ, Li Y, Kim SK (2011) 1-(5-bromo-2-hydroxy-4-methoxyphenyl)ethanone [SE1] suppresses pro-inflammatory responses by blocking NF- $\kappa$ B and MAPK signaling pathways in activated microglia. *Eur J Pharmacol* 670: 608-616.
54. Al-Waili NS (2004) Natural honey lowers plasma glucose, C-reactive protein, homocysteine, and blood lipids in healthy, diabetic, and hyperlipidemic subjects: comparison with dextrose and sucrose. *J Med Food* 7: 100-107.
55. Johnston JE, Sepe HA, Miano CL, Brannan RG, Alderton AL (2005) Honey inhibits lipid oxidation in ready-to-eat ground beef patties. *Meat Sci* 70: 627-631.
56. Turkmen N, Sari F, Poyrazoglu ES, Velioglu YS (2006) Effects of prolonged heating on antioxidant activity and colour of honey. *Food Chem* 95: 653-657.
57. Rakha MK, Nabil ZI, Hussein AA (2008) Cardioactive and vasoactive effects of natural wild honey against cardiac malperformance induced by hyperadrenergic activity. *J Med Food* 11: 91-98.
58. Al-Mamary M, Al-Meerri A, Al-Habori M (2002) Antioxidant activities and total phenolics of different types of honey. *Nutr Res* 22: 1041-1047.
59. Gheldof N, Engeseth NJ (2002) Antioxidant capacity of honeys from various floral sources based on the determination of oxygen radical absorbance capacity and inhibition of in vitro lipoprotein oxidation in human serum samples. *J Agric Food Chem* 50: 3050-3055.
60. Beretta G, Granata P, Ferrero M, Orioli M, MaffeiFacino R (2005) Standardization of antioxidant properties of honey by a combination of spectrophotometric/fluorimetric assays and chemometrics. *Anal Chim Acta* 533: 185-191.
61. Sereia MJ, Alves EM, Toledo VA, Marchini LC, Serine ES, et al. (2011) Physicochemical characteristics and pollen spectra of organic and non-organic honey samples of *Apis mellifera* L. *An Acad Bras Cienc* 83: 1077-1090.
62. Arráez-Román D, Gómez-Caravaca AM, Gómez-Romero M, Segura-Carretero A, Fernández-Gutiérrez A (2006) Identification of phenolic compounds in rosemary honey using solid-phase extraction by capillary electrophoresis-electrospray ionization-mass spectrometry. *J Pharm Biomed Anal* 41: 1648-1656.
63. Castro-Vázquez L, Diaz-Maroto MC, Gonzalez-Vinas MA, Pérez-Coell MS (2009) Differentiation of monofloral citrus, rosemary, eucalyptus, lavender, thyme and heather honeys based on volatile composition and sensory descriptive analysis. *Food Chem* 112: 1022-1030.
64. Chowdhury MM (1999) Honey: is it worth rubbing it in? *J R Soc Med* 92: 663.
65. Küçük M, Kolayl S, Karaoglu S, Ulusoy E, Baltaci C, et al. Biological activities and chemical composition of three honeys of different types from Anatolia. *Food Chem* 100: 526-534.
66. Frankel S, Robinson GE, Berenbaum MR (1998) Antioxidant capacity and correlated characteristics of 14 unifloral honeys. *J Apicul Res* 37:27-31.
67. Blasa M, Candiracci M, Accorsi A, Piacentini MP, Albertini MC, et al. (2006) Raw Millefiori honey is packed full of antioxidants. *Food Chem* 97: 217-222.
68. Rashed MN, Soltan ME (2004) Major and trace elements in different types of Egyptian mono-floral and non-floral bee honeys. *J Food Compos Anal* 17: 725-35.
69. Lachman J, Koliňová D, Miholová D, Kořata J, Titera D, et al. (2007) Analysis of minority honey components: Possible use for the evaluation of honey quality. *Food Chem* 101: 973-979.
70. Lee DC, Lee SY, Cha SH, Choi YS, Rhee HI (1998) Discrimination of native bee-honey and foreign bee-honey by SDS-PAGE. *Korean J Food Sci* 30: 1-5.
71. Alvarez-Suarez, Jagdish T, Joseph I (2004) Quantification of saccharides in multiple floral honeys using fourier transform infrared microattenuated total reflectance spectroscopy. *J Agric Food Chem* 52: 3237-3243.
72. Yaghoobi N, Al-Waili N, Ghayour-Mobarhan M, Parizadeh SM, Abasalti Z, et al. (2008) Natural honey and cardiovascular risk factors; effects on blood glucose, cholesterol, triacylglycerol, CRP, and body weight compared with sucrose. *Sci World J* 8: 463-469.
73. Inoue K, Murayama S, Seshimo F, Takeba K, Yoshimura Y, et al (1952) Identification of phenolic compound in manuka honey as specific superoxide anion radical scavenger using electron spin resonance (ESR) and liquid chromatography with colorimetric array detection. *J Sci Food Agric* 85:872-878, 2005. doi: 10.1002/jsfa.1952.
74. Münstedt K, Hoffmann S, Hauenschild A, Bülte M, von Georgi R, et al. (2009) Effect of honey on serum cholesterol and lipid values. *J Med Food* 12: 624-628.
75. Chepulis L, Starkey N (2008) The long-term effects of feeding honey compared with sucrose and a sugar-free diet on weight gain, lipid profiles, and DEXA measurements in rats. *J Food Sci* 73: H1-7.
76. Heman RH, Zakim D (1968) Fructose metabolism. I. The fructose metabolic pathway. *Am J Clin Nutr* 21: 245-249.
77. Buserrolles J, Gueux E, Rock E, Mazur A, Rayssiguier Y (2002) Substituting honey for refined carbohydrates protects rats from hypertriglyceridemic and prooxidative effects of fructose. *J Nutr* 132: 3379-3382.
78. Johnson RJ, Segal MS, Sautin Y, Nakagawa T, Feig DI, et al. (2007) Potential role of sugar (fructose) in the epidemic of hypertension, obesity and the metabolic syndrome, diabetes, kidney disease, and cardiovascular disease. *Am J Clin Nutr* 86: 899-906.
79. Zalibera M, Stasko A, Slebodova A, Jancovicova V, Cermakova T, et al. (2008) Antioxidant and radical-scavenging activities of Slovak honeys--An electron paramagnetic resonance study. *Food Chem* 110: 512-521.
80. Erejuwa OO, Sulaiman SA, Wahab MS, Sirajudeen KN, Salleh MS, et al. (2011) Glibenclamide or metformin combined with honey improves glycemic control in streptozotocin-induced diabetic rats. *Int J Biol Sci* 7: 244-252.