

# Honey as Nutrient and Functional Food

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## INTRODUCTION

As the only available sweetener honey was an important food for Homo sapiens since his very beginnings. Indeed, the relation between bees and Homo sapiens started as early as stone age <sup>77</sup>. In order to reach the sweet honey, man was ready to risk his life (Figure 1). Already the first written reference to honey, a Sumerian tablet writing, dating back to 2100-2000 BC, mentions honey's use as a drug and an ointment <sup>76</sup>. In most ancient cultures honey has been used for both nutritional purposes and for medicine <sup>24, 76, 78, 130</sup>. According to the bible, the wise Solomon has said: "Eat honey my son, because it is good" (Old Testament, proverb 24:13). The belief, that honey is a nutrient, drug and an ointment has been carried into our days. For a long time in human history it was the only known sweetener, until industrial sugar production began to replace it after 1800 <sup>76</sup>. In the long human history honey has been not only as a nutrient but also as a medicine <sup>130</sup>. A medicine branch, called apitherapy, has developed in recent years, offering treatments for many diseases by honey and the other bee products (see Chapter 7).

At present the annual world honey production is about 1.2 million tons, which is less than 1% of the total sugar production. Today, honey is one of the last untreated natural foods. The consumption of honey differs strongly from country to country. In the major honey producing and exporting countries China and Argentina the annual consumption is small: 0.1 to 0.2 kg per capita. It is higher in developed countries, where the home production does not always cover the market needs. In the European Union, which is both a major honey importer and producer, the annual consumption per capita varies from medium (0.3-0.4 kg) in Italy, France, Great Britain, Denmark, Portugal to high (1-1.8 kg) in Germany, Austria, Switzerland, Portugal, Hungary, Greece, while in overseas countries such as USA, Canada and Australia the average per capita consumption is 0.6 to 0.8 kg/year (see Honey Chapter on this homepage)

Different surveys on nutritional and health aspects of honey have been compiled <sup>14, 25, 28, 116, 119, 170, 176</sup>

## COMPOSITION AND NUTRITIONAL REQUIREMENTS

### Carbohydrates

Main sugars are the monosaccharides fructose and glucose. Beyond the two monosaccharides, about 25 different oligosaccharides have been detected, between them nutrition relevant ones such as panose, 1-kestose, 6-kestose, palatinose <sup>86, 217</sup>. The principal oligosaccharides in blossom honey are the disaccharides sucrose, maltose, trehalose and turanose. Honeydew honey compared to blossom honey contains higher amounts of oligosaccharides, and also trisaccharides such as melezitose and raffinose. During digestion the principal carbohydrates fructose and glucose are quickly transported into the blood and can be utilized for energy requirements of the human body. A daily dose of 20 g honey will cover about 3% of the required daily energy

### Proteins, enzymes and amino acids

Honey contains about 0.5% proteins, mainly enzymes and amino acids. Its contribution to human protein intake is marginal with respect to quantity (Table 2).

Three main honey enzymes are diastase (amylase), decomposing starch or glycogen into smaller sugar units, invertase (sucrase, glucosidase), decomposing sucrose into fructose and glucose, as well as glucose oxidase, producing hydrogen peroxide and gluconic acid from glucose. Since the saliva yields a sufficiently high activity of amylase and glucose oxidase, honey's contribution to sugar digestion is of minor importance. Honey glucose oxidase producing hydrogen peroxide, might exert an antibacterial effect in the oral cavity.

Table 1. A. Main honey nutrients, after<sup>54</sup>

Ingredient	Amount in 100 g	Recommended Daily Intake <sup>1</sup>			
		1-4 years old	4-15 years old	After 15 years old	
Carbohydrates	kcal	300	1000-1100	1400-2700	2400-3100
Proteins	g	0.5	13-14	17-46	44-59
Fats	g	0	-	-	-
<b>Minerals</b>	mg				
Sodium (Na)		1.6-17	300	410-550	550
Calcium (Ca)		3-31	600	700-1200	1000-1200
Potassium (K)		40-3500	1000	1400-1900	2000
Magnesium (Mg)		0.7-13	80	120-310	300-400
Phosphorus (P)		2-15	500	600-1250	700-1250
Zinc (Zn)		0.05-2	3	5-9.5	7-10
Copper (Cu)		0.02-0.6	0.5-1	0.5-1	0.5-1
Iron (Fe)		0.03-4	8	8-15	10-15
Manganese (Mn)		0.02-2	1-1.5	1.5-5	2-5
Chromium (Cr)		0.01-0.3	0.02-0.06	0.02-0.1	0.03-1.5
Selenium (Se)		0.002-0.01	0.001-0.004	0.001-0.006	0.003-0.007

Table 1. B Vitamins in honey, according to<sup>54, 72, 85</sup>

Vitamins	mg/kg			
Phyllochinon (K)	ca. 0.025	15	20-50	60-70
Thiamin (B <sub>1</sub> )	0.02-0.9	0.6	0.8-1.4	1-1.3
Riboflavin (B <sub>2</sub> )	0.01-0.9	0.7	0.9-1.6	1.2-1.5
Niacin <sup>2</sup> (B <sub>3</sub> )	0.10-2.7	7	10-18	13-17
Panθοthenic acid (B <sub>5</sub> )	0.02-1.9	4	4-6	6
Pyridoxin (B <sub>6</sub> )	0.01-0.32	0.4	0.5-1.4	1.2-1.6
Folic acid (B <sub>9</sub> )	0.01-0.7	0.2	0.3	0.4
Ascorbic acid (C)	0.1-2.5	60	70-100	100

<sup>2</sup> Niacin equivalents: 1 mg nicotinamide = 1 mg niacin = 60 mg tryptophan (= niacin-precursor)

Table 2 Other trace elements in honey, after<sup>54</sup>

Element	mg/100 g	Element	mg/100 g
Aluminium (Al)	0.01-2.4	Lead (Pb)*	0.001-0.03
Arsen (As)	0.014-0.026	Lithium (Li)	0.225-1.56
Barium (Ba)	0.01-0.08	Molybdenum (Mo)	0-0.004
Boron (B)	0.05-0.3	Nickel (Ni)	0-0.051
Bromine (Br)	0.4-1.3	Rubidium (Rb)	0.040-3.5
Cadmium (Cd)*	0-0.001	Silicium (Si)	0.05-24
Chlorine (Cl)	0.4-56	Strontium (Sr)	0.04-0.35
Cobalt (Co)	0.1-0.35	Sulfur (S)	0.7-26
Fluoride (F)	0.4-1.34	Vanadium (V)	0-0.013
Iodine (I)	10-100	Zirkonium (Zr)	0.05-0.08

\*- elements regarded as toxic, can be partially of anthropological origin

## Vitamins, minerals and trace compounds

The amount of vitamins and minerals is small and the contribution of honey to the recommended daily intake (RDI) of the different trace substances is marginal (Table 2). It must be born in mind that different unifloral honeys contain different amounts of minerals<sup>37</sup>.

Honey contains a number of other trace elements. From the nutritional point of view the minerals chrome, manganese and selenium are of nutritional importance, especially for children of the age of 1 to 15 year. The elements sulphur, boron, cobalt, fluorine, iodine, molybdenum and silicon can be important in human nutrition too, although there are no RDI values proposed for these elements (Table 2).

Honey contains 0.3-25 mg/kg choline and 0.06 to 5 mg/kg acetylcholine<sup>119</sup>. Choline is an essential for cardiovascular and brain function, and for cellular membrane composition and repair, while acetylcholine acts as a neurotransmitter.

## Aroma compounds, taste-building compounds and polyphenols

There is a wide variety of honeys with different tastes and colours, depending on their botanical origin<sup>79</sup>. The sugars are the main taste-building compounds. Generally, honey with high fructose content (e.g. acacia) are sweet compared to those with high glucose concentration (e.g. rape). Beyond sugars the honey aroma depends on the quantity and quality of honey acids and amino acids. In the past decades some research on honey aroma compounds has been carried out and more than 500 different volatile compounds have been identified in different types of honey. Indeed, most aroma building compounds vary in the different types of honey depending on its botanical origin<sup>55</sup>. Honey flavour is an important quality for its application in food industry and also a selection criterion for consumer's choice.

Polyphenols are another important group of compounds with respect to appearance and functional properties. 56 to 500 mg/kg total polyphenols were found in different honey types, depending on the honey type<sup>13, 111</sup>. Polyphenols in honey are mainly flavonoids (e.g. quercetin, luteolin, kaempferol, apigenin, chrysin, galangin), phenolic acids and phenolic acid derivatives<sup>228</sup>. The flavonoid content can vary between 2 and 46 mg/kg of honey and was higher in samples produced during dry season with high temperatures<sup>134</sup>. The polyphenols are responsible for the antioxidant properties of honey.

## ATHLETIC PERFORMANCE

The physiological action of gel and powdered forms of honey as a carbohydrate source for athlete performance, mainly cycling one, was studied recently under controlled conditions by Kreider and coworkers<sup>93, 95, 138, 139, 141, 142</sup>. Honey increases significantly the heart frequency and the blood glucose level during performance<sup>143</sup>. It did not promote physical or psychological signs of hypoglycemia in fasted subjects<sup>142, 152</sup>, during resistance training<sup>93</sup> or following resistance training<sup>93, 94</sup>. In another trial the effect of low and high glycemic index carbohydrate gels and honey were tested on 64 km cycling performance<sup>95, 143</sup>. Both high (glucose) and low GI (honey) gels increased cycling performance, honey being slightly better than glucose. The carbohydrate profile and GI response of honey was identical to that of a popular sports gel<sup>142, 203</sup>. According to these authors honey is well tolerated and can be an effective carbohydrate source for athletic performance. Summarising the research on honey and sport nutrition it is recommended that the amount of honey should be adapted to the body weight and to the ingestion time before exercise<sup>138</sup>:

- 4 hours before exercise: ingest 4 g per kg body weight
- 1 hour before exercise: ingest 1 gram per kg body weight
- 10 minutes before exercise: ingest 0.5 g per kg body weight
- During exercises 30 to 60 g can be ingested during each hour of exercise.

After physical exercise or competition carbohydrates should be supplemented by protein for optimal recovery. Dry honey, combined with whey protein was found to be more effective than protein combinations with glucose or maltodextrin<sup>138</sup>. For optimal recovery athletes should consume about 1 g honey per kg body weight within 15 minutes and repeat this procedure for the next 4 to 6 hours. Combining of honey with protein (3:1) may help to inhibit protein catabolism after the exercise<sup>138</sup>. The results by Kreider and coworkers<sup>93, 95, 138-140, 142</sup> should be confirmed by other researchers.

# GLYCEMIC INDEX, GLUCOSE AND FRUCTOSE

## Glycemic index, diabetes and the human diet

The impact of carbohydrates on human health is discussed controversially especially the understanding of how the carbohydrate content of a given food affects blood glucose levels. Today, the dietary significance of carbohydrates is often indicated in terms of the glycemic index (GI). Carbohydrates having a low GI induce a small increase of glucose in blood, while those with high GI induce a high blood glucose level. Fructose, besides glucose the main honey sugar, has a GI of 19, sucrose: 68. Theoretically high-fructose honeys like acacia, tupelo, chestnut, thyme, calluna should have a relatively lower GI. The only comprehensive data on honey GI is the one presented in table 3. It is based mainly on data of different Australian honeys<sup>31, 106</sup>. There was a significant negative correlation between fructose content and GI is probably due to the diverse fructose/glucose ratios of the various honey types testes. It is known that unifloral honeys have varying fructose content<sup>106, 194</sup>. Indeed, there is a significant negative correlation between honey GI and fructose concentration (Arcot & Brand-Miller, 2005). Some honeys, e.g. acacia and yellow box, with relatively high concentration of fructose, have a lower GI than other honey types (Table 3). A negative correlation between GI and fructose was established, while there was no significant correlation between GI and the other honey sugars. In a study with four North American honeys with different fructose content the resulting GI values were higher than those of the Australian study and varied between 69 and 74<sup>124</sup>. In another US investigation the GI of a honey of an unidentified botanical origin was found to be 35<sup>142</sup>. Recently a study with German honeys revealed GI values lying between 49 and 89<sup>41, 84</sup>. In these studies acacia, chestnut, linden and heather honey had GI between 49 and 55. A rape honey had a GI of 64 while a honeydew honey had the highest GI with 89, which was due to its high melezitose content.

In experiments with humans Ahmad et al showed that the honey induced glucose rise in blood is less pronounced than that after intake of artificial honey control and glucose<sup>5</sup>.

The effect of ingestion of a 75 g sugar solution containing linden honey or fructose/glucose control on serum insulin and C-peptide values of healthy humans was examined. These parameters were significantly lower for honey. The mean serum glucose concentration was also lower for honey, but direct comparisons at the various times showed no significant differences between the honey and the control. However, the area under the concentration-time profile for glucose response was lower for the honey than the control<sup>184</sup>.

The GI concept claims to predict the role of carbohydrates in the development of obesity<sup>156</sup>, meaning that low GI honeys could be a valuable alternative to high GI sweeteners. In order to take into consideration the quantity of ingested food, a new term, the glycemic load, is introduced. It is calculated as the glycemic index multiplied with the carbohydrate content in a given portion, divided by 100. Values lower than 10 are considered low, 10 to 20 are intermediate ones and above 20 belong to the category "high". For an assumed honey portion of 25 g the glycemic load of most honeys is low and some are in the intermediate range (Table 3).

The GI concept was developed to provide a numeric classification of carbohydrate foods on the assumption that such data would be useful in situations in which glucose tolerance is impaired. Therefore food with low GI should provide benefits with respect to diabetes and to the reduction of coronary heart disease<sup>129</sup>. Thus, consumption of honeys with a low GI, e.g. acacia honey might have beneficial physiological effects and could be used by diabetes patients. The consumption of 50 to 80 g honey of unspecified type by healthy people or diabetes patients leads to smaller increases of blood insulin and glucose than the consumption of the same amounts of glucose and of a sugar mixtures resembling to honey<sup>12, 18, 128</sup>. It was shown that consumption of honey had a favourable effect on diabetes patients, causing a significant decrease of plasma glucose<sup>16, 18, 191</sup>. Honey was well tolerated by patients with diabetes of unspecified type<sup>36</sup> and on diabetes type-2 patients<sup>56, 133, 208</sup>. According to recent studies, long term consumption of food with a high GI is a significant risk factor for type-2 diabetes<sup>154</sup>.

Relatively high amounts from 70 to 90 g honey were administered without any problems for the type 2 diabetes<sup>4, 18</sup>.

Honey seems to be also well tolerated by type 1 diabetes patients. Honey caused a higher c-peptide increase than comparable amounts of sucrose or glucose<sup>2</sup>. The c-peptide is a mass of the insulin increase in blood.

On the other hand it was found that linden honey caused lower c-peptide increase than comparable amounts of a fructose/glucose mixture<sup>184</sup>. The contradiction between the two studies should be resolved.

Table 3. Glycemic index (GI) and glycemic load (GL) for a serving (25 g) of honey, after <sup>31, 106</sup>

	honey origin	Fructose g /100 g	GI	AC g/serving	GL (per serving)
Acacia (black lockust)*	Romania	43	32	21	7
Yellow box	Australia	46	35±4	18	6
Stringy bark	Australia	52	44±4	21	9
Red gum	Australia	35	46±3	18	8
Iron bark	Australia	34	48±3	15	7
Yapunya	Australia	42	52±5	17	9
Pure Australia	Australia		58±6	21	12
Commercial blend	Australia	38	62±3	18	11
Salvation June	Australia	32	64±5	15	10
Commercial blend	Australia	28	72±6	13	9
Honey of unspecified origin	Canada		87±8	21	18
average		55	55±5	18	10
Glucose			100		
Fructose			19		

AC = available carbohydrate

## Fructose and obesity

Fructose is the main sugar in most honeys (Table 1). An over-consumption of fructose in today's American diet, mainly in the form of high-fructose corn syrup, is suspected to be one of the main causes for overweight problems<sup>97</sup>. After reviewing clinical studies these authors found that fructose ingestion leads to a rise of de-novo lipogenesis, which finally has an unfavourable effect on energy regulation and on body weight.

In rat feeding experiments the hypertriglyceridemic effect observed after intake of fructose alone does not take place after feeding of honey fructose. Compared to rats fed with fructose, honey-fed rats had higher plasma  $\alpha$ -tocopherol levels, higher  $\alpha$ -tocopherol/triacylglycerol ratios, lower plasma NO<sub>x</sub> concentrations and a lower susceptibility of the heart to lipid peroxidation. These data suggest a potential nutritional benefit of substituting fructose by honey in the ingested diets<sup>64</sup>.

It was shown that in patients with hypertriglyceridemia, artificial honey increased TG, while honey decreased TG<sup>9</sup>.

Recently it was found out that feeding rats by 10 % honey solution decreased the weight of the rats by decreasing their feeding frequency<sup>47</sup>.

Feeding of honey or sugar to Wistar rats resulted both in increase of weight in comparison to controls. Sucrose fed fat cells were significantly larger than the honey fed ones.<sup>205</sup>

Honey ingestion by humans leads to a rise of blood fructose concentration: in one case (rape honey), this rise was lower than that achieved after fructose/glucose controls, in the other cases it was same as after the controls (acacia honey). Fructose metabolism may be inhibited by unidentified substances present in the rapeseed honey<sup>183</sup>

***Summarising the above research, honey has probably no or a weak effect on obesity compared to pure fructose. However, there is need of further tests with human nutrition studies, carried with a variety of unifloral honeys.***

## INFANT NUTRITION

The application of honey in infant nutrition used to be a common recommendation during the last centuries and there are some interesting observations reported. Infants on a diet containing honey had better blood building and a higher weight increase compared to a diet without honey<sup>108</sup>. Honey was better tolerated by babies than sucrose<sup>180</sup> and compared to a water based placebo significantly reduced crying phases of infants<sup>201</sup>. Infants have a higher weight increase when fed by honey than by sucrose, and showed less throw up than the sucrose controls<sup>178</sup>. Compared to sucrose, ingestion of honey by infants resulted in an increase of haemoglobin content, better skin colour while no digestion problems were encountered<sup>222, 229</sup>. Infants exposed to a honey regimen had a better weight increase and during the regimen were less susceptible to diseases than infants fed normally or infants given blood building agents<sup>108</sup>.

The positive effects of honey in infant diet are attributed to effects on the digestion process. One possible cause is the well established effect of oligosaccharides on *B. bifidus*<sup>204</sup>. When fed on a mixture of honey and milk infants showed a regularly steady weight gain and had an acidophilic microorganism flora rich in *B. bifidus*<sup>121</sup>. In an other experiment with honey and milk it was shown that the infants were suffering less frequently from diarrhoea, and their blood contained more haemoglobin compared to a diet based on sucrose sweetened milk<sup>222</sup>. Feeding honey to infants improved calcium uptake into the blood, resulting in lighter and thinner faeces<sup>43</sup>.

There is a health concern for infants regarding the presence of *Clostridium botulinum* in honey. Since the presence of this bacterium in natural foods is ubiquitous and honey is a non sterilized packaged food from natural origin the risk of a low contamination cannot be excluded. Spores of this bacterium can survive in honey, but they cannot build toxin. But in the stomach of infants younger than one year the bacteria spores from honey can survive, grow, and theoretically build the toxin. On the other hand humans older than 12 months can ingest honey without any risk. In some cases, infant botulism has been explained by ingestion of honey<sup>75, 166, 181, 224</sup>. In Germany about one case of infant botulism per year is reported<sup>181</sup>. As a result of the reported infant botulism cases some honey packers (e.g. the British Honey Importers and Packers Association) place a warning on the honey label that “honey should not be given to infants under 12 months of age”. Recently, a scientific committee of the EU has examined the hazard of *Cl. botulinum* in honey. It has concluded, that no microbiological examinations of honey are necessary, as the incidence of *Cl. botulinum* is relatively low and tests will not prevent infant botulism. In the EU countries the health authorities have not issued a warning label on honey pots. Also, the counter-indication of honey in nourishing of infants in developing countries has been questioned<sup>100</sup>.

**For safety reasons honey should be given only to infants older than 1 year**

## ANTIMICROBIAL PROPERTIES

The antimicrobial action of honey has been extensively reviewed in 1992 by Molan<sup>173, 174</sup> and in 2011 by Al-Waili et al.<sup>10</sup>. It has both a direct and an indirect action.

### Indirect antimicrobial action

Honey can fight microbial infection by its immuno-activating, anti-inflammatory and prebiotic activity.

### Direct antimicrobial action



Honey inhibits the growth of microorganisms and fungi. The antibacterial effect of honey, mostly against gram-positive bacteria, is very well documented<sup>50, 171, 173, 175</sup>. Both bacteriostatic and bactericidal effects have been reported, against many strains, many of which are pathogenic (Table 5).

In 1937 Dold et al. determined the antibacterial activity as inhibine. The antibacterial assay carried out with *Staph. aureus* was sensitive to hydrogen peroxide. Researchers using this method found a good correlation between the capacity of honey to produce peroxide and the inhibine value. Honey glucose oxidase produces the antibacterial agent hydrogen peroxide<sup>244</sup>, while another enzyme, catalase breaks it down<sup>88</sup>. Honey with a high catalase activity have a low antibacterial peroxide activity<sup>70, 71</sup>. White established a good correlation between the peroxide accumulation capacity and the antibacterial activity expressed as inhibine<sup>90, 243</sup>. Lavie was the first to postulate the existence of other antibacterial substances in honey<sup>147</sup>.

Table 4 Infections caused by bacteria that have found to be sensitive to honey<sup>171, 175</sup>

Pathogen	Infection caused
<i>Bacillus anthracis</i>	anthrax
<i>Corynebacterium diphtheriae</i>	diphtheria
<i>Escherichia coli</i>	diarrhoea, septicaemia, urinary infections, wound infections
<i>Haemophilus influenzae</i>	ear infections, meningitis, respiratory infections, sinusitis
<i>Klebsiella pneumoniae</i>	pneumonia
<i>Mycobacterium tuberculosis</i>	tuberculosis
<i>Proteus sp.</i>	septicaemia, urinary infections
<i>Pseudomonas aeruginosa</i>	urinary infections, wound infections
<i>Salmonella sp.</i>	diarrhoea
<i>Salmonella cholerae-suis</i>	septicaemia
<i>Salmonella typhi</i>	typhoid
<i>Salmonella typhimurium</i>	wound infections
<i>Serratia marcescens</i>	septicaemia, wound infections
<i>Shigella sp.</i>	dysentery
<i>Staphylococcus aureus</i>	abscesses., boils, carbuncles, impetigo, wound infections
<i>Streptococcus faecalis</i>	urinary infections
<i>Streptococcus mutans</i>	dental carries
<i>Streptococcus pneumoniae</i>	ear infections, meningitis, pneumonia, sinusitis
<i>Streptococcus pyogenes</i>	ear infections, impetigo, puerperal fever, rheumatic fever, scarlet fever, sore throat, wound infections
<i>Vibrio cholerae</i>	cholera
<i>Actin. pyogenes, Kleb. Pneum., Noc. asteroides, Staph. aureus, Streptoc. agal., dysgal.,</i>	mastitis
<i>Epiderm floccosum, Microsp. canis, M. gypseum, Trichoph. rubrum, T. tonsurans, T. mentagr. var.</i>	tinea
<i>E coli, Salmonella, Shigella, Vibrio, Hel. pylori</i>	peptic ulcer

It was reported that depending on the antibacterial test it is possible to differentiate between the peroxide and non peroxide antibacterial action. Using this test different types of antibacterial substances have been determined, the chemical identity of which remains to be determined. The substances have different chemical characteristics: acidic, basic or neutral and that the main non-peroxide antibacterial activity is acidic<sup>50</sup>.

Studies with Malaysian Tualang honey showed also, that the main non-peroxide antibacterial activity is acidic<sup>135</sup>. Interestingly, honey acts best against bacteria in acedic medium. This is important from therapeutic point of view as the wound medium is also acidic<sup>17</sup>

Truchado et al, using another antibacterial test measured also mainly non-peroxide antibacterial activity<sup>231</sup>. Thus, depending on the antibacterial test different types of antibacterial activity can be determined. Summarising, antimicrobial effect of honey is due to different substances and depends on the botanical origin of honey<sup>50, 171, 173, 175</sup>. There are non-peroxide antibacterial substances with different chemical origin, e.g. and compounds with different chemical properties:

1. Phenolics and flavonoids, present in honey are also likely candidates, as many of them have been shown to have antibacterial activity<sup>22, 80, 99, 159, 179, 240</sup>, but there was no correlation between honey phenolics and antibacterial action<sup>231</sup>. In a study with Cuban unifloral honeys honeys with higher phenolic content tended to have a higher antibacterial activity<sup>27</sup>

2. The high sugar concentration of honey<sup>182</sup>, and also the low honey pH<sup>248</sup> can be responsible for the antibacterial activity.

3. Undetermined components of the water and methanolic extract of chestnut honey inhibit pathogenic bacteria like *Erwinia carotovora*, *Yersinia enterocolitica*, and *Aeromonas hydrophila* interfering in the quorum signal (QS) system of bacteria. The bacterial QS system is thought to determine the virulence of bacteria. The substances are thought to belong to the carbohydrate fraction of honey<sup>230</sup>.
4. Carbohydrate break-down Maillard products, present in Canadian honey<sup>61, 63</sup> and probably also in any honey, have an antibacterial activity. These substances are also present in fresh honey.
5. Antibacterial aromatic acids<sup>207</sup> and 10-HDA, the main royal jelly acid with antibacterial properties<sup>125</sup> have also been found in honey.
6. An antibacterial honey protein as defensin-1, which originates in royal jelly, was also found in honey<sup>145</sup>.
7. Honey bacteria produce antibiotic-like antifungal peptide compounds, e.g. bacillomycin F<sup>150, 151</sup>
8. The strong antibacterial activity of Manuka honey is due to the presence of the antibacterial substance methylglyoxal<sup>163</sup>.

Summarising, following antibacterial factors are responsible for the antibacterial action

- **Osmotic effect of sugars**
- **pH and honey acids**
- **Hydrogen peroxide**
- **Others: phenolics, carbohydrates, Maillard products, proteins, antibiotic-like peptides methylglyoxal, and other non-determined substances**

Contrary to the non-peroxide activity, the peroxide one can be destroyed by heat, by light and by storage<sup>50</sup> (Table 6). The antibacterial activity of light blossom honey was more influenced by these different factors than that of the dark honeydew honey. Thus, for optimum antibacterial activity, honey should be stored in a cool, dark place and should be consumed when fresh.

Some of the antimicrobial activity originates from the bees (the peroxide producing enzymes, the honey acids, carbohydrates, defensin-1, antibiotic-like compounds) while some of it originates from the plants (methylglyoxal, polyphenols) while a third part might be created during honey storage (Maillard products).

### **Influence of heat and storage**

Table 5. **Influence of heat, light and storage on the antibacterial activity of honey against *Staph. aureus* after**<sup>49, 52</sup>

	Non-peroxide activity		Peroxide activity	
	light	dark	light	dark
<b>Storage: 15 months at rt</b>				
Blossom honey	76	86	19	48
Honeydew honey	78	80	63	70
<b>Heat: 15 min 70°C</b>				
Blossom honey		86		8
Honeydew honey		94		78

antibacterial activity in % of the untreated controls, rt – room temperature 20-25 °C

Only fresh and unheated honey has optimum antibacterial activity. Early research showed that the peroxide activity is destroyed by heat and by storage in the light<sup>89, 241, 242</sup>. On the other hand it was shown that the non-peroxide activity is less susceptible to heat and light<sup>49, 52, 114</sup>. On the other hand, Maillard products which are produced upon heating and storage of honey have also antibacterial activity<sup>61, 63</sup>. The results are difficult to interpret as it is not clear which type of antibacterial activity has been tested in many studies. However, taken as a whole there is an overall decrease of all activity upon storage, less if stored in the dark.

***For optimum activity store unheated honey in a dark cool place.***

### **Bactericidal or bacteriostatic?**

In most of the reports on honey antibacterial action no distinction has been made between the two. Most experiments report on stop of bacterial growth after a certain time. The higher the concentration the longer is the period of growth inhibition. Complete inhibition of growth is important for controlling infections<sup>173</sup>.

The bactericidal action of honey seems to be dependent on the time of honey action. The time for bactericidal action depends on the bacteria type and vary from several to 40 hours. The concentration of honey also plays a role. Honey concentrations varying from 5 to 50 % have been found to be bactericidal. Generally, the higher the concentration, the faster the bactericidal action can take place<sup>173</sup>.

### **Antiviral, fungicide and anti-parasite activity**

It was reported that honey has been also shown to inhibit in vitro the *Rubella* virus<sup>251</sup> and *Herpes* virus<sup>19</sup> and three species of the *Leishmania* parasite<sup>252</sup>.

Honey has also **fungicide** activity, but not many fungi species have been tested. It has antifungal activity against dermatophytes, that can cause human mycoses (Tinea). Such mycoses is a common disease in humans. Honey has been shown to have a fungicide activity against dermatophytes from the genera *Epidermophyton*, *Microsporum* and *Trichophyton*, all species that can affect humans<sup>175</sup>.

Recently honey samples from different floral sources were evaluated for their ability to inhibit the growth of 40 yeast strains (*Candida albicans*, *C. krusei*, *C. glabrata* and *Trichosporon spp.*). Rhododendron and multifloral honeys have generally more inhibitory effect than eucalyptus and orange honeys ( $P < 0.05$ )<sup>137</sup>. Different unifloral honey from Slovakia also showed antifungal activity against *Penicillium crustosum*, *P. expansum*, *P. griseofulvum*, *P. raistrickii* and *P. verrucosum*, mostly at concentration higher than 10%<sup>131</sup>. Further studies are now required to demonstrate if this antifungal activity has any clinical application.

The fungicide effect of honey against *Candida albicans* is due to the effect of honey flavonoids<sup>65</sup>.

### **ANTIOXIDANT PROPERTIES**

The term “oxidative stress” describes the lack of equilibrium in the organism between the production of free radicals and the antioxidant protective activity. The protection against oxidation is thought to prevent some chronic diseases. The oxidative modification of the lipoproteins is considered to be an important factor for the pathogenesis of arteriosclerosis.

Honey has been found to contain significant antioxidant activity including glucose oxidase, catalase, ascorbic acid, flavonoids, phenolic acids, carotenoid derivatives, organic acids, Maillard reaction products, amino acids, proteins<sup>13, 23, 39, 48, 62, 81, 103, 107, 112, 112, 122, 186, 192</sup>. The main antioxidants seem to be the phenols and the Maillard products named melanoidins.

Different methods have been applied and also antioxidant activity units determined. The different methods for the determination of the antioxidant activity have been reviewed<sup>26</sup>.

There is a significant correlation between the antioxidant activity, the phenolic content of honey and the inhibition of the in vitro lipoprotein oxidation of human serum. It was found that honey intake caused a higher antioxidative effect in blood than the intake of black tea, although its in vitro effect measured as ORAC activity was five times smaller than that of black tea<sup>113</sup>.

Generally, the darker the honey, the higher its phenolic content and its antioxidant power<sup>42, 112, 162, 196, 237</sup>. Further, in a lipid peroxidation model system buckwheat honey showed a similar antioxidant activity as 1 mM  $\alpha$ -tocopherol<sup>186</sup>. Also, the influences of honey ingestion on the antioxidative capacity of plasma was also tested<sup>15, 211</sup>. In the first study the trial persons were given maize syrup or buckwheat honeys with a different antioxidant capacity in a dose of 1.5 g/kg body weight. In comparison to the sugar control honey caused an increase of both the antioxidant and the reducing serum capacity<sup>211</sup>. In the second study humans received a diet supplemented with a daily honey consumption of 1.2 g/kg body weight. Honey increased the body antioxidant agents: blood vitamin C concentration by 47%,  $\beta$ -carotene by 3%, uric acid by 12%, and glutathione reductase by 7%<sup>15</sup>. It should be borne in mind that the antioxidant activity depends on the botanical origin of honey and has remarkable variations in honey from different sources<sup>13, 35, 107, 112, 144, 237</sup>.

The antioxidant activity of honey is probably the reason of the protective effect of honey against damage and oxidative stress induced by CS in rat testis<sup>169</sup>.

The impact of heat on the antioxidant capacity of clover and buckwheat honey during storage was analysed recently. Processing clover honey did not significantly impact antioxidant capacity. Storage during 6 months reduced the antioxidant capacity of honeys by about 30%, with no impact of storage temperature or container type detected at the end point of the storage period. Antioxidant capacity of processed and raw honeys was similar after storage<sup>239</sup>. In another study both antioxidant activity and brown pigment formation increased with heat treatment and time<sup>233</sup>.

These results suggest that not only flavonoids, but also other substances formed under heating could be responsible for the honey antioxidant effect.

*Antioxidant scavenging activity is linked to the prevention of many chronic and age dependent pathological conditions like cancer, diabetes, atherosclerosis, cataract and chronic neurological conditions<sup>29</sup>. Thus the antioxidant activity of honey is linked to the observed anticancer and anti-atherosclerosis effects of honey.*

## ANTI-INFLAMMATORY EFFECTS



Anti-inflammatory effects of honey in humans were studied by Al Waili and Boni<sup>20</sup> after ingestion of 70 g honey. The mean plasma concentration of thromboxane B(2) was reduced by 7%, 34%, and 35%, that of PGE(2) by 14%, 10%, and 19% at 1, 2, and 3 hours, respectively, after honey ingestion. The level of PGF(2 $\alpha$ ) was decreased by 31% at 2 hours and by 14% at 3 hours after honey ingestion. At day 15, plasma concentrations of thromboxane B(2), PGE(2) and PGF(2 $\alpha$ ) were decreased by 48%, 63% and 50%, respectively.

Ingestion of honey had a positive effect in an experimental model of inflammatory bowel disease in rats<sup>45</sup>. Honey administration is as effective as prednisolone treatment in an inflammatory model of colitis. The postulated mechanism of action is by preventing the formation of free radicals released from the inflamed tissues. The reduction of inflammation could be due to the antibacterial effect of honey or to a direct antiinflammatory effect. A support of the latter hypothesis was shown in animal studies, where antiinflammatory effects of honey were observed in wounds with no bacterial infection<sup>198</sup>.

*Inflammation in specific parts of the human body is thought to be a major cause of cardiovascular diseases<sup>246</sup>. Thus, the positive effect of honey on cardiovascular health can be explained by the ant-inflammatory activity of honey.*

## ANTIMUTAGENIC AND ANTITUMOR EFFECTS

Mutagenic substances act directly or indirectly by promoting mutations of genetic structure. During the roasting and frying of food heterocyclic amines are built, e.g. Trp-p-1 (3-Amino-1,4-dimethyl-5H-pyridol [4,3-b] indole). The antimutagenic activity of honeys from seven different floral sources (acacia, buckwheat, fireweed, soybean, tupelo and Christmas berry) against Trp-p-1 was tested via the Ames assay and compared to that of a sugar analogue and to individually tested simple sugars. All honeys exhibited significant inhibition of Trp-p-1 mutagenicity. Glucose and fructose were found to be similar antimutagenic as honey and were more antimutagenic than maltose and sucrose<sup>238</sup>.

Stingless bee honeys from west Amazonian Ecuador showed anti-mutagenic activity assayed with *Saccharomyces cerevisiae* D7 strain, inhibiting back mutation over the entire tested concentration range<sup>117</sup>. Nigerose, another sugar, present in honey<sup>86, 217</sup>, has immunoprotective activity<sup>185</sup>.

The antimetastatic effect of honey and its possible mode of antitumor action was studied by applying honey in spontaneous mammary carcinoma, in methylcholanthrene-induced fibrosarcoma of CBA mouse and in anaplastic colon adenocarcinoma of Y59 rats<sup>188</sup>. A statistically significant antimetastatic effect was achieved by oral application of honey. These findings indicate that honey activates the immune system and honey ingestion may be advantageous with respect to cancer and metastasis prevention. In addition, the authors postulate that honey given orally before tumour cell inoculation may have an impact on tumour spreading. In another work of the same group the effect of honey on tumour growth, metastasising activity and induction of apoptosis and necrosis in murine tumour models (mammary and colon carcinoma) was

investigated. A pronounced antimetastatic effect was observed when honey was applied before tumour-cell inoculation (peroral 2 g kg<sup>-1</sup> for mice or 1 g kg<sup>-1</sup> for rats, once a day for 10 consecutive days)<sup>189</sup>.

The anti-proliferative effect of honey in colon cancer cells was explained by its antioxidant and anti-inflammatory properties<sup>126</sup>.

Honey exerted antiproliferative potential against the HCT-15 and HT-29 colon cancer cells as assessed by 3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyl tetrazolium bromide (MTT) assay. Flow cytometric analysis showed the increasing accumulation of hypodiploid nuclei in the sub-G(1) phase of cell cycle indicating apoptosis. Honey transduced the apoptotic signal via initial depletion of intracellular non protein thiols, consequently reducing the mitochondrial membrane potential (MMP) and increasing the reactive oxygen species (ROS) generation. An increasing earlier lipid layer break was observed in the treated cells compared to the control. Honey induced apoptosis was accompanied by up-regulating the p53 and modulating the expression of pro and anti-apoptotic proteins. Further apoptosis induction was substantiated using DNA fragmentation assay and YO-PRO-1 staining. Results showed honey as a plausible candidate for induction of apoptosis through ROS and mitochondria-dependent mechanisms in colon cancer cells. This will promote honey as a potential chemotherapeutic agent against colon cancer<sup>127</sup>.

Honey ingestion by rats induced antitumor and pronounced antimetastatic effects. The experimental evaluation of antitumor properties of honey was carried out using five strains of rat and murine tumors. Honey potentiated the antitumor activity of 5-fluorouracil and cyclophosphamide<sup>115</sup>

In another study the antitumor effect of bee honey against bladder cancer was examined in vitro and in vivo in mice<sup>220</sup>. According to these results honey is an effective agent for inhibiting in vitro the growth of different bladder cancer cell lines (T24, RT4, 253J and MBT-2). It is also effective when administered intravesically or orally in the MBT-2 bladder cancer implantation mice models.

Tsiapara et al. investigated the influence of Greek honey extracts (thyme, pine and fir honey) on the oestrogenic activity and cell viability of breast (MCF-7), endometrial (Ishikawa) and prostate (PC-3) cancer cells. Thyme honey reduced the viability of Ishikawa and PC-3 cells, whereas fir honey stimulated the viability of MCF-7 cells. The authors concluded that modulation of oestrogen activity was linked to the rich phenolic content of Greek honeys and suggested that a thyme honey-enriched diet may prevent cancer related processes in breast, prostate and endometrial cancer cells<sup>232</sup>.

The antiproliferative activity, apoptosis, and the antitumor effects of honey on human renal cancer cell lines (ACHN) were studied. Honey decreased the cell viability in the malignant cells in a concentration- and time-dependent manner. Honey induced apoptosis of the ACHN cells in a concentration-dependent manner. It is concluded that honey may cause cell death in the ACHN cells by inducing apoptosis<sup>209</sup>

HMF, a compound found in heated honey has been found to possess antitumor properties<sup>168</sup>. Thus, overheated honeys could potentially compensate the loss of quality by winning anti-cancer properties.

Jungle honey, collected from tree blossom by wild honeybees that live in the tropical forest of Nigeria) enhanced immune functions and antitumour activity in mice<sup>109</sup>.

Tualang honey from Malaysia has antiproliferative activity on OSCC and HOS cell lines, exerting early apoptosis effects<sup>110</sup>. This honey induces apoptosis and disrupts the mitochondrial membrane potential of human breast and cervical cancer cell lines<sup>104</sup> and inhibits also primary human keloid fibroblasts<sup>221</sup>

Honey has a supportive effect on human patients who have undergone a cancer radiation therapy, decreasing radiation mucositis. Patients with head and neck cancer treated with radiation therapy were given honey. There was a significant reduction in the symptomatic grade 3/4 mucositis among honey-treated patients compared to controls; i.e. 20 versus 75%. The compliance of honey-treated group of patients was better than controls. Fifty-five percent of patients treated with topical honey showed no change or a positive gain in body weight compared to 25% in the control arm, the majority of whom lost weight<sup>46</sup>. Febrile neutropenia is a serious side effect of chemotherapy. Honey was administered to chemotherapy patients with neutropenia and was found that it reduced the need for colony-stimulating factors<sup>253</sup>.

## IMMUNOACTIVATING AND IMMUNOSUPPRESSIVE PROPERTIES

### Immuno-activating properties

The effect of honey on the antibody production against thymus-dependent antigen sheep red blood cells and thymus-independent antigen (*Escherichia coli*) in mice was studied<sup>21</sup>. According to this study oral honey stimulates antibody production during primary and secondary immune responses against thymus-dependent and thymus-independent antigens.

It has been reported that honey stimulates T-lymphocytes in cell culture to multiply, and activates neutrophils<sup>3</sup>

In a study with humans receiving a diet supplemented with a daily honey consumption for two weeks of 1.2 g/kg body weight ingestion of honey following effects were observed: Increase of serum iron by 20% and decrease of plasma ferritin by 11%, an 50 % increase of monocytes and slight increases of lymphocyte and eosinophil percentages, reduction in serum of immunoglobulin E (34%) aspartate transaminase (22%) and alanine transaminase (18%), lactic acid dehydrogenase (41%), fasting sugar (5%) and creatine kinase and finally an increase in blood of copper (33%) and slight elevations of zinc and magnesium, hemoglobin and packed cell volume<sup>15</sup>

Honey increase proliferation of B- and T-lymphocytes and neutrophils in vitro<sup>3</sup>.

In another study with rats, feeding of honey caused an increase of lymphocytes in comparison with the sucrose fed controls<sup>69</sup>.

Apalbumine 1, the dominant royal jelly in honey with immunostimulating properties, is present in honey<sup>44</sup>

### Immuno-suppressive properties

In animal experiments honey showed an immunosuppressive activity<sup>87</sup>. In experiments with isolated leukocytes honey inhibited phagocytic myeloperoxidase activity<sup>167</sup>.

These findings is in line with the common belief that ingestion of honey can relieve pollen hypersensitivity. Immuno suppression plays also a positive role in autoimmune diseases.

*Honey causes both an enhancement of the immune response and an immuno-suppression. The immunoactivating effects are in line with the common belief that honey improves human reaction to viral infections. Honey may be also trigger immunoactivating activity by its stimulatory effects on lymphocytes and also by its probiotic effects (see above).*

*On the other hand the immunosuppressive activity of honey is probably due to its anti-inflammatory effect. These effects are in line with the belief that honey ingestion will decrease allergic reactions like hay fever.*

## CARDIOVASCULAR HEALTH

Feeding of honey or sugar to Wistar rats resulted both in increase of weight in comparison to controls. Sucrose fed fat cells were significantly larger than the honey fed ones. Compared to the controls (no sugars) sucrose feeding increased blood pressure, but not the honey fed rats<sup>205</sup>.

Ahmad et al. tested the effect of honey on bovine thrombin -induced oxidative burst in human blood phagocytes. Honey treatment of phagocytes activated by bovine thrombin showed effective suppression of oxidative respiratory burst. It can be assumed that this suppressive activity of honey could be beneficial in the interruption of the pathological progress of cardiovascular disease and may play a cardioprotective role<sup>6</sup>

Ingestion of honey by healthy humans has an effect on blood homostasis by inhibiting platelet aggregation. The anticoagulant effect of could be due to several substances present in honey: hydrogen peroxide, a platelet aggregation inhibitor, to honey flavonoids or sugars<sup>7</sup> or to by the influence on platelet function caused by honey induced LDL oxidation<sup>118</sup>.

Compared with fructose-fed rats, honey-fed rats had a higher plasma  $\alpha$ -tocopherol level, and an  $\alpha$ -tocopherol/triacylglycerol ratio, as well as a lower plasma nitrate levels and susceptibility of the heart to lipid peroxidation<sup>64</sup>

Honey ingestion improves experimental heart weaknesses as extrasystoles, arrhythmia and tachycardia of rats<sup>200</sup>

## PREBIOTIC AND PROBIOTIC EFFECTS

Other important honey effects on human digestion have been linked to honey oligosaccharides. These honey constituents has a prebiotic effect, similar to that of fructooligosaccharides<sup>210, 249</sup>. The oligosaccharide panose was the most active oligosaccharide. These compounds exert the prebiotic effect in a synergistic mode of action, rather to one of individual components, leading to an increase of bifidobacteria and lactobacilli<sup>234</sup>. According to an in vitro study on five bifidobacteria strains honey has a growth promoting effect similar to that of fructose and glucose oligosaccharides<sup>132</sup>. Unifloral honeys of sour-wood, alfalfa and sage origin honey stimulated also the growth of five human intestinal bifidobacteria<sup>216</sup>. In another study honey increases both in vivo (small and large intestines of rats) and in vitro the building of *Lactobacillus acidophilus* and *Lactobacillus plantarum*, while sucrose failed to produce any effect<sup>213</sup>.

Honey showed prebiotic activity towards 3 *Lactobacillus* species isolated from human faeces<sup>226</sup>

It is not clear whether all types of honey exhibit prebiotic effects and whether some honeys have a stronger prebiotic effect. Sour-wood, alfalfa and sage<sup>132</sup> and also clover honey<sup>132</sup> have been shown to have prebiotic activity.

The prebiotic activity of chestnut honey was found to be higher than that of acacia honey<sup>155</sup>.

Oligosaccharides from honeydew honey have prebiotic activity<sup>210</sup>. Theoretically honeydew honeys, containing more oligosaccharides should have a stronger prebiotic activity than blossom honeys. There is need of more research on prebiotic activity of unifloral honeys.

However the influence of the oligosaccharide content is questioned. Sage, alfalfa and sourwood honey, which vary in their oligosaccharide contents, were compared with sucrose, high fructose corn syrup and inulin in their ability to support growth, activity and viability of lactic acid bacteria and bifidobacteria typically used in yoghurt manufacturing. Growth and the end products of fermentation (lactic and acetic acids) were determined. Growth and acid production by organisms studied in the presence of different sweeteners were dependent on the specific organism investigated; however, it was not influenced by sweetener type, oligosaccharide content or the floral source of the honeys. All the sweeteners studied supported the growth, activity and viability of the organisms studied<sup>197</sup>

It has been shown that fresh honey has probiotic *Bifidus* and *Lactobacilus* bacteria. However these bacteria are viable only in fresh honey, about 2-3 months old<sup>187</sup>

## Other effects

### Antinociceptive activity

The antinociceptive (pain-soothing) is thought to be triggered by quinoline alkaloids. These quinoline alkaloids are present in exceptionally high concentration in chestnut honey, while they were present in much lesser quantities in honeydew, acacia, thyme, lavender, dandelion, sulla, thymus, sunflower and linden honeys<sup>38, 40</sup>.

### Antiacetylcholinesterase activity

Antiacetylcholinesterase activity is thought to be linked with the prevention of neurodegenerative diseases such as Alzheimer. Several Brazilian honeys have significant antiacetylcholinesterase activity, which depended on the floral source<sup>153</sup>

### Honey improving renal function

Experiments with rats showed that honey ingestion improves their renal function<sup>11</sup>

### Honey and the brain

Honey ingestion improves anxiety and the spatial memory of rats<sup>70</sup>

Research with different Nigerian honeys was carried out. The results showed that honey significantly ( $p < 0.05$ ) decreased locomotion and rearing behaviors in NIB and amphetamine-induced locomotor activity when compared to the control group. Exploratory behavior was significantly increased in both holeboard and elevated plus maze but had no significant effect on spatial working memory. Honey sample from Umudike has significant hypnotic and anticonvulsant effects. The antinociceptive models (hot plate and tail flick tests) showed that the honey samples significantly increased the pain reaction time and naloxone

blocked these central antinociceptive effects. The force swimming test showed that only the Idanre (ID) honey sample had antidepressant effect. In conclusion, some of these honey samples have central inhibitory property, anxiolytic, antinociceptive, anticonvulsant and antidepressant effects, thus may be used as nutraceutical. It can also be inferred that some of these effects are probably mediated through dopaminergic and opioidergic systems<sup>8</sup>.

### **Honey for good fertility**

Tualang honey from Malaysia was found to have a beneficial effect on menopausal rats by preventing uterine atrophy, increased bone density and suppression of increase of body weight<sup>250</sup>

Malaysian honey had a positive effect of testicular function in rats<sup>160</sup>. A study with Palestine honey showed that it increased spermatogenesis in rats<sup>1</sup>.

### **Against osteoporosis?**

Honey improves on the short term Ca absorption in rat bones in a positive dose response fashion, but this effect disappears on the long term<sup>32</sup>

### **Honey, oxidative stress, hypertension and diabetes**

Oxidative stress is implicated in the pathogenesis and/or complications of hypertension and/or diabetes mellitus. A combination of these disorders increases the risk of developing cardiovascular events. This study investigated the effects of streptozotocin (60 mg/kg; ip)-induced diabetes on blood pressure, oxidative stress and effects of honey on these parameters in the kidneys of streptozotocin-induced diabetic Wistar-Kyoto (WKY) and spontaneously hypertensive rats (SHR). Diabetic WKY and SHR were randomized into four groups and received distilled water (0.5 mL) and tualang honey (1.0 g/kg) orally once daily for three weeks. Control SHR had reduced malondialdehyde (MDA) and increased systolic blood pressure (SBP), catalase (CAT) activity, and total antioxidant status (TAS). SBP, activities of glutathione peroxidase (GPx) and glutathione reductase (GR) were elevated while TAS was reduced in diabetic WKY. In contrast, SBP, TAS, activities of GPx and GR were reduced in diabetic SHR. Antioxidant ( tualang honey) treatment further reduced SBP in diabetic SHR but not in diabetic WKY. It also increased TAS, GSH, reduced glutathione (GSH)/oxidized glutathione (GSSG) ratio, activities of GPx and GR in diabetic SHR. These data suggest that differences in types, severity, and complications of diseases as well as strains may influence responses to blood pressure and oxidative stress<sup>98</sup>

## **NUTRITIONAL AND FUNCTIONAL PROPERTIES OF UNIFLORAL HONEYS**



Due to different proportions of the possible sources, nectar and/or honeydew coming from a great variety of plants, no honey is completely the same as another one. This variability could be a handicap, given the market requirement for a consistent product, but when properly managed, it also could represent an opportunity for enhancing honey by offering to the consumer a number of typical products with special characteristics, according to the particular botanical origin.

Indeed, unifloral honeys are regarded as a more valuable class of honey, and botanical denominations are widely employed on the European market, often achieving higher prices than honey blends. Unifloral honeys have higher prices than blend honeys. In countries like France, Italy and Spain 30 to 50 % of the marketed honey is unifloral. In non-European countries, with the exception of the Manuka New Zealand honey, unifloral honeys have a smaller importance. Information on European unifloral honeys is compiled in the special Apidologie Issue 35 from 2004. In Europe there are more than 100 plant species that can give origin to unifloral honey, most of them having only a local importance<sup>193</sup>.

While the characterisation of microscopical, physical and physical properties of unifloral honeys is well advanced, the nutritional and health enhancing properties of unifloral honeys is quite a new field of research. The composition of honey depends on its botanical origin, regarding the main nutrients, the carbohydrates, and also the minor ones [Persano and Piro](#)<sup>194</sup>.

## Glycemic Index and fructose

The variation of the Glycemic Index (GI) varies according to the botanical origin of honey is described earlier in this chapter.

## Vitamins

Table 6: Average concentration of water-soluble vitamins in Sardinian monofloral honeys mg/kg +/- SD, after <sup>72</sup>

	<b>B<sub>2</sub></b>	<b>B<sub>3</sub></b>	<b>B<sub>5</sub></b>	<b>B<sub>9</sub></b>	<b>C</b>	<b>Sum</b>
Eucalyptus (n = 5)	<1.458	<2.262	<3.686	5.6 ± 0.4	3.2 ± 0.7	<16.2
Sulla (n = 3)	<0.417	5 ± 1	5.2 ± 0.7	<0.383	1.3 ± 0.8	<12
Citrus (n = 3)	2.2 ± 0.2	26 ± 2	<5.613	<0.383	2 ± 2	<36
Asphodel (n = 3)	3.7 ± 0.3	5.8 ± 0.1	16 ± 6	<1.1	2 ± 2	<28
Acacia (n = 2)	<0.25	5 ± 1	<1.75	<0.325	1.2 ± 0.2	<8.5
Lavender (n = 2)	4 ± 1	<3.125	<0.58	<1.575	2.2 ± 0.4	<11.5
Thistle (n = 3)	<4.16	8.6 ± 0.8	<1.75	<1.447	2.3 ± 0.3	<18.3
Strawberry-tree (n = 3)	<0.87	<4.633	<10.11	<0.39	4 ± 1	<20
Heather (n = 1)	<0.25	5.92 ± 0.01	<0.58	<0.50	2.7 ± 0.9	<10.0
Rosemary (n = 1)	<0.25	<0.75	<0.58	1.7 ± 0.2	1.5 ± 0.2	<4.8
Linden (n = 1)	<0.25	7.0 ± 0.3	<0.58	1.28 ± 0.05	<0.10	<9.2
Multifloral (n = 1)	1.1 ± 0.5	8 ± 1	<0.58	1.8 ± 0.3	<0.10	<11.6

## Antibacterial properties

Table 7. Antibacterial potency of unifloral honeys

Honey type	Antibacterial potency, type of antibacterial activity	Reference
<b>Dark colour</b>		
Buckwheat	high potency, undetermined type	172
Blueberry	high potency, undetermined type	60
Chestnut	average to high, both peroxide and non-peroxide	50, 173, 231, 247
Cotton	high, undetermined, peroxide	173, 244
Heather	low to high, undetermined type	50, 173
Honeydew, dark, both coniferous and non coniferous	high: both peroxide and non peroxide	50 59, 90, 161, 173
Jarraah	high: peroxide and non peroxide	123
Linen vine (Cuba)	high, undetermined type	27
Manuka	high: peroxide and non-peroxide	50, 173
Marri (red gum)	high: peroxide and non peroxide	123
Tualang	high: peroxide and non peroxide	135, 223
<b>Intermediate colour</b>		
Eucalyptus,	low to high: peroxide and non peroxide	50, 59, 231, 245
Linden,	low to high: peroxide and non peroxide	173, 231
Revanil	high: peroxide and non peroxide	146
Thyme	low to high: peroxide and non-peroxide	59, 66
Tupello	average: peroxide	244
Ulmo	High: probably peroxide	214

Light colour		
Acacia	low-average: undetermined, non-peroxide	50, 231
Christmas vine (Cuba)	low, undetermined type	27
Borage	low-medium	59, 177
Clover	Average, undetermined, peroxide,	59, 67, 173, 244
Lavender	medium: undetermined or non-peroxide	50, 231, 245
Lucerne	low: undetermined and peroxide	231, 244
Rosemary	low to high, undetermined, non-peroxide	245, 172
Orange	low-average: peroxide and non-peroxide	50, 231, 244
Rape	low to high: peroxide and non peroxide	34, 50, 59, 173
Rhododendron	low to high, undetermined or non-peroxide	50, 231
Sunflower	low-average: undetermined or non-peroxide	50, 231
Taraxacum	low-high: undetermined, non-peroxide	50, 231
Summary		
High activity	Intermediate activity	Low activity
blueberry, buckwheat, chestnut, cotton, heather, jarrah, honeydew, linen vine, manuka, red gum, revanil, tualang, ulmo	eucalyptus, clover, lavender, linden, rape, rhododendron, rosemary, thyme, tupello	acacia, Christmas vine, borage, , lucerne, orange

The antibacterial properties of honey have been reviewed above. The dependence of the antibacterial activity on the botanical origin is less clear cut than the antioxidant properties of honey. This can be explained by two facts. On one hand, there are different antibacterial factors: hydrogen peroxide, different honey components, most of all acids, and also phenolics, on the other a part of the antibacterial substances are added by the bees<sup>50</sup>.

The hydrogen peroxide in honey is produced by glucose oxidase and destroyed by catalase. The resultant between the two enzymes will determine the peroxide accumulation capacity of honey.

According to White and Dustmann the peroxide accumulation capacity of honey depends on the botanical origin of honey. Generally, dark honeys have a higher activity<sup>90, 243</sup>.

The non-peroxide, antibacterial activity depends also on the botanical source of honey<sup>50, 231</sup>, but there was no clear cut correlation between honey colour and non-peroxide activity. Taormina et al found that darker honeys (buckwheat, blueberry) have a significant non-peroxide activity<sup>225</sup>

Manuka is considered the honey with the strongest antibacterial properties<sup>175</sup>, but there is increasing evidence that other unifloral honeys, most of them with a dark colour have a similarly high antibacterial potency (table 7).

## Antioxidant properties

The antioxidant activity of honey has been reviewed above. The antioxidant properties of honey depend on the botanical origin of honey, the darker the honey the higher its antioxidative power<sup>42, 67, 73, 105, 107, 112, 136, 144, 162, 195, 196, 206, 237</sup>. This effect seems to be due to honey polyphenols (see section on antioxidant properties above). Following dark honey types have especially high antioxidant power:

- Buckwheat (*Fagopyrum sp.*)
- Chinese milk vetch (*Astragalus adsurgens*)
- Heather (*Caluna vulgaris*)
- Honeydew (all types of honeydew honeys)
- Manuka (*Leptospermum Scoparium*)
- Strawberry tree honey (*Arbutus menziesii*)
- Sweet chestnut (*Castanea sativa*)
- Tualang (*Koompassia excelsa*)

## Imunostimulating effects

Apalbumine 1, the dominant royal jelly in honey with immunostimulating properties, is present in unifloreal honeys in different quantities. The quantity of apalbumine decreases in the following order: Chestnut > dandelion > Rape, Linden, Acacia<sup>44</sup>

## Prebiotic properties

It is not clear whether all types of honey exhibit prebiotic effects and whether some honeys have a stronger prebiotic effect. Sour-wood, alfalfa, sage and clover honeys<sup>132</sup> have been shown to have prebiotic activity.

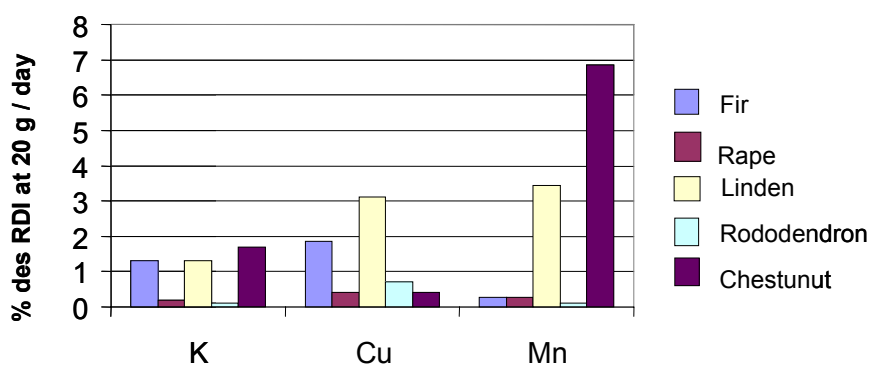
It was shown that the prebiotic activity of chestnut honey is bigger than that of acacia honey<sup>155</sup>.

Oligosaccharides from honeydew honey have prebiotic activity<sup>210</sup>. Theoretically honeydew honeys, containing more oligosaccharides should have a stronger prebiotic activity than blossom honeys. There is need of more research on prebiotic activity of unifloreal honeys.

## Mineral content

The mineral composition of honey depends on the botanical origin of honey<sup>37, 53, 158, 202, 227</sup>

### Variation of honey mineral content, after<sup>37</sup>



Lavandula stoechas, Citrus spp. and Echium plantagineum honeys collected in Portugal were determined by fluorometry after reaction with 2,3-diaminonaphthalene. The selenium levels of the honey samples studied were low, ranging from <math><1.0</math> to 2.91  $\mu\text{g}/100\text{ g}$  fresh weight. The honeys from Erica spp., C sativa and E. plantagineum presented the highest selenium values from all the honeys studied (median values 1.69, 1.51 and 1.51  $\mu\text{g}/100\text{ g}$  fresh weight), and the honeys from Eucalyptus spp., L. stoechas and Citrus spp. presented the lowest values (median values 1.33, 1.28 and 1.20  $\mu\text{g}/100\text{ g}$  fresh weight). The selenium content of Erica spp., was significantly higher than that observed for the Eucalyptus spp., L. stoechas and Citrus spp. and the selenium level of the Eucalyptus spp., was also significantly lower than that observed C. sativa and E. plantagineum honeys<sup>74</sup>.

## Gastroprotective properties

The content of nitrate ( $\text{NO}_3$ ) in honey is thought to be the causative action of the gastroprotective action of honey. Dark honeys like honeydew and sweet chestnut had considerably higher concentration than light honeys (acacia, orange blossom, lavender, sunflower, arbutus)<sup>40</sup>

## QUANTITY AND TIME OF HONEY INGESTION

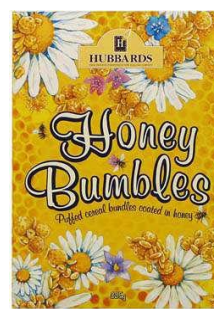
From nutrition point of view honey is a sugar. For sweeteners a maximum of 40 to 50 g per day is generally accepted. Taking into consideration that other sugars are also ingested a quantity of 20 g daily can be recommended. However it should be remembered, that for health enhancing and medical purposes higher amounts, 50 to 80 g of honey per day are recommended (see Chapter 8 on honey and medicine). But such high intake should be limited to a certain period of time.

## HONEY USES

### Food industry



great stuff!  
Heavenly  
Honey!



Due to its various favourable properties honey is used as an additive to a variety of food and beverages (see Table 5). The application of honey as a food additive is based on its manifold properties. The antibacterial effect of honey (see part II) counteracts microbial spoilage of food, e.g. of meat<sup>186</sup>. The antioxidant effect of honey prevents oxidation of food during storage. Honey acts against lipid oxidation of meat<sup>164, 186</sup> and is thus a efficient meat additive for preventing oxidation spoilage, e.g. to poultry<sup>30</sup> or to meat and muscle of unspecified origin<sup>186</sup>. Effects of honey against enzymatic browning of fruits and vegetables<sup>68</sup>, soft drinks<sup>148</sup> light raisin<sup>165</sup>, apple slices<sup>190</sup> have been reported. Honey enzymes have a clearing effect in fruit juices and fruit drinks manufacturing<sup>149, 190</sup>. Other physical and sensory properties make honey a good candidate for an additive to a wide variety of food: good sensory and rheological properties, superior microwave reactivity than synthetic sugars etc. More information on honey application in food is available through the American National Honey Board (<http://www.nhb.org/foodtech/index.html>).

Honey enhances the growth of dairy starter cultures in milk and milk products. Especially species with week growth rates in milk such as bifidobacteria are usually fortified by growth enhancers or by honey. The growth rate of two bifidobacteria Bf-1 and Bf-6 in milk can be stimulated by the addition of honey to milk<sup>235</sup>. The effect of honey was more pronounced than the one caused by common growth enhancers based on other oligosaccharides. Thus, honey can be used as a prebiotic additive to probiotic milk products.

Honey added to non fat dry milk has a favourable influence on some other “good bacteria”<sup>71</sup> The milk was incubated with *Streptococcus thermophilus*, *Lactobacillus acidophilus*, *Lactobacillus delbrueckii* subsp. *bulgaricus*, or *Bifidobacterium bifidum*. Honey supported the growth of all strains. The authors conclude that various oligosaccharides found in honey may be responsible for the enhanced lactic acid production by bifidobacteria.

Due to its antioxidant activity the addition of honey to patties seems to prevent formation of heterocyclic aromatic amine and overall mutagenicity in fried ground-beef patties<sup>215</sup>.

Acacia honey did not affect the survival of the microbial flora of yoghurt during a 6 week refrigerated storage period<sup>236</sup>. Also, honey had no effect on pH and lactic acid levels of the final products. In addition, at a rate of approximately 3.0% (w/v), it highly improves the sensory quality of the product without having a detrimental effect on characteristic lactic acid bacteria. Another study with sunflower honey showed that addition of honey (2,4 and 6 %) increased the values of *Streptococcus thermophilus* and *Lactobacillus delbrueckii* subsp. *bulgaricus* values, optimum sweetness was at 4 % honey<sup>212</sup>.

Another main application of honey in food industry is in baking, cereal and the confectionary industry. A review on these applications is summarised in a PhD study<sup>219</sup>. Proposed advantages of honey additions to baked goods are moisture retention, good texture, improved baking, flavour and sensory properties.

Acacia and chestnut honey had a stimulatory effect on the growth of *Lactobacillus casei* Lc-01 in cow's and goat's milk<sup>218</sup>

An overview of the different application of honey in food industry is given in the table below. A wide variety of the application research on different application of honey as a food additive has been commissioned by the American National Honey Board. ([www.honey.com](http://www.honey.com)) All the mentioned applications showcase a detailed description of the research carried out, together with comprehensive explanations of the honey use.

## Honey applications in the food industry

Use	Explanation
Sweetener for: sport beverages, non-alcoholic fruit beverages, ice tea, yoghurt drinks, chocolate milk beverages; fermented beverages; vinegar, vegetable juices; in mead production	supplies different natural honey flavours and colours; honey sugars are fermentable and give alcoholic drinks unique flavours; prevents browning due to antioxidative properties
Additive to poultry and other meat, to fruit and vegetable processing	Antioxidant and preservative (anti-bacterial) properties, reduces browning, improves sensory properties
Additive to microwave foods: cakes, muffins, cookies, glazes	Superior microwave reactivity and water activity managements than synthetic sugars
Additive to flour bagels, cereals, chicken marinades, French fries, bread, pasta, extruded snacks, corn chips, potato chips	Improves sensory properties, adds/retains moisture due to hygroscopic properties; improves browning due to reducing sugars;
Additive to frozen ice cream and dough	Better stability and sensory properties
Additive to fruit spreads, peanut butter, nut spread,	Better storability and sensory properties
Additive to salsas and sauces	Neutralises sour and burn intensity
Additive to fried or roasted beef, poultry	Reduces the formation of heterocyclic aromatic amines and their mutagenic effects
Dried honey	Convenient as consistent in texture, flavour and colour, allowing blending with other dry ingredients



## Honey in cosmetics

Since old times honey was used in cosmetics. Queen Cleopatra took a bath of honey and milk for her beauty. Today honey is also contained in many cosmetic products. It is a component of the water soluble part of cosmetic emulsions as a humifier for the cosmetics product and for the skin. Generally, honey cosmetics is suitable for all skin types. Honey is hygroscopic, antibacterial and fungicide, and its ingredients nurture the skin. It is mildly acetic and contributes to strengthening the upper acetic protective skin layer (pH of the skin is 5.5).

### Honey cosmetic products





Shampoo, Hairbalm and purifying lotion with honey A hand cream and sun cream with honey

Mask is the best form that complies with the consistency of honey. It nourishes the skin and keeps it moisturized. Regular use of them keeps skin juvenile and retards wrinkle formation. To mix the ingredients you can use mixer. They are left for about ½ an hour, then removed using a gauze and warm water and then washed.

## Simple recipes for honey cosmetics taken from different Internet sources

### Face Masks

#### Cleopatra mask

Honey 1 teaspoonful  
Milk 1 tablespoonful  
Egg white of 1 egg



#### Honey mask

Place a cloth in warm water and apply to your face to open the pores. Smear on honey, and leave on for 15 to 30 minutes. Rinse off with warm water, then use cold water to close the pores.  
Use once a week.

#### Egg yolk mask

Honey 1 teaspoonful  
Glycerin 1 teaspoonful  
Egg yolk of 1 egg

#### Egg white mask

Honey 1 teaspoonful  
Glycerin 1 teaspoonful  
Egg White of 1 egg

#### Fairness Mask

Honey 10 g  
Distilled water 155 ml + alcohol 70% 30 ml  
Borax 4 g  
Bergamot oil 3 drops + orange oil 2drops

#### Quick mask

Honey 100 g  
Alcohol 25 ml  
Water 25 ml

### Hand Care

#### Emulsion for hands

Honey 2 teaspoonful  
Almond oil 1 teaspoonful  
Perfume few drops  
Massage your hands, leave for a while and wash if you need.

#### Paste for hands

Honey 10 g  
Wheat flour 6 g  
Water 4 g  
Massage your hands



### Honey Bath

Add 200-250 g of honey to the bathing water.  
If used once in a while (e.g. every 2 weeks), it will keep on a good turger of the cells and nourishes the skin.



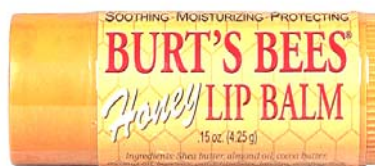
1/2 cup sea salt  
2 tablespoons baking soda  
1 cup boiling water  
1 cup honey  
2 cups milk  
10 drops of vanilla oil  
dissolve sea salt and baking soda in bathwater, dissolve honey in boiling water and add milk, add milk-honey mixture and vanilla oil to bathwater, swirl water to blend all ingredients

## Cracked Lips

Honey 10 g

Lemon juice 10 g

To be used concomitantly with lip moisturizer containing Panthenol.



Further reading for this section: <sup>82</sup>

## ALLERGY AND POTENTIAL HEALTH HAZARDS

### Allergy

Up to 5 % of the population is suffering from allergies. Compared to other foods allergy to honey seems relatively uncommon. Recently honey allergy was reviewed<sup>91</sup>. In epidemiological studies with normal people the allergy incidence is very low. In one study in Turkey with 4331 students no honey allergy could be detected, while in another Turkish study with 3810 patients searching consultation in an allergy clinic the honey allergy incidence was 1.8 %.

The incidence of honey allergy, reported in a group of 173 food allergy patients was 2.3% as reported by<sup>92</sup>. In this study with allergic patients the allergy honey allergy is explained by the presence of honey components of bee origin or by dandelion and *Compositae* pollen.

Allergies reported can involve reactions varying from cough to anaphylaxis<sup>120</sup>.

It was also reported that patients allergic to pollen are rarely allergic to honey, although there is one reported case of honey pollen allergy<sup>58</sup>.

### Toxic compounds in honey

Honey as any other natural food can be contaminated from the environment, e.g. heavy metals, pesticides, antibiotics etc. Generally, the contamination levels found in Europe do not present a health hazard.<sup>51</sup>

A few plants are known to produce nectar containing toxic substances. Diterpenoids and pyrazolidine alkaloids are two main toxin groups relevant in nectar. Some plants of the *Ericaceae* family belonging to the sub-family *Rhododendron*, e.g. *Rhododendron ponticum* contain toxic polyhydroxylated cyclic hydrocarbons or diterpenoids<sup>83</sup>. Honey containing *R. ponticum* is called mad honey and is found in some regions of Turkey. Ingestion of this type of honey is not lethal, it causes some complaints such as dizziness, nausea-vomiting, sweating, weakness, blurred vision, convulsions and loss of consciousness, extremity paresthesia, excessive perspiration and salivation<sup>57</sup>

Substances of the other toxin group, pyrazolidine alkaloids, are found in different honey types and the potential intoxication by these substances is reviewed by<sup>96</sup>

Cases of honey poisoning have been reported very rarely in the literature and concern mostly individuals from the following regions: Caucasus, Turkey, New Zealand, Australia, Japan, Nepal, South Africa and different countries in North and South America. The symptoms encountered after honey poisoning are vomiting, headache, stomach ache, unconsciousness, delirium, nausea and sight weakness. In general those poisonous plants are known to the local beekeepers, thus honey, which can contain poisonous substances is not marketed. To minimise risks of honey born poisoning in countries where plants with poisonous nectar are growing tourists are advised to buy honey from the market only and not from individual beekeepers.

### **Clostridium botulinum**

There is a health concern for infants regarding the presence of *Clostridium (Cl.) botulinum* in honey. Since the presence of this bacterium in natural foods is ubiquitous and honey is a non sterilized packaged food from natural origin the risk of a low contamination level cannot be excluded. Spores of this bacterium can survive in honey, but they cannot build toxin. Thus, in the stomach of infants younger than one year the

bacteria spores from honey can survive and theoretically build the toxin, while children older than 12 months can ingest honey without any risk. In some cases, infant botulism has been attributed to ingestion of honey<sup>75,224</sup>. In Germany one case of infant botulism per year is reported<sup>181</sup>. As a result of the reported infant botulism cases some honey packers (e.g. the British Honey Importers and Packers Association) place a warning on the honey label that “honey should not be given to infants under 12 months of age”.

In 2002 a scientific committee of the EU examined the hazard of *Cl. botulinum* in honey. It has concluded that microbiological examinations of honey are necessary for controlling the spore concentration in honey, as the incidence of *Cl. botulinum* is relatively low and sporadic and as such tests will not prevent infant botulism. Thus, in the EU countries the health authorities have not issued a regulation for placing a warning label on honey jars<sup>101</sup>.

## **HEALTH CLAIMS FOR HONEY**

According to the EU Regulation 1924/2006<sup>102</sup> different health claims can be made: The claims are classified using the Passclaim project classification of the International Life Science Institute (ILSI)<sup>33</sup>, wherever possible. In the Passclaim project the claims are classified into the following subject areas:

1. Diet-related cardiovascular disease
2. Bone health and osteoporosis
3. Physical performance and fitness
4. Body weight regulation, insulin sensitivity and diabetes risk
5. Diet-related cancer
6. Mental state and performance
7. Gut health, digestion and immunity

### **Honey health claims**

#### **Quantity and time of honey ingestion**

The health enhancing effects in human adults, described in this report were mostly achieved after ingestion of 50 to 80 g of honey per day.

The health claims of honey which are reported below are valid for intakes of following amounts of honey:

- *Adults: after ingestion of 50 to 80 g per day by adults,*
- *General (adults or infants): 0.8 g to 1.2 g honey per g human weight*

The health effects reported in the different publications reported above were measured mostly after 2 to 3 weeks of daily honey ingestion. Practical apitherapists suggest a daily honey ingestion for 1.5 to 2 months<sup>157, 199</sup>.

The main honey health claims for honey are

#### **Physical performance and fitness**

Honey is high carbohydrate food and its ingestion increases performance and fitness

*Ingestion of honey increases performance and fitness*

#### **Gut health and digestion**

*Long term ingestion of honey can improve gut and gastroenterological health*

#### **Immunity**

*Long term ingestion of honey can improve the immunological reaction towards infections*

### **Specific nutritional effects**

#### **Nutrition of infants**

- *Honey should not be given to infants less than one year old*
- *Honey can be recommended as food for infants older than one year..*

## Nutrition of Diabetes II patients

There evidence that honey can used as a sweetener by humans with diabetes II. Any honey can be used for this purpose, the most suitable honey is acacia honey (*Robinia pseudoacacia*), as it has the lowest GI.

### References

1. ABDUL-GHANI, A S; DABDOUB, N; MUHAMMAD, R; ABDUL-GHANI, R; QAZZAZ, M (2008) Effect of Palestinian Honey on Spermatogenesis in Rats. *Journal of Medicinal Food* 11 (4): 799-802.
2. ABDULRHMAN, M; EL-HEFNAWY, M; HUSSEIN, R; EL-GOUD, A (2009) The glycemic and peak incremental indices of honey, sucrose and glucose in patients with type 1 diabetes mellitus: effects on C-peptide level—a pilot study. *Acta Diabetol.* DOI:10.1007/s00592-009-0167-7
3. ABUHARFEIL, N; AL ORAN, L; ABO-SHEHADA, M (2008) The effects of bee honey on the proliferative activity of human B and T lymphocytes and activity of phagocytes. *Food and Agricultural Immunology* (11): 169-177.
4. AGRAWAL, O P; PACHAURI, A; YADAV, H; URMILA, J; GOSWAMY, H M; CHAPPERWAL, A; BISEN, P S; PRASAD, G B K S (2007) Subjects with impaired glucose tolerance exhibit a high degree of tolerance to honey. *Journal of Medicinal Food* 10 (3): 473-478.
5. AHMAD, A; AZIM, M K; MESAİK, M A; NAZIMUDDIN; KHAN, R A (2008) Natural honey modulates physiological glycemic response compared to simulated honey and D-Glucose. *Journal of Food Science* 73 (7): H165-H167.
6. AHMAD, A; KHAN, R A; MESAİK, M A (2009) Anti inflammatory Effect of Natural Honey on Bovine Thrombin-induced Oxidative Burst in Phagocytes. *Phytotherapy Research* 23 (6): 801-808.
7. AHMED, A; KHAN, R A; AZIM, M K; SAFEED, S; MESAİK, M A; AHMED, S; IMRAN, I (2011) Effect of Natural Honey on Human Platelets and Blood Coagulation Proteins. *Pak J Pharm Sci* 24: 389-397.
8. AKANMU, M A; OLOWOOKERE, T A; ATUNWA, S A; IBRAHIM, B O; LAMIDI, O F; ADAMS, P A; AJIMUDA, B O; ADEYEMO, L E (2011) Neuropharmacological Effects of Nigerian Honey in Mice. *African Journal of Traditional Complementary and Alternative Medicines* 8 (3): 230-249.
9. AL WAILI, N S (2004) Natural honey lowers plasma glucose, C-reactive protein, homocysteine, and blood lipids in healthy, diabetic, and hyperlipidemic subjects: Comparison with dextrose and sucrose 152. *Journal Med.Food* 7 (1): 100-107.
10. AL WAILI, N S; SALOM, K; BUTLER, G; AL GHAMDI, A A (2011) Honey and Microbial Infections: A Review Supporting the Use of Honey for Microbial Control. *Journal of Medicinal Food* 14 (10): 1079-1096.
11. AL WAILI, N S; SALOOM, K Y; AL WAILI, T N; AL WAILI, A N; AKMAL, M; AL WAILI, F S; AL WAILI, H N (2006) Influence of various diet regimens on deterioration of hepatic function and hematological parameters following carbon tetrachloride: a potential protective role of natural honey. *Natural Product Research* 20 (13): 1258-1264.
12. AL-KHALIDI, A; JAWAD, F H; TAWFIQ, N H (1980) Effects of bees honey, zahdi dates and its syrup on blood glucose and serum insulin of diabetics. *Nutrition Reports international* 21 (5): 631-643.
13. AL-MAMARY, M; AL-MEERI, A; AL-HABORI, M (2002) Antioxidant activities and total phenolics of different types of honey. *NUTRITION RESEARCH* 22 (9): 1041-1047.
14. AL-QUASSEMI, R; ROBINSON, R K (2003) Some special nutritional propeties of honey - a brief review. *Nutrition & Food Science* 33 (6): 254-260.
15. AL-WAILI, N S (2003) Effects of daily consumption of honey solution on hematological indices and blood levels of minerals and enzymes in normal individuals. *Journal of Medicinal Food* 6 (2): 135-140.

16. AL-WAILI, N S (2003) Intrapulmonary administration of natural honey solution, hyperosmolar dextrose or hypoosmolar distill water to normal individuals and to patients with type-2 diabetes mellitus or hypertension: Their effects on blood glucose level, plasma insulin and C-peptide, blood pressure and peaked expiratory flow rate. *European journal of medical research* 8 (7): 295-303.
17. AL-WAILI, N S (2004) Investigating the antimicrobial activity of natural honey and its effects on the pathogenic bacterial infections of surgical wounds and conjunctiva 154. *Journal of Medicinal Food* 7 (2): 210-222.
18. AL-WAILI, N S (2004) Natural honey lowers plasma glucose, C-reactive protein, homocysteine, and blood lipids in healthy, diabetic, and hyperlipidemic subjects: Comparison with dextrose and sucrose. *Journal of Medicinal Food* 7 (1): 100-107.
19. AL-WAILI, N S (2004) Topical honey applications vs. acyclovir for the treatment of recurrent herpes simplex lesions. *Medical Science Monitor* 10 (8): 94-98.
20. AL-WAILI, N S; BONI, N S (2003) Natural honey lowers plasma prostaglandin concentrations in normal individuals. *Journal of Medicinal Food* 6 (2): 129-133.
21. AL-WAILI, N S; HAQ, A (2004) Effect of honey on antibody production against thymus-dependent and thymus-independent antigens in primary and secondary immune responses. *Journal of Medicinal Food* 7 (4): 491-494.
22. ALJADI, A M; KAMARUDDIN, M Y (2003) Isolation and Identification of Phenolic Acids in Malaysian Honey with Antibacterial Properties. *Turk J Med Sci* 33: 229-236.
23. ALJADI, A M; KAMARUDDIN, M Y (2004) Evaluation of the phenolic contents and antioxidant capacities of two Malaysian floral honeys. *Food Chemistry* 85 (4): 513-518.
24. ALLSOP, K A; MILLER, J B (1996) Honey revisited: A reappraisal of honey in pre-industrial diets. *B.J.Nutr.* 75 (4): 513-520.
25. ALVAREZ-SUAREZ, J; TULIPANI, S; ROMANDINI, S; BERTOLI, E; BATTINO, M (2009) Contribution of honey in nutrition and human health: a review. *Mediterr.J.Nutr.Met.* 2: DOI 10.1007/s12349-009-0051-6.
26. ALVAREZ-SUAREZ, J; TULIPANI, S; ROMANDINI, S; VIDAL, A; BATTINO, M (2009) Methodological Aspects about Determination of Phenolic Compounds and In Vitro Evaluation of Antioxidant Capacity in the Honey: A Review. *Curr.Anal.Chem* 5: 293-302.
27. ALVAREZ-SUAREZ, J M; TULIPANI, S; DIAZ, D; ESTEVEZ, Y; ROMANDINI, S; GIAMPIERI, F; DAMIANI, E; ASTOLFI, P; BOMPADRE, S; BATTINO, M (2010) Antioxidant and antimicrobial capacity of several monofloral Cuban honeys and their correlation with color, polyphenol content and other chemical compounds. *Food and Chemical Toxicology* 48 (8-9): 2490-2499.
28. AMERICAN HONEY BOARD (2005) Honey-Nutrition and Health. *National honey board*: 1-27.
29. AMES, B N; SHIGENAGA, M; HAGEN, T (1993) Oxidants, antioxidants, and the degenerative diseases of aging. *Proc.Natl.Acad.Sci.USA* 90: 7915-7922.
30. ANTONY, S; RIECK, J R; DAWSON, P L (2000) Effect of dry honey on oxidation in turkey breast meat. *Poultry Science* 79 (12): 1846-1850.
31. ARCOT, J; BRAND-MILLER, J (2005) A preliminary assesment of the glycemic index of honey. <http://www.rirdc.gov.au/reports/HBE/05-027sum.html> (2005): 1-24.
32. ARIEFDJOHAN, M W; MARTIN, B R; LACHCIK, P J; WEAVER, C M (2008) Acute and chronic effects of honey and its carbohydrate constituents on calcium absorption in rats. *Journal of agricultural and food chemistry* 56 (8): 2649-2654.
33. ASP, N; BRYNGELSSON, S (2008) Health Claims in Europe: New Legislation and PASSCLAIM for Substantiation. *The Journal of nutrition* 138: 1210S-1215S.

34. BALTRUSAITYTE, V; VENSKUTONIS, P R; CEKSTERYTE, V (2007) Antibacterial activity of honey and beebread of different origin against S-aureus and S-epidermidis. *Food Technology and Biotechnology* 45 (2): 201-208.
35. BALTRUSAITYTE, V; VENSKUTONIS, P R; CEKSTERYTE, V (2007) Radical scavenging activity of different floral origin honey and beebread phenolic extracts. *Food Chemistry* 101 (2): 502-514.
36. BEJAN, V; LACATIS, D; PETRUS, V; BEJAN, V V; CRETEANU, G (1978) L'emploi du fructose dans le regime du diabete sucre insulino-dependant, *IIIe Symposium International d'Apitherapie, 11-15 Septembre 1978, Portoroz, Yougoslavie, Apimondia, Bukarest, 1978*: pp 382-384.
37. BENGSCHE, E (1992) Connaissance du miel. Des oligo-éléments pour la santé. *Rev.franç.apicult.* (521): 383-386.
38. BERETTA, G; ARTALI, R; CANEVA, E; ORLANDINI, S; CENTINI, M; FACINO, R M (2009) Quinoline alkaloids in honey: Further analytical (HPLC-DAD-ESI-MS, multidimensional diffusion-ordered NMR spectroscopy), theoretical and chemometric studies. *Journal of Pharmaceutical and Biomedical Analysis* 50 (3): 432-439.
39. BERETTA, G; GRANATA, P; FERRERO, M; ORIOLI, M; FACINO, R M (2005) Standardization of antioxidant properties of honey by a combination of spectrophotometric/fluorimetric assays and chemometrics. *Analytica Chimica Acta* 533 (2): 185-191.
40. BERETTA, G; VISTOLI, G; CANEVA, E; ANSELMINI, C; FACINO, R M (2009) Structure elucidation and NMR assignments of two new pyrrolidinyl quinoline alkaloids from chestnut honey. *Magnetic resonance in Chemistry* 47 (5): 456-459.
41. BERG, A; KONIG, D (2008) The glycaemic index of different German honeys. *Ernahrungs-Umschau* 55 (12): 720-725.
42. BERTONCELJ, J; DOBERSEK, U; JAMNIK, M; GOLOB, T (2007) Evaluation of the phenolic content, antioxidant activity and colour of Slovenian honey. *Food Chemistry* 105 (2): 822-828.
43. BIANCHI, E M (1977) Honey: Its importance in children's nutrition. *Amer.Bee J.* 117 (12): 733.
44. BILIKOVA, K; SIMUTH, J (2010) New Criterion for Evaluation of Honey: Quantification of Royal Jelly Protein Apalbumin 1 in Honey by ELISA. *Journal of agricultural and food chemistry* 58 (15): 8776-8781.
45. BILSEL, Y; BUGRA, D; YAMANER, S; BULUT, T; CEVIKBAS, U; TURKOGLU, U (2002) Could honey have a place in colitis therapy? Effects of honey, prednisolone, and disulfiram on inflammation, nitric oxide, and free radical formation. *Digestive Surgery* 19 (4): 306-311.
46. BISWAL, B M; ZAKARIA, A; AHMAD, N M (2003) Topical application of honey in the management of radiation mucositis. A preliminary study. *Supportive Care in Cancer* 11 (4): 242-248.
47. BISWAS, B K (2009) Effects of Honey on Feed Consumption and Body Weight of Sprague-Dawley and Obese Rats. *Journal of the American Association for Laboratory Animal Science* 48 (5): 613.
48. BLASA, M; CANDIRACCI, M; ACCORSI, A; PIACENTINI, M; ALBERTINI, M; PIATTI, E (2006) Raw *Millefiori* honey is packed full of antioxidants. *Food Chemistry* 97 (2): 217-222.
49. BOGDANOV, S (1984) Characterisation of antibacterial substances in honey. *Lebensmittel-Wissenschaft + [i.e.und] Technologie.Food science + technology.Science + technologie alimentaire* 17: 74-76.
50. BOGDANOV, S (1997) Nature and origin of the antibacterial substances in honey. *Lebensmittel-Wissenschaft + [i.e.und] Technologie.Food science + technology.Science + technologie alimentaire* 30 (7): 748-753.
51. BOGDANOV, S (2006) Contaminants of bee products. *Apidologie* 38 (1): 1-18.
52. BOGDANOV, S; BLUMER, P (2001) Natürliche antibiotische Eigenschaften des Honigs. *Schweizerische Bienen-Zeitung* 124 (2): 18-21.

53. BOGDANOV, S; HALDIMANN, M; LUGINBUHL, W; GALLMANN, P (2007) Minerals in honey: environmental geographical and botanical aspects  
19. *Journal of Apicultural Research* 46 (4): 269-275.
54. BOGDANOV, S; JURENDIC, T; SIEBER, R; GALLMANN, P (2008) Honey for Nutrition and Health: A Review. *J.Am..Coll.Nutr.* 27: 677-689.
55. BOGDANOV, S; RUOFF, K; PERSANO ODDO, L (2007) Physico-chemical methods for the characterisation of unifloral honeys: a review. *Apidologie* 35: S4-S17.
56. BORNET, F; HAARDT, M J; COSTAGLIOLA, D; BLAYO, A; SLAMA, G (1985) Sucrose or honey at breakfast have no additional acute hyperglycaemic effect over an isoglucic amount of bread in Type 2 diabetic patients. *Diabetologia* 28: 213-217.
57. BOSTAN, M; BOSTAN, H; KAYA, A O; BILIR, O; SATIROGLU, O; KAZDAL, H; KARADAG, Z; BOZKURT, E (2010) Clinical Events in Mad Honey Poisoning: A Single Centre Experience. *Bulletin of Environmental Contamination and Toxicology* 84 (1): 19-22.
58. BOUSQUET, J; CAMPOS, J; MICHEL, F B (1984) Food intolerance to honey. *Allergy* 39 (1): 73-75.
59. BRADY, N; MOLAN, P; BANG, L (2004) A survey of non-manuka New Zealand honeys for antibacterial and antifungal activities  
69. *Journal of Apicultural Research* 43 (2): 47-52.
60. BRUDZYNSKI, K (2006) Effect of hydrogen peroxide on antibacterial activities of Canadian honeys. *Canadian Journal of Microbiology* 52: 1228-1237.
61. BRUDZYNSKI, K; KIM, L (2010) Storage-induced chemical changes in active components of honey de-regulate its antibacterial activity. *Food Chem* doi:10.1016/j.foodchem.2010.11.151
62. BRUDZYNSKI, K; MIOTTO, D (2011) The recognition of high molecular weight melanoidins as the main components responsible for radical-scavenging capacity of unheated and heat-treated Canadian honeys. *Food Chem* 125 (doi:10.1016/j.foodchem.2010.09.049): 570-575.
63. BRUDZYNSKI, K; MIOTTO, D (2011) The relationship between the content of Maillard reaction-like products and bioactivity of Canadian honeys. *Food Chemistry* 124 (3): 869-874.
64. BUSSEROLLES, J; GUEUX, E; ROCK, E; MAZUR, A; RAYSSIGUIER, Y (2002) Substituting honey for refined carbohydrates protects rats from hypertriglyceridemic and prooxidative effects of fructose. *The Journal of nutrition* 132 (11): 3379-3382.
65. CANDIRACCI, M; CITTERIO, B; DIAMANTINI, G; BLASA, M; ACCORSI, A; PIATTI, E (2011) Honey Flavonoids, Natural Antifungal Agents Against *Candida Albicans*. *INTERNATIONAL JOURNAL OF FOOD PROPERTIES* 14 (4): 799-808.
66. CEYHAN, N; UGUR, A (2001) Investigation of in vitro antimicrobial activity of honey. *RIVISTA DI BIOLOGIA BIOLOGY FORUM* 94 (2): 363-371.
67. CHANG, X; WANG, J H; YANG, S H; CHEN, S; SONG, Y J (2011) Antioxidative, antibrowning and antibacterial activities of sixteen floral honeys. *Food & Function* 2 (9): 541-546.
68. CHEN, L; MEHTA, A; BERENBAUM, M; ZANGERL, A R; ENGESETH, N J (2000) Honeys from different floral sources as inhibitors of enzymatic browning in fruit and vegetable homogenates. *Journal of agricultural and food chemistry* 48 (10): 4997-5000.
69. CHEPULIS, L M (2007) The Effects of Honey Compared With Sucrose and a Sugar-free Diet on Neutrophil Phagocytosis and Lymphocyte Numbers after Long-term Feeding in Rats. *JCIM* 4: DOI: 10.2202/1553-3840.1098.
70. CHEPULIS, L M; STARKEY, N J; WAAS, J R; MOLAN, P C (2009) The effects of long-term honey, sucrose or sugar-free diets on memory and anxiety in rats. *Physiology & Behavior* 97 (3-4): 359-368.

71. CHICK, H; SHIN, H S; USTUNOL, Z (2001) Growth and acid production by lactic acid bacteria and bifidobacteria grown in skim milk containing honey. *Journal of Food Science* 66 (3): 478-481.
72. CIULU, M; SOLINAS, S; FLORIS, I; PANZANELLI, A; PILO, M I; PIU, P C; SPANO, N; SANNA, G (2011) RP-HPLC determination of water-soluble vitamins in honey. *Talanta* 83 (3): 924-929.
73. COSSU, M; ALMANINI, C (2008) Identification and quantification of antioxidant compounds and evaluation of correlated physical features of honeys from different floral sources, *Sardinia Chem*, Università di Sassari, Sassari, Sardinia, Italy: pp 56-57.
74. COSTA-SILVA, F; MAIA, M; MATOS, C C; CALCADA, E; BARROS, A I R N; NUNES, F M (2011) Selenium content of Portuguese unifloral honeys. *Journal of Food Composition and Analysis* 24 (3): 351-355.
75. COX, N; HINKLE, R (2002) Infant botulism. *American Family Physician* 65 (7): 1388-1392.
76. CRANE, E (1975) History of honey, In Crane, E (ed.) *Honey, a comprehensive survey*, William Heinemann; London; pp 439-488.
77. CRANE, E (1983) *The archaeology of beekeeping*. Gerald Duckworth & Co. Ltd. London
78. CRANE, E (1999) *The world history of beekeeping and honey hunting*. Gerald Duckworth & Co Ltd London
79. CRANE, E; WALKER, P; DAY, R (1984) *Directory of important world honey sources*. International Bee Research Association London; 384 pp
80. CUSHNIE, T; LAMB, A (2005) Antimicrobial activity of flavonoids. *International Journal of Antimicrobial Agents* 26 (5): 343-356.
81. D'ARCY, B R (2005) ... RIRDC Publication No 05/040 (report): 1.
82. DAVIS, E A (1995) Functionality of sugars: physicochemical interactions in foods. *The American Journal of Clinical Nutrition* 62 (1 Suppl): 170-177.
83. DE BODT, G (1996) Les miels de rhododendrons. *Les Carnets du CARI Abeilles et Cie* (50): 10-12.
84. DEIBERT, P; KOENIG, D; KLOOK, B; GROENEFELD, A; BERG, A (2009) Glycaemic and insulinaemic properties of some German honey varieties. *European journal of clinical nutrition* doi:10.1038/ejcn.2009.103: 1-3.
85. DEUTSCHE GESELLSCHAFT FÜR ERNÄHRUNG (2000) *Referenzwerte für die Nährstoffzufuhr*. Umschau/Braus Frankfurt am Main (1st edition. edition)
86. DONER, L W (1977) The sugars of honey - a review. *Journal of the Science of Food and Agriculture* 28: 443-456.
87. DUDDUKURI, G R; KUMAR, P S; KUMAR, V B; ATHOTA, R R (1997) Immunosuppressive effect of honey on the induction of allergen-specific humoral antibody response in mice. *International Archives of Allergy and Immunology* 114 (4): 385-388.
88. DUSTMANN, J H (1971) Über die Katalaseaktivität in Bienenhonig aus der Tracht der Heidekrautgewächse (Ericacea). *Z.Lebensm.Unters.Forsch.* 145: 292-295.
89. DUSTMANN, J H (1972) Über den Einfluss des Lichtes auf den Peroxid-Wert (Inhibin) des Honigs. *Z.Lebensm.Unters.Forsch.* 148 (5): 263-268.
90. DUSTMANN, J H (1979) Antibacterial effect of honey. *Apiacta* 14: 7-11.
91. DUTAU, G; RANCE, F (2009) Honey and honey-product allergies. *Revue Francaise D Allergologie* 49 (6): S16-S22.

92. DUTAU, G; RANCE, F (2009) Honey and honey-product allergies. *Revue Francaise D Allergologie* 49 (6): S16-S22.
93. EARNEST, C; KREIDER, R; LUNDBERG, J; RASMJSSEN, C; COWAN, P; GREENWOOD, M; ALMADA, A (2000) Effects of pre-exercise carbohydrate feedings on glucose and insulin responses during and after resistance exercise. *Journal of Strength and Conditioning Research* 361: 361.
94. EARNEST, C; KREIDER, R; LUNDBERG, J; RASMJSSEN, C; COWAN, P; GREENWOOD, M; ALMADA, A (2000) Effects of pre-exercise carbohydrate feedings on glucose and insulin responses during and after resistance exercise. *J.Strength Cond.Res.* 361: 361.
95. EARNEST, C; LANCASTER, S; RASMUSSEN, C; KERSKICK, C; LUCIA, A; GREENWOOD, M; ALMADA, A; COWAND, P; KREIDER, R (2004) Low versus high glycemic index meals carbohydrate gel ingestion during simulated 64 km cycling time trial performance. *Journal of Strength and Conditioning Research* 18 (3): 466-472.
96. EDGAR, J A; ROEDER, E L; MOLYNEUX, R J (2002) Honey from plants containing pyrrolizidine alkaloids: A potential threat to health. *Journal of agricultural and food chemistry* 50 (10): 2719-2730.
97. ELLIOTT, S S; KEIM, N L; STERN, J S; TEFF, K; HAVEL, P J (2002) Fructose, weight gain, and the insulin resistance syndrome. *The American Journal of Clinical Nutrition* 76: 911-922.
98. EREJUWA, O O; SULAIMAN, S A; AB WAHAB, M S; SIRAJUDEEN, K N S; SALLEH, M S M; GURTU, S (2011) Differential Responses to Blood Pressure and Oxidative Stress in Streptozotocin-Induced Diabetic Wistar-Kyoto Rats and Spontaneously Hypertensive Rats: Effects of Antioxidant (Honey) Treatment. *International Journal of Molecular Sciences* 12 (3): 1888-1907.
99. ESTEVINHO, L; PEREIRA, A P; MOREIRA, L; DIAS, L G; PEREIRA, E (2008) Antioxidant and antimicrobial effects of phenolic compounds extracts of Northeast Portugal honey. *Food and Chemical Toxicology* 46 (12): 3774-3779.
100. EUROPEAN COMMISSION (2002) Honey and microbiological hazards. *Report European Commission of Health & Consumer Protection Directorate-General*: 1-40.
101. EUROPEAN COMMISSION (2002) Honey and microbiological hazards. *Report European Commission of Health & Consumer Protection Directorate-General*: 1-40.
102. EUROPEAN PARLIAMENT AND COUNCIL (2007) REGULATION (EC) No 1924/2006 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 20 December 2006 on nutrition and health claims made on foods. *Official Journal of the European Union* L 404: L 12-3-L 12/17.
103. FAHEY, J W; STEPHENSON, K K (2002) Pinostrobin from honey and Thai ginger (*Boesenbergia pandurata*): A potent flavonoid inducer of mammalian phase 2 chemoprotective and antioxidant enzymes. *Journal of agricultural and food chemistry* 50 (25): 7472-7476.
104. FAUZI, A N; NORAZMI, M N; YAACOB, N S (2011) Tualang honey induces apoptosis and disrupts the mitochondrial membrane potential of human breast and cervical cancer cell lines. *Food and Chemical Toxicology* 49 (4): 871-878.
105. FERREIRA, I C F R; AIRES, E; BARREIRA, J C M; ESTEVINHO, L M (2009) Antioxidant activity of Portuguese honey samples: Different contributions of the entire honey and phenolic extract. *Food Chemistry* 114 (4): 1438-1443.
106. FOSTER-POWELL, K; HOLT, S H A; BRAND-MILLER, J C (2002) International table of glycemic index and glycemic load values: 2002. *The American Journal of Clinical Nutrition* 76: 5-56.
107. FRANKEL, S; ROBINSON, G E; BERENBAUM, M R (1998) Antioxidant capacity and correlated characteristics of 14 unifloral honeys. *Journal of Apicultural Research* 37 (1): 27-31.
108. FRAUENFELDER, R A (1921) *Der Honig als Genuss-, Nähr- und Kräftigungsmittel*. Buchdruckerei A. Umiker Biel-Madretsch; 32 pp

109. FUKUDA, M; KOBAYASHI, K; HIRONO, Y; MIYAGAWA, M; ISHIDA, T; EJIOGU, E; SAWAI, M; PINKERTON, K; TAKEUCHI, M (2009) Jungle Honey Enhances Immune Function and Antitumor Activity. *eCam* doi:10.1093/ecam/nen086
110. GHASHM, A A; OTHMAN, N H; KHATTAK, M N; ISMAIL, N M; SAINI, R (2010) Antiproliferative effect of Tualang honey on oral squamous cell carcinoma and osteosarcoma cell lines. *BMC Complementary and Alternative Medicine* 10
111. GHELDOF, N; ENGESETH, N J (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. *Journal of agricultural and food chemistry* 50 (10): 3050-3055.
112. GHELDOF, N; WANG, X H; ENGESETH, N J (2002) Identification and quantification of antioxidant components of honeys from various floral sources. *Journal of agricultural and food chemistry* 50 (21): 5870-5877.
113. GHELDOF, N; WANG, X H; ENGESETH, N J (2003) Buckwheat honey increases serum antioxidant capacity in humans. *Journal of agricultural and food chemistry* 51 (5): 1500-1505.
114. GONNET, M; LAVIE, P (1960) Influence du chauffage sur le facteur antibiotique présent dans les miels. *Annales de l'Abeille* 3 (4): 349-364.
115. GRIBEL', N V; PASHINSKII, V G (1990) [The antitumor properties of honey]. *Voprosy Onkologii* 36 (6): 704-709.
116. GROENEVELD, M (2004) Die Bedeutung von Honig in der Ernährung unter spezieller Berücksichtigung seiner Anwendungsgebiete in der Volksmedizin und seiner Wirkungen auf Fettstoffwechselfparameter.: 1-37.
117. GUERRINI, A; BRUNI, R; MAIETTI, S; POLI, F; ROSSI, D; PAGANETTO, G; MUZZOLI, M; SCALVENZI, L; SACCHETTI, G (2009) Ecuadorian stingless bee (Meliponinae) honey: A chemical and functional profile of an ancient health product. *Food Chemistry* 114 (4): 1413-1420.
118. HEGAZI, A; EL-HADY, F K A (2007) Influence of Honey on the Suppression of Human Low Density Lipoprotein (LDL) Peroxidation (In vitro). *eCam*: 1-9.
119. HEITKAMP, K (1984) Pro und kontra Honig - Sind Aussagen zur Wirkung des Honigs "wissenschaftlich hinreichend gesichert"? *Schriften zur Oecotrophologie*: 1-60.
120. HELBLING, A; PETER, C; BERCHTOLD, E; BOGDANOV, S; MÜLLER, U (1992) Allergy to honey: Relation to pollen and honey bee allergy. *ȳȳ* 47: 41-49.
121. HÜBNER, B (1958) Säuglingsernährung mit Honigmilch (Nektar-Mil). *MMW, Münchener medizinische Wochenschrift* 100 (8): 311-313.
122. INOUE, K; MURAYARNA, S; SESHIMO, F; TAKEBA, K; YOSHIMURA, Y; NAKAZAWA, H (2005) Identification of phenolic compound in manuka honey as specific superoxide anion radical scavenger using electron spin resonance (ESR) and liquid chromatography with coulometric array detection. *Journal of the Science of Food and Agriculture* 85 (5): 872-878.
123. IRISH, J; BLAIR, S; CARTER, D (2011) The Antibacterial Activity of Honey Derived from Australian Flora. *Plos One* 6 (3): e18229.
124. ISCHAYEK, J I; KERN, M (2006) US honeys varying in glucose and fructose content elicit similar glycemic indexes. *Journal of the American Dietetic Association* 106 (8): 1260-1262.
125. ISIDOROV, V A; CZYZEWSKA, U; JANKOWSKA, E; BAKIER, S (2011) Determination of royal jelly acids in honey. *Food Chemistry* 124 (1): 387-391.
126. JAGANATHAN, S; MANDAL, M (2009) Honey Constituents and their apoptotic effect in colon cancer cells. *JAAS* 1: 29-36.

127. JAGANATHAN, S K; MANDAL, M (2010) Involvement of non-protein thiols, mitochondrial dysfunction, reactive oxygen species and p53 in honey-induced apoptosis. *Investigational New Drugs* 28 (5): 624-633.
128. JAWAD, F H; AL-KHALIDI, A; TAWFIQ, N H (1981) Effects of bees honey, zahdi date and its syrup on blood glucose and serum insulin of normal subjects. *Journal of the Faculty of Medicine, Baghdad* 23 (2): 169-180.
129. JENKINS, D; KENDALL, C; AUGUSTIN, L; FRANCESCHI, S; HAMIDI, M; MARCHIE, A; JENKINS, A; AXELSEN, M (2002) Glycemic index: overview of implications in health and disease. *The American Journal of Clinical Nutrition* 76: 266S-273S.
130. JONES, R (2001) Honey and healing through the ages, In Munn, P; Jones, R (eds) *Honey and healing*, International Bee Research Association IBRA; Cardiff, GB; pp 1-4.
131. KACANIOVA, M; FATRCOVA-SRAMKOVA, K; NOZKOVA, J; MELICH, M; KADASI-HORAKOVA, M; KNAZOVICKA, V; FELSOCIOVA, S; KUNOVA, S; MARIASSYOVA, M (2011) Antiradical activity of natural honeys and antifungal effect against *Penicillium* genera. *Journal of Environmental Science and Health Part B-Pesticides Food Contaminants and Agricultural Wastes* 46 (1): 92-96.
132. KAJIWARA, S; GANDHI, H; USTUNOL, Z (2002) Effect of honey on the growth of and acid production by human intestinal *Bifidobacterium* spp.: An in vitro comparison with commercial oligosaccharides and inulin. *Journal of Food Protection* 65 (1): 214-218.
133. KATSILAMBROS, N L; PHILIPPIDES, P; TOULIATOU, A; GEORGAKOPOULOS, K; KOFOTZOULI, L; FRANGAKI, D; SISKOUDIS, P; MARANGOS, M; SFIKAKIS, P (1988) Metabolic effects of honey (alone or combined with other foods) in type II diabetics. *Acta diabetologica latina* 25 (3): 197-203.
134. KENJERIC, D; MANDIC, M L; PRIMORAC, L; BUBALO, D; PERL, A (2007) Flavonoid profile of *Robinia* hoenys produced in Croatia. *Food Chemistry*: in press.
135. KIRNPAUL-KAUR, B S; TSE TAN, H; BOUKRAA, L; HUA GAN, S (2011) Different Solid Phase Extraction Fractions of Tualang (*Koompassia excelsa*) Honey Demonstrated Diverse Antibacterial Properties Against Wound and Enteric Bacteria. *JAAS*: 59-65.
136. KISHORE, R K; HALIM, A S; SYAZANA, M S N; SIRAJUDEEN, K N S (2011) Tualang honey has higher phenolic content and greater radical scavenging activity compared with other honey sources. *NUTRITION RESEARCH* 31 (4): 322-325.
137. KOC, A N; SILICI, S; ERCAL, B D; KASAP, F; HORMET-OZ, H T; MAVUS-BULDU, H (2009) Antifungal Activity of Turkish Honey against *Candida* spp. and *Trichosporon* spp: an in vitro evaluation. *Medical Mycology* 47 (7): 707-712.
138. KREIDER, R (2001) Honey and sports nutrition: Report for the American Honey Board. *published on line* (4)
139. KREIDER, R (2001) Researches discover honey is good for muscles (Clinical Innovations) (Brief Article). *Assoc.Periooperat.Regist.Nurses J.* (10)
140. KREIDER, R; RASMUSSEN, C; LUNDBERG, J; COWAN, P; GREENWOOD, M; EARNEST, C; ALMADA, A (2000) Effects of ingesting carbohydrate gels on glucose, insulin and perception of hypoglycemia. *FASEB Journal* (14): A490.
141. KREIDER, R; RASMUSSEN, C; LUNDBERG, J; COWAN, P; GREENWOOD, M; EARNEST, C; ALMADA, A (2000) Effects of ingesting carbohydrate gels on glucose, insulin and perception of hypoglycemia. *FASEB Journal* (14): A490.
142. KREIDER, R; RASMUSSEN, C; LUNDBERG, J; COWAN, P; GREENWOOD, M; EARNEST, C; ALMADA, A (2000) Effects of ingesting carbohydrate gels on glucose, insulin and perception of hypoglycemia. *FASEB Journal* (14): A490.
143. KREIDER, R B; RASMUSSEN, C J; LANCASTER, S L; KERKSICK, C; GREENWOOD, M (2002) Honey: An alternative sports gel. *Strength Conditioning J.* 24: 50-51.

144. KUCUK, M; KOLAYLI, S; KARAOGLU, S; ULUSOY, E; BALTACI, C; CANDAN, F (2007) Biological activities and chemical composition of three honeys of different types from Anatolia. *Food Chemistry* 100 (2): 526-534.
145. KWAKMAN, P H S; TE VELDE, A; DE BOER, L; SPEIJER, D; VANDENBROUCKE-GRAULS, C M J E; ZAAT, S A J (2010) How honey kills bacteria. *The FASEB journal* doi: 10.1096/fj.09-150789
146. KWAKMAN, P H S; TE VELDE, A; DE BOER, L; VANDENBROUCKE-GRAULS, C M J E (2011) Two Major Medicinal Honeys Have Different Mechanisms of Bactericidal Activity. *Plos One* 6 (3): e17709.
147. LAVIE, P; GRASSÉ, P P (1963) Sur l'identification des substances antibactériennes présentes dans le miel. *Comptes rendus des Séances de l'Académie des Sciences* 256: 1858-1860.
148. LEE, C Y (1996) Substitution of honey for sulfur dioxide in grape juice processing. *American Bee Journal* 136 (12): 872-873.
149. LEE, C Y; SMITH, N L; UNDERWOOD, B A; MORSE, R A (1990) Honey protein from different bee species in relation to apple juice clarification activity. *American Bee Journal* 130: 478-479.
150. LEE, H; CHUREY, J J; WOROBO, R W (2008) Purification and structural characterization of bacillomycin F produced by a bacterial honey isolate active against *Byssoschlamys fulva* H25 116 77722. *JOURNAL OF APPLIED MICROBIOLOGY* 105 (3): 663-673.
151. LEE, H J; CHUREY, J J; WOROBO, R W (2008) Antimicrobial activity of bacterial isolates from different floral sources of honey 22 77723. *International Journal of Food Microbiology* 126 (1-2): 240-244.
152. LEUTHOLZ, B; KREIDER, R (2001) Optimising nutrition of exercise and sport, In Wilson, T; Temple, N (eds) Humana Press; Totowa, NJ; pp 207-235.
153. LIBERATO, M D T C; DE MORAIS, S M; SIQUEIRA, S M C; DE MENEZES, J E S A; RAMOS, D N; MACHADO, L K A; MAGALHAES, I L (2011) Phenolic Content and Antioxidant and Antiacetylcholinesterase Properties of Honeys from Different Floral Origins. *Journal of Medicinal Food* 14 (6): 658-663.
154. LIU, S M; MANSON J.E; STAMPFER M.J.; HOLMES M.D; HU F.B.; HANKINSON S.E; WILLETT W.C (2001) Dietary glycemic load assessed by food-frequency questionnaire in relation to plasma high-density-lipoprotein cholesterol and fasting plasma triacylglycerols in postmenopausal women. *The American Journal of Clinical Nutrition* 73: 560-566.
155. LUCAN, M; SLACANAC, V; HARDI, J; MASTANJEVIC, K; BABIC, J; KRSTANOVIC, V; JUKIC, M (2009) Inhibitory effect of honey-sweetened goat and cow milk fermented with *Bifidobacterium lactis* Bb-12 on the growth of *Listeria monocytogenes*. *Mljekarstvo* 59 (2): 96-106.
156. LUDWIG, D (2000) Dietary Glycemic Index and Obesity. *The Journal of nutrition* 130: 280S-283S.
157. LUDYANSKII, E A (1994) *Apiterapia*. Vologda, Russia; Poligrafist; 460 pp
158. MADEJCZYK, M; BARALKIEWICZ, D (2008) Characterisation of honey from different areas of Poland by their physico-chemical parametres and trace elements. *Proceedings of Ecopole 2007, Vol 2 2* (1): 59-63.
159. MADEO, M; GUGLIELMETTI, S; SPERANZA, G; LOZZIA, G C; GIORGI, A (2009) Evaluation of phenolic composition and a biological activity of honey. *Planta medica* 75 (9): 1053.
160. MAHANEEM, M; SULAIMAN, S; JAAFAR, H; SIRAJUDEEN, K; ISMAIL, Z; ISLAM, M (2011) Effect of Honey on Testicular Functions in Rats Exposed to Cigarette Smoke. *JAAS* 3: 12-17.
161. MAJTAN, J; MAJTANOVA, L; BOHOVA, J; MAJTAN, V (2011) Honeydew Honey as a Potent Antibacterial Agent in Eradication of Multi-drug Resistant *Stenotrophomonas maltophilia* Isolates from Cancer Patients. *Phytotherapy Research* 25 (4): 584-587.

162. MARGHITAS, L; DEZMIREAN, D; MOISE, A; BOBIS, O; LASLO, L; BOGDANOV, S (2009) Physico-chemical and bioactive properties of different floral origin honeys from Romania. *Food Chemistry* 112 (4): 863-867.
163. 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. *Molecular Nutrition & Food Research* 52 (4): 483-489.
164. MCKIBBEN, J; ENGESETH, N J (2002) Honey as a protective agent against lipid oxidation in ground turkey. *Journal of agricultural and food chemistry* 50 (3): 592-595.
165. MCLELLAN, M R; KIME, R W; LEE, C Y; LONG, T M (1995) Effect of honey as an antibrowning agent in light raisin processing. *Journal of Food Processing and Preservation* 19: 1-8.
166. MCMASTER, P; PIPER, S; SCHELL, D; GILLIS, J; CHONG, A (2000) A taste of honey. *Journal of Paediatrics and Child Health* 36 (6): 596-597.
167. MESAİK, M A; AZIM, M K; MOHIUDDIN, S (2008) Honey modulates oxidative burst of professional phagocytes. *Phytotherapy Research* 22 (10): 1404-1408.
168. MICHAİL, K; MATZI, V; MAIER, A; HERWIG, R; GREILBERGER, J; H. JUAN, H; KUNERT, O; R. WINTERSTEIGER, R (2007) Hydroxymethylfurfural: an enemy or a friendly xenobiotic? A bioanalytical approach. *Analytical and Bioanalytical Chemistry* 387: 2801-2814.
169. MOHAMED, M; SULAIMAN, S A; JAAFAR, H; SIRAJUDEEN, K N S (2011) Antioxidant Protective Effect of Honey in Cigarette Smoke-Induced Testicular Damage in Rats. *International Journal of Molecular Sciences* 12 (9): 5508-5521.
170. MOLAN, P (1999) Why honey is effective as a medicine. 1. Its use in modern medicine. 2. The scientific explanation of its effects 1907. *Bee World* 80; 82 (2; 1): 79-92.
171. MOLAN, P C (1992) The antibacterial activity of honey. 1. The nature of the antibacterial activity. *Bee World* 73 (1): 5-28.
172. MOLAN, P C (1992) The antibacterial activity of honey. 2. Variation in the potency of the antibacterial activity. *Bee World* 73 (2): 59-76.
173. MOLAN, P C (1992) The antibacterial activity of honey. 2. Variation in the potency of the antibacterial activity. *Bee World* 73 (2): 59-76.
174. MOLAN, P C (1992) The antimicrobial activity of honey 1. The nature of antibacterial activity. *Bee World* 73 (1): 5-28.
175. MOLAN, P C (1997) Honey as an antimicrobial agent, In Mizrahi, A; Lensky, Y (eds) *Bee Products. Properties, Applications, and Apitherapy, Symposium Tel Aviv*: pp 27-37.
176. MOLAN, P C (2001) Why honey is effective as a medicine - 2. The scientific explanation of its effects. *Bee World* 82 (1): 22-40.
177. MOLAN, P C; SMITH, I M; REID, G M (1988) A comparison of the antibacterial activities of some New Zealand honeys. *Journal of Apicultural Research* 27 (4): 252-256.
178. MOMMSEN, H (1957) Honig statt Zucker in der Ernährung des Säuglings. *Sonderdruck Deutsche Hebammen-Zeitschrift* 9 (1): 10-12.
179. MONTENEGRO, G; SALAS, F; PENA, R C; PIZARRO, R (2009) Antibacterial and antifungic activity of the unifloral honeys of *Quillaja saponaria*, an endemic Chilean species. *Phyton-International Journal of Experimental Botany* 78: 141-146.
180. MÜLLER, L (1956) Der Bienenhonig in der Säuglingsernährung bei Berücksichtigung einer neuen Fertignahrung. *Medizinische Monatsschrift* 10 (11): 729-732.

181. MÜLLER-BUNKE, H; HÖCK, A; SCHÖNTUBE, M; NOACK, R (2000) Säuglingsbotulismus. *Monatsschrift für Kinderheilkunde* 3: 242-245.
182. MUNDO, M A; PADILLA-ZAKOUR, O I; WOROBO, R W (2004) Growth inhibition of foodborne pathogens and food spoilage organisms by select raw honeys. *International Journal of Food Microbiology* 97: 1-8.
183. MÜNSTEDT, K; BÖHME, M; HAUENSCHILD, A; HRGOVIC, I (2011) Consumption of rapeseed honey leads to higher serum fructose levels compared with analogue glucose/fructose solutions. *European journal of clinical nutrition* 65: 77-80.
184. MÜNSTEDT, K; SHEYBANI, B; HAUENSCHILD, A; BRÜGGMANN, D; BRETZEL, R; WINTER, D (2008) Effects of Basswood Honey, Honey-Comparable Glucose-Fructose Solution, and Oral Glucose Tolerance Test Solution on Serum Insulin, Glucose, and C-Peptide Concentrations in Healthy Subjects. *J Med Food* 11: 424-428.
185. MUROSAKI, S; MUROYAMA, K; YAMAMOTO, Y; LIU, T; YOSHIKAI, Y (2002) Nigeroooligosacharides augments natural killer activity of hepatic mononuclear cells in mice (Preliminary study / report). *International immunopharmacology* 2: 151-159.
186. NAGAI, T; INOUE, R; KANAMORI, N; SUZUKI, N; NAGASHIMA, T (2006) Characterization of honey from different floral sources. Its functional properties and effects of honey species on storage of meat. *Food Chemistry* 15 (2): 256-262.
187. OLOFSSON, T C; VASQUEZ, A (2008) Detection and identification of a novel lactic acid bacterial flora within the honey stomach of the honeybee *Apis mellifera*. *Current Microbiology* 57 (4): 356-363.
188. ORSOLIC, N; BASIC, I (2004) Honey as a cancer-preventive agent. *Periodicum Biologorum* 106 (4): 397-401.
189. ORSOLIC, N; KNEZEVIC, A H; SVER, L; TERZIC, S; HECKENBERGER, B K; BASIC, I (2003) Influence of honey bee products on transplantable murine tumours. *Vet.Comp.Oncology* 1 (4): 216-226.
190. OSZMIANSKI, J; LEE, C Y (1990) Inhibition of polyphenol oxidase activity and browning by honey. *Journal of agricultural and food chemistry* 38: 1892-1895.
191. PERETTI, A; CARBINI, L; DAZZI, E; PITTAU, L; SPANU, P; MANAI, M (1994) Uso razionale del miele nell'alimentazione dei diabetici. *Clinica Dietologica* 21 (1): 13-21.
192. PEREZ, R A; IGLESIAS, M T; PUEYO, E; GONZALEZ, M; DE LORENZO, C (2007) Amino acid composition and antioxidant capacity of Spanish honeys. *Journal of agricultural and food chemistry* 55 (2): 360-365.
193. PERSANO ODDO, L; PIANA, L; BOGDANOV, S; BENTABOL, A; GOTSIU, P; KERKVLJET, J; MARTIN, P; MORLOT, M; VALBUENA, A O; RUOFF, K; VON DER OHE, K (2004) Botanical species giving unifloral honey in Europe. *Apidologie* 35 (special issue): 82-93.
194. PERSANO ODDO, L; PIRO, R (2004) Main European unifloral honeys: descriptive sheets. *Apidologie* 35 (special issue): S38-S81.
195. PICHICHERO, E; CANUTI, L; CANINI, A (2009) Characterisation of the phenolic and flavonoid fractions and antioxidant power of Italian honeys of different botanical origin. *Journal of the Science of Food and Agriculture* 89 (4): 609-616.
196. PILJAC-ŽEGARAC, J; STIPCEVIC, T; BELSCAK, A (2009) Antioxidant properties and phenolic content of different floral origin honeys. *JAAS* 1: 43-50.
197. POPA, D; USTUNOL, Z (2011) Influence of sucrose, high fructose corn syrup and honey from different floral sources on growth and acid production by lactic acid bacteria and bifidobacteria. *INTERNATIONAL JOURNAL OF DAIRY TECHNOLOGY* 64 (2): 247-253.

198. POSTMES, T (2001) The treatment of burns and other wounds with honey, *In* Munn, P; Jones, R (eds) *Honey and healing*, IBRA International Bee Research Association; Cardiff, GB; pp 41-47.
199. POTSHINKOVA, P (1992) *Bienenprodukte in der Medizin. Apitherapie*. Ehrenwirth Verlag München
200. RAKHA, M K; NABIL, Z I; HUSSEIN, A A (2008) Cardioactive and vasoactive effects of natural wild honey against cardiac malperformance induced by hyperadrenergic activity  
132. *Journal of Medicinal Food* 11 (1): 91-98.
201. RAMENGI, L A; AMERIO, G; SABATINO, G (2001) Honey, a palatable substance for infants: from De Rerum Natura to evidence-based medicine. *European journal of pediatrics* 160 (11): 677-678.
202. RASHED, M N; SOLTAN, M E (2004) Major and trace elements in different types of Egyptian mono- floral and non-floral bee honeys. *Journal of Food Composition and Analysis* 17 (6): 725-735.
203. RASMUSSEN, C; KREIDER, R; LUNDBERG, J; COWAN, P; GREENWOOD, M; EARNEST, C; ALMADA, A (2000) Analysis of glycemic index and insulin response index of various carbohydrate gels. *FASEB Journal* 14: A489.
204. RIVERO-URGELL, M; SANTAMARIA-ORLEANS, A (2001) Oligosaccharides: application in infant food (review). *Early Human Development* 65: 43-52.
205. ROMERO-SILVA, S; MIGUEL, A M R; ROMERO-ROMERO, L P; RODRIGUEZ, O; GERARDO, S G C; MOREL, N; LOPEZ-MUNOZ, F J; LIMA-MENDOZA, L A; BRAVO, G (2011) Effects of Honey Against the Accumulation of Adipose Tissue and the Increased Blood Pressure on Carbohydrate-Induced Obesity in Rat. *Letters in Drug Design & Discovery* 8 (1): 69-75.
206. ROSA, A; TUBEROSO, C I G; ATZERI, A; MELIS, M P; BIFULCO, E; DESSI, M A (2011) Antioxidant profile of strawberry tree honey and its marker homogentisic acid in several models of oxidative stress. *Food Chemistry* 129 (3): 1045-1053.
207. RUSSELL, K M; MOLAN, P C; WILKINS, A L; HOLLAND, P T (1988) Identification of some antibacterial constituents of New Zealand Manuka honey. *Journal of agricultural and food chemistry* 38 (1): 10-13.
208. SAMANTA, A; BURDEN, A C; JONES, G R (1985) Plasma glucose responses to glucose, sucrose and honey in patients with diabetes mellitus: an analysis of glycaemic and peak incremental indices. *Diabetic medicine* 2: 371-373.
209. SAMARGHANDIAN, S; AFSHARI, J T; DAVOODI, S (2011) Honey induces apoptosis in renal cell carcinoma. *Pharmacognosy Magazine* 7 (25): 46-52.
210. SANZ, M L; POLEMIS, N; MORALES, V; CORZO, N; DRAKOULARAKOU, A; GIBSON, G R; RASTALL, R A (2005) In vitro investigation into the potential prebiotic activity of honey oligosaccharides. *Journal of agricultural and food chemistry* 53 (8): 2914-2921.
211. SCHRAMM, D D; KARIM, M; SCHRADER, H R; HOLT, R R; CARDETTI, M; KEEN, C L (2003) Honey with high levels of antioxidants can provide protection to healthy human subjects. *Journal of agricultural and food chemistry* 51: 1732-1735.
212. SERT, D; AKIN, N; DERTLI, E (2011) Effects of sunflower honey on the physicochemical, microbiological and sensory characteristics in set type yoghurt during refrigerated storage. *INTERNATIONAL JOURNAL OF DAIRY TECHNOLOGY* 64 (1): 99-107.
213. SHAMALA, T R; JYOTHI, Y S; SAIBABA, P (2000) Stimulatory effect of honey on multiplication of lactic acid bacteria under in vitro and in vivo conditions. *Letters in Applied Microbiology* 30 (6): 453-455.
214. SHERLOCK, O; DOLAN, A; ATHMAN, R; POWER, A; GETHIN, G; COWMAN, S; HUMPHREYS, H (2010) Comparison of the antimicrobial activity of Ulmo honey from Chile and Manuka honey against methicillin-resistant *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa*. *BMC Complementary and Alternative Medicine* 10

215. SHIN, H S; STRASBURG, G M; USTUNOL, Z (2003) Influence of different unifloral honeys on heterocyclic aromatic amine formation and overall mutagenicity in fried ground-beef patties. *Journal of Food Science* 68 (3): 810-815.
216. SHIN, H S; USTUNOL, Z (2005) Carbohydrate composition of honey from different floral sources and their influence on growth of selected intestinal bacteria: An in vitro comparison. *Food Research International* 38 (6): 721-728.
217. SIDDIQUI, I R (1970) The sugars of honey. *Advances in Carbohydrate Chemistry and Biochemistry* 25: 285-309.
218. SLACANAC, V; HARDI, J; LUCAN, M; KUN, S; HAVAS, P; KRSTANOVIC, V (2011) Effect of Honey Addition on Fermentation Activity of *Lactobacillus Casei* Lc-01 in Cow'S and Goat'S Milk: A Kinetic Study. *Acta Alimentaria* 40 (2): 270-281.
219. STRAIT, M J (1997) The effect of liquid or dry honey as a partial replacement for sugar on the baking and keeping qualities of fat reduced muffins. Ph.D. Dissertation; Blacksburg, Virginia, USA Virginia Polytechnic Institute and State University; pp 1-175.
220. SWELLAM, T; MIYANAGA, N; ONOZAWA, M; HATTORI, K; KAWAI, K; SHIMAZUI, T; AKAZA, H (2003) Antineoplastic activity of honey in an experimental bladder cancer implantation model: in vivo and in vitro studies. *International journal of urology* 10 (4): 213-219.
221. SYAZANA, M S N; HALIM, A S; GAN, S H; SHAMSUDDIN, S (2011) Antiproliferative effect of methanolic extraction of tualang honey on human keloid fibroblasts. *BMC Complementary and Alternative Medicine* 11
222. TAKUMA, D T (1955) Honig bei der Aufzucht von Säuglingen. *Monatsschrift für Kinderheilkunde* 103 (2): 160-161.
223. TAN, H T; RAHMAN, R A; GAN, S H; HALIM, A S; HASSAN, S A; SULAIMAN, S A; KIRNPAL-KAUR, B S (2009) The antibacterial properties of Malaysian tualang honey against wound and enteric microorganisms in comparison to manuka honey. *BMC Complementary and Alternative Medicine* 9
224. TANZI, M G; GABAY, M P (2002) Association between honey consumption and infant botulism. *Pharmacotherapy* 22 (11): 1479-1483.
225. TAORMINA, P J; NIEMIRA, B A; BEUCHAT, L R (2001) Inhibitory activity of honey against foodborne pathogens as influenced by the presence of hydrogen peroxide and level of antioxidant power. *International Journal of Food Microbiology* 69 (3): 217-225.
226. TEJPAL, D; GOYAL, N (2009) Effect of Inulin, Honey and Gum Acacia on Growth of Human Faecal Potential Probiotic Lactobacilli. *The IUP Journal of Life Sciences* 3: 29-34.
227. TERRAB, A; GONZALEZ, A G; DIEZ, M J; HEREDIA, F J (2003) Mineral content and electrical conductivity of the honeys produced in Northwest Morocco and their contribution to the characterisation of unifloral honeys. *Journal of the Science of Food and Agriculture* 83 (7): 637-643.
228. TOMÁS-BARBERÁN, F A; MARTOS, I; FERRERES, F; RADOVIC, B S; ANKLAM, E (2001) HPLC flavonoid profiles as markers for the botanical origin of European unifloral honeys. *Journal of the Science of Food and Agriculture* 81 (5): 485-496.
229. TROPP, C (1957) Der Honig und seine Bedeutung in der Säuglings- und Kinderernährung. *Der Landarzt* 33 (9): 250-252.
230. TRUCHADO, P; GIL-IZQUIERDO, A; TOMAS-BARBERAN, F; ALLENDE, A (2009) Inhibition by Chestnut Honey of N-Acyl-L-homoserine Lactones and Biofilm Formation in *Erwinia carotovora*, *Yersinia enterocolitica*, and *Aeromonas hydrophila*. *Journal of agricultural and food chemistry* 57 (23): 11186-11193.

231. TRUCHADO, P; LOPEZ-GALVEZ, F; GIL, M I; TOMAS-BARBERAN, F A; ALLENDE, A (2009) Quorum sensing inhibitory and antimicrobial activities of honeys and the relationship with individual phenolics. *Food Chemistry* 115 (4): 1337-1344.
232. TSIAPARA, A; JAAKKOLA, M; CHINO, I; GRAIKOU, K; TINA TOLONEN, V V A P M (2009) Bioactivity of Greek honey extracts on breast cancer (MCF-7), prostate cancer (PC-3) and endometrial cancer (Ishikawa) cells: Profile analysis of extracts. *Food Chemistry* 116: 702-708.
233. TURKMEN, N; SARI, F; POYRAZOGLU, E S; VELIOGLU, Y S (2006) Effects of prolonged heating on antioxidant activity and colour of honey. *Food Chemistry* 95 (4): 653-657.
234. USTUNOL, Z (2000) The effect of honey on the growth of bifidobacteria: report for the National honey board.: 1-8.
235. USTUNOL, Z; GANDHI, H (2001) Growth and viability of commercial Bifidobacterium spp. in honey-sweetened skim milk. *Journal of Food Protection* 64 (11): 1775-1779.
236. VARGA, L (2006) Effect of acacia (*Robinia pseudo-acacia* L.) honey on the characteristic microflora of yogurt during refrigerated storage. *International Journal of Food Microbiology* 108 (2): 272-275.
237. VELA, L; DE LORENZO, C; PÉREZ, R A (2007) Antioxidant capacity of Spanish honeys and its correlation with polyphenol content and other physicochemical properties. *Journal of the Science of Food and Agriculture* 87 (6): 1069-1075.
238. WANG, X H; ANDRAE, L; ENGESETH, N J (2002) Antimutagenic effect of various honeys and sugars against Trp-p-1. *Journal of agricultural and food chemistry* 50 (23): 6923-6928.
239. WANG, X H; GHELDOF, N; ENGESETH, N J (2004) Effect of processing and storage on antioxidant capacity of honey. *Journal of Food Science* 69 (2): C96-C101.
240. WESTON, R J; MITCHELL, K R; ALLEN, K L (1999) Antibacterial phenolic components of New Zealand manuka honey. *Food Chemistry* 64 (3): 295-301.
241. WHITE, J W; SUBERS M.H. (1964) Studies on honey inhibine. 3. Effect of heat. *Journal of Apicultural Research* 3: 45-50.
242. WHITE, J W; SUBERS M.H. (1964) Studies on honey inhibine. 4. Destruction of the peroxide accumulation system by light. *Journal of Food Science* 29: 819-828.
243. WHITE, J W; SUBERS, M H (1963) Studies on honey inhibine. 2. A chemical assay. *Journal of Apicultural Research* 2 (3): 93-100.
244. WHITE, J W; SUBERS, M H; SCHEPARTZ, A J (1963) The identification of inhibine, the antibacterial factor in honey, as hydrogen peroxide and its origin in a honey glucose-oxidase system. *Biochimica et Biophysica Acta* 73: 57-70.
245. WILKINSON, J M; CAVANAGH, H (2005) Antibacterial Activity of 13 Honeys Against Escherichia coli and Pseudomonas aeruginosa. *J.Med.Food* 8: 100-103.
246. WILLERSON, J; RIDKER, P (2004) Inflammation as a Cardiovascular Risk Factor. *Circulation* 109: II2-II10.
247. WOO, K S; YONG-HO, C; EUN-MI, J (2009) Review of antioxidant activity and antibacterial capacity of Korean produced black locust honey and chestnut honey, *Proceedings of the 9th international conference on Apitherapy Health Care and International Forum of Apitherapy and Bee Products, Asoam Apicultural Association, Nopburee Press, Chiang Mai, Thailand, 14.Nov.2009: pp 30-39.*
248. YATSUNAMI, K; ECHIGO, T (1984) Antibacterial action of honey and royal jelly (japanisch). *Honeybee Science* 5 (3): 125-130.
249. YUN, Y W (1996) Fructooligosaccharides - occurrence, preparation and application. *Enzyme and microbial technology* 19: 107-117.

250. ZAID.S.; SULAIMAN, S; SIRAJUDEEN, K; OTHMAN, N (2010) The Effects of Tualang honey on Female Reproductive Organs, Tibia Bone and Hormonal Profile in Ovariectomised Rats - animal model for menopause. *BMC-CAM* 10:82: doi:10.1186/1472-6882-10-82.
251. ZEINA, B; OTHMAN, O; AL-ASSAD, S (1996) Effect of honey versus thyme on Rubella virus survival in vitro. *Journal of Alternative and Complementary Medicine* 2 (3): 345-348.
252. ZEINA, B; ZOHRA, B I; AL ASSAD, S (1997) The effects of honey on Leishmania parasites: an in vitro study. *Tropical Doctor* 27 Suppl 1: 36-38.
253. ZIDAN, J; SHETVER, L; GERSHUNY, A; ABZAH, A; TAMAM, S; STEIN, M; FRIEDMAN, E (2006) Prevention of chemotherapy-induced neutropenia by special honey intake. *Medical Oncology* 23 (4): 549-552.