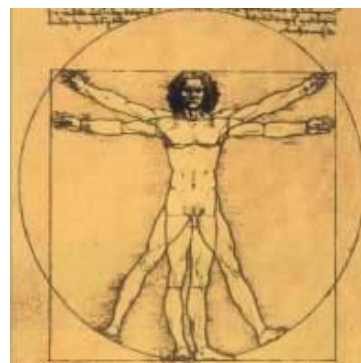




Functional and Biological Properties of the Bee Products: a Review

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Bee Products Science



In this presentation the most important functional and biological properties of honey, pollen, propolis, royal jelly (RJ) and bee venom (BV) as tested in cell and animal studies are reviewed.

COMMON PROPERTIES FOR ALL BEE PRODUCTS

Antimicrobial properties

Antimicrobial action comprises antibacterial, antifungal, antiviral action. These properties of the bee products are important for fighting infections provoked by these microbes. The two most important antimicrobial bee products are honey and propolis.

Honey: This topic has been extensively reviewed by Bogdanov, online article with original references on www.bee-hexagon.net/files/fileE/Honey/7HoneyNutrientFunctional.pdf The **antibacterial** effect of honey, mostly against gram-positive bacteria, both bacteriostatic and bactericidal effects have been reported, against many strains, many of which are pathogenic. Honey glucose oxidase produces the antibacterial agent hydrogen peroxide, while another enzyme, catalase breaks it down. Honey with a high catalase activity have a low antibacterial peroxide activity. Honey has both peroxide and non peroxide antibacterial action, with different non-peroxide antibacterial substances involved: acidic, basic or neutral (Bogdanov, 1997). Antimicrobial effect of honey is thus due to different substances e.g. aromatic acids (Russell et al., 1988) and compounds with different chemical properties (Dustmann, 1978; Dustmann, 1979; Bogdanov, 1997) and depends on the botanical origin of honey (Molan, 1992a; Molan, 1992b; Bogdanov, 1997; Molan, 1997).

The high sugar concentration of honey (Mundo et al., 2004), and also the low honey pH (Yatsunami and Echigo, 1984) is also responsible for the antibacterial activity.

Most experiments report on stop of bacterial growth after a certain time of honey action. The higher the concentration the longer is the period of growth inhibition. Complete inhibition of growth is important for controlling infections (Molan, 1992b).

Honey has also **antiviral** activity *Rubella* (Zeina et al., 1996), *Herpes virus* (Al-Waili, 2004).

Honey has also **fungicide** activity againsts different dermatophytes (Molan, 1997).

Propolis. The antimicrobial activity of propolis is by far the most important biological property of propolis, considering the high number of performed studies. In spite of the big compositional differences of the different propolis types they all have similar antimicrobial activity (Bankova, 2005; Bankova et al., 2007) (Kujumgiev et al., 1999). Poplar propolis gathered by *Apis mellifera caucasica* had a higher antibacterial activity than the one gathered by *Apis mellifera anatolica* and *Apis mellifera carnica* (Silici and Kutluca, 2005).

It has been proposed that propolis is more active against gram-positive pathogens (Grange and Davey, 1990) but many gram negative bacteria are also inhibited. With the increasing of antibiotic resistance in the last years there is a considerable interest of hospitals in propolis as an antibacterial agent. It has been shown that propolis has synergistic effects with antibiotic action against bacteria (Marcucci, 1995; Stepanovic et al., 2003; Speciale et al., 2006; Orsi et al., 2006; Scazzocchio et al., 2006; Onlen et al., 2007).

The antibacterial effect of propolis is bactericidal, (Grange and Davey, 1990; Mirzoeva et al., 1997; Pepeljnjak and Kosalec, 2004), by inhibiting their mobility (Mirzoeva et al., 1997). There are many antibacterial substances in propolis: polyphenols, flavonoids, caffeic acid phenethyl ester, terpenes, essential oils and furfuran lignans.

Poplar propolis gathered by *Apis mellifera caucasica* had higher antifungal activity than the one gathered by *Apis mellifera anatolica* and *Apis mellifera carnica* (Silici et al., 2005). On the other hand the antifungal and mostly antiviral properties of propolis from different botanical and geographical origin was similar (Kujumgiev et al., 1999).

Propolis kills the fungi and also the viruses, while the growth of the latter is also inhibited (Marcucci, 1995).

Pollen: Different flavonoids from *Ranunculus sardous* and *Ulex Europeans* had a marked antibiotic activity against *Pseudomonas aeruginosa*. On the other hand, *Eucalyptus globulus*, mainly rich in quercetin derivatives, did not show any antibacterial activity (Campos et al., 1998). In other study it was found that bee pollen hydrophobic compounds had antibacterial activity against *Viridans streptococci* (Tichy and Novak, 2000). Pollen bread was found to possess an antibacterial activity against *Staphylococcus aureus* and *S. epidermidis* (Baltrusaityte et al., 2007a). Pollen has also significant antifungal activity (Özcan et al., 2003; Ozcan, 2004).

Many studies have shown that RJ has antibacterial activity (LANGLADE et al., 1957; Yatsunami and Echigo, 1985; Fujiwara et al., 1990; Serra Bonvehi and Escola Jorda, 1991a; Abd-Alla et al., 1995; Xiao et al., 1996; Bachanova et al., 2002), fungicide (Sauerwald et al., 1998; Stocker, 2003), antiviral (Derevici and Petrescu, 1960; Stocker, 2003). RJ inhibits both gram-positive and gram-negative bacteria, many of these bacteria pathogenic. The antibacterial activity is due to 10-Hydroxydeceneoic acid (Blum et al., 1959; Serra Bonvehi and Escola Jorda, 1991b) and to different proteins and peptides (Fujiwara et al., 1990; Xiao et al., 1996; Stocker, 2003; Fontana et al., 2004).

BV is reported to have antibacterial activity against bacteria, fungi and viruses (Benton and Mulfinger, 1989; Ludyanskii, 1994; Ammentorp-Schmidt, 1994; Fenard et al., 1999; Yasin et al., 2000; Urtubey, 2005).

Antioxidant properties

The radical theory in human physiology claims that the active free radicals are involved in almost all the cellular degradation process and leads to cell death. An antioxidant is a molecule capable of slowing or preventing the oxidation of other molecules and so to prevent such changes. Oxidative stress is thought to contribute to the development of chronic and degenerative diseases such as cancer, autoimmune disorders, aging, cataract, rheumatoid arthritis, cardiovascular and neurodegenerative diseases (Pham-Huy et al., 2008). Propolis, pollen and honey have the highest antioxidant activities.

Propolis: Propolis is the most powerful antioxidant bee product. This effect is mainly due to the high concentration of phenolics. The antioxidant activity measured of propolis extracts in ORAC units was 4 times higher than that of vitamin E. Expressed in Trolox units it was 40-50 greater than that of forest fruits and 25-50 times greater than that of coffee and red wine (Bendini et al., 2009). Although the phenolic content seems to vary according to the botanical origin, antioxidant effects of many propolis types have been reported. In a study with propolis of different geographical and botanical origin it was found that the antioxidant activity correlates well with its total concentration of polyphenols (Kumazawa et al., 2004).

Pollen: In several studies a close relationship between pollen antioxidant bioactivity and phenolic compounds has been reported (Campos et al., 1994; Campos et al., 2003; Leja et al., 2007; Le Blanca

et al., 2009). It was also found that the bee pollen antioxidant activity is species-specific (Almaraz-Abarca et al., 2004; Leja et al., 2007; Le Blanca et al., 2009; Marghitas et al., 2009) and independent of its geographical origin (Almaraz-Abarca et al., 2004). Bee bread was also found to have a high antioxidant activity (Nagai et al., 2004; Baltrusaityte et al., 2007b). The free radical scavenging ability decreases with the storage of dried bee-pollen at room temperature and can lose about 50 % of the antioxidant power within 1 year (Campos et al., 2003).

Honey: This topic has been extensively reviewed by Bogdanov, online article with original references on www.bee-hexagon.net/files/file/fileE/Honey/7HoneyNutrientFunctional.pdf

Honey has been found to contain significant antioxidant compounds, but in lower concentration: glucose oxidase, catalase, ascorbic acid, flavonoids, phenolic acids, carotenoid derivatives, organic acids, Maillard reaction products, amino acids, proteins. 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 in ORAC units was five times smaller than that of black tea (Gheldof et al., 2003). Generally, the darker the honey, the higher its phenolic content and its antioxidative power. It should be borne in mind that the antioxidant activity depends on the botanical origin of honey and there is a remarkable variation in honey from different sources.

Antioxidant activity of BV and RJ has also been reported (Münstedt and Bogdanov, 2009).

Anti-inflammatory effects

Inflammation (inflammatio, to set on fire) is the complex biological response of vascular tissues to harmful stimuli, such as pathogens, damaged cells, irritants and free radicals. Inflammation in specific parts of the human body is thought to be a major cause of cancer, cardiovascular, arthritis and other chronic diseases. Thus, anti-inflammatory activity is thought to counteract the development of chronic diseases. All bee products have anti-inflammatory properties.

The most powerful anti-inflammatory product is undoubtedly **BV**. Different components such as melittin, mast cell degranulating- peptide, apamine and adolapine are powerful anti-inflammatory molecules (Shkenderov and Ivanov, 1983; Son et al., 2007).

Honey has also considerable anti-inflammatory properties. Anti-inflammatory effects of honey in humans plasma were measured by Al Waili and Boni (Al-Waili and Boni, 2003) after ingestion of 70 g honey. Ingestion of honey had a positive effect in an experimental model of inflammatory bowel disease in rats (Bilsel et al., 2002). The reduction of inflammation could be due to the antibacterial effect of honey or to a direct antiinflammatory effect.

All examined propolis types have anti-inflammatory activity, which is due to different anti-inflammatory compounds such as polyphenols, flavonoids, polyprenylated benzophenones and Artipellin C.

Anti-inflammatory activity has been reported also for pollen (Choi, 2007) and RJ (Kohno et al., 2004).

Immunomodulating and antitumor effects

Malignant tumors are linked with a decrease of the immune function. Stimulation of macrophages results in killing of cancer cells. Thus immunomodulating activity is often linked to anticancer action. All 5 bee products have immunomodulating and antitumor effects

Honey: stimulates T-lymphocytes in cell culture to multiply, and activates neutrophils (Abuharfeil et al., 2008). It was shown in a study with humans that honey causes an increase monocytes, lymphocyte and of eosinophil serum percentages (Al-Waili, 2003). Honey increase proliferation of B- and T-lymphocytes and neutrophils in vitro (Abuharfeil et al., 2008). In another study with rats, feeding of honey caused an increase of lymphocytes in comparison with the sucrose fed controls (Chepulis, 2007).

Honey antitumor effects have been recently reviewed (Orsolich, 2009). A significant antimetastatic effect of honey was demonstrated in methylcholanthrene-induced fibrosarcoma of CBA mouse and in anaplastic colon adenocarcinoma of Y59 rats (Orsolich and Basic, 2004). A pronounced antimetastatic

effect was observed when honey was applied before tumour-cell inoculation (peroral 2 g kg⁻¹ for mice or 1 g kg⁻¹ for rats, once a day for 10 consecutive days) (Orsolice et al., 2003). Jagathan and Mandal demonstrated an anti-proliferative effect in colon cancer cells (Jaganathan and Mandal, 2009).

Honey ingestion by rats induced antitumor and pronounced antimetastatic effects (Gribel and Pashinskii, 1990). In another study the antitumour effect of bee honey against bladder cancer was demonstrated *in vitro* and *in vivo* in mice (Swellam et al., 2003).

Greek honey extracts (thyme, pine and fir honey) had anticancer effects and suggested that honey-enriched diet may prevent cancer related processes in breast, prostate and endometrial cancer cells (Tsiapara et al., 2009). Jungle honey, collected from tree blossom by wild honeybees that live in the tropical forest of Nigeria) enhanced immune functions and has antitumour activity in mice (Fukuda et al., 2009).

Propolis: The immunomodulating activity of propolis has been reviewed by Sforcin. *In vitro* and *in vivo* assays demonstrated the modulatory action of propolis on murine peritoneal macrophages, increasing their microbicidal activity. It has stimulant action on the lytic activity of natural killer cells against tumor cells and on antibody production. Propolis inhibitory effects on lymphoproliferation may be associated to its anti-inflammatory property. In immunological assays, the best results were observed when propolis was administered over a short-term to animals (Sforcin, 2007).

Orsolice reviews the *antitumor and immunostimulating* effect of propolis, considering the inhibition of tumour growth by honeybee propolis and its polyphenolic compounds as well as the mechanisms involved based on *in vivo* and *in vitro* studies. The findings suggest that propolis and their polyphenolic/flavonoid components may serve as a potent adjunct to chemotherapy and radiotherapy in the treatment of cancers. Although many polyphenols have a anti-metastatic activity, caffeic acid phenethyl ester (CAPE) from poplar propolis and Artipillin C from Baccharis propolis have been identified as the most potent antitumor agents (Orsolice, 2009).

The immunoactivating and anticancer activity of **bee venom** has been reviewed (Krylov, 1995; Son et al., 2007). Antitumor effects have been reported on ovary, hepatoma, prostate, bladder, melanoma and renal cancers cells by different mechanisms of action depending on the tumor type.

Royal jelly: Immunoactivating activity of RJ has been reported in different studies (Wu et al., 1991; Watanabe et al., 1996; Sver et al., 1996a; Sver et al., 1996b; Krilov and Sokolskii C., 2000; Vučević et al., 2007) Anti-tumor effects in cell culture and animal experiments upon ingestion or injection of royal jelly have also been reported (Diomedea-Fresa et al., 1966; Tamura et al., 1987; Orsolice et al., 2005; Bincoletto et al., 2005; Nakaya et al., 2007; Orsolice et al., 2007b).

Hepatoprotective activity and anti-radiation activity

The hepatoprotective and the antiradiation activity are often closely correlated.

Hepatoprotective activity of **pollen** in rats was found in rats (Uzbekova et al., 2003), as well as specific decrease of carbaryl (Eraslan et al., 2008a) and pesticide (Eraslan et al., 2008b) induced intoxication of rats.

Propolis: (Banskota et al., 2001) and RJ (Krilov and Sokolskii C., 2000) hepatoprotective effects in animal experiments.

Antiradiation activity was shown in propolis (El-Ghazaly and Khayyal, 1995; Takagi et al., 2005; Orsolice et al., 2007a; Benkovic et al., 2008), in RJ (GIORDANO et al., 1959; PEJCEV et al., 1965; Wagner et al., 1970) and in pollen (Ananeva and Dvoretzkii, 1999).

SPECIFIC BIOLOGICAL EFFECTS OF THE BEE PRODUCTS

RJ has many specific biological effects in animal experiments. The most specific are:

- The bio-stimulating effects: anti-hypoxia, anti-fatigue effects, increases of growth, weight and oxygen consumption (Chauvin, 1968),(Krilov and Sokolskii C., 2000)-
- Its various effects on the central and peripheral nervous system (Krilov and Sokolskii C., 2000; Hattori et al., 2007a; Hattori et al., 2007b; Hattori et al., 2007c).

Besides RJ has anti-hypertensive, hypotensive, vasodilative effects (Shinoda et al., 1978; Kuzina, 1987; Tokunaga et al., 2003; Tokunaga et al., 2004a; Tokunaga et al., 2004b; Maruyama et al., 2005); and anti-atherosclerosis effects (Cho, 1977; Shen et al., 1995; Ragab and Ibrahim, 1999; Krilov and Sokolskii C., 2000).

BV: Most specific is its effect on the central and peripheral nervous system: stimulation of many peripheral chemoreceptors, cholinergic action, blockage of transmission of the vegetative synapse and the polysynaptic neuronal paths, pain-soothing aspirin-like action, influence of brain EEG and behaviour patterns of animals, inhibition of conditioned reflex patterns and increase of brain blood circulation.

Honey: has been shown to have a prebiotic effect, i.e. its ingestion stimulates the growth of healthy specific Bifidus and Lactobacillus bacteria in the gut. Sour-wood, alfalfa, sage and clover honeys have been shown to have prebiotic activity (Shin and Ustunol, 2005). The prebiotic activity of chestnut honey is bigger than that of acacia honey (Lucan et al., 2009). Oligosaccharides from honeydew honey have prebiotic activity (Sanz et al., 2005). Theoretically honeydew honeys, containing more oligosaccharides should have a stronger prebiotic activity than blossom honeys.

Pollen: a probiotic effect of fresh (deep frozen pollen) but not of dry pollen was announced (Percie du Sert, 2009). The probiotic lactic bacteria are not viable in dry pollen. In rat experiments it was shown that pollen ingestion improves food digestibility, stimulates growth and weight gain (Chauvin, 1968; Chauvin, 1987).

The functional properties of bee products

Product	Functional and biological properties of bee products
Honey:	antibacterial, antifungal, antiviral antioxidative, prebiotic, antiinflammatory, anticarcinogenic, prebiotic
Pollen	antibacterial, antifungal, antioxidative, immuno-modulating, radioprotective, hepatoprotective
Royal jelly	antibacterial, antifungal, antiviral antioxidative, biostimulating, immunomodulating, radioprotective, anticarcinogenic
Propolis	antibacterial, antifungal, antiviral antioxidative, antiparasitic, immunomodulating, antiinflammatory, analgesic, hepatoprotective, anticarcinogenic
Bee Venom	antibacterial, antiinflammatory, immunoactivating, immunosuppressive, analgesic, radioprotective, anticarcinogenic

CONCLUSIONS

The reviewed biological and functional properties of the bee products are mostly connected with their most frequent, but also potential use in medicine:

- Honey: for wound management and in gastroenterology
- Propolis in stomatology, odontology and gastroenterology, against skin lesions, otorhinolaryngologic and respiration diseases
- Pollen against prostatitis, hay fever and in gastroenterology
- Royal jelly: in geriatry, pediatriy and heart and blood circulation diseases,
- Bee venom against arthritis and different disease of the nervous system such as multiple sclerosis, Parkinson, Alzheimer and inflammations of the peripheral and central nervous system.

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