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## Honey Bee Products and their Contaminants: An Overview

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### Abstract

Apiculture is the art of rearing honey bees in artificial hives and collecting various bee products especially honey, bee bread, bee venom, bee pollen, propolis and royal jelly. Honey is a very sweet, viscous syrup produced by the honey bees as well as stingless bees which is probably the first natural sweetener ever discovered, widely used as a nutritious food supplement and medicinal agent. The physical, chemical and nutritive properties of honey fluctuate based on the floral preferences, floral sources, climatic conditions and geographic features. Honey exhibits antimicrobial, antioxidant, anti-inflammatory, anticancer, antihyperlipidemic, and cardioprotective properties. Due to these properties, it is used in the treatment of eye disorders, gastrointestinal tract diseases, neurological disorders, fertility disorders and wound healing activity. This review paper mainly focus on the biological and therapeutic effects of bee products and major contaminants in them. Bee products can be easily contaminated from different sources. The contamination can arise from beekeeping practices as well as from the environment. Environmental contaminants includes the heavy metals lead, cadmium and mercury, radioactive isotopes, organic pollutants, pesticides (insecticides, fungicides, herbicides and bactericides), pathogenic bacteria and genetically modified organisms. The contaminants from beekeeping includes acaricides: lipophylic synthetic compounds and non-toxic substances such as organic acids and components of essential oils; and antibiotics used for the control of bee brood diseases. Other substances used in beekeeping play a minor role: para-dichlorobenzene, used for the control of wax moth and chemical repellents. The degree of contamination of honey, pollen, beeswax, propolis and royal jelly by the different contaminants is reviewed.

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### Introduction

Apiculture is the art of rearing honey bees in artificial hives and collecting various bee products especially honey, bee bread, bee venom, bee pollen, propolis and royal jelly (Pasupuleti *et al.*, 2017; Vazhacharickal and Jose, 2016; Vazhacharickal and Jose, 2018). In the recent years honey bee products has gained much attention in traditional and modern medicine (Eteraf-Oskouei and Najafi, 2013; Meo *et al.*, 2017). Due to the health

benefits and pharmacological properties of bee products had created new horizons in the development of nutraceuticals and functional foods (Ruchi, 2017; Kataki *et al.*, 2019). Functional foods promote better physiological or psychological health conditions compared to normal food and leading to healthy condition (Roberfroid, 2000; Roberfroid, 2002).

Honey and other bee products are usually considered as natural, hygienic, healthy and fresh without any

adulterations. Due to agricultural intensifications and human interference, honey and various bee products are polluted by different source of contamination. The honey contamination especially with antibiotics and adulterations are very active news in media which completely vanish the apiculture field and create poor reputation of beekeepers. Therefore it is the need of the hour for the beekeepers to improve the quality of honey by excluding the different contamination sources and possibilities (Bogdanov, 2006).

In this review paper, attempts made to highlight and cover major contaminants of bee products which could be beneficial to apiculture and food researchers as well as beekeepers. Toxicological importance of residues were not discussed much but residue hazards effects mentioned briefly.

### Honey and bee products

Honey is a natural sweetener used widely across the world from ancient times (Kuropatnicki *et al.*, 2018; El-Soud and Helmy, 2012; Saranraj *et al.*, 2016). It is widely used for various applications including clinical and contains 200 distinct chemical compounds (Aparna and Rajalakshmi, 1999; Meo *et al.*, 2017).

Honey is viscous in nature and contains fructose and glucose (80-85%), water (15-17%), ash (0.2%), proteins and amino acids (0.1-0.4%) with trace amounts of enzymes, vitamins and phenolic compounds (Rao *et al.*, 2016; Balasooriya *et al.*, 2017). Honey composition varies depending on the plant sources from which bees collect nectar (Crane and Visscher, 2009; Ball, 2007; Kaškonienė and Venskutonis, 2010). In general all honey across the world contain similar types of phenolics acids, flavonoids, antioxidants with synergic action of components (Bogdanov *et al.*, 2008; Baltrušaitytė *et al.*, 2007). The physical and chemical properties of honey fluctuate based on the floral preferences and sources (Crane and Visscher, 2009; Ball, 2007; Kaškonienė and Venskutonis, 2010). In addition to floral sources, climatic conditions and geographic features influence physical, chemical and nutritive properties of honey (Kaškonienė and Venskutonis, 2010; Mohammed, 2020; Machado De-Melo *et al.*, 2018).

Honey is has been traditionally used by Egyptians, Greeks, Romans and Chinese to heal wounds, gastric ulcers, cough, sore throat, earaches and eye infections (Pasupuleti *et al.*, 2017; Molan, 1999; El-Soud and Helmy, 2012; Banerjee *et al.*, 2003). Honey is

considered as a functional food to provide energy and nourishment of the vital organs (Bogdanov, 2012; Luchese *et al.*, 2017; Pasupuleti *et al.*, 2017; Kostić *et al.*, 2020). The components like glucose, fructose, flavonoid, polyphenols and organic acids play a major role in quality and health benefits of honey (Cianciosi *et al.*, 2018; Abeshu and Geleta, 2016; da Silva *et al.*, 2016).

Honey is recognised world-wide as a medicine, energy source and well known for biological, physiological and pharmacological activities (Saranraj *et al.*, 2016; Mijanur Rahman *et al.*, 2014; Zulkhairi Amin, 2018).

Propolis is the bee glue refers to the resinous materials collected by bees from different plants (Bankova *et al.*, 2000; Burdock, 1998; Bankova *et al.*, 2014).

Being derived from Greek, “pro” means defence and “polis” means city or community (Castaldo and Capasso, 2002; Salatino *et al.*, 2005). Propolis is used as a sealant and construction material in the bee hive (Kasote, 2017; Fokt *et al.*, 2010; Wagh, 2013). It also maintain the internal temperature, protect form weathering and prevent invasion of the intruders (Kapare and Sathiyarayanan, 2020; Simone-Finstrom and Spivak, 2010). On heating propolis becomes soft and sticky, possess a pleasant smell and maintain an aseptic environment in the bee hive (Pasupuleti *et al.*, 2017; Chon *et al.*, 2020; Rahim, 2020). Propolis has antiseptic, anti-inflammatory, antioxidant, antibacterial, antimycotic, antifungal, antiulcer, anticancer, and immunomodulatory properties (Pasupuleti *et al.*, 2017; Martinotti and Ranzato, 2015; Cornara *et al.*, 2017; Anjum *et al.*, 2019; Rivero-Cruz *et al.*, 2020).

Royal jelly is the hypopharyngeal and mandibular secretion of the worker bee which is white in colour and viscous in nature (Buttstedt *et al.*, 2018; Chen and Chen, 1995; Ramanathan *et al.*, 2018; Miguel and El-Guendouz, 2017). It is a superfood consumed by the queen bee. On light doses, it is also fed to honey bee larvae in the first 2-3 days of maturation (Buttstedt *et al.*, 2018). Royal jelly is used by the queen throughout her life cycle. Royal jelly is responsible for the longevity of the queen bee and royalactin is the main component (Kunugi and Mohammed Ali, 2019; Kamakura, 2011; Detienne *et al.*, 2014). Royal jelly is widely used as a dietary supplement due to its antibacterial, antitumor, antiallergy, anti-inflammatory, and immunomodulatory effect (Viuda-Martos *et al.*, 2008; Ramadan and Al-Ghamdi, 2012; Pavel *et al.*, 2011; Khazaei *et al.*, 2018).

## Chemical constituents of honey, propolis and royal jelly

Honey is a supersaturated sugar solution comprising carbohydrates (82.4%), fructose (38.5%), glucose (31%), other sugars (12.9%), water (17.1%) and protein (0.5%) (Rossi and Marrazzo, 2021; Aurongzeb and Azim, 2011; Tappi *et al.*, 2019; Pavlova *et al.*, 2018). In addition, honey comprises organic acids, multi-minerals, amino acids, vitamins, phenols, and many other minor compounds especially phenolic acid, flavonoid and alpha tocopherol (Pashte *et al.*, 2020; Kumar *et al.*, 2010; Cianciosi *et al.*, 2018). Phenolic acids, flavonoids, ascorbic acid, proteins, carotenoids, enzymes like glucose oxidase and catalase enhances the health benefit of honey (Viuda-Martos *et al.*, 2008; Khalil *et al.*, 2010).

Propolis is the third important bee product after honey and wax which is mainly composed of resins (50%), wax (30%), essential oils (10%), pollen (5%) and other organic compounds (5%) (Kasote, 2017; Viuda-Martos *et al.*, 2008; Fokt *et al.*, 2010). The organic components in the propolis includes phenolic compounds, esters, flavonoids, terpenes, beta-steroids, aromatic aldehydes and alcohols (Kapare and Sathiyarayanan, 2020; Kayaoglu *et al.*, 2011). Propolis has diverse flavonoids especially pinocembrin, acacetin, chrysin, rutin, luteolin, kaempferol, apigenin, myricetin, catechin, naringenin, galangin, and quercetin; two phenolic acids, caffeic acid and cinnamic acid (Dezmirean *et al.*, 2021; Benhanifia and Mohamed, 2015). It is also a source of vitamins especially vitamins B1, B2, B6, C, and E and useful minerals such as magnesium (Mg), calcium (Ca), potassium (K), sodium (Na), copper (Cu), zinc (Zn), manganese (Mn), and iron (Fe) (Ahangari *et al.*, 2018; Sun *et al.*, 2000). In addition to this, enzymes like succinic dehydrogenase, glucose-6-phosphatase, adenosinetriphosphatase, and acid phosphatase are also present in propolis (Yousef *et al.*, 2010; Pasupuleti *et al.*, 2017).

The royal jelly has quite unique composition when compared to honey and propolis. Royal jelly consists of water (50%–60%), proteins (18%), carbohydrates (15%), lipids (3%–6%), mineral salts (1.5%), and vitamins (Kunugi and Mohammed Ali, 2019; Kamakura, 2011; Detienne *et al.*, 2014). With around 185 organic compounds, royalactin is the most important protein present in royal jelly (Kunugi and Mohammed Ali, 2019; Kamakura, 2011). Fatty acid, proteins, adenosine monophosphate (AMP) N1 oxide, adenosine, acetylcholine, polyphenols, and hormones such as

testosterone, progesterone, prolactin, estradiol and 10-hydroxy-2-decenoic acid (HAD) are the useful bioactive present in royal jelly (Pasupuleti *et al.*, 2017).

## Bioactive compounds in honey, propolis and royal jelly

Naturally occurring compounds especially polyphenols and vitamins as part of food chains are considered as bioactive (Sagar *et al.*, 2018; Biesalski *et al.*, 2009). Phenolic compounds are highly bioactive defined as organic compounds with an aromatic ring that is chemically bonded to one or additional hydrogenated substituents in the presence of corresponding functional derivatives (Delgado *et al.*, 2019; Pasupuleti *et al.*, 2017). Flavonoids are the major phenolic compounds present in honey, propolis and royal jelly (Viuda-Martos *et al.*, 2008). Phenolic compounds are responsible for the antioxidant, antimicrobial, antiviral, anti-inflammatory, antifungal, wound healing, and cardioprotective activities of bee products.

Major biological properties of honey includes antioxidant, anti-inflammatory, anti-bacterial, antiviral, anti-ulcer, antihyperlipidemic, antidiabetic and anticancer properties (Viuda-Martos *et al.*, 2008; Juszczak *et al.*, 2016; Buratti *et al.*, 2007). Honey lowers cardiovascular risks and shows ameliorative effect on plasma glucose, plasma insulin, cholesterol, triglycerides, blood lipids, C-reactive proteins and homocysteine (Al-Waili *et al.*, 2013; Bobiş *et al.*, 2018). Honey is proven to improve memory and learning process including enhanced morphology of memory-related brain areas, increased levels of brain-derived neurotrophic factor, reduced brain oxidative stress, increased acetylcholine concentration (Pasupuleti *et al.*, 2017; Othman *et al.*, 2015). The aim of this review is to summarize information on the traditional and clinical uses of honey to augment various biological activities and to treat diseases.

## Chemical constituents of honey

Around 200 compounds are present in honey which mainly comprises of water, sugars, vitamins, enzymes, amino acids and minerals (da Silva *et al.*, 2016; Eteraf-Oskouei and Najafi, 2013; Santos-Buelga and González-Paramás, 2017; Ahmad *et al.*, 2017). Sugars dominate 95-99% of honey's dry matter with fructose as the most prevalent (32-38% of total sugar) (Santos-Buelga and González-Paramás, 2017; Ahmad *et al.*, 2017). In addition to fructose and glucose other disaccharides and

oligosaccharides including maltose, maltotriose and panose (da Silva *et al.*, 2016; Eteraf-Oskouei and Najafi, 2013). In addition to this various organic acids, minerals and trace elements such as calcium, potassium, sodium, magnesium, phosphorous, sulphur, iron, zinc, copper and manganese (da Silva *et al.*, 2016; Eteraf-Oskouei and Najafi, 2013; Santos-Buelga and González-Paramás, 2017; Ahmad *et al.*, 2017).

Various vitamins, including ascorbic acid (Vitamin C), thiamine (Vitamin B1), pantothenic acid (Vitamin B5), riboflavin (Vitamin B2), nicotinic acid (Vitamin B3), pyridoxine (Vitamin B6), biotin (Vitamin B8), folic acid (Vitamin B9) and cyanocobalamin (Vitamin B12), are present. Enzymes and proteins are minor constituents, with the enzymes playing a vital role in various activities, including antimicrobial activity and facilitating calcium absorption (Ariefdjohan *et al.*, 2008). The antioxidant capacity of honey depends on total phenolic compounds and the presence of flavonoids which has an important role in reducing oxidative stress. A variety of flavonoids and terpenoids have been reported in various honeys. In manuka honey, pinocembrin (1), chrysin (2), pinobanksin (3), 8-methoxykaempferol (4), luteolin (5), isorhamnetin (6), galangin (7), kaempferol, sakuranetin (8), quercetin and magniferolic acid (9) and 3 $\beta$ -hydroxy-24-methylenecycloartan-26-oic acid (10) have been identified (Ahmed and Othman, 2013). The various physicochemical properties and therapeutic efficacies of honey and bee products are depicted in Fig. 1 and Fig. 2.

## Health benefits of honey

### Wound management

Honey is used as an effective agent to treat wounds, insect bites, burns, skin disorders, sores, and boils. The wound healing capacity is attributed as a promoter of wound repair and antimicrobial activity. Honey promotes the activation of dormant plasminogen in the wound matrix leading to the expression of proteolytic enzyme plasmin resulting in blood clot retraction and fibrin destructions. Plasmin breaks fibrin clots with attached dead tissues in the wound bed (Pasupuleti *et al.*, 2017).

The usage of honey in wound care is superior to conventional and modern wound care dressings. Honey stimulates wound healing properties of infected wounds that do not respond to antiseptics or antibiotics. Honey also aids autolytic debridement and accelerates the growth of healthy granulated wound bed (Pasupuleti *et al.*, 2017).

The application of honey in the case of Malodorous infections (*Bacteroides* spp. and *Peptostreptococcus* spp.) replaces the release of malodorous compounds (ammonia, amines, and sulfur) by lactic acids. The therapeutic effects observed after honey application include fast healing, wound cleansing, clearance of infection, tissue regeneration, minimized inflammation, and increased comfort during dressing due to lower extent of tissue adhesion (Pasupuleti *et al.*, 2017).

### Paediatric care

Honey enhances the epithelialization of skin surfaces and controls the skin damage near stomas. Honey is effective in eczema, psoriasis and pediatric dermatitis caused by the usage of napkins and diapers. Honey mixed with bee wax and olive oil significantly improves the psoriasis or atopic dermatitis condition. Various nitric oxide metabolites present in the honey reduce the incidence of skin infection in psoriasis.

### Diabetic Foot Ulcer (DFU)

Honey is considered as a low cost and effective therapy for the treatment of DFU which is often complicated by microbial infections. Honey is used in wound management and is effective among patients with locally infected wounds, DFU and Charcot foot ulcerations.

### Gastrointestinal (GI) disorder

Consumption of honey facilitates the absorption of molecules especially sugars and starch and aids in the digestive process due to minerals, phytochemicals and flavonoids. Honey has bactericidal properties against pathogenic bacteria and enteropathogens, including *Salmonella* spp., *Escherichia coli*, *Shigella* spp., and many other Gram negative species. The gastrointestinal tract (GIT) contains many important beneficial microbes like Bifidobacteria and consumption of probiotics increases the availability in the GIT. Honey is a good probiotic and dietary supplement that hastens the growth of Lactobacillus, Bifidobacteria and is beneficial for the intestinal microbiota.

### Oral health

Many oral diseases especially periodontal disease, stomatitis, and halitosis can be treated with honey. Honey is also popular for the prevention of dental plaque, gingivitis, mouth ulcers, and periodontitis. Honey stimulates the growth of granulation tissue leading

to the repair of damaged tissues. Honey has good antimicrobial activity against *Porphyromonas gingivalis* a Gram-negative bacteria that causes periodontitis. Honey is very effective against mouth ulcers and stomatitis conditions. Due to the presence of methylglyoxal component, the consumption of honey ameliorates halitosis (Pasupuleti *et al.*, 2017).

### Pharyngitis and coughs

Pharyngitis, commonly known as sore throat is an acute infection in the oropharynx and nasopharynx induced by *Streptococcus* spp. Honey is very effective in curing sore throat due to its anti-inflammatory, antiviral, and antifungal properties. Honey makes a smooth coat in the inner lining of the throat and destroys harmful microbes and soothing the throat. Honey is superior to dextromethorphan and diphenhydramine for the treatment of cough induced upper respiratory infections. Due to antioxidant and antimicrobial properties, honey minimize persistent cough, pneumonia and ameliorated sleep.

### Gastroesophageal Reflux disease

Gastroesophageal reflux disease (GERD) is a mucosal infection caused by contents of abnormal gastric reflux into the oesophagus and lungs. Symptoms of GERD include heartburn, inflammation, and acid regurgitation. Intake of honey make a coating on the oesophagus and stomach lining and prevent the upward flow of food and gastric juice. Honey stimulate the regrowth of tissues on the sphincter and reduce acid reflux (Pasupuleti *et al.*, 2017).

### Dyspepsia, Gastritis and peptic ulcer

Dyspepsia affect mainly stomach and small intestine and causes epigastric pain, heartburn, bloating and nausea. The preliminary symptom of peptic ulcer is dyspepsia which eventually cause cancer. Gastritis is the irritation and inflammation of the lining of the stomach wall. Honey is a very effective inhibitor for gastritis and the peptic ulcer causing agent, *Helicobacter pylori* (*H. pylori*), and decreased the secretion of gastric acid.

The high sugar content and low pH in honey are the results of glucose oxidative conversion to gluconic acid by glucose oxidase and eventually releases hydrogen peroxide. Glucose oxidase also acts on fibroblasts and epithelial cell activators required for the healing of ulcers caused by *H. pylori*.

### Gastroenteritis

Gastroenteritis is known as stomach or gastric flu and leads to the inflammation of the digestive tract. The symptoms of gastroenteritis include dehydration, watery diarrhoea, bloating, abdominal cramps, and nausea. Replacing the glucose in standard electrolyte oral rehydration solution (ORS) with honey reduced the recovery time of patients with gastroenteritis because the high sugar content in honey boosts electrolyte and water reabsorption in the gut.

### Constipation and diarrhoea

Chronic constipation is characterized by intolerable defecation, difficult stool passage characterized by straining, hard or lumpy stool and prolonged time to pass stool. Diarrhoea is defined as a high frequency of bowel movements with watery stool. Honey has minimized the pathogenesis and duration of viral diarrhoea compared to conventional antiviral therapy. Usage of honey on empty stomach prevents diarrhoea, constipation and stomach discomfort in the case of inflammatory bowel syndrome (IBS) (Pasupuleti *et al.*, 2017).

### Liver and pancreatic diseases

Honey balances liver systems and neutralize toxins and prevents oxidative damage. The antioxidant and hepatoprotective activity of honey minimized liver damage. Honey reduce the effect of fatty liver as it provide adequate glycogen storage in liver cells. Insufficient glycogen storage in the liver releases stress hormones that impair glucose metabolism over time. Impaired glucose metabolism leads to insulin resistance and is the main factor of fatty liver disease.

### Metabolic and cardiovascular health

Honey act as cardioprotective and therapeutic impacts against epinephrine-induced cardiac disorders and vasomotor dysfunctions. Honey exhibits cardioprotective effects such as vasodilation, balancing vascular homeostasis, and improvements in lipid profile. Flavonoids in honey improves coronary vasodilation, decreases the ability of platelets to form clots, prevents oxidation of low-density lipoproteins (LDL), increases high-density lipoproteins (HDL), and improves endothelial functions.

Honey has a good metabolic response against metabolic syndrome characterized by hyperglycemia, hypertension,

abdominal obesity, dyslipidemia, and intensified adaptability towards diabetes, kidney, and heart diseases. Polyphenols in honey reduce atherosclerotic lesions, honey decreased total cholesterol (TC) and noticeably prevented the rise in plasmaglucoase levels. Nitric oxide (NO) is a metabolite present in honey that also has cardioprotective functions.

## Cancer and oncogenesis

### Breast cancer

Imbalance in estrogen signalling pathways and propagating levels of estrogens have important roles in breast cancer growth and propagation. Targeting the estrogen receptor (ER) signalling pathway is the best way to prevent breast cancer. Honey is very efficient in modulating ER signalling pathway and has biphasic activity in MCF-7 cells. Cytotoxic activities of honey in human breast cancer cells were demonstrated by elevated secretion of lactate dehydrogenase (LDH). Honey shows highly specific and selective cytotoxic effects towards breast cancer cell lines and has a good potential as a chemotherapeutic agent.

### Liver cancer

The most common type of liver cancer is hepatocellular carcinoma (HCC). Treatment of HepG2 cells with honey minimized the amount of nitric oxide (NO) levels in the cells and decreased the HepG2 cell number greatly. Reduced reactive oxygen species (ROS) and enhanced antioxidant efficacy inhibit cancerous cell proliferation and lowered the number of HepG2 cells.

### Colorectal cancer

Most colorectal cancers begin as a polyp, which generally starts on the inner lining of the colon or rectum and grows towards the center. Honey inhibited the proliferation of colon cancer cells. Honey shows significant antiproliferative action against colon cancer cells due to the high phenolic content.

The molecular mechanisms resulting in the antiproliferative and anticancer effects of honey include cell cycle arrest, activation of mitochondrial pathway, induction of mitochondrial outer membrane permeabilization, induction of a poptosis, modulation of oxidative stress, reduction of inflammation, modulation of insulin signalling, and inhibition of angiogenesis in cancer cell.

## Health benefits of propolis

### Gastrointestinal disorder

Parasitic infection of the GI tract create abdominal pain, diarrhoea, bloating and nausea. Propolis has been reported to have several biological efficacies including anticancer, antioxidant, and anti-inflammatory activities. Propolis is also used clinically to treat viral infections. Propolis inhibits growth and adherence of the trophozoites, promote the detachment of parasitic worms and effective against giardiasis. Propolis also shows antihistaminergic, anti-inflammatory, antacid, and anti-*H. pylori* activities that can be used to treat gastric ulceration.

### Gynecological care

Widespread causes of indicative vaginitis are bacterial vaginosis (BV) and vulvovaginal candidiasis (VVC). The depletion of *Lactobacillus spp.* In the vagina is a distinguished feature of vaginal infections with yeast like fungi and elevated vaginal pH. Diabetes patients are more prone to having vaginal infections caused by *Candida albicans*. Application of 5% aqueous propolis solution resulted in an improvement in vaginal well-being. Propolis has antibiotic, antimycotic and anaesthetic action. Propolis may be used for Recurrent Vulvovaginal Candidiasis (RVVC) and alternative to antibiotics in patients involved with other medications and allergies. Propolis extract solution (PES) also show low toxicity in human cells and can be an alternative treatment for chronic vaginitis. Due to the antifungal properties PES can be used as an antibiofilm material for RVVC to counteract biofilm growth of *C. albicans* and antifungal drug resistance.

### Oral health

The excessive bacterial growth in oral cavity lead to several oral diseases. Propolis restrict bacterial-plaque development periodontitis causing pathogens. Propolis solutions exert a selectively lower cytotoxic action on human gum fibroblasts mouthwash containing propolis have shown effectiveness in healing surgical wounds.

Propolis solution is used to disinfect toothbrushes. A 3% ethanolic extract of propolis toothpaste gel showed good potency against gingivitis caused by dental plague. Propolis extracts have also helped cure halitosis; a condition of unpleasant bad breath due to poor oral hygiene. Propolis toothpaste or mouthwash is used for

their ability to reduce growth of bacterial plaque and pathogenic microflora that causes gingivitis and periodontitis.

### **Oncological treatment**

The propolis has good potential towards human breast cancer treatment due to its induction of apoptosis on breast cancer cells and proliferation. Due to the selective toxicity to only tumour cells, it exhibits low or no toxicity towards normal cells. Galangin, a common flavonoid in propolis induce apoptosis and inhibit melanoma cells. Propolis exert a selective cytotoxic action on human lung cancer cells by inducing endoplasmic reticulum stress, apoptosis, and caspase activity and by reducing the mitochondrial membrane potential.

### **Dermatological care**

Due to its anti-allergy, anti-inflammation, antimicrobial properties, and promotive action on collagen synthesis, propolis is widely used in skin care products especially creams and ointments. Propolis notably decreased free radical activity in healing the wound beds which supported the repair process and high efficacy in the treatment of acne vulgaris. Propolis also shows positive collagen metabolism in the wound during the healing process by increasing the collagen content of tissues. Propolis is used as an alternative therapy for wound healing to promote wound closure, under human diabetic foot ulcer (DFU).

### **Health benefits of royal jelly**

Royal jelly is one of the important honey bee products that have a good potential to treat various human diseases. The royal jelly possess antioxidant, antitumor, antiaging, neurotropic, and anti-inflammatory properties.

### **Reproductive health**

Royal jelly is effective in reducing premenstrual syndrome, treatment of urinary problems and promotion of life quality in postmenopausal women. Royal jelly has protective effects against Oxymetholone-induced reproductive toxin (OXM), which is an active steroid derived from testosterone and induce spermatogenesis. Royal jelly has been traditionally used to treat menopause symptoms by rebalancing the hormonal concentration in the blood, decreasing follicle-stimulating hormones (FSH).

### **Neurodegenerative and ageing diseases**

Royal jelly stimulates physical and mental functions for the elderly and increases their appetite and weight. Royal jelly exerted neuroprotective effects in Alzheimer's disease. Royal jelly contains longevity promoting factors and extends the lifespan and improve mental health.

### **Wound healing**

Royal jelly enhances wound-healing activity, under the effect of royal jelly, human fibroblasts were able to migrate and increase levels of sphingolipids by decreasing the secretion and formation of collagen. It shortens the curing period of desquamated skin lesions. Royal jelly exhibited protective action on human skin against ultraviolet B induced photoaging by promoting collagen production. Royal jelly dressing is also an effective way of treating diabetic foot ulcers due to its vasodilation effects around the affected wound and prevents infections.

### **Contaminants from environmental sources**

Contaminants can reach the raw materials of bee products especially nectar, honeydew, pollen, plant exudates by air, water, plants and soil and then be transported into the bee hive by the bees. Various contamination levels and causes will be discussed, without exploring the details of the contamination paths. The sources for contamination can be roughly divided into environmental and apicultural ones (Fig. 5).

### **Heavy metals**

Air and soil especially in urban areas contain heavy metals, mainly from industry and traffic which can contaminate the bee colony and its products. Lead (Pb) and cadmium (Cd) are of great significance due to their bioaccumulation, high toxicity in humans and animals. Lead is a major contaminant in polluted air and originating mainly from motor traffic can contaminate directly nectar and honeydew. Generally, Pb is not transported by plants while Cd originating from various metal industries and incinerators, is transported from the soil to plants and contaminate nectar and honeydew. The MRL (Maximum Residue Limit) values for Pb and Cd values in honey is 0.1 mg/kg for Cd and 1 mg/kg, proposed for the EU (EC, 2000a). Pb contamination has reduced, due to the advanced technologies used by the automobile manufacturers world-wide. A decrease of Pb in honey concentration was documented in Switzerland

in 1984 and 2002 with an average Pb concentration 0.2 mg/kg and 0.04 mg/kg respectively (Bogdanov *et al.*, 1986; Kantonales Laboratorium Basel-Stadt, 2002). Many global studies showed that lead contamination of honey in polluted and non-polluted areas is not significantly different, due to the considerable natural variation of the data and “filtering” by the bees (Höffel, 1982; Altmann, 1983; Bogdanov *et al.*, 1986; Jones, 1987; Conti *et al.*, 1998; Yazgan *et al.*, 2002; (Leita *et al.*, 1996; Fakhim-Zadeh and Lodenius, 2000; Porrini *et al.*, 2002).

Studies on heavy metal contamination of pollen, beeswax and propolis vary across a broad range (Altmann, 1983; Cesco *et al.*, 1994; MAFF, 1995; Leita *et al.*, 1996; Conti and Botre, 2001; Madras-Majewska and Jasinski, 2003).

Honey bees species vary widely with their foraging pattern and flight ranges usually limits a radius of up to 3 km. The honey bee products can serve as bio-indicators for the heavy metal contamination especially Pb in their flight ranges (Höffel, 1982; Altmann, 1983; Bromenshenk *et al.*, 1985; Bogdanov *et al.*, 1986; Jones, 1987; Balestra *et al.*, 1992; Cesco *et al.*, 1994; Conti and Botre, 2001; Yazgan *et al.*, 2002; Porrini *et al.*, 2002; Devillers *et al.*, 2002b; Lebedev and Murashova, 2004).

Heavy metals like mercury (Hg) and nickel (Ni) were not seriously studied in the case of honey with no specific global MRL levels. The MRL levels in Switzerland for Hg vary in different food between 0.01 mg/kg to 0.5 mg/kg for fruit juices and fish. The Swiss MRL for Ni varies between 0.1 mg/kg (beer) to 0.2 mg/kg (edible fat). In Slovakia honey, Hg levels ranged from 0.050 to 0.212 mg/kg and from 0.001 to 0.003 mg/kg, respectively (Toporèak *et al.*, 1992). The Hg levels in different bee products were reported: propolis: 0.001–0.07 mg/kg, beeswax: 0.0001–0.06 mg/kg and honey: 0.00001–0.006 mg/kg (Madras-Majewska *et al.*, 2002). Bee products may not be suitable to serve as indicators for the measurement of Pb and Cd pollution because of considerable natural variation while bees themselves seem to be serve this purpose better (Porrini *et al.*, 2002).

### Radioactivity

The main radioactive isotopes found in honey are <sup>40</sup>K and <sup>137</sup>Cs, the first being of natural origin, the latter originating from the Chernobyl atomic power station accident in 1986. The <sup>40</sup>K radioactivity in different types of honey from Poland varied from 39 to 123 Bq/kg (Borawska *et al.*, 2000). <sup>137</sup>Cs, with a half-life of thirty

years, is the most studied isotope, with a maximum limit of 370 Bq/kg for milk and 600 Bq/kg for all other products was set in the EU (EC, 1990). An average concentration of 4430 Bq/kg radioactive caesium in honey harvested in the Ukraine between 1986 and 1989 (Alexenitser and Bodnarchuk, 1999). The radioactive contamination, measured in other countries was much smaller, due to the distance from Chernobyl.

In Germany honey initially had relatively high contamination, averaging 51 Bq/kg, later level dropped by about 50% one year later and remained at an average level of about 10 Bq/kg in subsequent years (Horn and Vorwohl, 1986, 1987, 1988). German heather honey was highly contaminated, with an average of 532 Bq/kg in 1987 (Dustmann and von der Ohe, 1988) which may be due to different affinity of <sup>137</sup>Cs to the plants as well as isotope concentrations in the soil (Kubik *et al.*, 1991). The radioactive levels of honey samples from Croatia, Slovenia, Austria and Germany varied widely with a maximum of 425 Bq/kg (Barišic *et al.*, 2002).

The <sup>137</sup>Cs radioactivity of other bee products harvested in Ukraine between 1986 and 1989: pollen: 11070 Bq/kg, propolis: 34310 Bq/kg. In France and Italy, there is wide difference in the levels of radioactivity in pollen and propolis. Pollen and propolis are considered to be better indicators for radioactive contamination than honey (Alexenitser and Bodnarchuk, 1999). Studies also focus on the radioactivity due to different radioisotopes especially <sup>226</sup>Ra, <sup>214</sup>Pb, <sup>214</sup>Bi and <sup>40</sup>K measured across Japan, China, Hungary, Italy, and Australia (Handa *et al.*, 1997). Radioactivity is not currently a problem for honey and for other bee products unless in the case of a thermo-nuclear incidents/accidents.

### Organic contaminants

One of the major organic contaminants present in the environment are PCB's, (polychlorinated biphenyls) which originate from motor oil, coolants and lubricants, produced before 1980. These substances are still persistent in the environment and can contaminate plants and thus, the bees and their products. The quantities, found in honey are low and safe, while those found in wax are higher (Estep *et al.*, 1977; Gayger and Dustmann, 1985; Anderson and Wojtas, 1986; Morse *et al.*, 1987; Jan and Cerne, 1993). Small residues of polyaromatic compounds originating from oil were found in honeys produced near an oil factory in Germany (Horn and Martius, 1997).



## Pesticide used in agriculture

### Insecticides

The most common insecticides that have been examined in European honeys include:

Organochlorines (OC) such as lindane and its isomers, hexachlorocyclohexane (HCH), aldrin, dieldrin, endrin, DDT isomers, heptachlor, heptachlor epoxide, methoxychlor, endosulfan. Many OC are no longer used in agriculture, but are still present in the environment.

Organophosphorus pesticides (OP) like dialiphos, trichlorophon, and dichlorvos.

Carbamates: pesticides containing an amino group: R1-NH-CO-OR2.

Around 20% honey samples analysed in France between 1986 and 1996 contain pesticide residues (Fléché *et al.*, 1997). Honey samples from Spain and Portugal, showed residues of 42 different pesticides (OC, OP and carbamates) with majority of them belonging to organochlorines (Blasco *et al.*, 2003). Among them, gamma-HCH was found in 50% of the samples, followed by HCB (32%) and the other isomers of HCH (alpha-HCH and beta-HCH) in 28 and 26% of the samples, respectively. The low level pesticide content (below 0.5 mg/kg) in honey makes a minimal contribution to the acceptable daily intake (ADI) of pesticides.

Indian market honey samples were examined for residues of organochlorine (OC), synthetic pyrethroids (SP), organophosphates (OP) and carbamate insecticides (Anju *et al.*, 1997). Different OC pesticides varied between 0.01 and 6 mg/kg, while the residues of OP and carbamates varied between 0.1 and 9 mg/kg.

In Italy, OC pesticide residues were ranged from traces to 0.15 mg/kg (Roggi *et al.*, 1990). In Jordan, low levels of OC residues (lindane,  $\alpha$  HCH,  $\beta$  HCH and heptachlor) with values between 0.004 and 0.21 mg/kg (Al-Rifai and Akeel, 1997).

Imidacloprid is a systemic insecticide known under the name of Gaucho; found in honey, nectar and pollen. Very small residues (Schmuck *et al.*, 2001; Bonmatin *et al.*, 2003; Maus *et al.*, 2003; Rogers and Kemp, 2003; Schöning and Schmuck, 2003; Stadler *et al.*, 2003; Faucon *et al.*, 2004). There are no specific MRL values for bee products and the Swiss tolerance values for

imidacloprid are 0.01 mg/kg in maize and 0.05 mg/kg for fruits. Thus, the residues, found in honey and pollen are not considered to be a problem for human health. On the other hand, the effect of imidacloprid on bee health is highly controversial (Maus *et al.*, 2003; Faucon *et al.*, 2004). Residues from microencapsulated insecticides as methylparathion, which is toxic to bees, were found in US studies on honey and pollen (Atkins and Kellum, 1984; Russell *et al.*, 1998).

### Other pesticides, herbicides, bactericides, fungicides

Honey seems to be especially susceptible to residues from fungicides and pesticides used against various pests and diseases in crops. Levels ranging between traces and 0.11 mg/kg of some systemic fungicides have been found in honey (Rexilius, 1986; Kubik *et al.*, 1999). The fungicides have different level of persistence's in various bee products depending on the nature and active life span of the ingredients.

Residues in pollen were higher than in honey, especially herbicides, seem to contaminate mostly bees and pollen (Fléché *et al.*, 1997; Kubik *et al.*, 1999; Bogdanov, 2006).

Various antibiotics are also used as plant protections agents against bacterial plant pests. The fire blight on fruit trees is caused by the bacteria *Erwinia amylovora* which is controlled by the antibiotic streptomycin.

Many studies in Germany and European union showed that honey was often contaminated with streptomycin residues (Brasse, 2001) and banned in most countries of the EU due to contamination risk.

The herbicide asulam breakdown product sulphanilamide were found (0.005-0.70 mg/kg), together with asulam residues themselves (0.005-0.23 mg/kg) in Swiss honey samples (Kaufmann and Kaenzig, 2004; Bogdanov and Edder, 2004).

Bees are widely used as biological monitors for pesticide contamination of geographic regions rather than bee products (Celli *et al.*, 1996). The relatively low concentration of pesticides in honey seems to be due to a filtering effect of bees, so that the final concentration in honey was much lower, with dilution factors of about 1000 (Schur and Wallner, 1998; Schur and Wallner, 2000). Also, many of the modern pesticides used today are unstable and disintegrate quickly after use. Generally, there are no MRL's for pesticides in honey. In the EU an action level of 0.01 mg/kg.

Considering the fact that pesticide residues found in honey are comparably low (Kuchen *et al.*, 1998) and relatively low daily consumption, it can be concluded, that pesticide residues in honey are safe from toxicological point of view. To avoid residues pesticides should be used outside the bloom period or at least, not during the foraging time of bees or keeping the bee hives away from spraying areas.

### Pathogenic bacteria

The low water activity in honey, prevents the multiplication and growth of bacteria (Snowdon and Cliver, 1996; Snowdon, 1999). Presence of *Clostridium botulinum* in honey makes a severe health concern as the spores survive in honey. In some rare cases, infant botulism has been explained by ingestion of honey. From the other bee products only pollen might pose problems for bacterial and fungal contaminations.

### Genetically modified plants

Genetically modified organisms (GMO), such as rape and maize, are grown in some countries and might pose problems for bees and beekeepers (Williams, 2002).

In some countries such as USA and Canada genetically modified plants are commonly grown and accepted by the public, while in the European Union there is a wide opposition against the consumption of GMO – containing food.

There are very sensitive methods especially the of polymerase chain reaction (PCR) for the determination of genetically modified plants and pollen (Ramsay *et al.*, 1999). Bee pollen can be thus significantly contaminated, while honey, which contains less than 0.1% of pollen, will require no specific appellations.

**Table.1** Types of honey’s contamination. Al-Waili *et al.*, 2012

<b>A) The environmental contaminants</b>
1) Heavy metals such as lead, cadmium, and mercury
2) Radioactive isotopes
3) Organic pollutants, polychlorinated biphenyls (PCB’s)
4) Pesticides (insecticides, fungicides, herbicides, and bactericides)
5) Pathogenic bacteria
6) Genetically modified organisms
<b>B) The beekeeping contaminants</b>
1) Acaricides: lipophilic synthetic compounds and nontoxic substances such as organic acids and components of essential oils
2) Antibiotics used for the control of bee brood diseases, mainly tetracyclines, streptomycin, sulfonamides, and chloramphenicol.
3) Paradichlorobenzene, used for the control of wax moth and chemical repellents

**Table.2** Names of some plants whose nectar gives rise to toxichoney. Al-Waili *et al.*, 2012

<b><i>Rhododendron ponticum</i> (<i>Azalea pontica</i>) contains alkaloids that are poisonous to humans</b>
<b>Andromeda flowers contain grayanotoxins which are psychoactive and toxic to humans (paralyze limbs and diaphragm and result in death)</b>
<b><i>Kalmia latifolia</i>, the calico bush, mountain laurel, or spoon wood of the northern US, and allied species produce sickness or death</b>
<b>Wharangi bush, <i>Melicopeternata</i>, in New Zealand, produces toxic fatal honey</b>
<b>Datura plants in Mexico and Hungary</b>
<b>Belladonna flowers, henbane (<i>Hyoscamusniger</i>) plants in Hungary, <i>Serjanialethalis</i> in Brazil</b>
<b><i>Gelsemium sempervirens</i> in the American Southwest</b>
<b>Tutu (<i>Coriariaarborea</i>), in New Zealand, produce tutin which is a member of the picrotoxin group of poisons</b>
<b>Oleander in Mediterranean region</b>

Fig.1 Schematic representation of the therapeutic effects of honey. Adapted from Rao *et al.*, 2016.

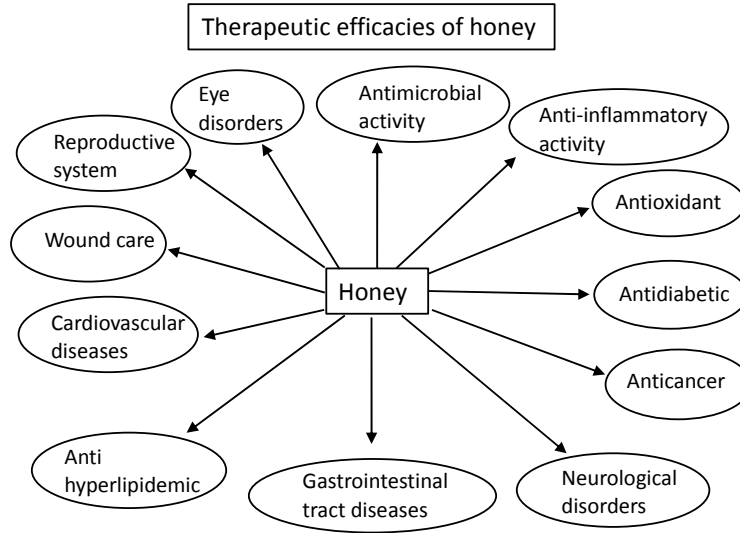
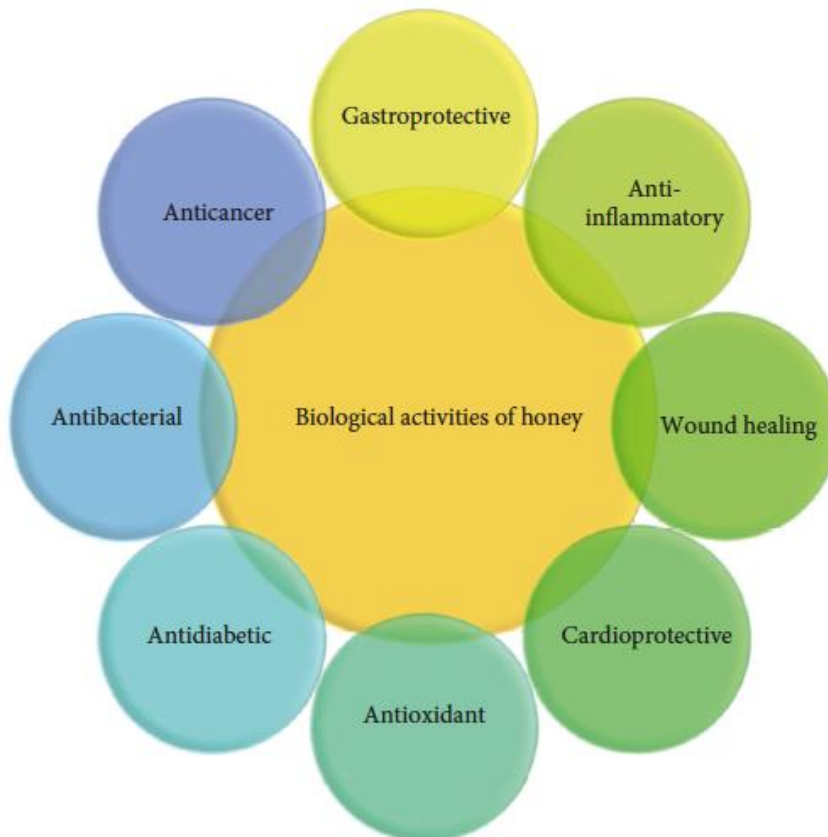
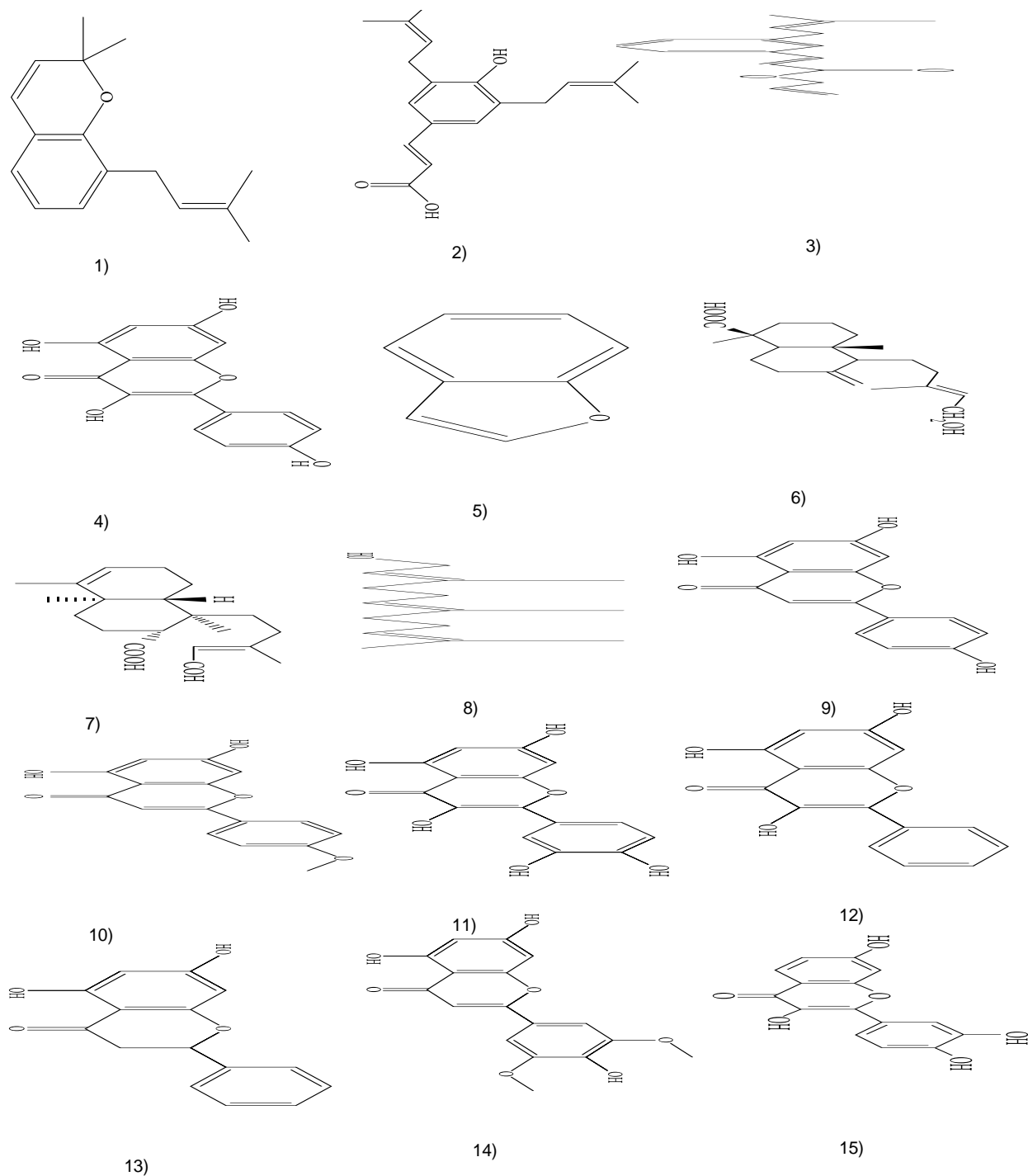


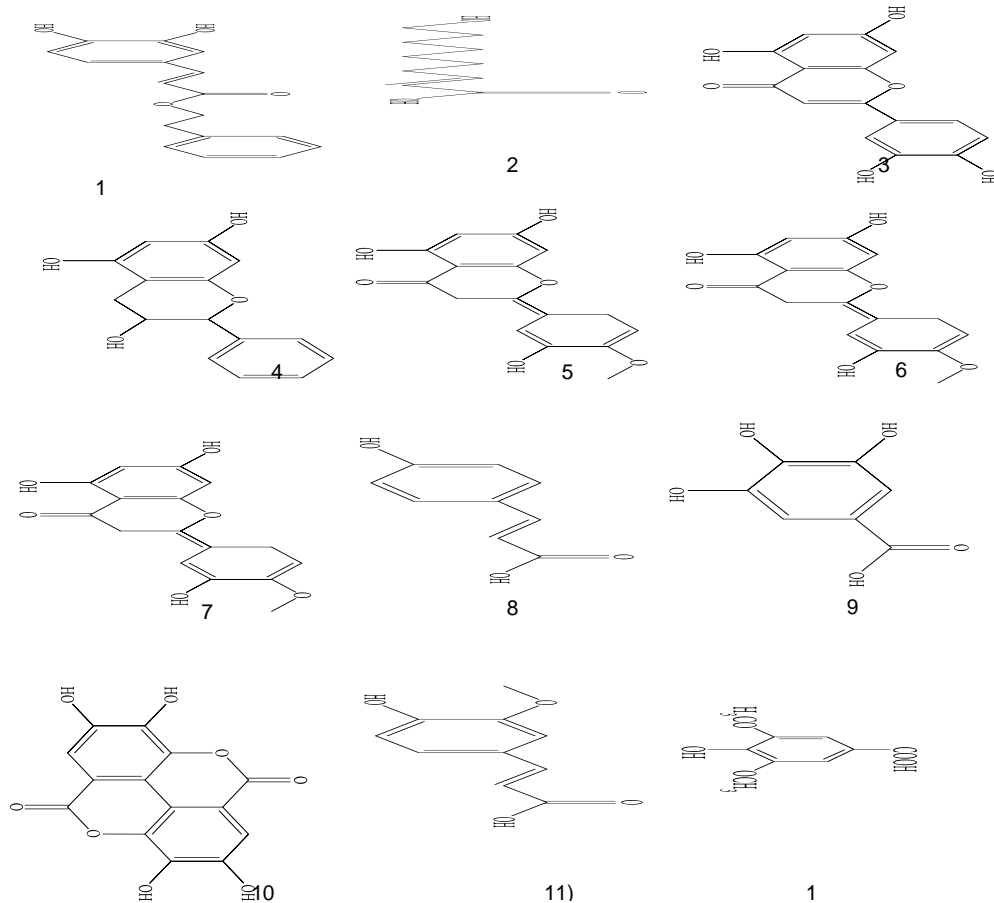
Fig.2 Various types of biological activities of honey products. Adapted from Pasupuleti *et al.*, 2017.



**Fig.3** Important bioactive compounds in honey, propolis and royal jelly; 2-dimethyl-8-prenylchromene (1), 4-hydroxy-3, 5-diprenyl cinnamic acid (2), 3-prenyl cinnamic acid allyl ester (3), kaempferide (4), benzofuran (5), isocupressic acid (6), 13C-symphoreticulinic acid (7), farnesol (8), apigenin (9), acacetin (10), quercetin (11), galangin (12), pinocembrin (13), chrysin (14) fisetin (15). Adapted from Rao *et al.*, 2016. Adapted from Pasupuleti *et al.*, 2017.



**Fig.4** Important bioactive compounds in honey, propolis and royal jelly; caffeic acid (1), 10-hydroxy-2-decenoic acid (2), luteolin (3), pinobanksin (4), hesperetin (5), naringenin (6), genistein (7), p-coumaric acid (8), gallic acid (9), ellagic acid (10), ferulic acid (11), syringic acid (12). Adapted from Pasupuleti *et al.*, 2017.



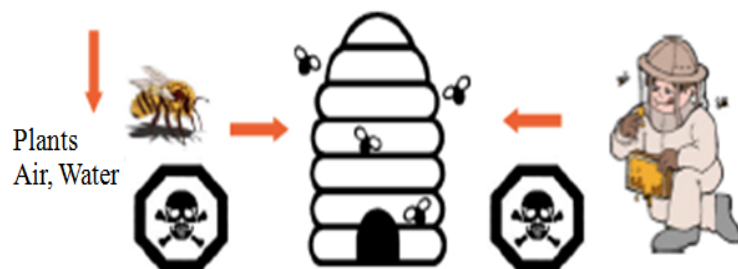
**Fig.5** The contamination sources for the bee colony. GMO: genetically modified organisms; AFB: American foul brood; EFB: European foul brood; SHB: small hive beetle. Bogdanov, 2006).

### Environment

- Pesticides
- Heavy metals
- Bacteria
- GMO
- Radioactivity

### Beekeeping

- Acaricides for Varroa control
- Antibiotics against AFB, EFB
- Pesticides for wax moth control
- Pesticide against SHB
- Bee repellents at honey harvest



## Contaminants from beekeeping

The most important contaminants are the substances used for the control of bee pests. At present, two of the most important pests worldwide are varroa and American Foul Brood.

### Acaricides

Varroacides are an important contamination source, as they have to be used for long-term Varroa destructor control (Wienands, 1987).

Synthetic, persistent substances

Natural non-toxic substances

A more complete list of more acaricides such as tetradion, chlorodimiform, cymiazole, can be found elsewhere. The majority of beekeepers world-wide use the acaricides mentioned to control the mite infections especially tetradion, chlorodimiform, cymiazole (Bogdanov, 2006; Wallner, 1999).

### Synthetic acaricides

Majority of the synthetic acaricides are mostly fat-soluble and persistent in wax. After acaricide treatments, they accumulate in wax and can contaminate honey. Acaricide residues were detected in many bee products (Wallner, 1999; Bogdanov *et al.*, 1998b).

The application of different synthetic acaricides results in different contamination levels in wax (brood combs and honey combs), sugar feed and honey. The acaricide levels including synthetic lipophylic acaricides found in the different products after treatment with the acaricides, decreased in the following order: brood combs > honey combs >> sugar feed ≥ honey.

The acaricide levels found in honey are generally lower and residues accumulate in wax (Muino *et al.*, 1997; Wallner, 1999). The residue amount in wax depends on the number of treatments and applications (Bogdanov *et al.*, 1998). The widely used acaricide amitraz is metabolised not only in honey (Bogdanov, 1988), but also in wax (Korta *et al.*, 2001, 2002).

Various theoretical models on the contamination of the bee colony by acaricides predict the contamination level of different colony matrices as bees, wax, pollen (Tremolada *et al.*, 2004). The Swiss bee research centre

has a monitoring program to model for a follow up of acaricide residues long-term behaviour in commercial beeswax (Bogdanov *et al.*, 1998). Due to the emergence of resistant mites, the use of alternative acaricides such as thymol and organic acids has become popular (Wallner, 1995, 1997; Menkissoglu-Spiroudi *et al.*, 2001; Bernardini and Gardi, 2001).

Acaricide residues have been found also in propolis (Bogdanov *et al.*, 1998; Wallner, 1999). For medical purposes only propolis produced in the frame of certified organic beekeeping should be used. Bogdanov, 2006

### Non-toxic natural acaricides

Non-toxic substances such as thymol and organic acids are widely used as a substitute for synthetic acaricides due to their persistence and resistance by the mites (Milani, 1999). Thymol is fat soluble and volatile, while organic acids are water soluble and non-volatile. These substances are natural honey and plant constituents which are non-toxic and considered as safe. Therefore, no MRL values have been fixed in the European Union (Mutinelli, 2003). Natural substances like thymol and organic acids are increasingly used for Varroa destructor control in many European countries, and also world-wide.

### Thymol

Honey bee colonies treated with thymol-based acaricides under moderate climate conditions after the honey harvest, the residues in honey will be marginal and safe. The residues in beeswax were much greater than those found in honey despite of the evaporation of Thymol with some times cause changes in the taste of honey (Bogdanov *et al.*, 1998; Wallner, 1997; Bogdanov *et al.*, 1999). The sensory threshold of thymol in honey is 1.1–1.5 mg/kg as international honey regulations do not allow that the natural taste of honey be changed (Bogdanov *et al.*, 1999).

### Organic acids

Oxalic and formic acids are natural honey constituents, which is widely used as an alternative V. destructor control which have a GRAS status (Generally Recognised As Safe) (Mutinelli, 2003). Single treatments with formic acid showed that the residue levels were within the natural variation of these acids while the long term usage may lead to change in the honey taste (Stoya *et al.*, 1986; Hansen and Guldborg, 1988; Krämer, 1994;

Capolongo *et al.*, 1996; Radtke and Hedtke, 1998; Prandin *et al.*, 1999; Bogdanov *et al.*, 2002a; Bogdanov *et al.*, 2002a).

Single or repeated treatments with oxalic acid do not lead to accumulation of residues in honey (Mutinelli *et al.*, 1997; del Nozal *et al.*, 2000; Bernardini and Gardi, 2001; Radetzki and Bärmann, 2001; Prandin *et al.*, 2002; del Nozal *et al.*, 2003; Moosbeckhofer *et al.*, 2003). Varroa control with natural acaricides like organic acids and thymol is a good alternative to treatments with synthetic substances in which the residue effect is marginally low and safe.

### **Antibiotics used against Foul Brood**

Antibiotic residues can originate from treatments against various bacterial brood diseases American Foul Brood (AFB) or European Foul Brood (EFB). Treatments with antibiotics are not allowed in the EU due to the antibiotic resistance and food chain contaminations while in many other countries they are widely used. In EU countries there are no MRL levels for antibiotics, which means that honey containing antibiotic residues are not permitted to be sold or marketed.

The detection of antibiotics in honey requires sensitive and precise detection methods and establishing a Minimum Required Performance Limit (MRPL), valid for testing laboratories.

At present, for most antibiotics the MPRL lies around 10 µg/kg, for chloramphenicol it is about 0.3 µg/kg, and for nitrofurans about 1 µg/kg. Routine analysis of antibiotics is carried out according to the “classical approach” in two steps. In the first one screening is carried out by the Charm test (Salter, 2003) or ELISA (Heering *et al.*, 1998).

In a second step the residues of the positively tested samples are quantified mostly by HPLC or LC-MS (Kaufmann *et al.*, 2001). The possibilities and the limits of the different analysis methods and instruments varied widely across the honey samples (Bogdanov, 2003).

The major antibiotics present in honey includes mostly streptomycin and sulfonamides, but also tetracyclines and chloramphenicol (Reybroeck, 2003; Bogdanov and Fluri, 2000). On the other hand, honey produced in Switzerland (Bogdanov and Fluri, 2000), Belgium (Reybroeck, 2003) and Germany (Wallner, 2003) had a lower residue level, varying from 1 to 7%.

### **Other substances used in beekeeping**

Some beekeepers use para-dichlorobenzene (PDCB) for the control of wax moth which enters the cycle of beeswax and contaminates commercial beeswax and also honey (Wallner, 1992; Seiler *et al.*, 2003; Bogdanov *et al.*, 2004). Naphthalene used for wax moth control, wood protectants and paints, used to protect the bee hive against spoilage, should not contain insecticides and fungicides, that might contaminate honey (Kalnins and Detroy, 1984; Bogdanov, 2006).

Storage of honey in inappropriate containers can also lead to undesirable residues of heavy metals. During the storage of honey, inorganic and organic components can diffuse from the inner surface of paraffinated, corrosive and painted vessels and contaminate it. Increased iron concentrations due to storage of honey in metal containers is a common problem (Morse and Lisk, 1980; Merin *et al.*, 1998).

### **Future prospects**

The present review article focusses on the health benefits of bee products especially, honey, propolis and royal jelly. Honey bee products possesses numerous biological, biochemical and physiological activities in animals as well as in humans. The efficacy of these properties depends on the types of phenolic and bioactive compounds present in the honey bee products.

They are effective in preventing diseases and promoting good health due to the presence of bioactive compounds such as flavonoids, phenolic acid, phenolic compounds, terpenes, and enzymes. The nutritional properties and functional values of honey, propolis and royal jelly differs widely.

These potent apitherapeutic products should be standardized for correct doses and checked for the allergic effects. The main contamination danger for bee products originates more from apicultural practices than from the environment. The main contamination risks for the different bee products are antibiotics (honey and royal jelly), lipophilic acaricides (wax and propolis) and pesticides (pollen). Beekeepers can take successful measures to prevent the contamination of bee products from beekeeping source with ecological alternatives.

Alternative bee pest control strategies and minimal use of synthetic chemicals in beekeeping can keep bee products clean and safe. The introduction of organic

beekeeping is an ecological means to avoid all major contamination sources for the production of high quality bee products.

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### Conflicts of interest

The author do not have any conflict of interest.

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