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Properties of Honey: Its Mode of Action and Clinical Outcomes

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Abstract

The medicinal use of honey is well established since time immemorable. Currently, there exists a large volume of clinical research wherein the benefits of honey in health and disease have been proven beyond doubt. By the very nature of its biochemical composition, it is a nutrient par excellence comprising carbohydrates, amino acids, minerals, and electrolytes. The main focus of this chapter is to highlight the important clinical uses of honey in light of modern day medical practice. Honey has broad-spectrum antimicrobial effect, covering diverse varieties of viruses, bacteria, and fungi. Other therapeutic properties of honey include antioxidant, anti-inflammatory, immunomodulatory, cytoprotective, and antineoplastic properties. Various components of honey have been isolated, and each of its actions is attributed to one or more of its constituents. The present day use of honey ranges from simple skin conditions to difficult surgical wounds to diverse cardiovascular and gastrointestinal pathologies to anticancer remedy.

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The benefits of honey as a therapeutic agent is its low cost, natural product with minimal adverse reactions, and minimal need for dose adjustments.

Keywords

Nutraceutical property · Antimicrobial agent · Wound healing · Pre- and probiotic · Honey polyphenols · Pediatric burns · Medihoney · Apitherapy

15.1 Introduction

Honey is a versatile natural product produced from plant nectars by the living machineries called honey bees. The biochemical properties of honey vary, depending mainly on the floral type. Based on the origin, honey has been classified as monofloral and polyfloral or multifloral. While monofloral honey is produced from single plant source, polyfloral honey has several botanical sources. Besides the floral honey, another variant is honeydew honey. Here honey bees feed on the plant secretions or excretion of certain plant-sucking insects belonging to genus Rhynchota. It is the source plant and the honey bee modifications thereof that imparts distinct physicochemical properties to the honey. Likewise the nutritive and medicinal properties of honey are due to the constituents present in it. At biochemical level, honey has antimicrobial, antioxidant, anti-inflammatory, immunomodulatory, cytoprotective, antiproliferative, and many other properties that make this natural substance such a versatile agent. This chapter will focus on certain clinical attributes of honey and the active chemical ingredients responsible for such properties. Before that, let us briefly discuss some physicochemical properties of honey.

15.2 Physicochemical Properties of Honey

Honey is a sweet viscous substance ranging in color from near transparent pale yellow through ambers to dark red amber to near black depending on the source, age, storage, and climatic conditions (Bertoncelj et al. 2007; Anupama et al. 2003). The viscous nature is because of the presence of very high sugar concentration. The supersaturated nature of the solution makes it highly dense, hygroscopic with a tendency to granulate if its moisture content drops further (Olaitan et al. 2007). Honey has acidic pH, ranging from 3.2 to 4.5 (Jeffrey and Echazarreta 1996). This is due to the presence of organic acids like gluconic acid, formic acid, citric acid, and acetic acid (Majewska et al. 2019). Undue fermentation can result in increased acidity due to conversion of alcohols into organic acids (Majewska et al. 2019). The very presence of phosphates, carbonates, and other mineral salts makes honey a good buffer.

Table 15.1 Main nutrient composition of honey[a]

	Floral honey		Honeydew honey	
Component	Range	Mean	Range	Mean
Water	15–20	17.2	15–20	16.3
Sugars (Total)		79.7		80.5
Fructose	30–45	38.2	28–40	31.8
Glucose	24–40	31.3	19–32	26.1
Sucrose	0.1–4.8	0.7	0.1–4.7	0.5
Erlose	0.5–6.0	0.8	0.1–6.0	0.1
Minerals	0.1–0.5	0.2	0.6–2.0	0.9
Amino acids	0.2–0.4	0.3	0.4–0.7	0.6
Organic acids	0.2–0.8	0.5	0.8–1.5	1,1
pH value	3.2–4.5	3.9	4.5–6.5	5.2

[a]Values in g/100 g of honey (Adapted from White (1975) and Bogdanov et al. (2003))

15.3 Nutraceutical and Pharmaceutical Properties of Honey

Honey has been used as a sweetener and health food. Literature in this regard dates back to 5500 BC. It has been used by all civilizations from time to time; be it Greeks, Romans, Chinese, Egyptians, or Indians. Though honey finds thousands of uses when both traditional and modern day medicine literature is taken into account, our emphasis will only be on the important and clinically significant ones.

15.3.1 Nutrition

Natural honey is a combination of carbohydrates, peptides and amino acids, organic acids, enzymes, minerals, and vitamins in aqueous base (Table 15.1). The composition varies depending on the floral type, geographical location, season of harvest, and thermal treatment (Alvarez-Suarez et al. 2010). The predominant component of honey is the carbohydrates; nearly 83% being simple sugars like fructose and glucose while rest 17% consisting of maltose, sucrose, isomaltose, erlose, maltulose, and many others (Khan et al. 2007; Jeffrey and Echazarreta 1996). Depending on the species of the honeybees, the protein content of honey is variable. For example, while protein content in *Apis cerana* varies from 0.1 to 3.3%, it varies from 0.2 and 1.6% in *Apis mellifera* (Won et al. 2008). Proline is the main amino acid in honey, constituting about 50–85% of the amino acid pool (Hermosin et al. 2003). Enzymes in honey has two sources: invertase, glucose oxidase, and amylase originate from hypopharyngeal glands of worker honeybees. On the other hand, catalase, acid phosphatase, and a little proportion of amylase come from plants (Jeffrey and Echazarreta 1996). The minerals and vitamins constitute about 0.02% of its weight (Jeffrey and Echazarreta 1996) (Table 15.2). Potassium comprises almost 30–35% of the total mineral content of honey. Other minerals like sodium, calcium, magnesium, iron, copper, silicon, and manganese are present in small quantities (Alqarni et al. 2014). Organic acids, which impart acidity to honey, constitute 0.57% of

Table 15.2 Mineral and vitamin composition of honey

Minerals	Amount (mg/100 g)	Vitamins	Amount (mg/100 g)
Sodium (Na^+)	1.6–17	Thiamine (B1)	0.00–0.01
Calcium (Ca^{2+})	3–31	Riboflavin (B2)	0.01–0.02
Potassium (K^+)	40–3500	Niacin (B3)	0.10–0.20
Magnesium (Mg^{2+})	0.7–13	Pantothenic acid (B5)	0.02–0.11
Phosphorus (P)	2–15	Pyridoxine (B6)	0.01–0.32
Selenium (Se)	0.002–0.01	Folic acid (B9)	0.002–0.01
Copper (Cu)[a]	0.02–0.6	Ascorbic acid (C)	2.2–2.5
Iron (Fe)[a]	0.03–4	Phyllochinon (K)	0.025
Manganese (Mn)[a]	0.02–2		
Chromium (Cr)[a]	0.01–0.3		
Zinc (Zn)[a]	0.05–2		

[a]Heavy metals (Adapted from White (1975) and Bogdanov et al. (2003))

honey. The chief organic acids in honey are gluconic acid and citric acid, which also help differentiate between floral and honey drew honey (Karabagias et al. 2014).

From nutritional point of view, natural honey is an instant energy dense food with added benefits of mineral and vitamins. This makes honey a good meal for body growth and metabolism. On an average 100 g of honey provides around 304 kilocalories of energy. Since the concentration of macro and micronutrients in honey is low (far below than recommended daily allowance), other supplements are needed in an adult human being to meet requirements on day-to-day basis. Scientific research showed adequate weight gain in rats fed on natural honey (Ajibola et al. 2011). In humans, the role of honey in infant nutrition is well described and has been found to be fairly tolerated with significantly lowered crying phases of babies as compared to placebo (Ramenghi et al. 2001). Studies have shown that feeding honey in infant diet had a better weight gain, increased hemoglobin levels and were less susceptible to diseases as compared to those fed normally or with sucrose supplemented diet (Samanta et al. 1985; Liu et al. 2001). Use of honey with milk is very common practice for premature babies and children with iron-deficiency anemia or jaundice. The beneficial effects of honey in athletics are also well documented (Hills et al. 2019).

Honey has other nutritional benefits like antioxidant potential, immune booster and pre and probiotic use. Metabolic activity in human body generates a class of highly unstable reactive oxygen species (ROS) and free radicals, which inflict damage at molecular level. These harmful agents are neutralized by the scavenger system within the body. However, disequilibrium between the production and the destruction of ROS and free radicals can result in oxidative stress and the subsequent detrimental effects in the body in the form of changes at cellular and molecular level. Certain extrinsic agents when consumed as food like honey can boost the protective mechanism by its antioxidant property. Honey is rich source of antioxidants like polyphenols/phenolic acids, flavonoids, carotenoid derivatives, organic acids, vitamins (ascorbic acid), amino acids, and proteins like glucose oxidase and catalase (Khalil et al. 2010). Some of the polyphenols of honey like Caffeic acid and its phenyl ester, Chrysin, Kaempferol, Galangin, Quercetin, Acacetin, Pinocembrin, Pinobanksin, and Apigenin have shown some promise as pharmacological agent in treatment of cancer (Jaganathan and Mandal 2009a, b).

The pre- and probiotic properties of honey have been validated by various studies (Gaifullina et al. 2017). Certain oligosaccharides and some low molecular weight polysaccharides present in honey exhibit prebiotic properties. These sugars evade digestion and undergo fermentation in large intestine and provide nutrition to resident microflora. On the other hand, probiotic effect of honey is mainly due to presence of microorganisms like Bifidobacteria and Lactobacilli in freshly harvested honey.

15.3.2 Antimicrobial

The broad-spectrum antimicrobial (antibacterial, antiviral and antifungal) activity of honey has been confirmed by vast majority of clinical and in vitro studies. The mechanism of antimicrobial action of honey has been attributed to several inherent components of the product like high sugar concentration, low pH value, glucose oxidase, bee defensin-1 and others (Molan 1992a, b; Mandal and Mandal 2011; Israili 2014; Kwakman et al. 2011; Kwakman and Zaat 2012). Due to high sugar content, certain bacteria which are osmosensitive are eliminated (bacteriocidal action), while as growth of few other bacteria resistant to changes in osmotic pressure is hampered (bacteriostatic action). Likewise acidic pH due to presence of organic acids like gluconic acid can have bacteriocidal or bacteriostatic action. The production of gluconic acid from glucose is catalyzed by enzyme glucose oxidase. The byproduct of this reaction is hydrogen peroxide which is a strong antimicrobial agent. Defensin-1 is a peptide secreted by the hypopharyngeal glands of honeybee and shows activity against Gram-positive bacteria, including *Bacillus subtilis* and *Staphylococcus aureus*. Some factors are typical of the variant of the honey like high methylglyoxal (MGO) levels in Manuka honey. However, the antimicrobial role of MGO and few others is still not clear. Other factors play an indirect role by exerting counter-productive response against the ill effects of microbial agents like anti-inflammatory action, antioxidant action, immunomodulation, and lysosomal cytolysis.

In clinical practice, honey has exhibited high anti staphylococcal and anti-*Helicobacter pylori* activity. Because of its excellent anti staphylococcal activity including Methicillin-resistent *Staphylococcus aureus* (MRSA), it can be used in wounds, burns, and certain soft tissue infections. Certain animal studies have shown that honey has a potential to be used in treatment of infected surgical wounds (Al-Waili 2004a, b). Local application of honey on infected wounds was found to hamper signs of inflammation and facilitated clearance of infection. Tissue erythema and edema was lessened, time for complete resolution of lesion and time for eradication of bacterial infection due to *S. aureus* or Klebsiella sp. was reduced. Its antimicrobial activity was found to be comparable to that of local antibiotics. Using agar diffusion assay, Nzeako and Al-Namaani investigated activity of different samples of honey against *Helicobacter pylori* (*H. pylori*) (Nzeako and Al-Namaani 2006). They concluded that all of them effectively inhibited the growth of *H. pylori*. Low gastric pH affects the activity of glucose oxidase enzyme present in honey, thus hampering generation of hydrogen peroxide, crucial antimicrobial agent. Thus, to execute anti *H. pylori* action in acid peptic disorders, components other than H_2O_2 come into play. Urease and xanthine oxidase, the important virulence factors of *H. pylori*, were found to be inhibited by phenolic components in honey (Sahin 2016). Further in one of the human clinical studies involving 150 patients with dyspepsia, consumption of honey at least once weekly significantly reduced the risk of development of *H. pylori* infection (Boyanova et al. 2015). In an in vitro study, researchers found that Mycobacteria failed to grow in culture media containing 10 and 20% honey (Asadi-Pooya et al. 2003). However in vivo studies supporting its role in tuberculosis are still at large. This future endeavor could solve the current problem of multidrug resistant (MDR) tuberculosis. It has been found that gram-negative bacteria are less sensitive to antimicrobial effects of honey, such as the lesser activity of honey against *P. aeruginosa* and *E. coli* in comparison with *S. aureus*. Honey effectively eradicates biofilms formed by *P. aeruginosa* (Cooper et al. 2014). The antibacterial spectrum of honey also includes organisms like *Salmonella* spp., *Campylobacter* spp., *Shigella* spp., and others. Due to its broad-spectrum antimicrobial action, honey is a potential wound dressing material.

Honey is effective antifungal with its antifungal action comparable to azole group of antifungals when used against Candida species (Irish et al. 2006; Majidi Poya and Khodavandi 2018). However, due to topical use, its role becomes limited in systemic fungal infections like candidemia, wherein it can act as an adjunct to antifungal medications. Virucidal action of honey is supported by its anti-influenza and anti-Varicella Zoster virus effects of honey (Watanabe et al. 2014; Shahzad and Cohrs 2012). MGO in Manuka honey has shown potent antiviral activity in in vitro studies (Watanabe et al. 2014). Other uses include labial and genital herpes.

15.3.3 Antioxidant

Honey polyphenols, catalase, peroxidase, glucose oxidase, vitamin C, and carotenoids are important dietary antioxidants present in honey. Antioxidant property of honey has important clinical implications such as use in cardiovascular diseases, diabetes, cancers, osteoporosis, neurodegenerative diseases, etc. One of the factors studied extensively in etiopathogenesis of aging and age-related disorders is oxidative stress. Free radicals and reactive oxygen species can harm cells by reacting with cell membrane components or proteins or DNA and can alter cell structure or function. Polyphenols and other antioxidants protect cells through scavenging of free radicals. Another action of polyphenols is pro-oxidant action that helps in apoptosis of cancer cells.

There seems to be a relationship between antioxidant potential and color of honey, with darker varieties of honey providing higher antioxidant levels. The antioxidant activity of honey polyphenols is measured in vitro by comparing the oxygen radical absorbance capacity (ORAC) with the total phenolic concentration.

15.3.4 Anti-inflammatory and Wound Healing

Various clinical observational and animal experimental studies have described the anti-inflammatory activity of honey (Efem 1993; Subrahmanyam 1996, 1998; Benhanifia et al. 2011; Oryan and Zaker 1998). The mechanism of action is an overlap between antimicrobial and antioxidant property and a direct anti-inflammatory role. The latter is the justification for its clinical use in nonmicrobial inflammatory conditions like arthritis, vasculitis, atherosclerosis, and senile neurodegenerative disorders like Parkinson's and Alzheimer's disease. Since the antimicrobial and antioxidant nature of honey has already been elaborated, the anti-inflammatory activity needs a word here. The anti-inflammatory effects of honey are mainly attributed to phenolic compounds and flavonoids present in the honey (Palmieri et al. 2012; Kassim et al. 2010). Chrysin, a flavonoid found in honey, has been reported to suppresses lipopolysaccharide-induced COX-2 expression (Woo et al. 2005) and thus the release of nitric oxide (NO) and pro-inflammatory cytokines such as tumor necrosis factor (TNF-α) and interleukin (IL-1β) gets inhibited (Palmieri et al. 2012). Researchers have isolated two more flavonoids from honey, namely apigenin and kaempferol. They act by suppression of TNF-α induced matrix metalloproteinase (MMP-9) expression in experimental human cell line, HaCaT (Majtan et al. 2013). In human endothelial cells, apigenin was also found to inhibit TNFα-induced MMP-9 expression by modulation of Akt signaling pathway (Palmieri et al. 2012). Further it has been found that IL-1β-induced MMP-9 mRNA expression in osteoblasts is inhibited by apigenin (Yang et al. 2012). Similarly there is evidence to support the role of kaempferol as a potent inhibitor of MMP-2 and MMP-9 (Li et al. 2009). Medicated manuka honey has been used effectively in conservative treatment of exomphalos major (Nicoara et al. 2006). Briefly the anti-inflammatory actions of honey can be summed up by its effect on various inflammatory mediatory pathways like: (a) inhibition of production and rapid scavenging of free radical and ROS (Zare et al. 2007), (b) inhibition of chemotaxis and thus decreased leukocyte infiltration (Leong et al. 2012), (c) inhibitory effect on cyclooxygenase-2 (COX-2) and iNOS expression (Hussein et al. 2012), (d) inhibition of matrix metalloproteinase-9 (MMP-9) (Majtan et al. 2013).

Another aspect of honey related to its anti-inflammatory potential is immunomodulation. Infact the anti-inflammatory and the immunomodulatory actions are intricately balanced to produce the desired effect. Honey can stimulate the expression of certain key mediators of immune system like TNF-a, IL-1b and IL-6. While TNF-a promotes macrophage activation, stimulates angiogenesis and re-epithelialization during wound healing; IL-1b stimulates the release of certain growth factors helpful in wound healing. IL-6 helps in proliferation of keratinocytes and attracts neutrophils. Honey also stimulates production of antibodies, T and B lymphocytes, neutrophils, monocytes, and natural killer (NK) cells during primary and secondary immune responses.

Honey is being indoctrinated as a novel dressing material with a strong backing from recent research. Molan had stated in 2002:

> "Dressing wounds with honey, a standard practice in past times, went out of fashion when antibiotics came into use. Because antibiotic resistant bacteria have become a widespread clinical problem, a renaissance in honey use has occurred."

Traditionally, honey has been used in acute and chronic non-healing wounds and ulcers. The wide spectrum of wounds includes burns, boils, venous and diabetic foot ulcers, pilonidal sinuses, malignant wounds, pressure sores, etc. Clinically, topical application of honey has been found to facilitate wound healing due to its antimicrobial, antioxidant and anti-inflammatory actions. Moreover, it also helps deodorize and debride deep dirty wounds and provides stimulus for tissue growth to heal wounds. As a bioactive dressing, honey surpasses or at least is equally effective, when compared with various standard treatments of modern times. It has heals superficial burns quicker than polyurethane film (OpSite™) and silver sulfadiazine (SSD) 1% ointment, the current treatment of choice in prevention of infection in burns (Pruitt 1987). Other advantages are its soothing effect on application and lesser scarring. Similarly, studies have shown honey to be a superior to conventional dressings in postoperative wounds and chronic complicated wounds like burst abdomen, venous ulcers, etc. (Cooper et al. 2001; Phuapradit and Saropala 1992). The use of some medically certified honey has become a standard practice in Europe. Medihoney, which is FDA approved for such use, is one such example. As certain microbial spores like Clostridium botulinum exist in our environment (soil, air dust, etc.), sterilization with gamma irradiation is a must before use. The use of Medihoney has been extended to fragile and immunocompromised patient population like wound management in cancer patients on chemotherapy, wound care in premature neonates and protection of catheter entry sites in chronic kidney disease patients on hemodialysis.

15.3.5 Gastrointestinal Diseases

Oral administration of honey can help in prevention and treatment of various gastrointestinal conditions like gastritis, duodenitis, gastroenteritis, diarrhea, peptic ulcers, constipation, jaundice, hepatitis, colorectal cancer, inflammatory bowel disease, hemorrhoids, anal fissure, perianal abscesses and many others (Tallet et al. 1977; Haffejee and Moosa 1985; Somal et al. 1994; Topham 2002; Alnaqdy et al. 2005). Honey is used in treatment of both NSAID-induced and *H. pylori* induced gastric ulcers. The mode of action is the interplay of antimicrobial, anti-inflammatory, and cytoprotective properties of honey. Besides this, honey is a versatile prebiotic and probiotic agent. One of the etiologies of colonic cancer and inflammatory bowel diseases is fiber-deficient diet, thus SCFA-replete diet. When ingested orally, partially and nondigestible sugars in honey reach colon and undergo fermentation with the aid of gut microbiota, resulting in production of short chain fatty acids (SCFAs). These SCFA have local effect on enterocytes or can reach blood stream by absorption across gut epithelium. SCFAs have anti-inflammatory, antimicrobial, immunomodulatory, and antitumorigenic actions. Two important SCFA-signaling pathways are well described: inhibition of histone deacetylases (HDACs) and activation of G-protein-coupled receptors (GPCRs).

15.3.6 Dermatological Conditions

The need for new agents to treat various dermatological conditions stems from the bucketful of adverse reactions of the available remedies. Honey has attracted concerned researchers due to its antimicrobial, anti-inflammatory, immunomodulatory, and regenerative properties. Besides a dressing for wounds and burns, it has been used in pityriasis, tinea, contact dermatitis, atopic dermatitis, dandruff, seborrhea, cutaneous leishmaniasis, and psoriasis (McLoone et al. 2016). It also acts as an emollient, humidifier, hair conditioner, and soothener in various cosmetic formulations. The ability of honey to inhibit proliferation of tumor cells and induce apoptosis has found a role in skin cancers like melanoma (Pichichero et al. 2010). Certain components of honey impart protective effect against ultraviolet radiations (Ahmad et al. 2012).

15.3.7 Oral Health

Honey has found its use as a cost-effective treatment in various oral and dental conditions like oral ulcers, stomatitis, oral candidiasis, dental caries, and periodontitis (El-Haddad and Al-shawaf 2013; Nayak et al. 2010; El-Haddad et al. 2014). Peridontitis starts as acute inflammatory response secondary to bacterial infection which progresses to chronic stage resulting in destruction of gums and supporting tissues around the teeth. The protective effect of honey comes into play by virtue of its antimicrobial, antioxidative, anti-inflammatory, and tissue-healing properties. Similarly, due to its inhibitory effect on Candida species, honey is used as an effective treatment for oral thrush.

15.3.8 Ophthalmological Conditions

Globally honey is finding its place as a the treatment modality for various ophthalmological conditions like conjunctivitis, blepharitis, corneal diseases like keratitis, corneal ulcerations, bullous keratopathy and thermal and chemical burns to eyes (Shenoy et al. 2009). The protective effect of honey in senile cataract is also well documented (Golychev 1990).

15.3.9 Diabetes

Honey has a low glycemic index (GI) which makes it beneficial in type I and type II diabetes. Besides this, honey stimulates insulin secretion, decrease blood glucose levels, elevates hemoglobin concentration and improves lipid profile (Al-Waili and Haq 2004). With its regular use, honey helps correct dyslipidemia, reduces blood homocysteine and C-reactive protein (CRP) levels in normal and hyperlipidemic subjects (Al-Waili 2004a, b).

15.3.10 Cardiovascular Diseases

Diabetes, hypertension, obesity, and dyslipidemia are important risk factors for cardiovascular diseases. These are clustered together as an entity known as metabolic syndrome. There are many preclinical and human studies supporting protective effects of honey in metabolic syndrome. The pathophysiology of cardiovascular diseases starts with an endothelial intimal injury due to predisposing factors like hypertension, age-related changes in vessel wall and oxidant stress. This is followed by cascade of thrombotic and inflammatory changes ultimately resulting in deposition of atherosclerotic plaque at the site of initial intimal insult. This process is favored by proatherogenic agents like oxidized LDL, pro-inflammatory cytokines (TNF-a, IFN-y, IL-1 and IL-6) and angiotensin 2, which cause endothelial dysfunction. There is simultaneous inefficiency of nitric oxide (NO), which is a potent vasodilator. As the cellular and lipid content continues to swell the plaque, followed by calcium deposition, there occurs narrowing of vascular lumen. These changes lead to impaired perfusion to target organs resulting in ischemia. For example, myocardial ischemia due to impaired blood supply to cardiac musculature. Honey reduces the risk of cardiovascular disease by its anti-inflammatory, antioxidant, anti-thrombotic, vasodilatory, and anti-atherogenic properties.

Polyphenols and flavonoids in honey exert their therapeutic effects by reducing the risk factors such as improving endothelial function, inhibition of LDL oxidation, reduction in blood pressure, correction of dyslipidemia, obesity and hyperinsulinemia and antiplatelet action.

15.3.11 Anti-neoplastic

The anticancer property of honey is extensively researched. Various phenolic compounds like Caffeic acid, Kaempferol, Chrysin, Galangin, Quercetin, Apigenin, etc. have been shown to impart honey its anticancer property (Jaganathan and Mandal 2009a, b). The possible mechanisms involved are apoptosis, antiproliferation, antioxidation, anti-inflammation, and immunomodulation. Polyphenols in honey cause depolarization of mitochondrial membrane of cancer cells resulting in apoptosis. Other actions of honey polyphenols are due to increased expression of p53, caspase 3, and proapoptotic protein Bax. Honey also downregulates the expression of antiapoptotic protein like Bcl-2. Various in vitro studies and clinical trials have shown certain cancer cell lines to be sensitive to honey polyphenols. It has also been shown to potentiate action of certain chemotherapeutic drugs like 5-fluorouracil and cyclophosphamide (Abubakar et al. 2012; Jaganathan and Mandal 2009a, b). Examples of human cancers where antitumor action of honey has shown promise include leukemia, breast, colorectal cancer, renal, prostatic, endometrial, cervical, oral and skin cancers (Tsiapara et al. 2009; Gribel and Pashinski 1990; Jaganathan and Mandal 2009a, b; Samarghandian et al. 2011; Ghashm et al. 2010).

15.3.12 Pediatric Use

Honey has been used in treatment of pediatric wounds and burns. Despite limited clinical data, positive role in difficult postoperative wounds in normal and immunocompromised pediatric population has been found in few studies (Vardi et al. 1998; Simon et al. 2006). Oral intake after tonsillectomy has been found to decrease pain and thus lessened the need for postoperative analgesia (Ozlugedik et al. 2006). Honey is a good antitussive probably by virtue of its sweet syrupy nature per se. Due to issues of safety and efficacy with the currently available drugs like dextromethorphan, diphenhydramine, codeine and others, the use of honey has been revisited in this regard and has held promise as a safe and effective alternative (Paul et al. 2007; Shadkam et al. 2010). Other indications are acute gastroenteritis, gastritis, constipation, etc. Besides a blanket antimicrobial cover against the enteritis-causing group of bacteria, its composition makes it a good oral rehydration solution.

15.4 Toxicity of Honey

Every molecule used in clinical practice has some adverse action and honey is no exception to it. The adverse effects of honey are as under:

Plant Toxins: There are examples of honey containing plant toxins which can have deleterious effects on humans. For example, honey produced from the nectar of Rhododendron ponticum, also called “maddening honey” due to its action on central nervous system. Other examples are honey produces from plants like Kalmia, Andromeda, Datura, Hyoscamus, etc. Symptoms of poisoning may include dizziness, vomiting, headache, convulsions, respiratory distress, palpitations, or even death.

Hydroxymethylfurfural (HMF): HMF is a cyclic aldehyde produced as a result of sugar degradation. It is usually absent in fresh and untreated sugar rich foods but the concentration increases due to long-term storage or heat treatment. HMF is thus a parameter for quality and freshness of honey. At high concentrations, HMF has been found to be cytotoxic. It can cause irritation to eyes, skin, respiratory tract, and other mucous membranes. Further, carcinogenic potential of HMF has been studied in animal studies.

Infantile Botulism: Infantile botulism is caused by ingestion of spores of Clostridium botulinum. Since this bacterium is ubiquitous in nature, the untreated natural honey is considered to be a commonly implicated dietary source of Clostridium spores. The child presents with constipation, muscle weakness, difficulty swallowing and breathing, excessive drooling, slow or no reflexes.

Allergy: Allergic reactions due to honey are very uncommon and range from milder reactions to anaphylaxis. The cause for these reactions is proteins produced by bees or proteins derived from plant pollens. Individuals allergic to pollen of certain plants are more likely to have allergies to honeys produced from nectar of such plants.

15.5 Conclusion

Backed by recent research regarding nutraceutical and pharmaceutical properties, the list of clinical uses of honey seems to be ever expanding. The central theme of honey being used as a medicine revolves around its antimicrobial, antioxidant, anti-inflammatory, and immunological properties. In fact, this field of medicine has been named as apitherapy. Modern medicine acknowledges the beneficial effects of honey ranging from nutrition to wide array of infective pathologies (bacterial, viral, fungal) to life style disorders like obesity, hypertension, diabetes, cardiovascular diseases to diseases of skin, genitals, eyes, and oral cavity to various malignancies. Honey is like an elixir that keeps us healthy, prolongs our lives and acts as a shield against wear and tear and degenerative processes involving central nervous system, bones and joints. Other advantages of honey as a drug are low cost and safety. Given the economic impact, adverse reactions or emerging resistance of present day conventional pharmacotherapy, more research is needed to illustrate complete clinical profile of honey.

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