Chapter

Health Benefits of Honey

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Abstract

In addition to being used as food, honey has been used as an alternative medicine for thousands of years. Honey has a great potential to be used as a medicine because it is not suitable for micro-organisms, it is very acidic and has a very high sugar content, which causes an osmotic effect that prevents the growth of some micro-organisms, moreover, in some honey, hydrogen peroxide is found, which has a strong antibacterial effect. However, properties and appearances of honey vary greatly according to the floral source in which the bee collects the nectar, so some honey also have a strong antioxidant and anti-inflammatory activity. Recently, there are several studies, mainly *in vitro*, that prove the effectiveness of honey for various medical purposes due to its components and its antibacterial, anti-inflammatory, antioxidant, antiviral, antifungal, and anticancer properties.

Keywords: anti-inflammatory, antioxidant, bee, cancer, medicine

1. Introduction

Honey is a compound widely used as a medicine and food source for thousands of years [1]. Several natural products that have been used as medicine have been replaced by modern pharmaceuticals, but recently they have returned to the world stage due to the growing public interest [2]. In ancient Egypt, beekeeping has been practiced for more than 4000 years, and honey has been used as a medicine in the treatment of wounds, ulcers, burns, abscesses, gastrointestinal diseases, inflammations, rigid joints, and even as a contraceptive method [1, 3]. In Asia, honey is recognized for its medicinal value since 2000 BC [1]. There are also references to different uses of honey in the bible and in the Qur'an [1]. The ancient Greek Hippocrates, known as the father of modern medicine, used honey to clean wounds, gastrointestinal diseases, and ulcers [1, 3]. In Ancient Rome, honey was also prescribed alone or in combinations, often used to treat throat problems, pneumonia, and even snake bites [1].

The main components of honey are sugars, among which are predominantly fructose and glucose [4, 5]. However, there are other compounds in smaller quantities and very variable depending on the type of each honey, from the floral source where the bee collects the nectar, such as water and free amino acids [4, 5]. Among them, the most found is proline [4, 6]. Some specific enzymes are also found, the main enzymes of honey are invertase, amylase, and glucose oxidase, but other

enzymes such as catalase and phosphatase [6–8]. Honey is also composed of organic acids that contribute to its characteristic flavor and are responsible for the excellent stability of honey against micro-organisms, for example, formic, acetic, butyric, oxalic, lactic, succinic, folic, malic, citric, and glycolic [6, 7]. Gluconic acid is considered one of the most important organic acids in honey; it is the product of catalytic oxidation of glucose oxidase, in this oxidation, hydrogen peroxide is also formed, which has a strong antibacterial effect [4–7].

Honey may still have some mineral substances, such as potassium, magnesium, sodium, calcium, phosphorus, iron, manganese, cobalt, and copper; studies show that honey can contain several types of minerals, but potassium is the most abundant in various types of honey [6, 8–10]. Carotenoids, flavones, and anthocyanins can still be found, which contribute to the antioxidant action of honey [6]. About 80 aromatic compounds have been detected in honey, including carboxylic acids, aldehydes, ketones, alcohols, hydrocarbons, and phenols [6]. These compounds also contribute to the organoleptic properties of honey. The appearance of honey varies from almost colorless to dark brown; it can be liquid, viscous, or solid. Its flavor, aroma, and composition vary enormously, depending on the floral source in which the honeybee collects the nectar. However, some environmental factors can strongly influence honey composition, such as temperature and humidity [6, 7, 11].

Honey is a food that contains high energy carbohydrates, being that 95–99% of the total solids are composed by sugars, which are easily digestible, since they are similar to many fruits [7, 12]. Proteins and enzymes in honey often have no significant nutritional value, as they are usually not present in sufficient amounts [7]. Several of the essential vitamins are present in honey, such as vitamin K, B1, B2, B6, and C, but generally at insignificant levels [7, 8, 13]. The mineral content of honey is variable, usually darker honeys have significant amounts of minerals, but honey can be considered a nutritive sweetener, mainly due to its high fructose content [7, 13].

In addition to its food value, honey has great potential in medicine; it has been used for thousands of years, and has now been widely studied as an alternative medicine. Honey is not a suitable medium for bacteria, since it is very acidic and has a very high sugar content. This causes an osmotic effect that prevents the growth of bacteria, this effect works literally drying the bacteria [7, 13]. Another type of antibacterial property of honey was called inhibition in 1940 by Dold [7]. And in 1963, Jonathan White proposed that this inhibitory effect described in 1940 was due to the hydrogen peroxide produced and accumulated in the diluted honey, which we know today, is a by-product of the formation of gluconic acid by the enzyme glucose oxidase [5, 7, 11].

Historically, honey has been used for various medical purposes; and recent research has confirmed the effectiveness in the treatment of several diseases due to its components and its properties antibacterial, anti-inflammatory, antioxidants, antiviral, and others that will be addressed in this chapter.

2. Properties of honey

2.1 Anti-inflammatory

Inflammation is nothing more than a defense response of the body to a tissue that has suffered a certain damage, which consists of the recruitment of leucocytes and plasma proteins of the blood [14, 15]. This damage can be caused by physical, chemical, or even microbial agents; inflammation is characterized by edema, erythema, pain, and increased temperature [15, 16].

It is well known that propolis, another product from honeybee colony, has potential anti-inflammatory properties, including *in vivo.* But studies on the anti-inflammatory power of honey also are promising, such as the study that evaluated the anti-inflammatory and antioxidant effects of Tualang honey against conventional treatment in alkaline lesions in the eyes of rabbits and the results showed that there was no difference in the clinical inflammatory characteristics between the group treated with honey and the group with conventional treatment, so it is possible to infer that Tualang may be an alternative treatment [17, 18]. Other studies have also been depending on the use of honey, such as chronic ocular surface diseases and infectious conjunctivitis [19, 20].

Gastric ulcers are among the most common diseases affecting humans, a study demonstrated that the use of honey in conjunction with other compounds may promote gastroprotection. Later, a recent study investigated the effect of gastric protection using only honey against gastric ulcers induced by ethanol in rats and also suggested this effect as gastroprotection [21, 22]. Manuka honey significantly decreased the ulcer, completely protected the mucus of the lesions and preserved the gastric mucus glycoprotein, significantly increased the mucus levels of gastric nitric oxide, reduced glutathione, glutathione peroxidase, and superoxide dismutase, and also decreased lipid peroxidation of the mucus and tumor necrosis factor-α, interleukins-1β, and concentrations of interleukins-6 [21]. Honey has been shown to be efficient in other types of ulcers, and this Manuka honey exerted an antiulcer effect, keeping enzymes and antioxidants, non-enzymatic and inflammatory cytokines reduced [21, 23].

In addition to the Manuka honey and the Tualang honey, the anti-inflammatory effect of Malaysia's Gelam honey was also studied, which is associated with anti-inflammatory effects on tissues [24, 25]. Malaysia Gelam honey was tested in rats induced by inflammation [25]. Paw edema was induced by a subplantar injection and the rats were treated with either the anti-inflammatory drug Indomethacin or Gelam honey. Results showed that Gelam honey can reduce dose-dependent edema in inflamed rat paws, decrease the production of nitric oxide, prostaglandin, tumor necrosis factor-α, and interleukin-6 in plasma, and suppress expression of synthase inducible nitric oxide, cyclooxygenase-2, tumor necrosis factor-α, and interleucine-6 in paw tissue [25]. The oral pre-treatment of Gelam honey at 2 g/kg body weight at two times (1 and 7 days) showed a decreased production of proinflammatory cytokines, which was similar to the effect of the anti-inflammatory indomethacin, both in plasma and in the tissue, and Gelam honey has anti-inflammatory effects and is potentially useful for the treatment of inflammatory conditions [25]. Another study demonstrated that different types of honey promoted increased release of TNF-α, IL-1β, and IL-6 from monocytes, which are cells that assist in healing [26].

We can also compare the anti-inflammatory activity of honey with another herbal remedy in a study carried out in 2012 to test the activity of honey and brown sugar, surgically treated guinea pigs that were treated with honey, brown sugar, and a control group treated with saline solution, it is already known that sugar can help healing [27, 28]. The honey group showed a decrease in the area of the wound and the formation of granulation tissue before the brown sugar group and control; the honey group was still the only one that presented no crust in any wound and promoted a faster healing by stimulating the faster formation of granulation tissue and re-epithelization [28]. In addition, honey showed a higher antibacterial effect in relation to brown sugar and control group [28]. Another study had the same result, honey was effective in reducing bacterial contamination and wound healing [29].

Recent studies proved the anti-inflammatory activity of honey; different types of honey, different regions and different floral sources, were studied and both

showed anti-inflammatory responses [17, 21, 25, 28]. Treatment with Tualang honey and Gelam honey showed similar responses to conventional anti-inflammatories used for specific treatments [17, 25]. Honey still has a better anti-inflammatory activity than brown sugar, promoting faster healing [28]. Also, honey is a relatively cheap and easily accessible anti-inflammatory compound that needs to be further studied and later applied in modern medicine [17, 21, 25, 28].

2.2 Antibacterial

One of the advances of modern medicine has been the development of antibiotics; these antibiotics can be bactericidal, which kill the micro-organisms directly, or bacteriostatic, which prevent the growth of micro-organisms [30]. However, micro-organisms are increasingly developing resistance to these antibiotics, which is a major concern. In addition to antibiotics, the prevention of bacterial diseases can be carried out with the use of vaccines and with basic sanitary methods [30, 31].

Many different micro-organisms can cause disease and be transmitted even by contaminated water, and among the major aquatic pathogens are *Escherichia coli* and *Pseudomonas aeruginosa. S*ome studies have already shown that honey can combat these pathogens [14, 18, 32, 33]. A study in 2011 tested the bacterial activity of honey, for which the Revamil® and Manuka honey were used, and it was found that both honeys had activity against *Escherichia coli*, *Pseudomonas aeruginosa*, and also against *Bacillus subtilis* [34]. Manuka honey still had a greater efficacy than Revamil® against *Staphylococcus aureus-methicillin resistant* bacteria after 24-h incubation [34]. Despite the efficiency of honey, propolis has higher antibacterial activity against *Staphylococcus aureus* [35]. Overall, Revamil® honey clearly had more potent bactericidal activity than Manuka after 2 h of incubation, while Manuka honey was more potent after 24 h [34].

The bacteria *Streptococcus pyogenes* and *Streptococcus pneumoniae* are important human respiratory pathogens; *Streptococcus pneumoniae* can cause invasive lung infections that can develop in secondary infections and other respiratory disorders [14]. The antibacterial activity of honey was tested using dressings soaked with two types of honey, including Aquacel-Tualang honey and Aquacel-Manuka honey, the conventional dressing for burn treatment, Aquacel-Ag and only the curative Aquacel (control), against bacteria isolated from patients with burns (*in vitro*) [30]. Seven organisms were isolated from burns, four types of Gram-negative bacteria, *Enterobacter cloacae*, *Klebsiella pneumoniae*, *Pseudomonas* spp., and *Acinetobacter* spp., and three Gram-positive bacteria, *Staphylococcus aureus*, Coagulase-negative *Staphylococcus aureus*, and *Streptococcus* spp. Aquacel-Ag and Aquacel-Manuka dressings provided a better zone of inhibition for Gram-positive bacteria. However, similar results between Aquacel-Manuka and Aquacel-Tualang were obtained against Gram-negative bacteria [36].

Salmonellosis is a gastrointestinal disease caused by eating food contaminated with *Salmonella*, such as eggs, chicken, meat, and raw vegetables, or by handling animal or animal products contaminated by the bacterium [14, 37]. It is the most common bacterial food infection in the United States. However, most *Escherichia coli* strains are not pathogenic to humans, but the few pathogenic strains of *Escherichia coli* are transmitted by food and produce potent enterotoxins [14]. In the literature, there are several studies that demonstrate the efficiency of honey against bacteria important to human health, one of them demonstrated the antibacterial potential of honey against clinical isolates of *Escherichia coli*, *Pseudomonas aeruginosa*, and *Salmonella enterica Typhi* by *in vitro* methods [38]. Honey showed excellent antibacterial activity against all bacteria studied, which are related, respectively, to urinary tract infection, skin lesion, and enteric fever in human

patients; and thus, honey can be considered an alternative treatment against such infection [38]. In addition to honey being effective against bacterial infections, it can be used as a treatment for one of the most common bacterial contamination symptoms, when honey is administered as oral rehydration fluid, it can decrease the duration of bacterial diarrhea [39].

Another form of food poisoning is caused by enterotoxins produced by Gram-positive bacteria, such as *Staphylococcus aureus*; these toxins cause nausea, vomiting, diarrhea, and dehydration, and is a major public health problem [14, 40]. The antibacterial action of Tualang, Gelam, and Durian honeys was tested against *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Enterococcus faecium*, *Enterococcus faecalis*, *Escherichia coli*, *Salmonella enterica Typhi*, and *Klebsiella pneumoniae* [41]. Durian honey did not produce substantial antibacterial activity, while Tualang and Gelam honey showed a spectrum of antibacterial activity with its growth inhibitory effects against all bacterial species tested, including vancomycin-resistant *Enterococci* (VRE), the results still suggest the Gelam honey has the highest antibacterial effect among the honey samples from Malaysia tested [41].

Clostridiums are anaerobic bacteria that are capable of growing up in canned food [14]. In addition to the antibacterial activity of honey against the bacteria dating to the top, Manuka honey still has antibacterial effect on *Clostridium difficile*, which is a Gram-positive anaerobic bacillus, which was associated with approximately 29,000 deaths in 2001 in the United States [42, 43]. A recent study has shown that Manuka honey exhibited a bactericidal action against *Clostridium difficile*; this is yet another feature that makes Manuka honey highly attractive in the treatment of bacterial infections [42]. However, Manuka honey was considered ineffective against other bacteria *Helicobacter pylori* when tested *in vivo*, despite having been found effective *in vitro* [44, 45].

Honey has an excellent antibacterial effect against different types of bacteria, as previously mentioned; honey is very acidic and has a very high sugar content, which does not serve as a suitable medium for bacteria [4–7]. Moreover, in some honeys, the peroxide of hydrogen is found, which has a strong antibacterial effect [4–7]. Remavil® honeys, Manuka honey, Tualang honey, and Gelam honey were tested with different types of bacteria and had positive results [34, 36, 41, 42]. The bacteria tested and susceptible to some of these honeys were *Escherichia coli*, *Pseudomonas aeruginosa*, *Pseudomonas* spp., *Bacillus subtilis*, *Staphylococcus aureus*, *Staphylococcus aureus-resistant methicillin*, *coagulase-negative Staphylococcus aureus*, *Staphylococcus epidermidis*, *Enterobacter cloacae*, *Klebsiella pneumoniae*, *Acinetobacter* spp., *Streptococcus* spp., *Enterococcus faecium*, *Enterococcus faecalis*, *Salmonella enterica serovar Typhimurium*, *vancomycin-resistant Enterococci*, and *Clostridium difficile* [34, 36, 38, 41, 42].

2.3 Antivirals

Of all human infectious diseases, the most prevalent and difficult to treat are those that are caused by viruses, because viruses usually remain infectious in dry mucus for a long time [14]. Also, viruses need a host cells to occur its replication; so killing the virus means killing your host cell as well. Hence, vaccination is the most efficient way to prevent these diseases [14, 46].

Chickenpox is caused by the varicella-zoster virus and it is a very common childhood disease that usually does not cause many problems; but when it affects the elderly, it can be easily fatal [14, 47]. Varicella-zoster is highly contagious and is transmitted by infectious droplets, which results in a systemic rash on the skin [14]. As honey can be conveniently applied to the skin, it is easily found and relatively inexpensive, it can be considered an excellent remedy against Zoster rash, especially

in developing countries, or in countries where antiviral drugs are relatively expensive and difficult to access. Therefore, a study determined *in vitro* antiviral effect of honey against the varicella-zoster virus; two types of honey were used, Manuka honey and clover honey, and both types showed antiviral activity against the varicella-zoster virus, showing that honey has significant antiviral activity against varicella-zoster [48]. A study on the relationship of honey to another virus, analyzed *in vivo*, showed that the use of topical honey is safe and effective in the treatment of recurrent herpes and genital herpes lesions [49].

Respiratory syncytial virus is the most common cause of viral respiratory infections in infants and young children, also seriously affects adults, the elderly and immunocompromised, causing deaths mainly in the elderly [50, 51]. The antiviral activity of honey was tested for its action against the respiratory syncytial virus. A variety of tests using cell culture was developed to assess the susceptibility of respiratory syncytial virus to honey. The results confirmed that treatment with honey promoted inhibition of viral replication [50]. Attempts to isolate the antiviral component in honey demonstrated that sugar was not responsible for the inhibition of respiratory syncytial virus, but could be methylglyoxal; this component of honey may play a role in the increased potency of Manuka honey against respiratory syncytial virus [50]. Thus, honey may be an alternative and effective antiviral treatment for the therapy of respiratory viral infections, such as respiratory syncytial virus; however, other measures, such as an effective vaccine, are still necessary for the control of this disease [50, 52].

Influenza is a highly infectious respiratory disease of viral origin that causes even more deaths than the respiratory syncytial virus at all ages, except in children less than a year old [14, 51]. Influenza viruses are transmitted from person to person through the air, especially from droplets expelled during coughing and sneezing and are a serious threat to human health, and there is an urgent need for the development of new drugs against these viruses. Therefore, the anti-influenza virus activity of honey from several sources was studied [53]. The results showed that honey, in general, and particularly Manuka honey, has potent inhibitory activity against the influenza virus, demonstrating a potential medicinal value [53]. In addition to honey, propolis has also been studied against the influenza virus and appears to decrease the activity of the influenza virus [54].

Honey, especially Manuka honey, has strong antiviral properties. Studies show that honey has action against the varicella-zoster virus, the respiratory syncytial virus, and also has anti-influenza activity [47, 50, 53]. New studies on this property of honey are necessary, mainly with other types of honey.

2.4 Antifungal

Most people associate fungi with organic matter decomposition or superficial fungal infections, but fungi can cause various human diseases, from mild to firmly established systemic diseases; the most serious infections can even be fatal [14]. The incidence of *Candida* infections is increasing worldwide. *Candida albicans* is present in the normal human microbiota; however, this fungus can cause a variety of diseases, such as vaginal, oral, and systemic infections, especially in immunosuppressed patients, as carriers of the HIV virus, these infections can be further aggravated by the increase in resistance levels of this fungus to the medicines [14, 55, 56]. Clinical isolates of *Candida albicans*, *Candida glabrata*, and *Candida dubliniensis* were tested against four different honeys. The antifungal activities of floral honeys were significantly higher than artificial honey against *Candida albicans* and *Candida glabrata*; but for *Candida dubliniensis*, only Jarrah honey was significantly active [56]. *Candida glabrata*, which is innate less susceptible to many conventional antifungals, was also the least susceptible to the honey tested [56].

As previously stated, honey has antifungal properties and may act against *Candida* [57]. A study in 2012 evaluated the clinical and mycological cure rates of a mixture of honey and vaginal mucus compared to local antifungal agents for the treatment of patients with vulvovaginal candidiasis during pregnancy, recurrent asymptomatic candidiasis in early pregnancy is associated with preterm birth [57, 58]. The clinical cure rate was significantly higher in the honey and mucus group than in the conventional antifungal group, while the mycological cure rate was higher in the conventional antifungal group than in the mucus and honey group; therefore, the mixture of honey and mucus can be used with a complement or an alternative to antifungal agents, especially in patients with vulvovaginal candidiasis during pregnancy [57].

In addition to the antifungal activity of honey against *Candida albicans*, the antifungal activity against *Rhodotorula* sp. was studied; this fungus can also affect humans, cases of meningitis caused by *Rhodotorula* species in immunosuppressed people have been reported [59, 60]. Four honeys from Algeria from different botanical origins were analyzed to test the antifungal effect against *Candida albicans* and *Rhodotorula* sp., different concentrations of honey were studied *in vitro* for antifungal activity, and the study demonstrated that, *in vitro*, these natural products clearly show antifungal activity against *Rhodotorula* sp. and *Candida albicans* [60].

Aspergillus spp. is a saprophyte commonly found in nature as a mold of leaves, produces potent allergens, and often causes asthma and other hypersensitivity reactions [14]. The antifungal activities of some samples of honey obtained from different geographic locations in Nigeria were tested against some fungal isolates [61]. Honey samples were examined for antifungal activity against *Aspergillus niger*, *Aspergillus flavus*, *Penicillium chrysogenum*, *Microsporum gypseum*, *Candida albicans*, and *Saccharomyces* sp., and results show that honey samples had different levels of inhibitory activity at various concentrations against the fungi tested, with zones of inhibition increasing with increasing honey concentration; *Microsporum gypseum*, which can infect immunosuppressed patients, was the most sensitive of all fungal isolates studied, while *Candida albicans* was the least sensitive, other studies have shown efficient inhibitory activity of honey against the growth of *Candida albicans* [61–64]. Honey samples used in the study showed spectrum and promising antifungal activity, the honey from Nigeria may serve as a source of antifungal for possible development of antifungal drugs for the treatment of fungal infections [61].

Besides the antibacterial and antiviral properties, some honeys also have antifungal properties [56, 57, 59, 61]. Recent studies showed some honey have properties against *Candida albicans*, *Candida glabrata*, *Candida dubliniensis*, *Rhodotorula* sp., *Aspergillus niger*, *Aspergillus flavus*, *Penicillium chrysogenum*, *Microsporum gypseum*, and *Saccharomyces* sp., which make these honey as possible alternative medicines, especially against candidiasis, a disease that is growing worldwide [24, 56, 59, 61].

2.5 Anticancer

In 2016, the cancer mortality rate has dropped 23% since 1991 [65]. Despite this progress, mortality rates are increasing for liver, pancreatic, and uterine cancers; and cancer is now the leading cause of death in 21 states from United States, lung cancer is still the most lethal, followed by breast cancer [65, 66]. The advance for cancer treatment needs more clinical and basic research [65].

Many scientists have focused on the antioxidant property of honey. Studies indicate that ingestion of honeybee products, such as honey, can prevent cancer [67, 68]. Through the use of human renal cancer cells, the antiproliferative activities, apoptosis, and the antitumor activity of honey were investigated [67]. Honey decreased cell viability in malignant cells regardless of concentration and time [67]. Honey induced

apoptosis of human renal cancer cells according to honey concentration, and apoptosis plays an important role, most of the drugs used in the treatment of cancer are apoptotic inducers, so the apoptotic nature of honey is considered vital [67].

The anticancer activity of honey samples was extracted from three different Egyptian floral sources and was tested against colon, breast, and liver tumor lineage [69]. Cassia honey showed moderate cytotoxic activity against colon cancer and breast cancer, with the weakest cytotoxic activity against liver cancer; Citrus honey exhibited the highest cytotoxic activity against breast cancer; and Ziziphus honey showed potent efficiency against colon, liver, and breast cancer [69]. Breast cancer, which is the type of cancer that most affects and kills women, was also tested for another type of honey, the Manuka honey, and the results showed that it is cytotoxic to MCF-7 breast cancer cells *in vitro* and the effects are mainly correlated with the total content of phenols and their antioxidant power [65, 70].

The phytochemical content and antioxidant activity of melon honey and Manuka honey and their cytotoxic properties were tested against human and metastatic colon adenocarcinoma. The ability to induce apoptosis in colon cancer cells depends on the concentration of honey and type of cell line, in addition to having a great relation with the phenolic content and residues of tryptophan. Honey was analyzed for phenolic, flavonoid, amino acid, and protein contents, as well as their free radical scavenging activities [71, 72]. Melon honey presented the highest amount of phenolics, flavonoids, amino acids, and proteins, as well as antioxidant capacity in relation to Manuka honey [71]. Both melon honey and Manuka honey induced cytotoxicity and cell death independently of dose and time in human and metastatic colon adenocarcinoma cells [71]. Melon honey showed to be more efficient in concentrations [71]. The results indicate that melon honey and Manuka honey can induce inhibition of cell growth and the generation of reactive oxygen species in colon adenocarcinoma and metastatic cells, which may be due to the presence of phytochemicals with antioxidant properties. These results suggest a potential chemo-preventive agent against colon cancer; in addition, honey can improve the functioning of other substances already used in cancer treatment [71, 73].

Research on cancer control has shown the importance of adjuvant therapies [74]. *Aloe vera* may reduce tumor mass and rates of metastasis, and its association with conventional therapy can produce benefits for the treatment, while honey may inhibit tumor growth [74, 75]. The influence of *Aloe vera* and honey on tumor growth and the apoptosis process was evaluated by evaluating tumor size, the rate of cell proliferation for Walker 256 carcinoma [74]. Tumor-bearing mice received a daily dose of *Aloe vera* and honey, and the control group received only sodium chloride solution [74]. The effect of *Aloe vera* and honey against tumor growth was observed through a decrease in relative weight (%) [74]. The results suggested that *Aloe vera* and honey can modulate tumor growth, reduce cell proliferation, and increase susceptibility to apoptosis. Studies have shown that honey has antiproliferative activity because of its ability to induce apoptosis, so this combination is a possible adjuvant therapy [74, 76, 77].

Several types of honey have been studied because of their anticancer properties [65, 67, 69–71, 74]. Currently, cancer is one of the world's leading diseases, requiring further studies [65]. Some honey have already been tested against colon, breast, and liver tumor, as well as human kidney cancer and Ehrlich ascites carcinoma cell lines, where most have weak to strong cytotoxic activity depending on the type of honey tested and depending on the dose of honey [67, 69–71]. The effect of *Aloe vera* on honey has also been studied, and the whole has the capacity to modulate tumor growth, reducing cell proliferation, and also increasing susceptibility to apoptosis [74]. The antitumor effects of honey were highly correlated with their ability to induce apoptosis of cells and with their antioxidant power [65, 67, 69–71, 74]. The

effect of *Aloe vera* along with honey has also been studied, and the set has the capacity to modulate tumor growth, reducing cell proliferation, and also increasing susceptibility to apoptosis [74]. The antitumor effects of honey were highly correlated with its ability to induce cell apoptosis and with its antioxidant activity [65, 67, 69–71, 74].

2.6 Antioxidants

Antioxidants, which are present in large amounts of honey, making it a food with great antioxidative potential, are free radical scavengers that reduce the formation or neutralize free radicals [11, 78]. A comparative analysis of total phenolic content and antioxidant potential of commercially available common honey was performed along with Malaysia's Tualang honey. Biochemical analyzes revealed a significantly high phenolic content in Tualang honey [78]. In addition, the antioxidant capacity of Tualang honey was higher than that of common honey; these data suggested that the high activity of elimination of free radicals and antioxidant activity observed in Tualang honey were due to the increase in the level of phenolic compounds, it was also observed that the antioxidant activity of honey depends on its botanical origin [78, 79]. Therefore, the favorable antioxidant properties of Tualang honey can be important for nutrition and human health [78].

Type 2 diabetes consists of progressive hyperglycemia, insulin resistance, and β-pancreatic cell failure, which may result from glucose toxicity, inflammatory cytokines, and oxidative stress, and is responsible for 90–95% of all cases of diabetes [80, 81]. A study investigated the effect of pre-treatment with Gelam honey, and the individual flavonoid components chrysin, luteolin, and quercetin on the production of reactive oxygen species, cell viability, lipid peroxidation, and insulin in hamster pancreatic cells, cultured under normal conditions and hyperglycemic, the pre-treatment of cells with Gelam honey extract or flavonoid components showed a significant decrease in the production of reactive oxygen species, glucose-induced lipid peroxidation, and a significant increase in insulin content and viability of cultured cells under hyperglycemic conditions. The results indicated the *in vitro* antioxidant property of Gelam honey and flavonoids on hamster β cells, creating a protective effect against hyperglycemia [80]. Another study demonstrated the effect of honey on diabetics, the study with rats concluded that the pancreatic tissues of rats with diabetes were exposed to great oxidative stress and that supplementation with other honey, Tualang honey, had protective effects in the pancreas [80, 82].

Honey contains antioxidants, such as phenolic compounds that prevent cellular oxidative damage that leads to aging, disease such as cancer, metabolic disturbances, cardiovascular dysfunction and even death [83, 84]. The antioxidant effect of honey in young and middle-aged rats was compared, the rats were fed with pure water (control), those supplemented with 2.5 and 5.0 g/kg of Gelam honey for 30 days. Results showed that Gelam honey supplementation reduced DNA damage, plasma malondialdehyde level, and glutathione peroxidase. Liver activity superoxide dismutase also decreased in young rats supplemented with 5 g/kg of Gelam honey [84]. Gelam honey reduces the oxidative damage of young and middle-aged rats by modulating the activities of the antioxidant enzymes that were more prominent in higher concentration compared to the lower concentration [84]. Another study indicates that honey has these antioxidant and free radical sequestering properties, mainly due to its phenolic compounds [85].

Honey has antioxidant properties that can be further explored and studied, because antioxidants reduce free radicals and oxidative stress, which can help to promote and maintain health [80, 82, 84]. Besides the previously described, the antioxidant effect of honey can be an important property to help in the anticancer effect [67, 71].

3. Conclusions

Several studies have proven the effectiveness of honey as an alternative medicine; some have even shown that honey is as good a medicine as conventional medicine. Use of different types of honeys showed anti-inflammatory effect very similar to the conventional drug and that can be used as an alternative medicine in the treatment of diseases or inflammations. Honey can also be used as an antimicrobial agent anti-inflammatory, antibacterial, antivirals, antifungal, anticancer, and antioxidants. However, there is still a need to increase research on honey, especially in its potential as a medicine and also a dissemination of this knowledge to the population and the medical community, so an increase in the use of this powerful compound will be possible.

Conflict of interest

The authors declare that there is no conflict of interest.

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