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Quality, composition and health effects of natural honey: a review

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ABSTRACT: One of the most important foods produced and consumed worldwide is natural honey. This substance features nice sensory qualities such as a light hue as well as a familiar scent and flavor. It also contains organic acids, sugars, minerals, enzymes, phenolic and volatile chemicals, methylglyoxal, amino acids, vitamins etcetera which have been linked to potential biological activities. All of these features make this viscous substance extremely desirable by consumers thus raising its market value. Natural honey is however prone to contamination upon improper storage so that its natural quality and authenticity can be jeopardized. In this regard, the purpose of this study is to provide updates to the literature available on the physicochemical, sensory features, content, economic value, medicinal benefits, contamination, originality, and adulteration of natural honey. With this context, we hope to provide data that can help guide future honey study.

1. INTRODUCTION

Honey is an all-natural substance that has been used for thousands of years as a medicine. It's chemical make-up varies depending on certain factors namely; the kind of flowers used to produce it, the time of year, the weather and the processing methods used (Adgaba et al., 2017). The unique nutritional and therapeutic benefits of this sweet and viscous substance have been confirmed by current science (Nainu et al., 2021), as it has been demonstrated to be effective against a wide variety of bacteria, including Salmonella spp and E. coli (Obey et al., 2022). Additionally, honey has been shown to be effective in the treatment of a variety of skin conditions, including ulcers, bedsores, acne, burns, and wounds (Nainu et al., 2021). The flavonoids and polyphenols in propolis, which are present in high concentrations in natural and high-quality honey are significant antioxidants (Habryka et al., 2020), and these antioxidants benefit cardiovascular health through lowering of blood pressure and reducing of the likelihood of heart attacks and strokes (Duman, 2019). Moreover, these antioxidants may improve eye health and perhaps lower the risk of some types of cancers (Yelin & Kuntadi, 2019). It has been pointed out that the high levels of amino acids, vitamin B6, thiamine, niacin, riboflavin, and pantothenic acid present in honey make it an effective immune system booster, however the precise amounts for this action depend on both the floral origin and quality of the honey (Hrubša et al., 2022). Honey also contains significant amounts of other minerals, such as calcium, copper, iron, magnesium, manganese, phosphorus, potassium, sodium, and zinc (Ani et al., 2020). The iron, copper, and manganese concentrations in this substance are primarily responsible for its extraordinary ability to increase hemoglobin production in the body (Ani et al., 2020). According to Ayurvedic scriptures, the substance aids in regulating hemoglobin and red blood cells counts (RBCs) (Kuhn et al., 2017).

Several enzymes, including glucose oxidase, invertase, amylase, catalase, diastase and many more are contained in honey (Porcza et al., 2016), with invertase (saccharase), diastase (amylase), and glucose oxidase been the most abun-

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dant (Samarghandian et al., 2016). These enzymes play crucial roles in the turning of sugar into honey (Đogo Mračević et al., 2020). Glucose oxidase for instance, converts glucose into hydrogen peroxide (with antibacterial characteristics) and gluconic acid (which aids in calcium absorption) Bobis et al. (2020), invertase breaks down sucrose into simpler sugars like fructose and glucose, amylase breaks long chains of starch into dextrin and maltose and catalase aids in the breakdown of hydrogen peroxide into oxygen and water (Porcza et al., 2016). It is the aim of this study is to provide updates to the literature available on the physicochemical, sensory features, content, economic value, medicinal benefits, contamination, originality, and adulteration of natural honey hoping that this information should aid further research on honey.

2. THE PHYSIOCHEMICAL COMPOSITIONS OF NATURAL HONEY

2.1. MOISTURE

One most distinguishing feature which impacts the viscosity, specific gravity, maturity, crystallization, taste, preservation, shelf life, and palatability of honey is its water content Zolghadri et al. (2019). That is to say that the sensory qualities, nutritional properties, self life and etcetera of honey may all be adversely impacted (crystallization may be caused and the growth of osmophilic microbes responsible for fermentation may be encouraged) by an excess of moisture (above 19%) (Petrillo et al., 2018). Several other variables, including the kind of bees, the flowers they forage from, the time of the year and the weather all play roles in determining the quality of honey (Pasupuleti et al., 2017).

2.2. PH

Hydrogen ion concentration in honey solutions (pH) is measured because it affects the synthesis of compounds like hydroxymethylfurfural (HMF) (Rahman et al., 2014). Honey's buffer acids and minerals are also helpful supplementary variables in determining the product quality and as a metric for measuring overall acidity (L.R. Silva et al., 2009). Honey's pH may vary from around 3.5 to about 5.5, depending on the plant it came from, the pH of the nectar, the soil it was grown in, and the amounts of various acids and minerals present, such as calcium, sodium, potassium, and other ash components (Wagner et al., 2002). Value changes might suggest fermentation or tampering (Kalogeropoulos et al., 2009). The honey vesicle is used to convey nectar to the hive but on the way, the bees may add chemicals from their mandibles to the nectar which might alter the honey's pH (L.R. Silva et al., 2009). Speaking of the acidity of honey, which may occur from the activity of the enzyme glucose oxidase generated in the hypopharyngeal glands of the bees which results in the production of gluconic acid. The acidity may vary depending on the levels of certain organic acids and inorganic ions like phosphate and the nectar supply. The glucose oxidase enzyme is not destroyed by heat or acid during processing thus, may continue to impact the honey even after it has been refined and stored (Balouiri et al., 2016). Honey's organic acids make up only around 0.5% of the solids, yet they provide a lot of flavor (Zainol et al., 2013).

2.3. ASH

Honey's high ash level is indicative of its high mineral concentration Mandal and Mandal (2011). There are trace quantities of the minerals calcium (Ca), magnesium (Mg), iron (Fe), copper (Cu), cadmium (Cd), and zinc (Zn) in the form of sulfate (SO_4^{2-}) and chloride ions (Cl^-) (M.S. Silva et al., 2017). Honey's color may be affected by the presence of minerals which are usually more prevalent in dark than in light honey (Nwuche et al., 2013).

2.4. ELECTRIC CONDUCTIVITY

The capacity of ions in a solution to transport electrons is what gives the solution its electrical conductivity. It correlates with ash level, pH, acidity, minerals, proteins and other chemicals in honey (Faustino & Pinheiro, 2021), and it may help identify honey's botanical origin. The conductivity of honey is a useful measure of whether or not it has been altered from its natural state which is either nectar (with significant variation across species) or honeydew (Bogdanov et al., 2008).

2.5. COLOR

The factor for customer choice in honey is its color and this affects its pricing which is especially significant on the global market (dine et al., 2019). Color change can occur depending on a number of factors including; the minerals it contains, how it was stored and processed, the weather conditions during the nectar flow, the temperature at which it ripens in the hive, the ratio of fructose to glucose, nitrogen content and the instability of fructose in an acid solution.

2.6. REDUCING SUGARS, TOTAL REDUCING SUGARS, SUCROSE AND HYDROXYMETHYLFURFURAL

Honey is mostly composed of water and sugars (which account for 95% of the dry weight). The monosaccharides: glucose and fructose which together account for around 85 percent of the carbohydrates in honey from the Apis genus, are called reducing sugars because of their capacity to decrease copper ions in an alkaline solution. Although both fructose and glucose contribute to honey's sweetness, fructose's strong hygroscopicity makes it more palatable while glucose's weak solubility has a tendency to affect crystallization (Truzzi et al., 2014). Fructose is the most common form of sugar in honey because it affects the honey's ability to crystallize thus making liquid honey more stable. Succrose and maltose, two disaccharides make up 10% of the sugars in honey (Idris et al., 2011). In general, honey from the Apis genus contains between 2% and 3% sucrose. Honey with a relative humidity exceeding 20% (Aumeeruddy et al., 2019) is likely to be tainted or collected prematurely

To produce hydroxymethylfurfural (HMF), sugars are dehydrated directly under acidic circumstances, mostly from the breakdown of fructose which occurs during the heating process of the Maillard reaction (Z. Wang et al., 2021). When present in large concentrations, it may be harmful to human health, when present in trace amounts however, HMF is a quality indication that may aid one to tell the difference between an aged honey and one freshly harvested. Concentrations beyond the legal limit may indicate any one of the following; that inverted sugar (syrup) was added during processing, that the product was improperly kept, that it was heated, or that it was contaminated with acid, water, or minerals (Bobis et al., 2020).

2.7. PROTEIN

The proteinaceous substances (major royal jelly) which are found only in trace amounts in honey can be utilized to identify suspected adulterations in the commercial product (Guerrini et al., 2009). They are also a way to tell when honey has reached peak flavor (Ellah & G, 2020). Plants and animals both contribute to honey's protein content. For example, the bee's own salivary gland secretions and other materials gathered during the collection of nectar and honey ripening make up the animal protein source (D. Silva et al., 2016), while nectar and pollen gathered from the wild provide the plant protein source

2.8. VISCOSITY

The viscosity and other physicochemical qualities of honey are sensitive to a wide range of variables, including its chemical make-up and temperature. Since viscosity typically decreases with increasing water content, water content is one of the most crucial elements for viscosity (Živkov Baloš et al., 2018). It is crucial in understanding its quality because the resulting rheological models may be used to correlate the concentration, temperature, pH, and maturation index of a fluid with its rheological characteristics. This information is crucial for ensuring the quality of equipment and processes across production lines during the intermediate control stage Kivrak et al. (2016).

2.9. DIASTASE ACTIVITY

A wide variety of enzymes although only in trace amounts are contained in honey. Honeybees and nectar plants produce these enzymes and pollen grains contain them in trace amounts (Bogdanov, 2009). Diastase is a crucial enzyme and its amount contained in honey varies depending on its place of origin and botanical inspiration. Hydrolyzing the starch molecule is its primary function but it also serves as a quality indicator (Radia et al., 2015), and as well, the digestion of pollen may need the presence of this enzyme. Denaturing the honey by heating it over its melting point reduces its quality and alters the diastase activity which is intimately linked to the honey's structure (Ajlouni & Sujirapinyokul, 2010). Samples of honey collected at times of rapid nectar flow show signs of lower enzyme levels owing to the buildup of the material processed inside the hive.

2.10. WATER ACTIVITY

Water is an important component of many diets, hence the idea of water activity has been used to examine how water interacts with other dietary components da Silva et al. (2020). Microbial activity in honey is hindered by the fact that its water activity is low. Water activity is a metric that affects the amount of water in a meal and how readily it can be used for microbial metabolism. Because of this attribute, the product has greater microbial stability (Qi et al., 2020). This improves its quality, preservation and shelf life. The water activity measurement is set to 0.0 when there is no water present in the meal, and to 1.0 (da Silva et al., 2020) when the sample is made up completely of pure water.

3. MEDICINAL BENEFITS OF HONEY

3.1. WOUND HEALING EFFECTS

Wound healing is one most well-researched and beneficial applications of honey Huyck et al. (2012). During World War I, the Russians found that using honey on wounds helped keep them from becoming infected and sped up the healing process. Also in order to heal wounds such as ulcers, burns, fistulas, and boils, the Germans used a combination of cod liver oil and honey (Hseu et al., 2020). Honey has therefore been shown to be effective in the treatment of a wide variety of wounds, including those caused by abrasions, abscesses, amputations, bed sores/decubitus ulcers, burns, chill blains, burst abdominal wounds, cracked nipples, fistulas, diabetes, malignancy, leprosy, trauma, cervical, varicose, sickle cell, and septicemia. There are several overlapping processes at work during normal wound healing, such as coagulation, inflammation, cell proliferation, tissue remodeling, and replacement of injured tissue (Taranto et al., 2017). Wound healing is aided by honey since it helps get rid of necrotic tissue during the inflammatory phase, speeds up the remodeling phase and slows down the bacterial growth phase (Terrab et al., 2002). In laparoscopic oncological surgery, honey has been utilized to prevent tumors from implanting themselves in wounds. The substance has also been used to treat open wounds without reports of infection. There is also thought to be a possible therapeutic use of honey in the management of gingivitis and periodontal disease (Boora et al., 2014). A young boy's knee amputation wound which got infected with Pseudomonas aeruginosa and Staphylococcus aureus so that it became resistant to standard therapy healed completely in ten weeks after being dressed with sterilized active manuka honey dressing pads (Herald et al., 2014). Recent research on Fournier's gangrene has also shown encouraging results including a quick reduction in edema and discharge, a speedy recovery with little scarring, successful wound debridement and a lower risk of death upon the application of honey (Chandra et al., 2014).

Other research published recently shows that honey promotes wound healing in IL-6-deficient mice by increasing IL-6 and TNF- production at the wound site (Noreen et al., 2017). The healing process is sped up by the cytokines and interleukins (cytokines) that are released by honey-stimulated lymphocytes, phagocytes, monocytes, and/or macrophages. These include TNF-alpha, IL-1beta, and IL-6 (Mujeeb et al., 2014). Honey's osmolarity and high sugar content also aid in the healing process for should the blood circulation at the wound site be adequate, honey's osmotic impact will drive water out of the wound bed by a straightforward outflow of lymph (Feás et al., 2010). Furthermore, by stimulating the production of 5adenosine monophosphate-activated protein kinase (AMPK) and antioxidant enzymes to reduce oxidative stress, honey has been proven to speed up the healing process after an injury. Endogenous antioxidants are produced by the body and exist in two types: those that rely on enzymes and those that don't. Superoxide dismutase, catalase and glutathione peroxidase are examples of enzymatic antioxidants (GPx) while vitamins E and C, glutathione (GSH) and some other small molecules are among the non-enzymatic antioxidants (Karabagias et al., 2018). All these antioxidants aid wound healing through promotion of mitochondrial activity and the proliferation and migration of human dermal fibroblasts (Karabagias et al., 2018).

The presence of serine proteases and matrix metalloproteases near injury sites is another way by which protein degradation may be facilitated in wounds but there be some inhibitors that prevent these protease enzymes from functioning normally. Hydrogen peroxide ($H_2O_{2)}$ acts to render these inhibitors ineffective so that the proteases may work normally. H_2O_2 therefore operates as a physiological switching stimulus both activating and deactivating these enzymes. Usually, proteases functioning in the body break down the debris and germs in the wound so that the osmotic outflow from honey clears out the broken-down debris with ease. In addendum, H_2O_2 promotes the development of repair cells like fibroblasts and epithelial cells during inflammation. H_2O_2 many also promote cell proliferation and wound healing through activation of nuclear transcription factors (NTFs) (Karabagias et al., 2018).

H_2O_2 in addition activates insulin receptor complexes which in turn set off a cascade of molecular processes in the cell. As a consequence, amino acids and glucose may be taken in more easily promoting cellular development. It is possible that the vitamins, minerals, carbohydrates and amino acids in honey are what fuel the developing cells. Phagocytes are hence better able to consume invading bacteria by using glucose as fuel. New tissue regeneration is also promoted by honey via increased monocyte and lymphocyte proliferation both of which are influenced by cytokines. (Elfirdoussi et al., 2020).

3.1.1 BENEFITS FOR WOUND DRESSING

When honey is applied to a wound, it speeds up the healing process and gets rid of any infection that might have been there. The situation is analogous with burns. A honey dressing may hasten the healing process, disinfect the wound, and ease the discomfort (Onyibe et al., 2021). Both the osmotic outflow and the bioactive impact of honey contribute to the remarkable speed with which it disinfects wounds. Honey's acidity also helps fight germs (Batool et al., 2019). The direct nutritional influence of a variety of amino acids, vitamins and trace minerals on repairing tissues is also important. When honey is put on a wound, the osmotic outflow helps to flush away dirt and other particles lying at the wound's base. Therefore, the dressing is not sticky and may be removed without any discomfort. In cases however where some people may still experience acute pain or distress, a possible explanation is that the acidity of honey irritates exposed nerve terminals (Terrab et al., 2002). Honey's antimicrobial effects may not be the only reason it helps wounds heal as recent studies show that honey, even at concentrations as low as 0.1%, may activate phagocytes and increase the growth of B- and T-lymphocytes in cell culture from peripheral blood (Yücel & Sultano⊠lu, 2013). One research found that natural honey dramatically boosted the production of immune-activating cytokines such as tumor necrosis factor-α (TNF-α), interleukin (IL)-1β, and IL-6 from MonoMac-6 cells (and human monocytes). Because of this, it was hypothesized that honey's wound-healing properties may stem from its ability to activate monocytic cells, which then release inflammatory cytokines (Azonwade et al., 2018). Honey dressing also provides financial benefits for the patient as costs associated with hospital stays, bandages, and surgeries are minimized since patients recover quickly.

Studies comparing honey dressing for burns to amniotic membrane treatment, silver sulfadiazine dressing, and boiling potato peel dressing have also been undertaken. Early healing with a reduced degree of contracture and scarring was seen in instances treated with honey dressing (Edo, Makinde, et al., 2022). Even skin grafts treated with honey according to research show good histological preservation. Using natural honey for the treatment of radiation-induced mucositis has been shown to be successful, as described by (Akpoghelie et al., 2022). In a surprising turn of events, honey was formerly used to diagnose measles in its earliest stages. Massages with honey were said to make measles eruptions worse the day after they are applied but upon repeated application the rash clears up completely (Guerrini et al., 2009).

3.2. EFFECTS OF HONEY IN THE TREATMENT OF INFECTIONS

3.2.1 IN THE TREATMENT OF FUNGAL INFECTIONS

Both in its pure and diluted forms, honey have been shown to have antifungal and antitoxin effects. Aspergillus niger, Aspergillus flavus, Penicillium chrysogenum, Microsporum gypseum, Candida albicans, Saccharomyces, and Malassezia species are all killed by this substance according to studies (Bakier et al., 2016). Honey has also been reported to be effective against cutaneous and superficial mycoses including ringworm and athletes' foot. The high sugar content, glucose oxidase, and methylglyoxal present in honey all contribute to its possible antibacterial impact (Özkök et al., 2010). Although the exact process is still unclear but researchers have proposed a few possible explanations;

Since honey prevents biofilm development, disrupts already-established biofilms and induces changes to the exopolysaccharide structure, it could act as an antifungal agent. Its ability to disrupt the integrity of cell membranes leads to a reduction in biofilm cell surface area and ultimately, cell death or growth inhibition (Achilonu & Umesiobi, 2015). Using an atomic force microscope, researchers found that honey effectively removed all traces of biofilm after halving the thickness of the exopolysaccharide layer (Larayetan et al., 2019). Poor membrane growth in fungi is linked to the suppression of germ-tube development and Scientists have discovered that the flavonoid component of honey suppresses several cellular processes involved in germ tube formation and as well slows the development of the microbe by altering its outer shape and membrane integrity. The proportion of cells in the G0/G1 phase and/or the G2/M phase have also been observed to be decreased by the flavonoid extract of honey thus influencing hyphal transition (Achilonu & Umesiobi, 2015).

3.2.2 IN THE TREATMENT OF VIRAL INFECTIONS

Infections and lesions caused by viruses are often brought about either by naturally occurring or ubiquitous triggers (Larayetan et al., 2019). The results of recent research have shown that honey may have antiviral properties. Several of honey's components including copper; a trace metal that inactivates viruses are responsible for its antiviral properties. The ascorbic acid and flavonoids components of honey similarly impede viral development by preventing viral transcription and translation (Achilonu & Umesiobi, 2015). Evidence from in vitro research indicates that honey may inhibit the growth of several viruses, including those responsible for the spread of herpes simplex and zoster (Edo, Onoharigho, Akpoghelie, et al., 2022). Furthermore, there has been recent discoveries of nitrite and nitrate; two metabolites of nitric oxide (NO) in the salivary gland of bees (Edo, Onoharigho, et al., 2022). The energy molecule NO is known to induce host defense against viruses, including DNA and RNA so that while terminating viral replication, NO also inhibits the growth of viral lesions (Edo, 2022b). The mechanism through which NO inhibits replication is by blocking the production of viral proteins such as polymerase, nucleic acid, and capsid. (Hassan et al., 2020).

3.2.3 HONEY'S SENSITIVITY IN RELATIONS TO OTHER PATHOGENS

It has been shown that honey inhibits the growth of over 60 different bacterial species including both aerobic and anaerobic gram-positive and gram-negative strains (Sajid et al., 2020). There is a wide variety of pathogens that honey has been shown to be effective against including Bacillus anthracis, Corynebacterium diphtheriae, Haemophilus influenzae, Klebsiella pneumoniae, Listeria monocytogenes, Mycobacterium tuberculosis, Pasteurella multicoda, Yersinia enterocolitica, Proteus species, Pseudomonas aeruginosa (Edo, Onoharigho, et al., 2022). Natural honey also displayed an antibacterial action against the community-associated methicillin-resistant S. aureus (MRSA) germ in in-vitro condition, according to a limited number of case studies (Boussaid et al., 2018). Researchers showed that honey had a MIC (minimum inhibitory concentration) against bacteria ranging from 1.8% to 10.8% (v/v) meaning that it was effective against bacteria even after being diluted nine times. (Parvate et al., 2020). Some bacteria responsible for UTIs the likes of E. coli, Proteus species, and S. faecalis, have been shown to be susceptible to the antibacterial action of honey, leading to claims that honey when diluted appropriately may cure UTIs.

The gastritis-causing H. pylori isolate was demonstrated to be suppressed by a 20% honey solution in in vitro tests. Isolates that showed resistance to other antimicrobials nevertheless responded to this treatment (Tornuk et al., 2013). In addition, honey unlike most traditional antibiotics, reportedly does not promote the growth of antibiotic-resistant bacteria and may be used indefinitely Edo (2022a).

Depending on the concentration, honey exhibits bacteriostatic and bactericidal effects. Bacteriostatic activity was attained at concentrations of 5%-11% in both pasture honey and manuka honey (v/v), whereas bactericidal activity was achieved at concentrations of 8%-15% in both. Instead of killing bacteria, fake honey (a sugar solution that mimics honey's composition) only slowed their growth by 20% to 30% (Ruiz-Matute et al., 2007).

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3.3. EFFECTS AGAINST CARDIOVASCULAR DISEASES

Blood glucose, cholesterol, C-reactive protein (CRP) and body weight are all cardiovascular risk factors that honey may help control (Karabagias et al., 2018). Drug treatment particularly anti-arrhythmic medications may be lifesaving in the management of cardiovascular disorders. However, the risks associated with anti-arrhythmic medicines (including potentially fatal arrhythmias in certain patients) have resulted in restrictions on their use Gidamis et al. (2004). As a result, there is a push to provide medications that have fewer side effects and yet, do not sacrifice effectiveness. Historically, people utilized honey for its therapeutic properties. However, much of the research done on its benefits against cardiovascular risk factors including hyperlipidemia and free radical generation has been conducted on animals (Iglesias et al., 2012).It was suggested after one such experiment that the possible function of honey in reducing cardiovascular risks may be due to its content of glucose, fructose, and trace minerals like copper and zinc. In human subjects also, low-density lipoprotein (LDL), high-density lipoprotein cholesterol (HDL-C), triacylglycerole, body fat, glucose and cholesterol levels were all seen to be lowered in the subjects that took 70 g of honey for 30 days. This effect is shown in both cardiac patients and healthy human subjects. Adding to that, honey contains several antioxidants including vitamin C, monophenolics, flavonoids, and polyphenols. Again, it is worthy of note that the risk for cardiovascular diseases is inversely proportional to the regular consumption of these antioxidants and that is to say that the antioxidants work to provide antithrombotic, anti-ischemic, antioxidant and vasorelaxant benefits against coronary heart diseases. Furthermore, flavonoids have been hypothesized and seen to reduce the incidence of CHD via three main mechanisms: enhanced coronary vasodilatation, reduced blood clotting due to impaired platelet function and protection against LDL oxidation (Azonwade et al., 2018). An experiment to ascertain the effects of natural honey on total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triacylglycerole, C-reactive protein (CRP), fasting blood glucose, and body weight was carried out in 38 obese people. Total cholesterol, LDL-C, triacylglycerole, and CRP levels were all seen to be lowered among those who consumed 70 grams of natural honey daily for 30 days. The authors thus found that natural lowers cardiovascular risk factors, especially in people with increased risk factors, and does not cause additional weight gain in subjects who are already overweight or obese (Amit et al., 2017). Human subjects were in another experiment put through a series of tests to compare the effects of consuming 75 grams of real honey to the same quantity of manufactured honey (fructose + glucose). The spikes in insulin and CRP after consuming glucose were much larger than those after consuming honey. Honey moreover lowered total cholesterol, LDL-C and TG while marginally increasing HDL-C. The people with hypertriglyceridemia saw a rise in their TG levels when given imitation honey, whereas those given real honey saw a drop. Synthetic honey was associated with a rise in LDL-C in hyperlipidemic individuals whereas natural honey was associated with a decrease. Although both honey and dextrose raised plasma glucose levels, honey had a far smaller effect on diabetic individuals. Another mechanism of anticardiovascular activity by honey is via nitric oxide (NO) metabolites. Research suggests that the high NO content in honey may provide protection against cardiovascular diseases (Aazza et al., 2018) by the following; controlling blood pressure and vascular tone, blocking platelet aggregation and leukocyte adhesion and stopping the proliferation of smooth muscle cells (Edo, 2022b). Blood arteries are also seen to relax and widen when NO levels rise. Renal regulation of extracellular fluid balance is also dependent on nitric oxide's (NO) vasodilatory function, which is essential for the control of blood pressure and blood flow. Additionally, honey contained flavonoids have been studied for their potential to reduce oxidative stress and boost NO's bioavailability. Two of the most abundant flavonoids in honey cartechin and quercetin have also been recently demonstrated to limit the growth of aortic atherosclerotic lesions and the atherogenic alteration of LDL (Nainu et al., 2021).

Another in vitro investigation found that 45 days of chronic oral treatment of natural honey had powerful anti-arrhythmic and anti-infarction benefits in rats (Eteraf-Oskouei & Najafi, 2021). They found that giving normal or stressed rats natural honey (5 g/kg) for 1 hour prior to an injection of adrenaline (100 mcg/kg) prevented epinephrine-induced vasomotor dysfunction and cardiac abnormalities and maintained the favorable inotropic effect of adrenaline. The authors concluded that the cardioprotective and therapeutic effects of natural honey against adrenaline-induced cardiac and vasomotor dysfunction could either be directly (via its high total antioxidant capacity and enzymatic and non-enzymatic antioxidants, in addition to its substantial quantities of mineral elements such as magnesium, sodium, and chlorine) or indirectly (via the influence of vitamin C on the release of nitric oxide from endothelium) (Kivrak et al., 2016).

Superoxide dismutase, glutathione peroxidase, and glutathione reductase, together with creatine kinase-MB, lactate dehydrogenase, aspartate transaminase, and alanine transaminase, were observed in another study to be restored to pretreatment levels from isoproterenol-induced myocardial infarction in Wistar rats upon treatment with honey. This demonstrates that honey provides protection against the deleterious effects induced by free radicals that are known to be fatal. Honey also demonstrated another effect of decreasing cardiac troponin I (cTnI), triglycerides (TG), total cholesterol (TC), and lipid peroxidation (LPO) products in a rat model of myocardial infarction (Sajid et al., 2020).

3.4. EFFECTS ON GASTROINTESTINAL TRACT DISEASES

The use of honey for the prevention and treatment of bacterial and rotavirus-caused gastrointestinal infections such as gastritis, duodenitis, and gastric ulcers after oral administration has been documented (Manzanares et al., 2014). The first step in the progression of a bacterial infection of the gastrointestinal tract is the attachment of bacteria to mucosal epithelial cells lining the gastrointestinal system. One method for preventing illness is to prevent harmful germs from attaching to the intestinal epithelium. Honey's ability to inhibit bacterial adhesion was shown to be independent of its impact on epithelial cells, as shown by (da Silva et al., 2020). This ability to inhibit bacterial adhesion may be attributed to a number of factors and some of the fractions inside honey may affect the electrostatic charge or hydrophobicity of bacteria, both of which have been documented to be essential variables in the interaction of bacteria with host cells.

Furthermore, Honey has been discovered to be an effective treatment for diarrhea and gastroenteritis (Pasupuleti et al., 2017). When used in replacement fluid at a concentration of 5% (v/v), honey was shown to be more effective than sugar in reducing the length of diarrhea in instances of bacterial gastroenteritis. And in virus-caused stomach flu that showed no signs of abating, honey improved rehydration fluid by boosting potassium and water intake while decreasing salt intake. It acts as an anti-inflammatory agent, aiding in the healing of injured intestinal mucosa and promoting the development of new tissue (Radia et al., 2015). Oral pretreatment with honey (2 g/kg) reduced gastric indomethacin-induced lesions, microvascular permeability, and myeloperoxidase activity, as shown by (Nasution & Zahrah, 2014). Honey's antibacterial activity is around average, making it effective against H. Pylori owing to the presence of hydrogen peroxide at a concentration of 20%.

The extent of the lesions induced by ethanol was significantly reduced after perfusion of the stomach with isotonic honey to test the cytoprotective capabilities of natural honey (Sanz et al., 2005). Natural honey may also be used in place of sucralfate in the treatment of peptic ulcer disease, since it has been shown to have curative effects for the recovery of antral ulcers (Yelin & Kuntadi, 2019).

3.5. ANTIOXIDANT ACTIVITY

We now know that radicals change molecules and genes in many different kinds of organisms. In fact, oxidative stress has been linked to 86 different illnesses. Antioxidants are substances that prevent further damage from occurring due to free radicals in lipid bilayers and membranes. Many long-lasting, chronic and degenerative diseases including cancer, aging, atherosclerosis, and mutagen synthesis are due to oxidative stress (George & Abrahamse, 2020). To combat free radicals, the body produces endogenous antioxidants such as vitamin C, vitamin E, and glutathione (Kečkeš et al., 2013). Other protective agents include catalase, superoxide dismutase, peroxidase, ascorbic acid, and tocopherol and sugars, proteins, fats, and nucleic acids (Sharifi-Rad et al., 2020). Significant antioxidant activity has also been reported in honey. Apigenin, pinocembrin, kaempferol, quercetin, galangin, chrysin, and hesperetin are some of the flavonoides found in it that elicit these actions. Phenolic acids like ellagic acid, caffeic acid, p-coumaric acid, and ferulic acid, vitamin C, tocopherols, catalase, superoxide dismutase, and reduced glutathione too are present. A synergistic antioxidant action is produced by the majority of the chemicals listed. Due to its antioxidant properties, honey has been proposed as a safe and effective substitute for artificial preservatives such sodium tripolyphosphate in food storage (Chua & Adnan, 2014).

Most of honey's antioxidant activity is determined by its plant origin, whereas the rest is only somewhat influenced by its processing, handling, and storage conditions (Edo, Onoharigho, et al., 2022). Strongly linked with antioxidant activity is honey's total phenolic content. Additionally, a robust relationship was discovered between the hue of honey and its antioxidant power. For instance, the overall phenolic content of black honey is greater and hence its antioxidant activity says a number of studies (Damto, 2019). The antioxidant qualities of honey may be quantified by testing its ability to scavenge free radicals using assays including the oxygen radical absorbance capacity (ORAC) assay, the 1,1-diphenyl-2-picrylhydrazyl (DPPH) scavenging assay and the ferric reducing antioxidant power (FRAP) assay (Escriche et al., 2014). High antioxidant capabilities in honey have been said to vary depending on the floral variety and region (Onoharigho et al., 2022). Honey (1.2 g/kg) was in a certain study shown to increase beta-carotene, vitamin C, glutathione reductase, uric acid levels and antioxidant activity in healthy adult volunteers Geană et al. (2020). There is debate about the precise antioxidant mechanism however. Some hypothesized processes include free radical sequestration, hydrogen donation, metallic ion chelation, flavonoids' substrate action for hydroxyl, and superoxide radical activities.

3.6. ANTI-INFLAMMATORY EFFECTS

When vascular tissues are exposed to harmful stimuli, they respond with a complicated biological process known as inflammation. It's a protective mechanism that the body employs to get rid of whatever infections or stimuli caused the harm. Inflammation may be either acute or chronic. Acute inflammation occurs quickly after a stimulus has entered the body and also manifests clinically as redness, discomfort, itching, and functional impairment (D. Wang et al., 2021). Acute inflammation not properly addressed in a timely manner might progress into chronic inflammation. Many chronic illnesses and disorders point to it as a primary contributor. Consequently, liver disorders (Gulec et al., 2014), renal diseases (Kharchoufa et al., 2020), and different cancers (Edo, 2022a) are thought to be combatable through anti-inflammatory activity. Cytokines, cyclooxygenases (COXs), lipoxygenases (LOXs), mitogens, macrophages, tumor necrosis factor (TNF) and many other elements of inflammatory pathways (Mitogen-activated protein kinase (MAPK) and nuclear factor kappa B (NF-B)) (Hseu et al., 2020) are also involved in the inflammation process and several additional inflammatory mediators, enzymes, cytokines, proteins and genes are induced after MAPK and NF-B activation, including cyclooxygenase-2 (COX-2), lipoxygenase-2 (LOX-2), C-reactive protein (CRP), interleukins (IL-1, IL-6, and IL-10) and tumor necrosis factor alpha (TNF-) too.

It is widely established that honey has anti-inflammatory effects although it is still unclear how exactly it does this. Studies on many organisms, from cell cultures to animal models to humans have however all shown honey's anti-inflammatory effects (Ranneh et al., 2021). Recent in vivo investigations have proven that honey's anti-inflammatory properties work. Edema and plasma levels of inflammatory cytokines such IL-6, TNF-, PGE2, NO, iNOS, and COX-2 were shown to be reduced by honey in these investigations. In addition, studies conclude that honey inhibits the degradation of the protein IB (inhibitor of kappa B) and reduces nuclear translocation of NF-B (Farràs et al., 2019). Proinflammatory enzymes including cyclooxygenase-2 (COX-2), prostaglandins (Johnson et al., 2020), and inducible nitric oxide synthase (iNOs) (Jung et al., 2018) have as well been shown to be inhibited by phenolic acids and flavonoids like chrysin, quercetin, and galangin. Other studies have revealed that the flavonoid concentration of honey reduces the development of MMP-9 (matrix metalloproteinase 9), an inflammatory mediator responsible for chronic inflammation. Anti-inflammatory cytokines like IL-1 and IL-10, as well as growth factors may also be dramatically suppressed by honey. Other evidence suggests that macrophages, monocytes, and neutrophils create reactive oxygen species that promote inflammation. To counteract inflammation, honey prevents the release of these cells. It does this by reducing inflammation through prevention of the formation of keratinocytes and leukocytes. Honey's H_2O_2 generation during an inflammatory reaction has also been shown to encourage the development of repair cells like fibroblasts and epithelial cells. Honey's anti-inflammatory properties set it apart as a potential new agent for disease modulation (Mărgăoan et al., 2021)

Inflammation is linked to abnormalities in arachidonic acid metabolism. Arachidonic acid is converted into leukotrienes through the LOX pathway (LTs). The LOX isozymes come in three different forms: 12-LOX, 15-LOX, and 5-LOX. When activated, 12-LOX may cause inflammatory/allergic problems, whereas 15-LOX can produce 15-HETE, which has anti-inflammatory properties, and 5-LOX can produce 5-HETE as well as LTs. It has been shown that several polyphenols in honey may inhibit LOXs (Hajeyah et al., 2020). Honey's phenolic components and flavonoids are generally responsible for its anti-inflammatory activity (Mărgăoan et al., 2021).

3.7. HONEY AS FOOD

Honey is consumed fresh in most cases either in the liquid form or semi-solid processed form. Consumption of 100 g of honey provides the body with nearly 320 kcal (Boussaid et al., 2018). The benefits accrued with the intake of honey as food has been verified by several researchers. Consumption could be either for medicinal purposes, as food or as additives in several food systems (Chin & Sowndhararajan, 2020). In the food industry, it is common for honey to be produced in large quantities either for consumption by itself or in combination with other local products before consumption. For example, in the production of dairy products like yoghurts where honey is used as a sweetener so as to extend the shelf-life of the product for reasonably longer periods (El-Haskoury et al., 2018). Honey is sometimes used as flavoring additive in the manufacture of gum products. In addendum, it has been reported that honey has been utilized in the manufacture of non-alcoholic drinks like fruit juices in Japan where it is employed as a flavoring agent and sweetener (Ratiu et al., 2019).

The addition of honey to infant formulas and its use as a flavoring agent have notonly gained worldwide recognition but also improved the nutritional status of the food products (Zarei et al., 2019). Honey is easily digestible and is a rich source of energy to the body. It contains all the classes of food in the correct proportion with glucose and fructose forming a bulk of the carbohydrate fraction (Duman, 2019). The amount and type of proteins contained in honey can be attributed to the origin of the honeybee. Vitamins present include the B complex vitamins and ascorbic acid. Honey also contains trace minerals like Calcium, Iron, Copper, Manganese, Phosphorus, Potassium, and Zinc (Padhan et al., 2020). The nutritional status of honey posits it as an ideal candidate for food for humans of all age grades. Honey consumed as food helps boost energy, enhance physiological processes like growth and promotes health maintenance regimes like exercises and sporting activities (Flores et al., 2015). It has been reported by several researchers that consumption of honey could help in weight gain due to facilitated bone mass increase and impregnation with minerals (Antia et al., 2015). It has also been reported that consumption of honey has an effect on the enhancement of gastrointestinal function. The use of honey in making sweets and candies for children could be more beneficial instead of the artificial sweeteners that are commonly used which are detrimental to the health of the children. This submission has been supported by several researchers who revealed the use of honey in palliating the extreme consequences of neonatal diarrhea and gastroenteritis (Castro-Vargas et al., 2020).

3.8. AS A FOOD PRESERVATIVE

Food spoilage is defined as microbiological, chemical or physical alterations in food which makes it undesirable and unacceptable to consumers. Food spoilage is mainly caused by the activities of microorganisms (Sereia et al., 2017). Food preservation involves the application of food processing practices which will hinder the proliferation of microorganisms and retard the oxidation of fats that cause rancidity (Boussaid et al., 2018). It is therefore imperative that the activities of these organisms be checked in foods using a hurdle approach which should involve the use of natural food additives like honey as a food preservative (Ibrahim et al., 2021).

The antimicrobials and antioxidants present in honey promote its function as a food preservative. Honey functions as a food preservative based on its high sugar concentration which tends to "squeeze" the water out of microbial cells that could be responsible for spoilage of the food. This process causes a drying up of the cells ultimately leading to their death Chin and Sowndhararajan (2020). Some of the antimicrobials present in honey which help to prevent the proliferation of microorganisms in foods include high sugar concentration, low pH value, glucose oxidase and bee defensin-1 (Đogo Mračević et al., 2020). Honey also contains antioxidants and phytochemicals like phenols, hydrogen peroxide, flavonones, and carotenes which inhibits the proliferation of bacteria like Listeria, Monocytogenes, Staphylococcus aureus etc. The bioactive compounds present in honey which work in synergy to produce their antioxidant effect include flavonoids, phenolic acids, tocopherols, catalase, superoxide dismutase, glutathione, ascorbic acid, and peptides (Bonvehi et al., 2019).

The detection of minute amounts of Clostridium botulinum in honey has been reported to enhance its use as a food preservative since the bacterium provides a natural source of antioxidants and has been used to ameliorate the negative effects of browning in fruits and vegetable processing caused by polyphenol oxidase (Farràs et al., 2019).

The antioxidant activities of honey are correlated to its use in foods as a sweetening agent as it helps protect consumers from tissue damage caused by free radicals and oxidative compounds (Bobis et al., 2020). The glucose oxidase in honey also supplies a regular amount of hydrogen peroxide (H_2O_2) at concentrations which enhances antibacterial function but which will not cause damage to the tissues of the body. It has been reported that honey has a preservative effect on prolonging the shelf-life of fruits and vegetables such as strawberries and tomatoes without the assistance of chemical preservatives. According to the study, the fruits appeared much more appealing to consumers and was recommended to farmers as a better preservative tool especially as it better suited to consumers allergic to chemicals (Erhonyota et al., 2022).

4. CONCLUSION

Honey is an all natural substance that features nice sensory qualities such as a light hue as well as a familiar scent and flavor. Within it is contained organic acids, sugars, minerals, enzymes, phenolic and volatile chemicals, methylglyoxal, amino acids, vitamins etcetera which have been linked to potential biological activities and so has been used for thousands of years as a medicine. Its chemical make-up varies depending on factors like the time of its production, the kind of flowers used to produce it, the weather/ time of year and the processing methods used. The unique nutritional and therapeutic benefits of honey have been confirmed by current science (Nainu et al., 2021), as it has been demonstrated to be effective as an anti-cardiovascular diseases agent, anti-inflammatory agent, antimicrobial agent, wound healing aid etcetera. Honey has also been seen to be an effective agent in the treatment of a variety of skin conditions, including ulcers, bedsores, acne and burns. However, some of the mechanisms by which honey elicits these biological properties remain unknown, further research is therefore needed for a better understanding of these before it can be used as an alternative treatment in modern medicine. Natural honey is nonetheless recommended as a good dietary supplement.

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CONFLICTS OF INTEREST

Authors declare there is no conflict of interest.

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