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Honey is a natural food that is packed with vitamins, minerals, enzymes, proteins, organic acids, and many other biologically active compounds. Its exact components may vary based on the unique collection of flowers and plants that honeybees pollinate. The nutrient dense quality of honey has different health benefits. People all around the world are currently suffering from chronic illnesses such as obesity, diabetes, hypertension, and dyslipidemia at unprecedented rates. When patients experience a combination of these disease states, it is known as metabolic syndrome (MetS). MetS is correlated with urbanization in developing countries, with sedentary lifestyle and poor diet as the biggest risk factors. Studies have shown that honey is able to help manage and reverse all four disease states that make up MetS. While the exact mechanisms are still being investigated, honey's positive health effects may suggest that it could play a role in helping patients manage and ultimately reverse these chronic diseases.

Keywords: *honey, metabolic syndrome, chronic disease*

People all around the world are currently suffering from chronic illnesses at unprecedented rates. Global obesity rates have tripled from 1975 to 2015, and in America alone, nearly 70% of adults are overweight or obese.[1,2] Diabetes is growing at an even faster rate. In 2001, the American Diabetes Association estimated that 29 million Americans will be diabetic by the year 2050.[3] These projections were much too low, as the CDC reported 37.3 million diabetic Americans (11.3% of the population) in 2022.[4] Hypertension is currently one of the most prevalent chronic diseases in the world, with rates as high as 47% as of 2020.[5] Dyslipidemia is also a problem. The CDC reports that 12% of adults have total cholesterol over 240 mg/dL.[6] When patients experience a combination of these four disease states it is known as metabolic syndrome (MetS).[7] MetS exhibits a strong correlation with urbanization in developing/developed countries, with a sedentary lifestyle and poor diet as the largest risk factors.[8,9] With these frightening trends of chronic illness, polypharmacy is not enough to keep up with the American diet and lifestyle. Patients are left struggling with handfuls of daily medications, potentially steep healthcare costs, and no answers to where to go from here. Will they be taking an endless list of medications for the rest of their lives? Perhaps alternative methods that may help prevent or reverse these diseases should be considered. Changing the American diet and incorporating foods like honey may be a viable option for managing metabolic syndrome.

COMPOSITION OF HONEY

Honey is a natural product mainly composed of water (15–20%), carbohydrates (75–80%), and small amounts of at least 22 additional complex sugars. It is also made up of varying amounts of organic acids, proteins, vitamins, minerals, enzymes, and other biologically active compounds.[10] The three basic types of honey are single-origin, multi-flower, and local. Single-origin honey is made from the nectar of one specific plant, such as clover. Multi-flower honey is produced from the nectar of multiple different plants, which produces variability in flavor and appearance. Local honey comes from a specific region or area, with countless types available throughout the world.[11] In addition to these broad categories, honey can either be raw or pasteurized, which refers to whether it was treated with high heat to destroy sugar-tolerant yeasts. While pasteurizing honey extends the shelf-life and prevents crystallization, raw honey contains more amino acids, antioxidants, vitamins, minerals, and enzymes, and thus be more nutrient-dense.[12]

WEIGHT LOSS

A large amount of data supports honey's ability to decrease body weight and help with weight loss. Honey's mechanism for weight loss is multi-faceted and not fully understood. However, it is believed to be attributed to its antioxidant effects, and its ability to regulate enzymes and receptors involved with glucose and lipid regulation.[7] Sugars and phenolic compounds found in honey have been tied to reductions in adipose tissue in obese rats.[15] While most of the data supporting honey's anti-obesity effects have been seen in animals, there are a few published human studies. An 8-week randomized control study by Bahrami and colleagues compared body weight and lipid values in 48 type-II diabetics who consumed honey to a control group.[13] The treatment group was fed incremental amounts of honey per day: 1 g/kg/day in the first 2 weeks, 1.5 g/kg/day for weeks 3-4, 2 g/kg/day for weeks 5-6, and 2.5 g/kg/day for weeks 7-8. For reference, this is equivalent to >10 tablespoons of honey in a 200-pound subject. The control group did not consume any honey. The results

showed a statistically significant amount of weight loss in the treatment group, an average of 5 pounds, while the control group did not lose any weight.[13] It is important to note that patients did not change their energy output or intake during the 8 weeks, meaning the weight loss was not attributed to a change in diet or exercise. Another study, by Yaghoobi and colleagues, focused on honey's effects in obese and overweight individuals. Over a 30-day period, 38 subjects were given 70 g of honey per day, while 17 subjects in the control group were given 70 g of sucrose per day. On day 31 the investigators found that the honey group exhibited a 1.3% reduction in body weight and 1.1% reduction in body fat, while the control group exhibited a 0.6% and 0.9% increase respectively.[14] Both studies demonstrated that adding to and/or substituting honey in a patient's diet leads to steady decreases in body fat without increasing body weight. However, more research on the impact of honey on weight loss is needed.

DIABETES

Honey has also shown favorable effects on blood sugar in diabetic patients, despite being composed mostly of sugar. Its proposed anti-diabetic effect has two probable mechanisms. The first is honey's ability to inhibit alpha-amylase and alpha-glucosidase enzymes, which leads to slower digestion of complex carbohydrates into absorbable glucose. This effectively helps reduce glucose spikes and keeps diabetic patients at their target glucose levels for longer periods of time.[7,18,19] The second is honey's ability to mitigate insulin resistance, or in other words, allow insulin to work more efficiently. Multiple studies have demonstrated that certain components in honey help upregulate insulin receptor substrates 1 and 2 in muscle tissue. This allows insulin to work better and in turn improves blood glucose regulation.[7,15] Due to these effects, studies suggest that honey can be a better alternative to sugar for diabetic patients. The previously mentioned study by Bahrami and colleagues reported significant reductions in fasting blood glucose (FBG), an average of 29%, in the patients fed weight-based amounts of honey.[13] However, this study did not show positive effects on hemoglobin A1C, a lab value that measures average three-month blood sugar levels. The study by Yaghoobi also found improvements in FBG levels with honey consumption. The honey-fed group experienced a 4.2% decrease in FBG while the sucrose group experienced a 2.2% increase.[14] One shortcoming of this study was that they did not measure honey's effect on A1C levels. A different study by Al-Waili and colleagues also showed better FBG levels with honey compared to dextrose. They found that the diabetic group who received honey had significantly lower plasma glucose levels for the 180 minutes following administration. The average FBG level was 169 mg/dL compared to 311 mg/dL in the dextrose group.[16] This sizeable difference, with average blood glucose nearly 85% higher in those who consumed dextrose, demonstrates that honey is a better option for diabetic patients. Another clinical trial, done at the National Institute for Diabetes and Endocrinology in Egypt, studied honey's effects on 40 type-1 diabetic patients aged 4-18 years old. This 12-week trial, using 0.5 g/kg of daily honey consumption, found statistically significant reductions in FBG and hemoglobin A1C levels. The study's duration may be the reason why positive effects were seen in both levels.[17] While honey itself does temporarily raise blood sugar following consumption, as do most foods, these studies show that honey has a much more favorable effect on blood glucose than other common sugars. Therefore, diabetic patients could potentially benefit from prolonged use of honey in the management of their disease.

DYSLIPIDEMIA

Honey has been shown to have a positive effect on all major lipids, including triglycerides, apolipoprotein B (apo B)-containing lipoproteins, low-density lipoprotein (LDL), very low-density lipoprotein (VLDL) and high-density lipoprotein (HDL). The previously mentioned studies that assessed honey's effects on body weight and blood glucose also found positive effects on lipid levels. Those who consumed honey had significant reductions in LDL (14%, 5.8%), total cholesterol (17%, 3%), and triglycerides (22%, 11%), as well as an increase in HDL (12%, 3.3%).[13,14] The mechanisms that may cause lipid control in honey overlap with its anti-obesity and anti-diabetes effects. A possible mechanism that may explain the link between insulin and lipid levels is that insulin resistance is partially defined by a lack of HDL production and overproduction of VLDL in the liver. Thus, honey consumption may lead to the restoration of proper lipid levels by allowing insulin to work more efficiently in the body.[21] This is an example of how the individual disease states that make up MetS are complexly intertwined and can easily compound on one another.

HYPERTENSION

Honey's ability to control hypertension is a unique quality that is backed by both human and animal data.[7] Two studies support honey's immediate hypotensive effects. One included 140 healthy male (18-25 years old) and female (19-23 years old) subjects that tested the ability of 20 mL of honey to reduce blood pressure immediately after consumption. The researchers found that honey was able to significantly decrease systolic blood pressure by an average of 10 mmHg and decrease diastolic blood pressure and heart rate for up to 60 minutes. These results were consistent in both men and women, though greater effects were seen in women.[21] The second of these studies looked exclusively at 50 healthy, young males from a similar population set. Using 20 mL of honey as the intervention, the investigators found a decrease in systolic blood pressure by 7 mmHg for up to 60 minutes.[22] While not applicable to eating honey, an interesting study by Al-Waili found that intrapulmonary inhalation of a honey solution led to significant decreases in systolic and diastolic blood pressure for up to 120 minutes.[23] Although these studies had positive

results, additional data is needed to conclude any long-lasting hypotensive effects with honey.

Explanations for honey's hypotensive effects are again tied to insulin. Hyperinsulinemia is understood to activate the sympathetic nervous system (SNS), leading to increased cardiac output and vasoconstriction. Thus, honey's ability to regulate insulin activity may play a role in reducing the hypertensive effects of the SNS. Oxidative stress is also a huge risk factor for not only hypertension, but the other components of MetS. Prolonged oxidative stress exposure leads to inflammation of the vascular walls, reduced vasodilatory nitric oxide, and increased arterial wall proliferation/stiffness which contributes to hypertension.[7] Since honey contains antioxidant properties, reversing this oxidative stress may be how it helps reverse hypertension, and ultimately mitigate MetS.

OPTIMIZING PATIENT OUTCOMES

The diseases that comprise MetS are highly correlated with one another because they all share underlying causes: insulin resistance, oxidative stress, and inflammation. Thus, once patients develop any one of those chronic conditions, they are at increased risk of experiencing another. Instead of treating each disease with a unique set of medications, patients could benefit from a single product like honey that can help address all these underlying issues simultaneously. The antioxidant effects of honey are linked to its phenolic compounds which consist of flavonoids (such as quercetin, apigenin, luteolin, kaempferol, chrysin, and galangin), phenolic acids, carotenoid, ascorbic acid, and antioxidant enzymes like catalase and glucose oxidase.[24-26] The anti-inflammatory effects of honey are tied to its ability to reduce C-reactive proteins (CRP), with one study having a 3.2% decrease in CRP.[14] Dozens of animal models have also displayed reduced inflammatory markers from honey consumption.[14] Honey's ability to mitigate insulin resistance is yet to be fully explained, but its ability to upregulate insulin receptors and the improvement seen in insulin sensitivity by diabetic patients may help piece together this mechanism of action.[15,27]

One of the greatest challenges to testing honey's efficacy is honey itself. Honey is 100% natural and is affected by many complex processes in nature. Thus, it is nearly impossible to recreate the same batch twice. Factors such as geographic region, conditions of the hive, the bees' sources of nectar, and temperature are all factors that can affect the chemical composition of honey.[15] There are also human factors involved, such as adulterated honey, misbranded honey, and low-quality storage that can jeopardize the integrity of the product. Despite this lack of standardization, studies to date show positive results on honey's ability to reverse MetS, with minimal to no negative effects. However, more longitudinal studies that include patients with metabolic syndrome are needed to determine honey's exact role in managing these diseases.

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