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A FOLKLORE MEDICINAL STUDY ON EFFICACY OF HONEY

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ABSTRACT

Honey is a natural gift to man from Mother Nature which is made available to us from the mysterious kingdom of the bees. It is a sweet, flavourful liquid substance with several beneficial constituents. Extensive research has shown the therapeutic promise of the use of honey in enhancing health values and improving body systems. This manuscript documents the ancient medicinal uses of honey and provides evidence-based data demonstrating its benefits in animal models, patients, and healthy individuals. Honey is also evaluated for its wide acceptability as a complementary and alternative medicine for most ailments. All types of honey exhibit different biochemical activities and show greater variability in their potency as apitherapeutic agents than conventional medicines. The mechanisms of action conferring honey's protective effects, as suggested by various authors, are documented. The use of apitherapy in synergy with chemotherapy to manage microbial and cancer ailments is also helpful in reducing drug-induced cytotoxicity.

KEYWORDS: *Honey, Therapeutic, Nutraceutical, Apitherapy, Health, Medicine*

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INTRODUCTION

Natural honey can be defined as a sweet, flavourful liquid with high nutritional value and immense therapeutic benefit (1). This natural product is produced mainly by bees from the secreted nectars of various flowers; this type is regarded as blossom or floral honey. A less common type, honeydew or forest honey, is produced from the exudates of plant sucking insects called aphids. Natural honey has more than 300 constituents, but its main composition is sugars, primarily fructose and glucose, with small amounts of fructo-oligosaccharides (1,2). The contents of raw honey vary in different geographical locations. These compositional varieties are greatly influenced by the botanical origin of the honey, which is a consequence of the diet of the bees. It is noteworthy that, irrespective of its floral source, honey contains phytochemicals, flavonoids, catalase, phenolic acids, ascorbic acid, antibiotic-rich inhibine, tocopherols, and peptides, and most of these substances work in synergy to provide its beneficial effects (1–3). The other substances identified in natural honey include proteins, amino acids, enzymes (amylase, catalase, invertase, oxidase), and vitamins (including niacin, riboflavin, and pantothenic acid), as well as minerals (mainly calcium, copper, iron, magnesium, manganese, phosphorus, potassium and zinc) (3,4). Some of these macro and micronutrients found in natural honey, as documented in previous reviews by Eteraf-Oskouei and Najafi (1) and by Ajibola et al. (5) with modifications by Ajibola (6), are listed in Table 1. The other chemical components

of honey also identified by these reviewers (1,5), with inputs from Rashed and Soltan (4), are shown in Table 2.

Table 1: Some Macro and Micro Nutrients of Natural Honey (Mean (SD))*

Proximate Analyses	Amount	Proximate analyses	Amount
Water (%)	15.92 (SD 0.07)	Protein (%)	0.42 (SD 0.06)
Carbohydrate (g/100g)	88.97 (SD 1.71)	Fat (%)	0.53 (SD 0.01)
Fructose (g/100g)	43.35 (SD 0.02)	Thiamine (mg/100g)	0.01 (SD 0.00)
Glucose (g/100g)	37.64 (SD 0.01)	Riboflavin (mg/100g)	0.02 (SD 0.00)
Sucrose (g/100g)	2.03 (SD 0.05)	Niacin (mg/100g)	0.15 (SD 0.01)
Maltose (g/100g)	2.75 (SD 0.02)	Vitamin B5 (mg/100g)	0.07 (SD 0.03)
Oligosaccharides (g/100g)	3.11 (SD 0.08)	Pyridoxine (mg/100g)	0.17 (SD 0.02)
Energy (MJ/Kg)	15.56 (SD 0.21)	Folic acid (mg/100g)	0.006 (SD 0.00)
		Ascorbic acid (mg/100g)	2.35 (SD 0.25)
		Vitamin K (mg/100g)	0.025 (SD 0.00)
		Other nutrients (%)	0.53 (SD 0.00)

*Adapted from Eteraf-Oskouei and Najafi (1), Ajibola et al. (5), Ajibola (6).

Table 2: Chemical Elements Found in Natural Honey*

Element	Amount	Element	Amount
Aluminium (Al)	0.01 – 2.4	Magnesium (Mg)	0.7 – 13
Arsenic (As)	0.014 – 0.026	Manganese (Mn)	0.02 – 2
Barium (Ba)	0.01 – 0.08	Molybdenum (Mo)	0 – 0.004
Boron (B)	0.05 – 0.3	Nickel (Ni)	0 – 0.051
Bromine (Br)	0.4 – 1.3	Phosphorus (P)	2 – 15
Cadmium (Cd)	0 – 0.001	Potassium (K)	40 – 3500
Calcium (Ca)	3 – 31	Rubidium (Rb)	0.040 – 3.5
Chlorine (Cl)	0.4 – 56	Selenium (Se)	0.002 – 0.01
Chromium (Cr)	0.01 – 0.3	Sodium (Na)	1.6 – 17
Cobalt (Co)	0.1 – 0.35	Silicon (Si)	0.05 – 24
Copper (Cu)	0.02 – 0.6	Strontium (Sr)	0.04 – 0.35
Fluoride (F)	0.4 – 1.34	Sulphur (S)	0.7 – 26
Iodide (I)	10 – 100	Vanadium (V)	0 – 0.013
Iron (Fe)	0.03 – 4	Zinc (Zn)	0.05 – 2
Lead (Pb)	0.001 – 0.03	Zirconium (Zr)	0.05 – 0.08
Lithium (Li)	0.225 – 1.56		

*Data in mg/100g, Adapted from Eteraf-Oskouei and Najafi (1), Rashed and Soltan (4), Ajibola et al. (5).

The oral consumption of raw honey by man has been in vogue for centuries. An abundance of reports confirm that pure natural honey is the most ancient sweetener and has been in use since antiquity (1). The honey serves as a complementary and alternative medicine (CAM) for most diseases. The traditional and therapeutic use of NH has been to abate infections, mitigate ailments, give health benefits to patients, and provide succour to healthy individuals (5–7).

The wide acceptability and successful use of honey as a CAM and apitherapeutic agent has prompted several studies aimed at gaining some scientific insights and generating evidence-based data. Collation of some of these scattered data is also required for further investigation of honey's nutraceutical properties and its relevance in modern day health care. Hence, the documentation of the known medicinal uses of honey in one manuscript becomes imperative for providing further insight into the apitherapeutic and health values of natural honey.

Haematopathology

The daily intake of natural honey is associated with various beneficial effects on haematological parameters and blood concentrations of metabolic catalysts, namely enzymes and minerals (7). The use of natural honey in apitherapy has been shown to ameliorate anaemic effects, thereby providing succour to patients. One dietary enrichment study (8) confirmed an enhanced haematological value in adult rats fed Nigerian Jungle honey when compared to controls. The authors found improved haemoglobin concentration, elevated red blood cell counts and enhanced haematocrit values in the raw honey eaters. In a similar experimental study from another laboratory, Chepulis (9), also reported improved haematological profiles and immunity boost in rats nurtured with 10% New Zealand forest honey as a dietary supplement. This researcher also documented a higher lymphocyte count and enhanced phagocytosis by neutrophils in rats fed natural honey relative to control rats. This aligns with a previous study that verified that prebiotics can improve immunity (10) and that honey contains oligosaccharides and other prebiotics (1). In addition, natural honey has immuno-protective ingredients. According to Al-Waili and Haq (11-12), the oral consumption of Asian polyfloral honey from Al-Theed City, UAE stimulates and increases antibody production during various immune responses against the T-cells antigens of the thymus-independent and dependent origin.

Dental Care

The oral use of raw honey can positively influence dental health and oral wellness, and is assuming importance during dental surgery (13). A very recent article indicates that the use of Asian polyfloral honey as an apitherapeutic agent mitigates pain associated with tooth extraction and prevents oral infections, such as gingivitis and dental caries, in patients undergoing orthodontic treatment (13). According to Mohapatra et al. (14), raw and processed honey have a broad-spectrum antibacterial activity with high potential for the reduction of dental caries susceptibility (13,14). In addition to the carioprotective potential of New Zealand manuka honey, English et al. (15) report, and Atwa et al. (13) concur, that this natural product prevents dental plaque and gingivitis as well as other oral ailments. The report from Steinberg and co-researchers also show that raw honey is non-cariogenic or less cariogenic than sugar (16).

Natural honey is not only non-cariogenic, but is also anti-cariogenic, as shown by Khamverdi and co-workers, who evaluated the antibacterial potency of Iranian honey (17) in apitherapy. The oral health effect of honey is due to its antibacterial potential, which prevents bacterial growth, thereby mitigating the pathogenesis of dental caries (13,16). In addition, recent research shows that eating raw honey is safe and does not give rise to oral health hazards such as gingivitis and periodontal disease (15). In this study (15), volunteers who chewed New Zealand manuka honey as "honey leather" had highly significant reductions in mean plaque scores (0.99 reduced to 0.65; $P = 0.001$) compared to the control group, suggesting a potential therapeutic role for honey in oral health. As discussed in previous studies, the non-cariogenic potential of honey might be due to the protective role of honey's synergistic constituents (1,5,6). These chemical substances include calcium, fluoride, phosphorus and other colloidal constituents of honey. In summary, honey is a potent analgesic agent in dental surgery, in addition to its nutraceutical value when consumed

by individuals and/or used as an apitherapeutic agent in the management of patients with oral ailments.

Eye Diseases

The therapeutic use of natural honey in the treatment and management of eye ailments is on record. The ancient use of honey as curative substance for eye diseases cuts across geographical barriers, and involves people from Attica, Europe, India, Asia and Africa (18–20). The efficacy of honey as a potent apitherapeutic agent in the management of eye infections was also recently shown by Salehi and co-workers, in their clinical trial on vernal keratoconjunctivitis patients (21). These authors show the relevance of natural honey in modern ophthalmology by documenting effective treatment of these patients by topical honey application. The African people in Mali also used natural honey for therapeutic control of measles (18). Natural honey was mostly applied on the eyes for the prevention of the corneal scarring sequelae of measles and other eye infections (19–22).

According to the findings reported in the reviewed manuscripts, the antimicrobial and anti-inflammatory properties of honey are highly beneficial in the treatment of different eye ailments. These ailments could be caused by chemical and thermal injuries to the eyes, as well as by conjunctival and corneal infections (21,22).

The apitherapeutic use of varieties of honey in the field of ophthalmology is comprehensively discussed by Ajibola et al. (5) in a review on the nutraceutical value of honey. The ophthalmological effects of natural honey mentioned by these researchers in their recent discourse are further elaborated above as honey therapy against various eye pathologies.

Cardiovascular Diseases

The oral administration of medical honey abates cardiovascular risk factors in animal models, human participants, susceptible healthy individuals, and patients (23–26). Other studies involving animal models and human participants nurtured with natural honey relative to controls (fed a fructose/sucrose mixture) report higher blood concentrations of antioxidants, which reduce the risk of development of cardiovascular diseases.

In 2012, some nutritional physiologists performed a comparative study in male rats fed sugar or South African monofloral sunflower honey (27). They found that excessive sugar consumption significantly ($P < 0.05$) elevated blood concentrations of circulating substrates (glucose and triglycerides) amidst several pathological changes, including hypercholesterolaemia, hyperinsulinaemia, and hepatomegaly, and significantly increased ($P < 0.001$) visceral adiposity and fat molecules in the liver (27). These risk factors of cardiovascular diseases were not seen in the honey-fed rats during the study. The absence of these pathologies confirms the cardioprotective capability of sunflower honey; thus, natural honey intake is devoid of health hazards (5,27). These results justify the conclusion that eating natural honey instead of artificial sugars has health benefits (23). Experimental procedures and clinical trials also affirm the apitherapeutic value and the significance of eating honey in mitigating cardiovascular ailments, as shown by health index records (25,26). Gharekhani et al. (24) give credence to this affirmation in their test of the efficacy of natural honey on cardiac arrhythmias and infarct size when it is used during ischemia in isolated rat hearts.

The apitherapeutic and beneficial effects of Malaysian honey have been demonstrated in animal models with hypertension alone (28), or with hypertension and diabetes (29), as well as those of Nigerian Jungle honey in a clinical trial involving healthy human participants (30). This cardiovascular section can be concluded with the ‘cure all’ claim associated with therapeutic potency of honey, as the literature search shows its positive influence as an apitherapeutic agent on various body organs and systems, ranging from the body metabolic sites (e.g., the liver) to the heart, kidney, blood and gastrointestinal tract.

Metabolic Disorders

Natural honey is also beneficial as a glycimic food in maintaining blood-sugar concentration (31,32). Several studies show that oral consumption of varieties of honey abates metabolic disorders in animal models, patients and susceptible healthy individuals (25,31–33). In one dietary supplementation study, male and female rodents were fed diets enriched with either South African sunflower honey or liquid sugar from 7 days old to 13 weeks of age in order to compare their metabolic health and to document the effects of natural honey against metabolic dysfunction and/or syndrome (6). Metabolic syndrome is a condition characterized by central obesity, hyperglycaemia, hypertension and dyslipidaemia, and thus increased susceptibility to diabetes mellitus and other metabolic ailments (34). In male rodents, sugar significantly ($P < 0.05$) elevates the blood concentrations of glucose and triglycerides and promotes enhanced visceral adiposity, hypercholesterolaemia, hyperinsulinaemia, hepatomegaly, and accumulation of fat droplets in the liver (31). These risk factors, which are associated with metabolic dysfunctions, were not seen in the honey-nurtured or in female rodents in this trial, which indicated the health potentials of monofloral sunflower honey. These results confirm the conclusion drawn from one study done elsewhere, by Busserolles and other researchers, that eating natural honey instead of artificial sugars has health benefits (23). The trials involving animal models and human participants also affirm the apitherapeutic value of medicinal honey in the management and control of metabolic diseases. Several biomarkers confirm this, including reduction in the plasma concentrations of total cholesterol and low density lipoprotein (LDL)-cholesterol (23,25,26); triglycerides (25,26), and glucose in healthy humans, as well as in patients with diabetes mellitus and C-reactive protein (23,25,26,32) and patients with elevated blood concentrations of high density lipoprotein (HDL)-cholesterol (23,25,26).

Unlike artificial sugars, this natural sweetener, honey, can be consumed by diabetic patients with beneficial results (25,32,33). However, there is need for caution and honey consumers, especially diabetic patients, should still be wary of possibilities for health hazard(s). As mentioned by Ajibola and colleagues in their study on the nutraceutical value of honey and contributions to human health, honey, like any other products with human involvement, is not devoid of contamination and adulteration (5). Some apiculturists feed the bees in their colonies with refined sugars, while some honey vendors even engage in the crude, inimical, and unwholesome practice of direct honey adulteration with sugars and other artificial sweeteners (5,6,33). As such, if diabetic patients consume a honey sample that is adulterated with as high as 70% artificial sugars, their health conditions may deteriorate.

Erejuwa provides possible explanations for such a potential negative effect of honey in diabetic patients (33), including the ingestion of higher than pharmacological doses of honey without therapeutic monitoring and/or consumption of honey with a low fructose: glucose ratio, as used in Bahrami's clinical trial (33,35). Hence, natural honey should be provided in its genuine, original state and administered at appropriate therapeutic doses for desired positive results.

Antimicrobial Effects

The antimicrobial potential of natural honey is the most widely investigated apitherapy, alongside its use in wound management. To date, several studies have been conducted on different bacterial species to investigate the antibacterial properties of honey from different geographical locations of the world (2,5,13,36–40). Most bacteria, viruses and fungi are sensitive to medicinal honey, as it is a very effective broad-spectrum antimicrobial agent (1,2,3,6,41,42). Researchers have demonstrated the antimicrobial activity of natural honey against *Bacillus subtilis*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Staphylococcus aureus,* as well as other Gram-positive and Gram-negative bacteria (2,3,13). These authors opine that the formation of hydrogen peroxide (H2O2) enhances the antibacterial capability of honey.

$$Glucose + H_2O + O_2 \text{ ----------} Gluconic\ acid + H_2O_2$$

Hydrogen peroxide is produced through the action of enzymes, mainly glucose oxidase, in natural honey. The hypopharyngeal gland of the bee facilitates the enzymatic secretion of glucose oxidase into the nectar of flowers during honey production (3), (39). In general, apitherapeutic investigations on the antibacterial activities of honey show both bacteriostatic and bactericidal effects (13), and these could be due to peroxide and non-peroxide constituents of honey (39,40,43).

Treatment with natural honey is also of therapeutic value against Candida albicans, Leishmania parasites, *Trichophyton mentagrophytes*, and influenza and rubella viruses, as well as other pathogenic microbes (2,5,13,41,42). In addition, other studies also document the anti-mycotic effects of honey (22, 36-43). Cutaneous and superficial fungal infections, like athlete's foot and ringworm, are sensitive to apitherapy. This sensitivity partially results from fungal growth inhibition and is partially due to prevention of secondary infection by opportunists like bacteria (22,36).

The various studies discussed in this section show that diluted and/or undiluted natural honey has antiseptic, anthelminthic and antimicrobial activities when used alone; while it shows enhanced antipathogenic potency when apitherapy is combined with chemotherapy. This synergistic potency was shown in an in vitro study by Watanabe et al. (41) using New Zealand manuka honey in combination with antiviral chemotherapeutic agents (zanamivir or oseltamivir) against influenza virus. The reports of potent inhibitory activity by these authors demonstrate a potential enhanced apitherapeutic value of honey.

Wound Cure

Medical honey is an antiseptic agent, effective against burns, ulcers (including recalcitrant ones), surgical wounds (even when infected), fungating wounds, pressure sores, and cancer or broken skin (42). According to an expert, applying honey topically as dressings in surgical patients was successful where conventional treatments (including radiation therapy) failed to produce the desired results (43-44). In one study, Ajibola (45) also obtained excellent results from experimentally created surgical wounds in West African Dwarf (WAD) goats treated with Nigerian Jungle honey as an apitherapeutic agent. The researcher documented epithelialisation and enhanced contraction of the honey treated wounds when compared with untreated wounds.

An abundance of evidence supports the topical application of medical honey for different types of wounds. These include apitherapeutic studies involving the use of honey in hospital surgical wards and laboratory experimentation (45–47). The presence of various bioactive substances in honey (2,4,48) gives rise to its different biological properties (5,6) promoting wound healing amidst other several protective effects, as shown by molecular evidence from several studies (39,49–51). Comprehensive overviews of the effects of honey on various types and classes of wounds are available in Molan's popular treatise: "Why honey is effective as a medicine" (22), and a recent publication by Ajibola (42) titled: "Physiological effects of natural honey on wounds in animals."

The apitherapeutic use and application of honey for wound care also involves paediatric patients (48). Honey causes enhanced epithelialisation and minimises scar formation with an anti-microbial effect. These researchers opine that medical honey is a safe and natural substance that induces wound healing at a greater rate than conventional methods of treatment.

The key findings for the use of honey in wound management are intertwined with those of the previous section (Antimicrobial & antiparasitic effects). These entail wound dressing with honey as an age-long practice, pre-dating antibiotic use (22,42). Honey is a potent broad-spectrum antibacterial agent, with both bacteriostatic and bactericidal properties (hydrogen peroxide, antioxidants, lysozyme, polyphenols, phenolic acids, flavonoids, methylglyoxal and bee peptides) higher than those of conventional drugs (1,14,40,43). Antibiotic-resistant microbes are sensitive to honey treatment (38–40); Medical grade wound honey care creams, gels, impregnated gauzes and dressings for wound management have been developed for public use (39,42). Minor cuts, bruises, chronic ulcers, burns, diabetic foot, gangrene, oncological wounds and other wounds, such as those caused by surgical removal of tumours, radiotherapy, and mucositis sequelae to chemotherapy, have been successfully treated with honey (22,39,42).

These various beneficial effects of apitherapy involve several mechanisms, as suggested by different workers (1,22,39,42), using varieties of honey from different geographic, botanic and entomologic origins, and can be summarised as follows: the physicochemical properties of honey curtail malodour of wounds and infected sites; the hygroscopic nature of honey facilitates moisture withdrawal from infected sites and surrounding tissues, thereby dehydrating bacteria, yeasts and other microbes; a protective layer forms between the wound bed and the highly viscous honey dressing; the low pH inhibits bacterial growth; a synergistic interaction occurs with the phenolic acids and other non-peroxide bioactive phytochemicals contained in honey.

Other Health Benefits

The other beneficial health effects of varieties of natural honey and apitherapeutic practices include treatment of general body pain, chest pain, menstrual pain, fatigue, vertigo, postnatal disorders, male impotence, and respiratory distress such as cough, bronchitis, pharyngitis, throat aches, and urinary tract infection (URTI) (1,22,39,43,49,50). These effects might be connected with the high energy content of honey, in addition to its effects against bacterial infection and inflammatory processes (42,51,50). In one reproductive study, Zaid et al. (51) reported the effects of tualang honey from Malaysia on menopausal rodents. The observation of uterine atrophy prevention informed the suggested use of honey as an alternative to hormone replacement therapy by these authors.

The contributions of medical honey in radiology and nuclear medicine have also been documented (52). According to Makpol et al. (52), Malaysian Gelam honey attenuates radiation-induced cell death and radiation-induced deoxyribonucleic acid (DNA) damage by promoting cell cycle progression and inhibiting apoptosis, indicating its molecular mechanism as a radioprotector against radiation damage. However, apitherapeutic management with honey prior to radiation exposure is advisable as it provides the best beneficial effect against ionizing radiation (52).

Another important medicinal use of natural honey is its age-long therapeutic effect against gastrointestinal tract ailments (22,53,54). Present statistics support this ancient practice, as honey is being used for the management and control of gastrointestinal pathologies like ulcers, diarrhoea, gastritis and gastroenteritis (55–57). The potency of this natural product as a gastro-protective agent, as reported by Osato et al. (58), includes inhibition of Helicobacter pylori, the causative agent of gastritis and peptic ulcers. The protective and other health benefits of honey are due to its bioactive

constituents interacting synergistically for positive effects, as proposed by Ajibola (6). This hypothesis of SMIF in honey has also been mentioned by other researchers. Eteraf-Oskouei and Najafi (1) concur with this proposition that most compounds in honey work together to produce a synergistic antioxidant effect. Vit and Huq (39) also lend credence to the synergism of the phytochemicals of natural honey in their 'Systematic reviews on interventions with honey in cancer.'

The 'cure-all' effects of natural honey can partly be attributed to its hepatoprotective potential, as the liver is the chief metabolic site of the entire body. In one molecular study, honey produced by stingless bees from Ecuador (Meliponinae) prevented DNA damage, as shown by measured antioxidant capacity (59). Other authors also have significantly contributed to mechanistic insights into honey's action through its chemotherapy against the oxidative stress and cell death (apoptosis) caused experimentally by hepatic obstructive jaundice (60). Natural honey curtails the ill effects of bile duct ligation to preserve the ultrastructural anatomy of the liver. The conclusion can be drawn that the antioxidant constituents, anti-inflammatory activity, free radical scavenging capability, reduction in necrotized tissue and the provision of a rich energy source are among the more important mechanisms of honey's effects (3,36), including the cardioprotective effect (24).

CONCLUSION

The oral and topical uses of honey as CAM show therapeutic promise, as honey improves functional body systems, reverses pathological conditions and gives enhanced health values. Natural honey contains antioxidants, phytochemicals and other bioactive substances that produce desired beneficial effects in almost all organs of the human and animal body. The different honey types show biochemical activities, adding value to honey's apitherapeutic potency and promoting natural honey as a choice therapeutic agent, even when conventional therapy appears ineffective. The superior efficacy of honey, coupled with its wide application in apitherapy, makes it a complementary and alternative medicine for most ailments. The biological, physical and chemical properties derived from honey's constituents interact uniquely and work synergistically to bring forth the desired beneficial effects. Hence, the mechanistic insights into the overall protective effects of honey indicates the presence of a unique 'synergistic multiple ingredients factor'.

Conflict of Interest

None.

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