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Therapeutic Potential of Apitherapy: A Comprehensive Review on the Health Benefits of Honey and Propolis

Katarzyna Żak, Hubert Jucha, Katarzyna Madyniak, Agnieszka Kluz, Aleksandra Pliszka, Michał Mazur, Weronika Jarych, Krystian Zukierski, Katarzyna Michalak

1. Katarzyna Żak

Saint Adalbert Hospital in Gdańsk, aleja Jana Pawła II 50, 80-462 Gdańsk, Poland katarzynazakeu@gmail.com
https://orcid.org/0009-0006-4036-090X

2. Hubert Jucha

Fundacja Zdrowie, Wilhelma Konrada Roentgena 23, 02-781 Warszawa, Poland hubert.jucha@outlook.com
https://orcid.org/0009-0002-0182-627X

3. Katarzyna Madyniak

Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warszawa, Poland kasiamadyniak@onet.pl
https://orcid.org/0009-0003-6927-3832

4. Agnieszka Kluz

Wolski Hospital, Marcina Kasprzaka 17, 01-211 Warszawa, Poland agnieszka.kluz@op.pl
https://orcid.org/0009-0006-7427-5818

5. Aleksandra Pliszka

Saint Adalbert Hospital in Gdansk, aleja Jana Pawła II 50, 80-462 Gdańsk, Poland Aleksa.pliszka@gmail.com https://orcid.org/0009-0003-5938-5929

6. Michał Mazur

Saint Adalbert Hospital in Gdansk, aleja Jana Pawła II 50, 80-462 Gdańsk, Poland Michal98mazur.med@gmail.com
https://orcid.org/0009-0007-8157-5293

7. Weronika Jarych

Szpital Morski im. PCK in Gdynia, Powstania Styczniowego 1, 81-519 Gdynia, Poland weronikajarych@gumed.edu.pl
https://orcid.org/0009-0009-1335-8072

8. Krystian Zukierski

Szpital Morski im. PCK in Gdynia, Powstania Styczniowego 1, 81-519 Gdynia, Poland krystian.zukierski@gmail.com
https://orcid.org/0009-0008-1428-5744

9. Katarzyna Michalak

Szpital Morski im. PCK in Gdynia, Powstania Styczniowego 1, 81-519 Gdynia, Poland kamichalak3@wp.pl
https://orcid.org/0009-0005-0856-1536

Abstract

Apitherapy has been developed in recent years, providing treatments using honey and other bee products to combat various diseases.

Honey and propolis contain bioactive compounds such as flavonoids and phenolic acids, minerals, vitamins, enzymes and many more which are responsible for numerous health-promoting features. [1] Among this benefits are anti-diabetic, cardioprotective, wound healing, antiviral, antimicrobal, anti-aging, immunomodulatory effects.

The purpose of this review is to summarize and update the current information regarding the role of honey and propolis in health and diseases.

Aim of the study

This study reviews recent research on honey and propolis, highlighting their key healing compounds and clinical applications in treating various diseases. The study proposes directions for future research and highlights knowledge gaps.

Materials and methods

To evaluate studies on the therapeutic effects of honey and propolis, we conducted a comprehensive literature review using databases, including PubMed, Google Scholar, and ScienceDirect. The main keywords used in the search included: apitherapy, honey, propolis.

Conclusions

In conclusion, honey and propolis are emerging as promising therapeutical options, with evidence supporting their effectiveness in treating various health conditions (cardiovascular diseases, prediabetes, hypertension, infections, pain, and wound healing).

Given their safety, efficacy, and inexpensiveness, they could be viable alternatives to conventional treatment. However, further research is crucial to better understand the active ingredients and mechanisms of action, ultimately guiding the development of effective therapies and clear clinical guidelines.

Keywords:

apitherapy, honey, propolis, wound, antiviral, pain, polyphenols, antibacterial, flavonoids, infection

Introduction

Honeybees and its products such as propolis, honey, bee pollen, bee venom, beeswax, royal yelly have been used for centuries to prevent and cure diseases. While the origins of apitherapy cannot be determined precisely, it is known to have been practiced in ancient Egypt, Greece as well as China 3000-5000 years ago.

The first written record of honey and it's healing properties was compiled in Ancient Egypt about 2600-2200 BCE in medical text named nowadays The Edwin Smith Papyrus.[2] The author describes how to prevent and cure infection with honey in cervical vertebral compression fracture or cervical sprain. [3]

Hippocrates, one of the most exceptional figures in the history of medicine, credited with the eponymous oath which every new physician swears, advised honey for treating the wounds of the head, ears, and penis. [4]

In recent decades research on pharmacological activity of bee products has increased and correspondingly many molecules and bioactive compounds which play a therapeutic role have been characterized which play a therapeutic role.

Currently, many lines of evidence, including clinical and experimental research indicate that bee products have numerous functional properties with antioxidant, antiviral, antimicrobial, antifungal, anti-inflammatory, anti-aging and wound healing effects. [5]

This article aims to synthesize evidence from many studies to provide updated facts about bioactive compounds in honeybee products such as honey and propolis and its healing properties based upon extensive research in several medical journals and web-based studies.

Materials and methods

We reviewed literature from The PubMed database, Google Scholar and Sciencedirect to evaluate studies involving honey and propolis. Keywords used in the search included: apitherapy, honey, propolis, wound, antiviral, pain, polyphenols, antibacterial, flavonoids, infection. A review of publications from the last 10 years was carried out. Few older studies were included as well, given that they contained reliable and established knowledge Ali FR et al. (2013), van Middendorp JJ et al. (2010), Bogdanov S et al. (2003), Kenjeric D et al. (2007), Rice-Evans C et al. (2011), Poljsak B et al. (2013), Yaghoobi N et al. (2008), Ahmadi M et al. (2013), Boroumand P et al. (2013)

Filters applied: Books and Documents, Clinical Trial, Meta-Analysis, Randomized Controlled Trial, Systematic Review.

1. Honey

Honey is mainly constituted by carbohydrates and water. Furthermore, honey contains numerous minor compounds in lower amount such as minerals, polyphenols, carotenoids, organic acids, proteins, amino acids, enzymes (glucose oxidase, catalase), vitamins and odorants. Most of honey's reported biological properties and many of its uses can be attributed to these minor components. [6,7,8]

Polyphenols are major group of compounds found in plant foods which include phenolic acids, flavonoids, stilbenes, and lignans but only flavonoids and phenolic acids are present in honey. Particularly, among flavonoids, only the flavonols (such as quercetin, kaempferol, myricetin, and fisetin), flavones (such as genkwanin, luteolin, apigenin, tricetin and chrysin) and flavanones (such as pinocembrin and pinostrobin) sub-groups are present in honey.

Phenolic acids are mainly divided in to two sub-groups: hydroxybenzoic and hydroxycinnamic acid. The four most common hydroxycinnamic acids are ferulic, caffeic, p-coumaric, and sinapic acids. The four commonly found hydroxybenzoic acids are p-hydroxybenzoic, protocatechuic, vanillic, and syringic acids. [1]

They are acknowledged as stupendous antioxidants also having a key role as anti-inflammatory, antidiabetic, antimicrobial, antiallergic, antiviral, antithrombotic, hepatoprotective and neuroprotective. [9]

Honey antioxidant activity is provided fundamentally by phenolic compounds rather than other components.[10] Whats more, phenolic acids exhibit significantly higher in vitro antioxidant activity than vitamins E or C.[11] In addition exogenous intake of antioxidants can diminish oxidant stress through counteracting the action of free radicals which prevents cell aging.[12]

1.1 Cardioprotective, antidiabetic properties

According to various studies, regular phenolic compound intake shows a negative correlation to risk of cardiovascular diseases. Phenols have an antithrombotic, antioxidant, anti-ischemic and vasorelaxant effect, therefore being beneficial in patients with coronary heart disease. Flavonoids are said to reduce coronary heart disease risk through three main mechanisms: improved coronary vasodilatation, suppression of thrombocyte activity resulting in slower clot formation and prevention of low-density lipoprotein (LDL) oxidization.[5,13,14]

Moreover, a cohort study of 18000 people in China shown that regular intake of honey had minimized the risk of prediabetes. The association persisted after detailed adjustment for confounders. Furthermore, the results of sensitivity analyses demonstrated the validity of these associations. Authors also showed that higher consumption of honey diminished prevalence of prediabetes. Compared to participants who rarely consumed honey, the multivariable OR of prediabetes were 0.94 (95 % Confidence Interval (CI) 0.86, 1.02) for \leq 3 times/week, 0.77 (95 % CI 0.63, 0.94) for 4–6 times/week and 0.85 (95 % CI 0.73, 0.99) for \geq 1 time/d (p for trend \leq 0.01).[15]

Although honey consumption has positive effects on diabetes, randomized controlled crossover clinical trial showed that 8 week intake of 50 g/day honey nonsignificantly increased glycated haemoglobin (HbA1c) (+0.17%, p = 0.22), which suggests honey should be consumed with special caution in people with diagnosed diabetes.[16]

Furthermore, recent randomized, double-blinded study shown that supplementation of honey lowers diastolic blood pressure from 77.92 mmHg at baseline to 73.45 mmHg (F-statistic = 2.55, p-value = 0.047) and fasting blood sugar from 6.11 mmol/L at baseline to 5.71 mmol/L (F-statistic = 4.03, p-value = 0.021) in 12 months' time in postmenopausal women.[17]

Despite honey ameliorating cardiovascular risk factors, clinical trials have not shown its supplementation to cause any significant changes in body mass in men, women and prepubertal girls. [13,18,19]

1.2 Infections and antimicrobial properties

Honey has a healing property due to its antibacterial activity which is mainly attributed to low water activity, low pH and hydrogen peroxide. two major non-peroxide antibacterial factors are methylglyoxal (MGO) and defensin-1. Due to high concentrations of methylglyoxal in manuka honey it's possible to kill bacteria such as metycylin resistant staphylococcus aureus MRSA. [25,26]

Honey is well known traditional remedy for symptoms deriving from upper respiratory tracts. Its included in practical algorithm created by the Italian Society of Pediatric Allergy and Immunology for acute cough in children and adolescents as natural remedy.[20]

In a systematic review and meta-analysis by Abeulgasim H. et al. 2020 was found that honey likely improved symptoms of upper respiratory tract infections with a significantly greater reduction in combined symptom score (three studies, mean difference -3,96 95% CI -5.42 to -2.51, I2=0%), cough frequency (eight studies, standardized mean difference (SMD) -0,36, 95% CI -0.50 to -0.21, I2=0%) and cough severity (five studies, SMD -0,44, 95% CI -0.64 to -0.25, I2=20%) compared to usual care. Adverse effects of consuming honey were not observed in most patients. Research suggests that due to frequent prescription of antibiotics despite lack of guidance, with little improvement of upper respiratory track symptoms and numerous adverse effects, honey can be a rational alternative for adults and children demanding such treatment. [21]

F O Anisaba et al. (2022) carried out a randomized study to assess the role of honey on upper respiratory tract infection symptoms compared to Diphenhydramine. Night-time honey doses given to children with cough from upper respiratory tract infection significantly reduces cough severity (4.00 and 0.00 vs 4.00 and 3.00, p<0.001) and frequency (5.00 and 0.00 vs 5.00 and 3.00, p<0.001) and improves children and caregivers sleep compared to Diphenhydramine which is consisted with Ahmadi M et al.(2013). research. [22,23]

What is interesting, In a multicenter, placebo-controlled randomized clinical trial evaluating the effects of Honey and Nigella sativa (HNS) on COVID-19, HNS reduced time needed to relieve symptoms compared to placebo for 50% (moderate cases: 4 vs. 7 days, Hazard Ratio [HR]: 6.11; 95% CI: 4.23-8.84, p < 0.0001 and for severe cases: 6 vs. 13 days, HR: 4.04; 95% CI: 2.46-6.64; p < 0.0001). What is more HNS reduced mortality in severe cases by 25%, cleared the virus earlier than placebo (4% vs. 18.87%, OR: 0.18; 95% CI: 0.02-0.92, p = 0.029) and remarkably alleviated symptoms. [24]

1.3 Wound healing

Another important function is stimulating the migration of fibroblast and promotion of collagen deposition during skin healing. [27]

The clinical application of honey's properties are effective wound healing as well as contributing to pain relief. The mechanism of pain relief in wounds is related to the presence of antioxidants in honey such as flavonoids, polyphenols, vitamin C and many more.

Fujie Zhang et al. (2021) analyzed in the review and meta-analysis the evidence to compare the efficacy of honey and povidone iodine-based dressings on mean healing duration, mean hospital stay duration and visual analogue scale (VAS) score of pain. They included 12 studies with a total of 1236 participants. The honey-based dressings showed moderate-to-large impact in reducing mean healing duration, shortened the length of hospital stay and decreased VAS score in contrast to the povidone iodine-based dressings. [28]

Evidence suggest that honey is effective in diabetic foot ulcer in reducing wound recovery time and rate, time of hospital stay and also ameliorate pain. What is more honey stimulate granulation in diabetic foot ulcer wounds. [29]

Honey can be used for every stage of wound healing, but it should be prepared properly. Honey should be always sterilized by gamma-irradiation because it does not impact honey antibacterial activity contrary to heat. Mild pain may occur when applying honey to infected wounds. Honey, when gelled or released gradually, is less acidic than regular honey or honey-soaked gauze dressings, lessening the nociceptive reaction, hence decreasing pain during treatment. [30]

Moreover, honey's strong antibacterial ability is connected to an improvement in delaying the onset of mucositis, decreasing the risk of treatment interruptions in patients with head and neck cancer with ongoing radiotherapy with or without coincidental chemotherapy. A reduction in the peak mucositis score due to honey was not observed. [31]

Honey possesses anti-inflammatory effects and aids in tissue re-epithelialization, accelerating healing and reducing pain.

1.4 Pain management

The role of honey for cicatrization and pain control of obstetric wounds was analyzed. There was no difference in the final wound healing between placebo and honey group (MD -0.34; 95% CI -1.13, 0.44; p=0.39). Nonetheless, the process in the honey group was much more convenient for the patient: lowers pain levels (SMD -0.54; 95% CI 0.83 to 0.25, p=0.03) (and therefore lower analgesic consumption), fewer complications and an increase in the overall satisfaction after the intervention (Overall response rate (ORR) 0.81; 95% CI 0.65, 0.98). [32] Data also indicated that honey has been employed to treat pain in women with primary dysmenorrhea as effectively as mefenamic acid. [33]

Studies have shown that honey consumption can benefit in lowering the frequency of analysics intake and pain levels post-operatively without side effects or allergies. The findings indicated that honey decreased pain perception, particularly in cases of inflammatory pain. [34.35.36]

2. Propolis

Propolis and its extracts are commonly employed in the treatment of numerous conditions. Propolis contains a high concentration of flavonoids, phenolic acids (caffeic and cinnamic acids), and resveratrol. It also contains vitamins B1, B2, B6, C, E, and minerals like magnesium, calcium, potassium, sodium, copper, zinc, manganese, and iron, as well as enzymes such as succinic dehydrogenase and glucose-6-phosphatase. They contain substances like caffeic acid phenethyl ester and artepillin C, known for their antiviral, anti-inflammatory, and immunomodulatory effects. [37,38,39]

2.1 Anti-inflammatory properties

Studies have shown that propolis supplementation has beneficial effect of inflammatory biomarkers such as IL-6 (95% CI: -4.62, -0.34; p = 0.023) and TNF-alfa (95 % CI: -1.45, -0.26; p = 0.005) but does not reduce the concentration of CRP (95 % CI: -0.03, 0.05, p = 0.646). It may act as a useful adjunct therapy for conditions where inflammation is a primary contributing factor. [40] On the other hand, another meta-analysis showed that propolis decreased serum levels of CRP and other inflammatory markers. The decrease was proportional to propolis dose and greater when Asian propolis was used. [41,42]

Given the limited studies, clinical variability, and other constraints, more high-quality research is needed for clearer and more detailed recommendations.

2.2 General diseases

Data showed evidence that propolis has positive effect on diabetes, regulates glycemic control and also may help improve other metabolic factors that are linked to type 2 diabetes.[43,44,45] Administering 300 mg of propolis twice daily for 12 weeks led to a significant reduction in fasting plasma glucose (FPG) (p=0.004) and 2-hour post-glucose levels (p=0.034). [43] Daily doses of 1000 and 1500 mg of propolis help decrease insulin levels and improve insulin resistance. The findings suggest that propolis can lower glucose levels after a 75g oral glucose load, increasing the study's relevance, as 2-hour post-glucose levels are associated with higher cardiovascular morbidity and mortality. [44,45]

Both high insulin levels and dyslipidemia are the key features in polycystic ovarian syndrome (PCOS). Supplementation with propolis elicited positive effects on fasting insulin and insulin resistance, in addition to reducing the testosterone level (p=0.004), low-density lipoprotein (LDL)/high-density lipoprotein(HDL) (p=0.02), and hip circumference (p=0.03), in PCOS women.[46]

What is more propolis has beneficial effect on liver enzymes such as alanine transaminase (95% CI, -4.58 to -0.61) and and aspartate aminotransferase (95% CI, -3.05 to -1.09). [45] Data showed that 8 week Propolis supplementation combined with a reduced-calorie diet improve liver function, the non-alcoholic fatty liver disease (NAFLD) fibrosis score (p = 0.013) and glucose parameters, fasting blood sugar (p = 0.037), the serum insulin level (p = 0.040) in patients with NAFLD compared to placebo. [47]

It also shown beneficial effects on cardiovascular risk factors. Propolis consumption led to a significant decrease in triglycerides levels, significant decrease in LDL-cholesterol levels, significant enhancing influence on HDL-cholesterol levels but no significant impact of propolis intake on total cholesterol (TC) levels compared with control groups. Furthermore, propolis consumption resulted in a significant decrease in the serum level of C-reactive protein high-sensitivity (hs-CRP). [48,49]

Propolis is also beneficial for improving health-related quality of life in chronic kidney disease (P < 0.05) [50]. In a randomized double-blind, placebo-controlled trial women receiving 500mg capsules of propolis had improved urinary frequency (p < 0.001), dysuria (p = 0.005) and urgency (p = 0.03), but did not relieve suprapubic pain and hematuria (p > 0.05). [51]

2.3 Cancer

Many in vitro studies show a promising and positive anticancer effect of propolis, suggesting its potential as a natural therapeutic agent in cancer treatment. Recently, this anticancer effect has also been investigated in human trials, providing further insights into its efficacy and potential applications in oncology.

Davoodi SH et al. (2022) investigated propolis effects vs. placebo on the nutritional status and quality of life in patients diagnosed with breast cancer who are receiving chemotherapy. After 3 months of receiving propolis 250 mg/two times per day , there was a significant improvement in energy intake in patients who were treated with propolis compared to place group $\,$ (p <0.001) and in quality of life.[52]

Also, safety and efficacy of propolis mouthwash in cancer patients with therapy-induced oral mucositis was evaluated. The results indicate that the occurrence of severe oral mucositis was notably reduced in the propolis group compared to the control group (OR = 0.35, 95% CI: 0.18 to 0.70 , p=0.003). [53]

2.4 Dental care

The oral cavity has the most diverse microbiological environment in humans, and excessive bacterial growth may lead to cavities and other oral diseases.

Studies aimed to assess the clinical efficacy of propolis containing mouthwash in oral diseases. It seems that propolis mouthwash can effectively decrease gingival inflammation and bleeding, without causing tooth discoloration or staining in gingivitis. [54]

Moreover, a potential beneficial role of propolis on reducing plaque has been reported.[55] Propolis extracts have also been proven to play a beneficial role in alleviating dentin hypersensitivity, offering a natural remedy for discomfort and sensitivity in patients experiencing the symptoms of this condition.[56]

Due to the recently discovered link between COVID-19 infection and periodontal diseases, the properties of propolis were evaluated in reducing the severity of COVID-19 symptoms by alleviating periodontal disease. Propolis has been known to mitigate bacterial infections through immune system activation and anti-inflammatory function, as well as its direct antibacterial properties. It can therefore mediate periodontitis development and symptoms. Studies have shown that the flavonoids contained in propolis inhibit the replication of the virus in some strains, including coronaviruses. The components of propolis show aminopeptidase inhibitor activity, which block the main proteases of SARS viruses and appear to inhibit spike proteins - the sites of most mutations in SARS-CoV strains. It can therefore be summarized that propolis reduces COVID-19 severity both through its antibacterial and antiviral properties, therefore affecting both COVID-19 itself and closely related periodontitis.[57]

2.5 Wound healing

Propolis can also be useful due to its skin regeneration stimulation and enhancement of reepithelialization. It can also reduce the inflammatory response and attain a more effective healing process.

Due to its anti-inflammatory and antioxidant properties propolis can be helpful as a supplementary treatment in the healing of human diabetic foot wounds. A study reported that propolis reduced wound area by 4 cm², increased connective tissue, boosted glutathione (GSH) levels and the GSH/GSSG ratio (p < 0.02), decreased TNF- α , and raised IL-10 levels. [58] Another study investigating the effect of Brazilian green propolis in chronic ulcer treatment suggested that propolis-based ointment has healing potential and aids in wound cleaning and debridement.[59]

The studies reported that propolis can be more effective in healing herpes simplex virus(HSV)-induced ulcers compared to acyclovir (95% CI: 2.70 to 8.25; p = 0.0001). Its effectiveness in treating and re-epithelialization HSV-induced ulcers in the oral and genital regions has been proven to surpass that of acyclovir. In addition, honey is equally effective as acyclovir in relieving pain from herpetic lesions.[60]

2.6 Depression

Depressive disorder is a common mental disorder affecting a variety aspects of patients well-being. Clinically it is treated with medicines that have numerous obstacles and side effects. Preclinical trials emerge the role of the potential of flavonoids and phenolic acids role to diminish depressive symptoms. [61,62] In a randomized placebo-controlled clinical trial showed that propolis with a combination of SSRI could safely alleviate symptoms of moderate-severe major depressive disorder. [63]

Conclusions

Pharmaceutical and clinical applications of bee products such as honey and propolis are attracting significant interest from researchers. Numerous clinical trials and meta-analyses have been conducted to assess health benefits for many different diseases. Honey due to its properties presents a very promising potential to be used in cardiovascular diseases, prediabetes, ischemic disease, hypertension and infectious diseases. According to the study's results, honey treatments showed greater efficiency and provided benefits to the patients by accelerating wound healing and decreasing reported pain and hospital stay but a good-quality, placebocontrolled randomized controlled trials are needed to clarify these findings and enable widespread use of this form of treatment. The approaches utilized are more budget-friendly, straightforward, safer, and more readily available. Moreover, honey is both accessible and inexpensive. Propolis shows a positive impact on wound healing, liver and kidney diseases, glycemic control and lipid profile. What is more, propolis extract can be regarded as an efficient, safe, and affordable alternative to conventional dental treatments due to its therapeutic effect on oral health. Many lines of evidence suggest that they can be beneficial in a combination with other therapeutic substances. Such approach can minimize the risk of side effects and lower doses of medications. Owing to its safety, efficacy, good-tolerability and cost-effectiveness, they may be regarded as a viable alternative to conventional treatments. Nevertheless, further research into the active ingredients that give honey and propolis its numerous therapeutic effects along with a better understanding of how these chemicals produce their effects on diseases in a large-scale randomized controlled trials (RCTs) are necessary. Consistent data could help guide the development of effective therapies and straightforward guidelines.

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Authors do not report any disclosures.

Authors' contributions

Conceptualization: Katarzyna Żak, Agnieszka Kluz; Methodology: Katarzyna Żak, Katarzyna Madyniak; Software: n/a; check: Hubert Jucha, Michał Mazur; Formal analysis: Katarzyna Żak, Hubert Jucha;

Investigation: Katarzyna Żak;

Resources: Katarzyna Żak, Hubert Jucha;

Data curation: Agnieszka Kluz;

Writing - rough preparation: Katarzyna Żak;

Writing - review and editing: Hubert Jucha, Katarzyna Madyniak;

Visualization: Katarzyna Michalak, Krystian Zukierski;

Supervision: Katarzyna Madyniak, Aleksandra Pliszka, Michał Mazur;

Project administration: Katarzyna Żak, Weronika Jarych;

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