



Shilajit and Honey: Hypothesizing Synergy and Nature's Power for Holistic Wellness

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ABSTRACT: Recently, significant lifestyle changes have led to metabolic syndrome, anxiety, depression, and a decline in quality of life. Additionally, the combination of increased workload, ambitious career goals, and the desire to match or exceed others' socio-economic status often results in poor nutrition, which causes various health problems, fatigue, reduced strength, and stamina. Therefore, there is a clear need for nutritional supplements to address these issues. Shilajit and honey are two natural compounds from different sources that offer powerful nutritional benefits. Both are effective antioxidants and anti-inflammatories with considerable nutritional value. In this manuscript, we explore the chemical compositions, pharmacological activities, mechanisms of action, and health benefits of Shilajit and honey. Based on this, we suggest combining them for synergistic health effects. We also identify current gaps in regulation, safety, and toxicology studies, and emphasize the need for well-designed research. Furthermore, a clinical trial is needed to confirm the effectiveness of this formulation.

KEYWORDS: Antioxidant; Anti-inflammatory; Natural product: Synergistic effect and Quality of life.

1. INTRODUCTION

Could an ancient Ayurvedic combination unlock new health benefits? Market options such as honey, Shilajit sticks, or syrups are emerging, indicating consumer interest in their “synergistic” effects. Both ingredients are well-known: honey, a natural sweetener high in antioxidants, has proven antimicrobial and anti-inflammatory properties [1]. At the same time, Shilajit is a mineral resin rich in fulvic acid and other components that has long been used in traditional Indian medicine as a rejuvenator and potent antioxidant [2]. Both compounds complement the antioxidant property and demonstrate increased free radical scavenging activity.

Honey is a natural substance synthesized by *Apis mellifera* bees using floral nectar, plant exudates, or the secretions of insects, which they enzymatically modify and dehydrate through evaporation [1]. China is the world's largest honey producer, accounting for about 28% of total production. Other key producers include Turkey (5.9%), Iran (4.5%), the United States (4.1%), and India (3.5%). Leading honey-exporting countries are China, New Zealand, Argentina, and India, while the leading importers are the United States, Germany, Japan, and the United Kingdom [3]. Renowned for being a nutritious and wholesome food, honey's composition varies widely based on its floral source and geographic region [4]. Honey mainly consists of sugars, making up about 80–85%, along with 15–17% water, and trace amounts of proteins ranging between 0.1% and 0.4% [5]. This composition includes enzymes, acids, vitamins, and phenolics, which shape flavor, aroma, and bioactivity [5]. The color of honey, ranging from white to deep brown, is mainly influenced by its mineral and phenolic content [5]. Based on its botanical origin, honey is classified into two types: monofloral honey, which mainly comes from a single plant species, and multifloral honey, which is made from nectar from various plant species [6].

Shilajit is a sticky, blackish-brown substance that oozes from mountain cliffs. It is biologically active and has a distinct odor similar to cow urine (gomutra). In simple terms, Shilajit is a natural substance with a tar-like consistency, appearing in irregular shapes with porous or smooth surfaces, and emitting a unique balsamic smell [7]. Over centuries of natural composting, plant and microbial matter create a resin rich in humic substances: about 60–80% of Shilajit's active fraction is fulvic acid, along with trace minerals like selenium [8]. In Ayurveda, it is valued as a “rasayana” or anti-aging tonic that boosts strength and longevity. Modern research and market analyses highlight Shilajit's powerful antioxidant and anti-inflammatory properties and explore its effects on energy, cognitive health, and healthy aging [9].

Given their complementary bioactive profiles and increasing popularity, the combined use of honey and Shilajit warrants scientific investigation. This review explores the hypothesis that honey and Shilajit work together synergistically. We will review relevant literature, including traditional reports and modern studies, on their individual and combined effects, looking for evidence that their pairing could enhance benefits beyond those of either ingredient alone. By incorporating market context and biochemical insights, this work aims to inform the scientific community about the potential of this innovative combination.

2. CHEMICAL COMPOSITION OF HONEY

Honey's chemical combinations form the basis of its medicinal uses in both traditional and modern medicine. Its primary components are sugars, making up about 80% of its total composition. Fructose (roughly 38.5%) and glucose (approximately 31.0%) are the main simple sugars, providing energy, sweetness, and contributing to honey's distinct viscosity. In addition to these main sugars, honey contains smaller amounts of disaccharides like sucrose and maltose, along with trace levels of trisaccharides such as maltotriose and melezitose. Beyond serving as an energy source, honey also contains various health-promoting bioactive compounds [10].

The biological activity of honey is mainly affected by enzymes added by bees, such as invertase, diastase, catalase, and glucose oxidase [11]. These enzymes generate hydrogen peroxide, which gives honey its antimicrobial properties that inhibit harmful microbes [12,13]. These enzymes break down complex sugars

into simpler forms, resulting in the formation of gluconic acid and hydrogen peroxide—compounds that increase honey's acidity and antimicrobial properties [14]. The proteins in honey mainly come from bee secretions and pollen, adding to its overall nutritional content [15-19]. Honey's flavonoids complement its polyphenols, promoting overall health and wellness [19]. Chrysin, a compound found in honey, exhibits potent antioxidant, anti-inflammatory, and anticancer properties, emphasizing its role in supporting disease prevention [16]. Luteolin, present in honey, possesses anti-inflammatory properties and helps protect cells against oxidative stress [20]. Likewise, other flavonoid in honey offers anti-inflammatory benefits and shield cells from oxidative stress [21]. These flavonoids in honey combine to support overall health and address various health issues [22].

3. HONEY'S TRADITIONAL APPLICATIONS

Honey has played an essential role in medicine for more than two millennia [23]. Classical medical texts emphasize its notable healing abilities, acknowledging it as both a therapeutic agent and a nutritional supplement [24,25]. In Traditional Medicine, honey is known for relieving dryness and is particularly useful for conditions related to fluid imbalance in the body [23]. For example, honey is often used to help soothe dry coughs, sore throats, and breathing difficulties [26]. Honey is believed to soothe and hydrate the lungs, making it an essential remedy for respiratory issues caused by dryness or yin deficiency [27].

Honey is also valued for its soothing effects on digestion [28]. It soothes and regulates the stomach, helping to relieve issues like bloating, stomach pain, and indigestion [29]. Its moisturizing properties make it a gentle remedy for constipation. [29]. Recently, honey-based suppositories have become a modern method to help relieve constipation [30]. Applied to the skin, honey's antibacterial and anti-inflammatory properties aid in healing wounds, burns, and ulcers [31,32]. Honey aids in healing damaged skin by promoting tissue regeneration and shielding against infections, strengthening its role in treating skin injuries [33]. Honey frequently acts as a carrier in herbal medicine, improving how herbal remedies are delivered [31,34]. Its natural sweetness masks bitter herbal flavors, and its viscosity preserves herbal extracts, improving absorption [35,36].

4. MOLECULAR MECHANISM OF HONEY

Honey's molecular mechanisms operate through the modulation of multiple signaling pathways that are central to cellular homeostasis and disease pathogenesis, as shown in Figure 1 [37]. The main pathways involved include the nuclear factor-kappa B (NF- κ B) signaling cascade, mitogen-activated protein kinase (MAPK) pathways, and the intrinsic apoptotic machinery. These pathways work together to produce honey's overall therapeutic effects, with crosstalk between different molecular targets enhancing the overall biological response [38]. The NF- κ B signaling pathway is a key mechanism through which honey provides its therapeutic effects. Honey notably prevents NF- κ B from moving into the nucleus by stopping the breakdown of inhibitor κ B α (I κ B α) and blocking the nuclear buildup of p65 and p50 subunits [39]. This inhibition occurs through various mechanisms, including the suppression of the I κ B kinase (IKK) complex activation and the subsequent prevention of I κ B α phosphorylation and degradation. The result is a significant decrease in the expression of pro-inflammatory mediators such as tumor necrosis factor- α (TNF- α), interleukin-1 β (IL-1 β), interleukin-6 (IL-6), cyclooxygenase-2 (COX-2), and inducible nitric oxide synthase (iNOS) [40].

Along with NF- κ B inhibition, honey influences the MAPK signaling pathway, especially affecting the phosphorylation of extracellular signal-regulated kinases (ERK1/2), p38, and c-Jun N-terminal kinase (JNK). This combined suppression of NF- κ B and MAPK pathways results in a comprehensive reduction of inflammatory responses since both pathways are vital for activating inflammatory genes. The coordinated blocking of these pathways highlights honey's ability to target multiple molecular mechanisms at once,

offering a more effective therapeutic strategy than targeting a single pathway. Additionally, the apoptotic machinery is another key target for honey's therapeutic effects, particularly as a natural approach to prevent cellular damage and cancer [41]. Honey induces apoptosis through several mechanisms, mainly involving the mitochondrial pathway. The process starts with mitochondrial membrane depolarization, which leads to the release of cytochrome c and other apoptogenic factors from the intermembrane space [38]. This release activates caspase-9, which then activates the executioner caspase-3, leading to the characteristic features of apoptosis, including DNA fragmentation and cell death [41].

Cell cycle regulation is another key mechanism by which honey provides therapeutic benefits. Honey treatment causes cell cycle arrest, especially in the G₀/G₁ and G₂/M phases, preventing abnormal cell growth. This arrest occurs through the regulation of cell cycle proteins, including increased levels of p21 and changes in cyclin expression [38]. The ability to stop cell cycle progression is especially important in preventing damaged cells from proliferating and in maintaining tissue homeostasis. These detailed molecular mechanisms demonstrate that honey is a versatile therapeutic agent capable of addressing different aspects of disease development all at once. The combination of multiple pathways, along with honey's natural origin and excellent safety profile, makes it a valuable addition to treatment options.

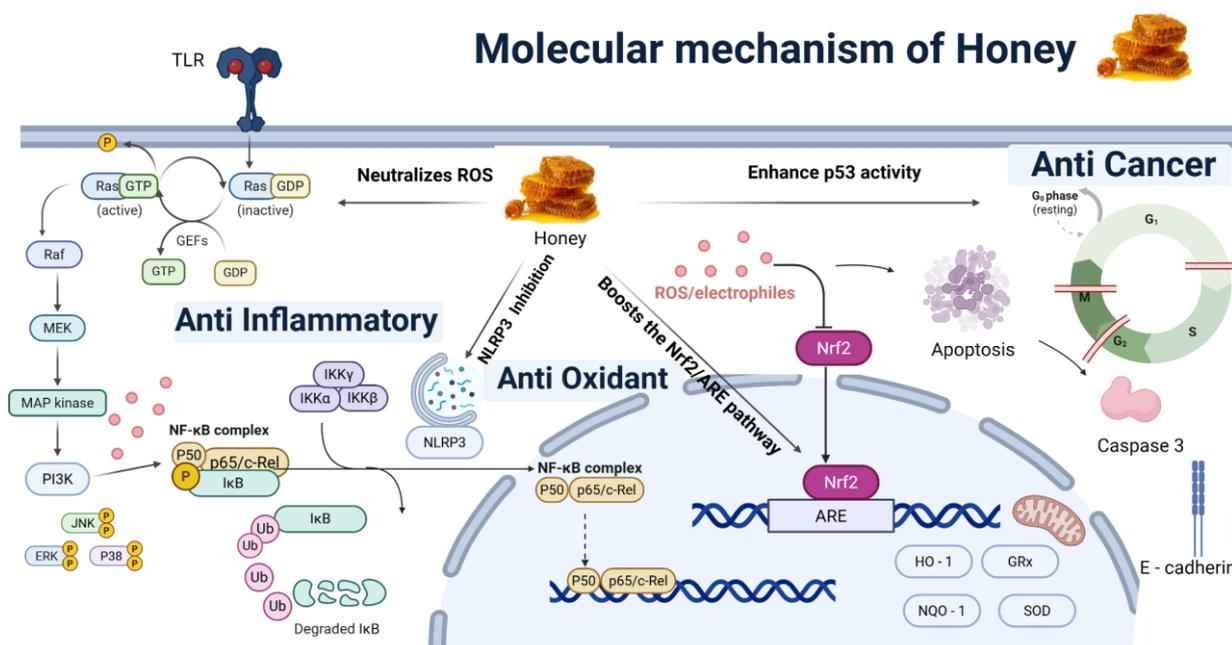


Figure 1. Showing the molecular mechanism of Honey, and its various benefits.

4.1 Antioxidant Effects

The antioxidants in honey, such as phenolic acids and flavonoids, help neutralize free radicals, reduce oxidative stress, and may lower the risk of chronic diseases like cancer and heart disease [42,43]. Honey's antioxidant potential has been confirmed through multiple analytical methods, including DPPH, FRAP, ORAC, and Trolox-equivalent antioxidant capacity assays [44,45]. Phenolic compounds like caffeic acid and quercetin in honey display potent antioxidant and anti-inflammatory effects, strengthening the body's capacity to combat oxidative stress [46,47]. Regularly consuming honey may boost antioxidant enzymes like superoxide dismutase (SOD) and glutathione peroxidase (GPx), which help protect cells from damage caused by reactive oxygen species (ROS) [46,48]. Beyond combating oxidative stress, honey's antioxidant properties are key to its health benefits, like aiding wound healing, supporting heart health, and possibly offering anticancer effects. [49]. Honey's flavonoids neutralize free radicals, reduce inflammation, and prevent tissue damage, demonstrating its therapeutic benefits [43].

The chemical structure of phenolic acids and flavonoids influences their biological effects [50]. Honey is rich in potent antioxidants such as quercetin, caffeic acid, gallic acid, chrysin, luteolin, and kaempferol, all known for their effective ability to neutralize free radicals [51,52]. The effectiveness of these compounds in fighting oxidative damage depends on their molecular structure, particularly the placement of hydroxyl groups [53]. The antioxidants in honey help protect the body from conditions related to oxidative stress, such as diabetes, cardiovascular diseases, and cancer [54]. Honey's antioxidants fight oxidative stress by reducing reactive oxygen species, minimizing lipid damage, and decreasing inflammation, making it an effective natural remedy. More research on its compounds could lead to new functional foods and nutraceuticals.

4.2 Wound-Healing Benefits

Honey has been valued for wound healing since ancient times because of its ability to fight microbes, support the immune system, and provide antioxidants. These qualities make it a strong natural choice for aiding tissue repair and preventing infections [55]. Honey creates a moist environment for wound healing while serving as a protective barrier against contamination. Its acidity and low moisture content inhibit bacterial growth, reducing the risk of infection. [56]. Its high sugar concentration creates an osmotic effect that draws excess moisture away from the wound, helping to reduce swelling and promote healing [57].

Honey contains the enzyme glucose oxidase, which allows a gradual release of hydrogen peroxide. This provides continuous antimicrobial protection while being gentle on tissues, unlike the damaging effects sometimes caused by synthetic antiseptics [58]. Additionally, honey accelerates wound healing by aiding in debris removal and removing dead tissue, thereby creating an ideal environment for recovery. Clinical studies support honey's superior effectiveness in wound care, with research indicating better healing results compared to traditional wound dressings [59]. Manuka honey has received FDA approval for medical use in wound care and is highly valued for treating infections caused by resistant organisms [60]. Different types of honey, such as wildflower honey, also demonstrate notable healing properties [61].

In conclusion, honey's various wound-healing properties make it a promising natural treatment, but medical supervision is advised for safe and effective use.

4.3 Cardioprotective Effects

Honey supports heart health by improving fat metabolism and reducing levels of total cholesterol, LDL cholesterol, and triglycerides, which helps lower the risk of atherosclerosis [62]. Bioactive substances such as flavonoids and polyphenols offer antioxidant benefits that help decrease oxidative stress and promote heart health [63]. Honey's anti-inflammatory effects play a vital role in managing chronic inflammation, which is a crucial factor in the development of cardiovascular diseases. By reducing inflammation, honey may help prevent the buildup of atherosclerotic plaques and promote heart health [64]. Recent studies suggest that eating honey regularly might help lower blood pressure slightly, which could assist in managing hypertension [65]. Honey may improve endothelial function, support blood vessel health, and potentially reduce the risk of heart-related problems [65]. Honey's combination of antioxidant, anti-inflammatory, and cholesterol-lowering effects suggests it could reduce the risk of atherosclerosis, which involves plaque buildup in the arteries.

Research indicates honey may indirectly promote heart health by affecting obesity and diabetes, which are major risk factors for cardiovascular disease [54]. Its vasodilatory effects and endothelial benefits may enhance circulation, lessen heart strain, and promote blood vessel health [65]. Early research suggests that honey's antioxidant and anti-inflammatory properties could help lower the risk of heart attacks, but more studies are necessary to confirm this [66,67]. Honey's heart-protective benefits can differ based on its plant source and processing methods. It's best enjoyed in moderation as part of a healthy lifestyle, and those with existing heart conditions should consult their doctor for personalized advice.

4.4 Antihypertensive Effect

High blood pressure plays a key role in causing heart diseases by affecting the coronary arteries, altering the structure of the heart muscle, and potentially leading to heart failure [68]. Recent research points to honey's potential role in lowering blood pressure through several biological pathways, indicating its value as a supportive dietary option for managing hypertension. Evidence shows that honey consumption may help reduce blood pressure by influencing different physiological systems. Research on rats with high blood pressure has been demonstrated that honey may help lower systolic blood pressure and block the activity of the angiotensin-converting enzyme, which plays a key role in regulating blood pressure [69]. Additionally, studies on animals have found that honey drinks fortified with γ -aminobutyric acid can lower high blood pressure, with significant reductions in systolic pressure seen after seven weeks of use [69].

The primary mechanism through which honey exerts its antihypertensive effects appears to involve lowering oxidative stress in the kidneys. Studies have demonstrated its ability to reduce oxidative stress by lowering markers such as malondialdehyde and increasing antioxidant enzymes like catalase and glutathione-S-transferase [70]. Honey activates nuclear factor erythroid 2-related factor 2 (Nrf2), boosting antioxidant defences, which helps reduce oxidative stress and lowers systolic blood pressure in rats with hypertension [71]. Honey may help lower high blood pressure by reducing cortisol levels and relaxing blood vessels, which decreases overall vascular resistance and eases stress-related hypertension [69]. The cardiovascular advantages of honey should be considered supportive alongside conventional methods for managing high blood pressure. Maintaining a healthy lifestyle, such as balanced nutrition, consistent exercise, stress reduction, and following medical treatments, is crucial. It's vital to consult healthcare providers before adding honey to a personalized treatment plan. More clinical studies are needed to establish appropriate dosages, understand long-term impacts, and clarify how honey works in humans.

4.5 Antidiabetic Effects

Despite progress in medical treatment, type 2 diabetes remains a significant worldwide health issue [72]. The unique balance of fructose and glucose in honey, along with its relatively low glycemic index, may help lower blood sugar levels by activating enzymes like glucokinase and promoting glycogen storage, thus aiding better blood glucose regulation [46]. Honey's antioxidant properties may decrease oxidative damage in pancreatic β -cells, aiding in preserving their insulin production and enhancing blood sugar regulation [18,46].

Animal and lab studies have indicated that honey may lower blood sugar, enhance insulin response, and reduce markers like glycated hemoglobin and fructosamine, suggesting it could help manage blood glucose. Additionally, the oligosaccharides in honey might positively influence gut bacteria, which in turn may improve glucose metabolism and blood sugar regulation [72]. Due to its glycemic properties, honey consumption requires careful portion control in diabetic individuals. Although some evidence suggests honey may offer mild benefits over refined sugars in terms of insulin sensitivity and postprandial glucose response, variability in honey composition and study methodologies prevents definitive conclusions. Therefore, honey can be included in a well-balanced diet for individuals with diabetes, but only with guidance from a healthcare professional and regular blood sugar monitoring. It should complement, not replace, other essential aspects of diabetes care.

4.6 Anti-inflammatory Effects

Honey's notable anti-inflammatory effects result from its diverse range of bioactive molecules, such as phenolic acids and flavonoids, which help regulate inflammatory responses by inhibiting the activation of nuclear factor kappa B (NF- κ B), a key regulator of inflammation [73]. Honey helps control inflammation by blocking the activation of I κ B α , which is a crucial step for the movement of NF- κ B-p65 into the cell nucleus. This action decreases the production of inflammatory substances such as TNF- α , IL-1 β , and MCP-1. This

precise regulation at the molecular level explains honey's effectiveness in reducing inflammation and alleviating related issues. Furthermore, honey's blend of phenolic compounds, antioxidants, and natural enzymes works synergistically to reduce oxidative stress and inflammation. It does this by neutralizing reactive oxygen species and inhibiting the activity of enzymes like COX-1 and COX-2, which lowers prostaglandin production and helps relieve inflammation-related symptoms [74]. The anti-inflammatory effectiveness of honey depends on its type and how it's processed. Darker honey, such as buckwheat honey, generally exhibits stronger anti-inflammatory properties because it contains higher levels of phenolic compounds and flavonoids. Also, raw or minimally processed honey preserves more bioactive compounds, enhancing its therapeutic potential compared to heavily processed varieties [1]. Altogether, these attributes emphasize honey's value as a natural remedy for reducing inflammation and boosting the immune system balance.

4.7 Immunomodulatory Effects

Honey supports immune system regulation through its diverse components, such as polyphenols, flavonoids, and natural sugars. These compounds work together to stimulate immune cell growth and promote the release of key signaling molecules like TNF- α , IL-1 β , and IL-6 [75]. Certain flavonoids found in honey, such as quercetin and luteolin, help regulate immune function and reduce inflammation. They achieve this by decreasing the production of pro-inflammatory cytokines and inhibiting the expression of genes involved in inflammatory responses, which may assist in managing autoimmune conditions and chronic inflammation [37,73]. Honey promotes wound healing by stimulating the local immune system and increasing the release of cytokines at the site of injury, which aids in tissue repair and the regeneration process [76]. Although the sugars in honey are not the main drivers of its immunomodulatory effects, they might support it indirectly, possibly by producing short-chain fatty acids (SCFAs) [76]. Together, these different actions highlight honey's potential as a natural remedy for enhancing immune responses, promoting skin regeneration, and assisting in managing conditions caused by inflammation.

4.8 Antiviral Activity

Honey demonstrates antiviral effects due to several factors in its composition, including its naturally low pH, elevated osmolarity, and the slow release of hydrogen peroxide through glucose oxidase activity. These elements work together to create an environment that can hinder viral activity and replication [77]. Honey exerts antiviral effects through multiple mechanisms. Its high sugar concentration creates a hypertonic environment that draws moisture away from viral particles, impairing their integrity. The naturally acidic pH of honey also disrupts viral structures and reduces their ability to infect host cells. Additionally, honey contains bioactive compounds like flavonoids and phenolic acids, which may hinder viral replication while also providing antioxidant and antimicrobial support. Recent studies suggest that honey may be effective against SARS-CoV-2, the virus responsible for COVID-19. It has demonstrated the ability to inactivate various enveloped viruses such as influenza, herpes simplex, varicella-zoster, and HIV, highlighting its wide-ranging antiviral effects [78,79]. Computer-simulated studies suggest that bioactive components in honey could block SARS-CoV-2 proteases, potentially disrupting the virus's ability to replicate. Moreover, methylglyoxal (MGO), a key compound in manuka honey, has demonstrated antiviral effects against influenza viruses and may also help inhibit SARS-CoV-2, highlighting honey's potential as a therapeutic option [80].

Honey boosts the immune system by encouraging the production of cytokines, which help improve the body's ability to fight viral infections [81]. Its anti-inflammatory effects help reduce excessive inflammation during viral infections, which is especially important in COVID-19, where inflammation significantly worsens the illness [82]. Honey's antioxidant and anti-inflammatory components help regulate immune function and reduce the risk of complications [83]. Honey may help relieve symptoms of viral infections like sore throats

and coughs, although its effectiveness can vary depending on the virus. Ongoing clinical trials are exploring honey's potential to ease COVID-19 symptoms. It's important to avoid giving honey to infants under one year old and to be cautious with individuals allergic to bee products. Honey should be seen as a supportive remedy rather than a standalone treatment, and more research is needed to confirm its benefits.

4.9 Anticancer Activity

Honey contains a variety of bioactive compounds, especially phenolics, that show promise in cancer treatment by triggering programmed cell death in malignant cells. It activates enzymes like caspase-3 and influences regulatory proteins, including P53, Bax, and Bcl-2, encouraging apoptosis and blocking pathways that prevent cell death, which highlights its potential as a therapeutic agent, as shown in Figure 1. [37,84]. Honey's antioxidants fight oxidative stress, which contributes to cancer development, and its ability to prevent mutations helps reduce cancer risk [85]. Additionally, it interferes with cell signaling pathways and cell cycle progression, stopping cancer cell growth in various types, including glioma, colon, and melanoma cells [86]. Studies explore honey's role in cancer prevention, though results vary depending on the cancer type and processing methods. It should be viewed as a supplementary option rather than a primary treatment for cancer.

4.10 Gut Microbiota Modulation

Honey contains oligosaccharides like fructo-oligosaccharides and inulin that serve as food for beneficial gut bacteria, including Bifidobacterium and Lactobacillus, helping to maintain a balanced and healthy digestive system [87]. These carbohydrates pass through the digestive system without being broken down and reach the gut, where they are fermented by beneficial bacteria. This process promotes a healthy balance of gut microbes and supports overall metabolism [88]. Honey boosts probiotic viability and growth, both in vitro and during gut transit, leading to increased short-chain fatty acid production, which supports gut health and may prevent diseases [87]. Furthermore, manuka honey and probiotics work synergistically, promoting the growth of beneficial bacteria while suppressing harmful pathogens [89].

Honey's encapsulating properties protect probiotics, such as Bifidobacterium, from harsh gut conditions, similar to traditional agents [90]. Research shows that formulations with honey can boost the levels of lactic acid bacteria in both animals and humans, highlighting honey's ability to promote the growth of beneficial Research shows that formulations with honey can boost the levels of lactic acid bacteria in both animals and humans, highlighting honey's ability to promote the growth of beneficial gut microbes. gut microbes [91]. Although honey-derived oligosaccharides might not be as strong as fructo-oligosaccharides (FOS) as prebiotics, they are selectively fermented by specific gut bacteria, supporting the survival and activity of probiotics [92]. These findings emphasize honey's capacity to act both as a prebiotic and as an ingredient that supports symbiotic products, aiding in regulating gut microbiota and enhancing the body's natural defense against harmful microbes.

5. TRADITIONAL USAGE OF SHILAJIT AROUND THE WORLD

Mummiyo, another name for Shilajit, was widely used by Hakims, Ayurvedic, and Siddha vaidhis for treating inflammatory and genitourinary disorders and as an aphrodisiac [93]. In Tajikistan, Shilajit is commonly added to the daily diet, and various food supplements containing Shilajit are available on the market there [94]. It is commonly recognized as an immunostimulant and anabolic dietary additive [95]. In Russia and other former Soviet republics, Shilajit has been used to manage diabetes, slow the aging process, and treat arthritis [6]. Shilajit is a naturally occurring, mineral-rich substance that is usually dark in color and comes from rock formations in high-altitude areas in various parts of the world [96]. Recently, Shilajit has become popular in Germany for treating various ailments in phytotherapy [97]. Additionally, Shilajit is commonly used in the Gulf countries, Pakistan, and Iran as a Vajikaran Dravya (aphrodisiac) [98].

6. CHEMICAL CONSTITUENTS

Shilajit from various regions contains a wide range of organic compounds, mainly consisting of humic acids (about 80–85%) and the rest made up of non-humic substances (roughly 15–20%) [9]. On average, it contains approximately 14–20% water, 18–20% minerals, 13–17% protein, 4–4.5% fats, 3.3–6.5% steroidal compounds, 18–20% nitrogen-free extracts, 1.5–2% carbohydrates, and trace amounts (0.5–0.8%) of alkaloids, amino acids, and other bioactive elements. [8]. Shilajit consists of a complex mixture of natural substances, including humins, humic acids, and fulvic acids. These components are always present and help carry other active compounds [99]. It also contains various active substances, including benzoic acid, benzoates, and hippuric acid. Research has identified numerous compounds, such as Shilajityl acetate, lipids, steroids, carbohydrates, alkaloids, amino acids, and vitamins. Additionally, Shilajit contains polyphenols, essential oils, and other bioactive molecules like ellagic acid, triterpenes, and phenolic acids [99, 100].

7. BIOACTIVITY OF SHILAJIT

Research shows Shilajit has a range of bioactivities, including antioxidant, anti-inflammatory, antiviral, and immunomodulatory effects [9]. These findings, supported by animal studies, in vitro research, and clinical models, demonstrate Shilajit's potential. However, some conclusions need further investigation and more targeted studies.

7.1 Immunomodulatory Effects

Fulvic acid and other components in Shilajit boost immune function by increasing ROS and nitric oxide production in macrophages and stimulating lymphocyte activity. Shilajit also enhances T-cell-mediated cytotoxicity and helps restore lymphocyte counts after radiation exposure, with its effects on white blood cells being dose-dependent [101].

7.2 Antioxidant Properties

Shilajatu demonstrates strong free radical scavenging activity. In a study assessing oxidative stress caused by CCL4, Shilajatu was found to boost antioxidant activity in rat liver homogenate [102]. Additionally, the antioxidant effect of Shilajit was tested by measuring its ability to prevent lipid peroxidation caused by iron (Fe²⁺) in rat liver tissue samples. It was summarized that a 300 mg/kg daily dosage significantly enhances antioxidant activity [101]. Native Shilajatu from Bahr Aseman Mountains showed moderate antioxidant properties, whereas Shilajatu from Pakistan and Afghanistan exhibited stronger antioxidant effects [101]. Additionally, Shilajatu completely protected methyl methacrylate (MMA) from hydroxyl radical-induced polymerization.

7.3 Anti-diabetic effects

A comparative study on an animal model found that 100 mg/kg of Shilajit administered daily effectively reduced the hyperglycemic effects of streptozotocin. Improvement was observed as early as the 14th day with continued Shilajit treatment [77]. In another study, it was concluded that at the same dose level (100 mg/kg/day), adding Shilajit to conventional antidiabetic medications could improve glycemic control. [78]. Furthermore, a clinical study involving diabetic individuals used Shilajit that led to a significant decrease in postprandial (P<0.001) and fasting blood glucose (P<0.001) [79].

7.4 Anti-Microbial Effects

UV-treated Shilajit exhibits strong antimicrobial effects against different bacteria and some fungi, including *Penicillium chrysogenum* [103]. An in vitro study demonstrated Shilajatu's ability to inhibit bacterial growth, especially against human pathogens. Shilajatu extracts at various concentrations inhibited *S. aureus* in vitro, but there was no effect on *E. coli* [104]. Other studies have demonstrated Shilajatu's ability to decrease microbial activity, with *E. coli* being the most impacted [105]. Studies show that adding Shilajit to the diet

enhances antioxidant defenses, strengthens the immune system, and improves resistance to disease in *M. rosenbergii* when challenged with *A. hydrophila* [106]. Furthermore, Shilajit has been shown to shorten treatment duration in patients with pulmonary tuberculosis, emphasizing its potential therapeutic benefits.

7.5 Anti-Viral Properties

Shilajit shows dose-dependent antiviral effects against several viruses, including HSV1, HSV2, HCMV, and RSV. However, it was ineffective against HRV and VSV. Fulvic acids found in Shilajit have demonstrated antiviral properties. Clinical research indicates that Shilajit could improve the effectiveness of antiretroviral therapy (ART) in people with HIV and might help inhibit HIV enzymes when used alongside *Andrographis officinalis* [107].

7.6 Effects on Anxiety, Adaptogenic Properties, and Cognitive Function

Shilajatu has shown anxiolytic effects in ethanol-induced anxiety models in mice, with results that depend on the dose [108]. Furthermore, both processed Shilajatu and its active constituents, such as Fulvic acids, improved learning and memory retrieval in battery tests [109]. Clinical studies on Alzheimer's patients showed a decrease in cognitive decline among those treated with Shilajatu compared to a placebo group. [9]. Pre-treatment with Shilajatu extract effectively protected mice from haloperidol-induced catalepsy, indicating its potential to prevent extrapyramidal side effects of antipsychotic drugs [110].

7.7 Anabolic Properties

In athletes, Shilajatu has been shown to activate anabolic processes in cells and tissues. Daily administration of 500 mg of Shilajatu was found to promote favorable muscle and connective tissue adaptations. In animal studies, Shilajit increases protein and nucleic acid synthesis, enhances liver energy metabolism, and promotes mineral transport to muscles and bones, including calcium, phosphorus, and magnesium [111].

7.8 Endocrine and Anti-Diabetic Effects

Animal studies showed that Shilajatu, when used with traditional medicines, improved blood sugar management [112]. Other research found that Shilajatu helped reduce the hyperglycemic response caused by streptozotocin. In clinical trials, significant improvements were observed in fasting and postprandial blood sugar levels in diabetic patients treated with Shilajatu. Shilajatu also contains α -Lipoic acid, which is beneficial in treating type-2 diabetes, supporting its use in Ayurvedic diabetes management [113].

7.9 Anti-Ulcerogenic Effects

Research has demonstrated that Shilajit supports wound healing, boosts mucosal barrier protection, and shows notable anti-inflammatory effects in experimental models. Furthermore, Shilajit has been observed to lower the gastric ulcer index and prevent duodenal ulcers, likely due to the presence of Fulvic acids and other bioactive compounds [114].

7.10 Effects on Infertility and Testosterone

A clinical trial found that taking Shilajit for 90 days resulted in a significant increase in free testosterone and dehydroepiandrosterone (DHEAS) levels, showing better results compared to the placebo group [115]. Animal studies also showed that Shilajatu increased sperm volume, motility, and other parameters in male rams. Additionally, a clinical evaluation revealed improvements in sperm count, motility, and morphology, while reducing the number of pus and epithelial cells [9].

7.11 Cardioprotective Effects

In animal studies with induced myocardial injury, Shilajatu preserved heart function, lowered serum cardiac troponin levels, and decreased the severity of cardiac lesions [116]. Clinical trials also showed the beneficial

effects of Shilajatu on endothelial function and lipid profile, demonstrating more positive results than simvastatin in certain cases [117].

7.12 Miscellaneous Effects

Shilajit has been shown to reduce symptoms of chronic fatigue syndrome by affecting the hypothalamus-pituitary-adrenal (HPA) axis and supporting mitochondrial health. It also demonstrated promising effects in reducing cartilage degeneration in rats with induced osteoarthritis and possesses anti-arthritic properties in dogs. Shilajatu was effective in improving symptoms of polycystic ovarian syndrome (PCOS) in rats [118]. Combining approaches in medicinal plant therapy has shown greater effectiveness compared to using single drugs for treating various diseases. Combination therapies have transformed traditional medicine, providing new hope for patients with infectious diseases and cancer by using multiple treatments [119]. While the specific mechanisms are still unclear, medicinal plant combinations are often used in toxicological settings. Ayurvedic medicine frequently includes metals in herbal formulations, called Rasasadhies (Herbo-Mineral Metal Preparations), to harness their therapeutic effects, even though there is general caution about heavy metals in medicinal products. These preparations are believed to provide benefits such as improved taste, extended shelf life, no taste, quicker action, and smaller doses [120].

In traditional Indian medicine, polyherbal formulations, which combine multiple plant extracts, are favored over remedies that use only a single plant. Ayurvedic treatments mainly rely on such polyherbal formulations. [121,122]. Research has highlighted potential interactions between plant components and their combined use in herbal formulations, which may involve complementary, supportive, or mutually beneficial effects [121]. The Unani medical system has also gained global popularity for its notable therapeutic effectiveness, leading to increased adoption of these practices worldwide. However, progress in regulation has been slower due to the lack of standardized assessments [122]. Studies have shown that combining plants rich in flavonoids and phenolics, like green tea, in polyherbal blends can produce potent antioxidant extracts. [122]. Traditional medicine often favors using combinations of herbs rather than single herbs, relying on synergistic effects to boost effectiveness and reduce side effects, especially for conditions like diabetes [123]. A study showed that a polyherbal cream for diabetic foot ulcers is just as effective and safe as conventional silver sulfadiazine cream [124].

Herbal formulations, which leverage the complex pharmacological properties of combined botanicals, have been used in various global herbal medicine traditions [125]. Each herbal blend contains particular chemical compounds that, when combined, can achieve the intended therapeutic effects [126]. Ayurvedic products are gaining popularity due to increased interest in plant-based formulations. Synergism in herbal combinations can happen through pharmacokinetic or pharmacodynamic interactions [127]. While herbal remedies are widely used, their combinations, often sourced from different plants, can pose unique challenges due to variations in species, growing conditions, and active ingredients. However, combining different active components can improve overall effectiveness compared to single-component treatments, providing a clear advantage over traditional medications. The complex interactions between active compounds in polyherbal formulations can lead to synergistic, potentiative, or antagonistic effects [128]. Combining plants can boost potency compared to individual extracts, but adding multiple ingredients may also cause chemical incompatibilities and stability problems [129]. The regulatory oversight of Ayurvedic herbal formulations in India is less strict than that for pharmaceuticals, which can impact the quality and standardization of these products in both domestic and international markets [130]. Notably, Ayurvedic formulations don't need mandatory toxicity studies or clinical trials to obtain patents or manufacturing licenses [131].

Understanding herb-herb interactions is crucial for maximizing the benefits of plant-based treatments. Combining plant extracts or their active ingredients can create synergistic effects that boost effectiveness

while reducing side effects and the needed doses of each component [132]. To better understand these effects, using molecular, cellular, and analytical techniques together can help investigate the outcomes of multi-ingredient prescriptions [133]. However, traditional pharmacological methods may not fully explain the combined effects of multiple herbs. New "omic" technologies and systems biology could develop innovative strategies for studying phytopharmaceutical combinations to reveal their full potential. [133]. The word "herbomics" refers to the application of "omics" approaches to the study of herbs, highlighting the role of systems biology in understanding herbal medicine [134]. Phytomedicines, with their multi-target approach and lower doses, may provide a safer and more effective alternative to single-target chemical treatments. [135].

8. ADVANTAGES OF USING COMBINED METHODS IN HERBAL TREATMENTS: [136].

- When different components are combined, their interaction can enhance the overall therapeutic effect, leading to results that might not be achieved by using each one alone.
- Formulations with multiple herbs often provide a wider range of effective doses, allowing them to work well at lower amounts and remain safe even at higher doses, which improves their overall risk-to-benefit ratio.
- Herbal blends with various ingredients can target multiple biological pathways simultaneously, offering a comprehensive approach to managing health conditions.
- When two herbs are combined, they can interact to boost treatment effects by improving how the body absorbs, processes, or responds to the compounds involved.
Using herbal blends can deliver the desired benefits with smaller doses, reducing the risk of side effects compared to standard pharmaceutical drugs.
- By adopting a holistic approach, herbal combinations can work together to address complex health issues while minimizing side effects, utilizing traditional knowledge, and enhancing treatment outcomes through personalized plans, stress resilience, and better absorption.

9. COMBINATION OF HONEY AND SHILAJIT

Both honey and Shilajit contain bioactive compounds and have long-standing traditions of use in traditional medicine [137,138]. The reason why Shilajit should be combined with honey is its complementary properties. The antimicrobial and wound healing properties of honey may enhance the bioavailability and effectiveness of the bioactive constituents ingested with Shilajit [138]. Additionally, honey could improve the flavor and acceptance of Shilajit, which tastes resinous and very sweet [139]. This synergistic effect is expected to enhance health benefits, such as immune support, anti-inflammatory properties, and tissue and wound healing. The fulvic acid in Shilajit improves the bioavailability of nutrients by forming complexes that are easier to transport across cell membranes [140]. When combined with honey's natural sugars and bioactive compounds, this creates an optimal delivery system that enhances absorption while providing sustained energy without blood sugar spikes, as shown in an 8-week randomized controlled trial by Bahrami et al., where honey consumption made no significant difference in fasting blood sugars [141].

Both Shilajit and honey are rich in antioxidants. The fulvic and humic acid content of Shilajit (60-80 percent of the material) has "powerful antioxidant effects," with the ability to produce one of the strongest known Oxygen radical absorbance capacities (ORAC) in natural substances [142]. Flavonoids (quercetin) and phenolic acids (gallic acid) in honey also help neutralize free radicals and reduce oxidative stress [143]. This dual antioxidant action provides a complete protective effect against oxidative stress and inflammation.

The combination has demonstrated strong potential in boosting energy production within cells through various pathways. Shilajit is abundant in bioactive compounds that optimize mitochondrial efficiency by stabilizing complex enzyme activities and preventing the loss of mitochondrial membrane potential, as shown by Keller

et al. 2019 [144]. This results in higher production of adenosine triphosphate (ATP), the primary form of cellular energy. Honey enhances this process by providing easily accessible natural sugars, which can also be efficiently utilized by an improved mitochondrial system [145]. These mechanisms have clinical evidence, as research indicates that Shilajit supplementation suppresses the occurrence of mitochondrial dysfunction and fiber reversion related to chronic fatigue syndrome, particularly in behavioral patterns associated with a lack of muscular energy [118]. The honey mixture might boost these functions even more because it provides both immediate and sustained energy through different metabolic pathways.

Both Honey and Shilajit are immune-modulators and anti-inflammatory agents. Honey is believed to have wound-healing and anti-inflammatory properties, meaning it induces the release of cytokines (IL-6, TNF-alpha, and others) to the site of injury and inhibits bacterial growth, thereby speeding up the healing of wounds and burns [74]. Fulvic acid-rich Shilajit has been reported to stabilize the immune system and possess anti-inflammatory, antiallergic, and immunomodulatory properties [9]. They could strengthen the immune system, reduce chronic inflammation, and support healing from infections or wounds when combined.

Honey has the potential to influence the blood sugar profile and lipids positively, and Shilajit can supplement the effect through its adaptogenic properties [139]. Clinical studies and animal research indicate that consuming honey lowers blood glucose, LDL cholesterol, and C-reactive protein levels, while increasing nitric oxide bioavailability, which protects the cardiovascular system [28]. Shilajit is also antidiabetic in models (enhancing insulin response) and may be considered an adaptogen, with beneficial effects on stress response [72]. The combination of them could be helpful in regulating blood pressure, glucose, and lipid metabolism simultaneously. That is, honey offers quick, natural carbohydrates for energy, and the mineral-rich matrix of fulvic acids in Shilajit enhances metabolic absorption and stamina.

This interest is evident in the commercial market. Honey is a standard natural product (with the world market valued at \$8.94 billion expected in 2023), and it is growing (~6.5%) as consumer demand shifts toward nutraceuticals and healthier sweeteners [146]. Similarly, a supplement of Shilajit is a growing segment in ethnobotany (market ~\$175.6 million in 2023, ~9% CAGR) driven by the demand for traditional medicines with scientifically validated benefits [147]. The two are already combined in many products, such as honeys called Shilajit-infused or honey sticks. Briefly, both ancient tradition and modern science provide reasons to combine Shilajit and honey: specifically, their potential to supplement each other through their antioxidative, anti-inflammatory, and adaptogenic properties, along with consumer demand in the natural, health-boosting functional foods market. We have attempted to document, based on our understanding of the individual effects of honey and Shilajit, as well as their combination, on various health and wellness-related parameters in Table 1.

Table 1: Effect of Shilajit, honey, and their combination on various health and wellness-related parameters

Features	Shilajit	Honey	Shilajit + Honey
Composition	Fulvic acid Humic acids Polyphenols Amino acids Trace elements Minerals Vitamins Fatty acids Antioxidants	Natural sugars Enzymes Polyphenols Trace elements Minerals Vitamins Fatty acids Antioxidants	Synergistic effect
Antioxidants	+++	+++	+++

Oxygen Radical Absorbance Capacity	+++	++	+++
Effect on blood sugars	No effect	+	+++
Low energy	+++	++	+++
Hormonal balance	+++	+	+++
Cold and cough	+	+++	+++
Physical performance	+++	+	+++
Immunity	++	+++	+++
Pre and post workout	+++	+	+++
Physical Performance	+++	+	+++

+ indicate mild effect, ++ indicate moderate effect and +++ indicate strong effect.

10. COMBINED MECHANISM OF ACTION OF SHILAJIT AND HONEY

We hypothesize that the combination of rich fulvic and humic acids found in Shilajit, along with the high polyphenol and flavonoid content in honey, helps to downregulate the Toll-like receptor (TLR) signaling of inflammation. Shilajit with fulvic acid downregulates the IKK complex, prevents I κ B degradation, and stops the nuclear translocation of NF- κ B, p50, and p65 subunits (Figure 2). [148]. In parallel studies, floral honeys (Gelam, Manuka, Acacia) have been reported to inhibit the same cascade by stabilizing I κ B, suppressing the formation of pI κ B, and reducing the expression of COX-2 and TNF- α . Co-administration could therefore introduce dual checkpoints upstream (IKK) and midstream (I κ B) that synergistically blunt NF- κ B-associated transcription of pro-inflammatory mediators, Figure 2.

Shilajit up-regulates Nrf2, prevents Keap-1-mediated ubiquitination, restores SOD activity, and reduces lipid peroxidation in oxidative models [151]. Honeys containing flavonoids also promote Nrf2 binding to Keap-1, increase nuclear localization, and boost phase II enzymes, including HO-1 and NQO1 [152]. A combined formulation could enhance Nrf2 signaling through distinct chemical triggers, such as electrophilic fulvic acids and phenolic flavones, resulting in a broader ARE-gene response and improved ROS buffering capacity (Figure 2). Both agents target components of the MAPK pathway: Shilajit reduces phosphorylation of JNK, ERK, and p38 downstream of Ras-Raf-MEK, while honey polyphenols prevent MAPK/ATF2 activation in macrophages stimulated with LPS [153]. At the same time, honey flavones and fulvic acid have been found to interact with PI3K/Akt, which then stabilizes Nrf2 and inhibits the GSK-3-mediated degradation. [149]. Akt-dependent cytoprotective signals may also counteract the MAPK dampening phenotype, shifting the combined cell-survival signatures toward oxidative-stress resolution (Figure 2). Shilajit's fulvic fraction functions as a direct electron donor, neutralizing reactive species and reducing NLRP3 inflammasome priming. Honey polyphenols provide non-enzymatic antioxidant capacity and can chelate transition metals that promote radical formation. Collectively, they may decrease intracellular ROS below the threshold needed for NLRP3 activation, further preventing IL-1 β release and tissue damage.

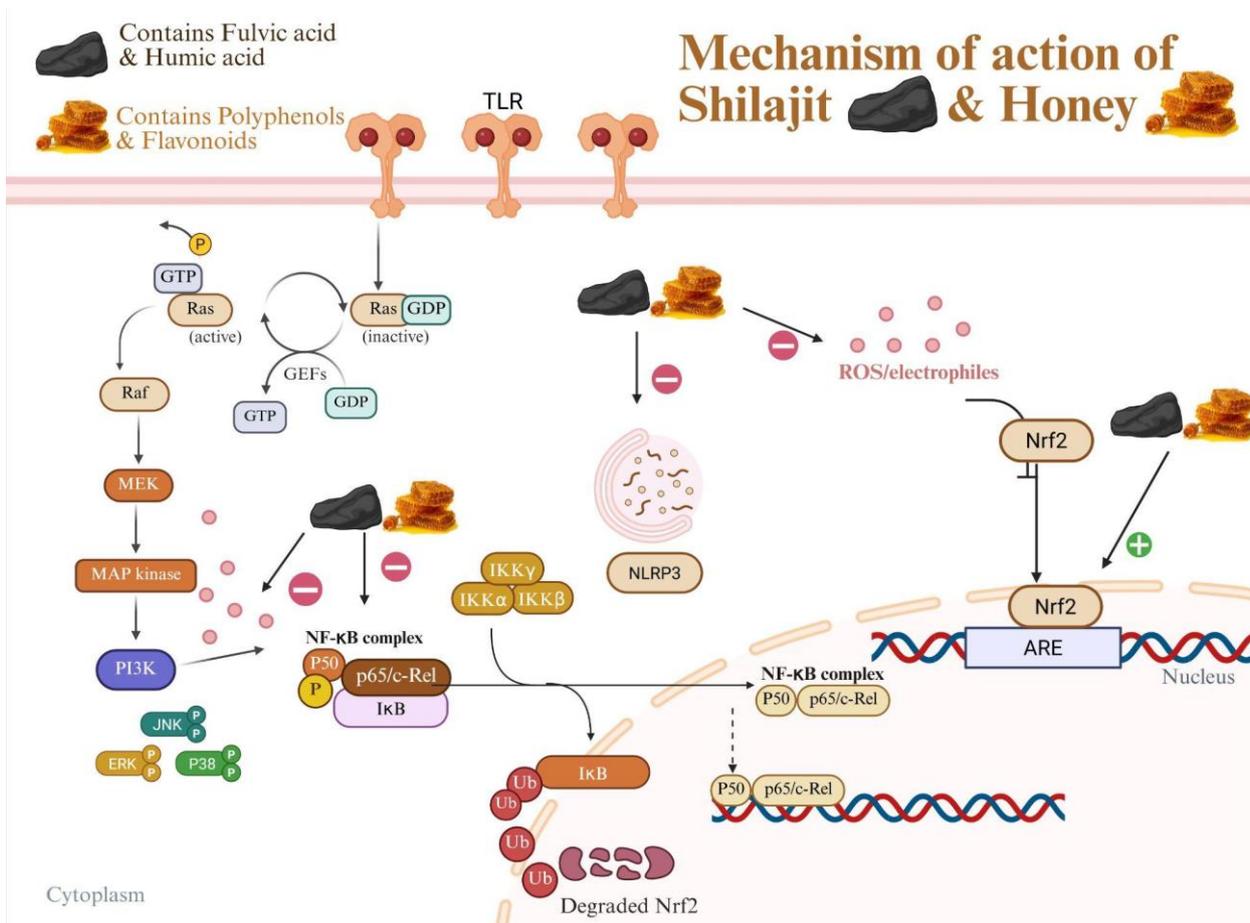


Figure 2. Proposed Mechanism of Action of Honey and Shilajit.

11. DISCUSSION

While modern research shows promise for Shilajit's therapeutic potential, supporting Charaka's claims, the field is limited by a lack of rigorous, peer-reviewed studies, and many reports are based on observational data and non-standardized materials [93]. The collapse of the USSR revealed previously unpublished research on Shilajit, which had been widely used by Soviet athletes and military personnel to boost physical and mental performance, with studies supporting its revitalizing effects [8]. No adverse effects have been reported in either animal or human studies available in the literature. While Shilajit is often considered a miracle drug, it should not be used arbitrarily. The effectiveness of Shilajit depends on various factors, including patient characteristics, preparation methods, and dosage. Notably, despite traditional references to Shilajit bhasma for certain ailments, modern research on this specific preparation is lacking, creating an opportunity for further investigation.

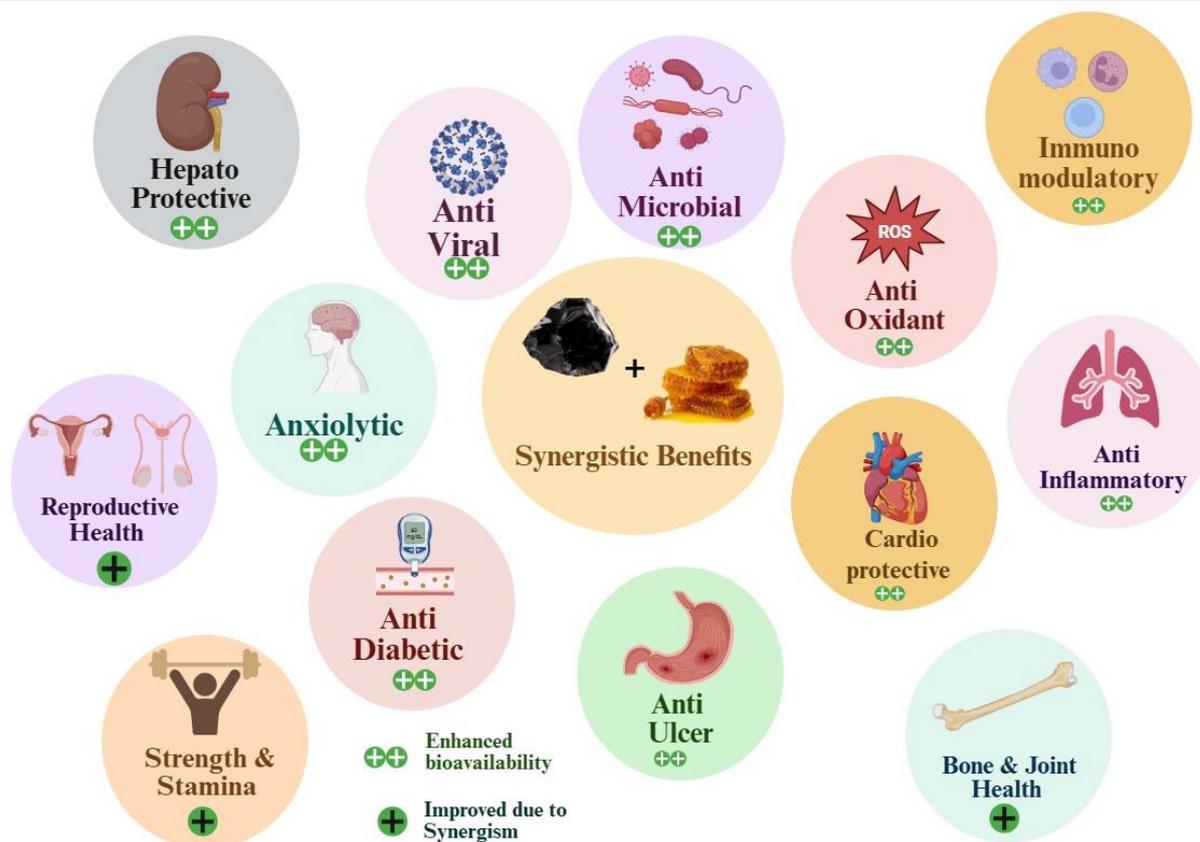


Figure 3: Combined synergistic effect of Honey and Shilajit

By combining traditional wisdom with modern research, the combination of honey and Shilajit provides a compelling example of functional synergy (Figure 3). Their complementary antioxidant, anti-inflammatory, and bioavailability-improving properties indicate real potential for tackling oxidative stress, metabolic issues, wound healing, compromised strength-stamina, and overall wellness. Going forward, the field should focus on rigorous clinical trials, detailed molecular research, and standardized manufacturing practices. An evidence-based approach will help a combination of honey and Shilajit products become safe and effective nutraceuticals that connect Ayurvedic tradition with modern medicine.

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REFERENCES

1. Kumar R, Kumar S, Herbal SK-BP of, 2024 undefined. Biomedical perspectives of herbal honey. SpringerR Kumar, S Kumar, SS KanwarBiomedical Perspectives of Herbal Honey, 2024•Springer 2024:89–167. https://doi.org/10.1007/978-981-97-1529-9_7.
2. Iqbal A, Rehman SA, Khan N, Qadir A. Asphaltum Punjabianum (Shilajit): Unraveling Myths with Scientific Evidence. *International Journal of Ayurveda and Pharma Research* 2025:137–45.
3. Prendergast KS, Garcia JE, Howard SR, Ren ZX, McFarlane SJ, Dyer AG. Bee Representations in Human Art and Culture through the Ages. *Art & Perception* 2021;10:1–62. <https://doi.org/10.1163/22134913-BJA10031>.

4. Matos LC, Machado JP, Monteiro FJ, Greten HJ. Understanding Traditional Chinese Medicine Therapeutics: An Overview of the Basics and Clinical Applications. *Healthcare* 2021, Vol 9, Page 257 2021;9:257. <https://doi.org/10.3390/HEALTHCARE9030257>.
5. Babal K. *The Yin-Yang Diet: For Balance Nutrition, Health, and Harmony*. 2019.
6. Zhang Y, Fang XM. The Pan-liver Network Theory: From Traditional Chinese Medicine to Western Medicine. *Chinese Journal of Physiology* 2023;66:401–36. <https://doi.org/10.4103/CJOP.CJOP-D-22-00131>.
7. Barros A, Abraão A. *The Power of Antioxidants-Unleashing Nature’s Defense Against Oxidative Stress* 2025.
8. Qadir A, Ali A, Singh T. Phyto-Therapeutic Potential and Pharmaceutical Impact of Shilajit (*Asphaltum punjabianam*): Current Research and Future Prospects 2024.
9. Iqbal A, Qadir A. Clinical studies and safety evidence for human consumption of Shilajit: a herbo-mineral compound with multifaceted health benefits. *Int J Basic Clin Pharmacol* 2025;14:630–40. <https://doi.org/10.18203/2319-2003.ijbcp20251850>.
10. Cornara L, Biagi M, Xiao J, Burlando B. Therapeutic properties of bioactive compounds from different honeybee products. *Front Pharmacol* 2017;8. <https://doi.org/10.3389/FPHAR.2017.00412>.
11. Da Silva PM, Gauche C, Gonzaga LV, Costa ACO, Fett R. Honey: Chemical composition, stability and authenticity. *Food Chem* 2016;196:309–23. <https://doi.org/10.1016/J.FOODCHEM.2015.09.051>.
12. Brudzynski K, Abubaker K, St-Martin L, Castle A, Hayashi MAF, Liu J, et al. Re-examining the role of hydrogen peroxide in bacteriostatic and bactericidal activities of honey. *Frontiers in Microbiology*, 2011•frontiersinOrg 2011;2. <https://doi.org/10.3389/FMICB.2011.00213/FULL>.
13. Al-Waili NS, Salom K, Butler G, Al Ghamdi AA. Honey and microbial infections: A review supporting the use of honey for microbial control. *J Med Food* 2011;14:1079–96. <https://doi.org/10.1089/JMF.2010.0161;ISSUE:ISSUE:10.1089/JMF.2011.14.ISSUE-10;PAGE:STRING:ARTICLE/CHAPTER>.
14. Brudzynski K. A current perspective on hydrogen peroxide production in honey. A review. *Food Chem* 2020;332:127229. <https://doi.org/10.1016/J.FOODCHEM.2020.127229>.
15. Ranneh Y, Akim AM, Hamid HA, Khazaai H, Fadel A, Zakaria ZA, et al. Honey and its nutritional and anti-inflammatory value. *BMC Complement Med Ther* 2021;21. <https://doi.org/10.1186/S12906-020-03170-5>.
16. Wilczyńska A, Żak N. Polyphenols as the Main Compounds Influencing the Antioxidant Effect of Honey—A Review. *International Journal of Molecular Sciences* 2024, Vol 25, Page 10606 2024;25:10606. <https://doi.org/10.3390/IJMS251910606>.
17. Silva B, Biluca FC, Gonzaga LV, Fett R, Dalmarco EM, Caon T, et al. In vitro anti-inflammatory properties of honey flavonoids: A review. *Food Research International* 2021;141:110086. <https://doi.org/10.1016/J.FOODRES.2020.110086>.
18. Ilie A;, Fikai C-I;, Fikai D;, Andronescu A;, Synergic E, Spoială A, et al. Synergic Effect of Honey with Other Natural Agents in Developing Efficient Wound Dressings. *Antioxidants* 2023, Vol 12, Page 34 2022;12:34. <https://doi.org/10.3390/ANTIOX12010034>.
19. Pasupuleti VR, Arigela CS, Gan SH, Salam SKN, Krishnan KT, Rahman NA, et al. A review on oxidative stress, diabetic complications, and the roles of honey polyphenols. *Oxid Med Cell Longev* 2020;2020. <https://doi.org/10.1155/2020/8878172>.
20. Cianciosi D, Forbes-Hernández TY, Afrin S, Gasparrini M, Reboredo-Rodriguez P, Manna PP, et al. Phenolic Compounds in Honey and Their Associated Health Benefits: A Review. *Molecules* 2018, Vol 23, Page 2322 2018;23:2322. <https://doi.org/10.3390/MOLECULES23092322>.

21. Deadman B. The flavonoid profile of New Zealand manuka honey 2009.
22. Alvarez-Suarez JM, Giampieri F, Battino M. Honey as a Source of Dietary Antioxidants: Structures, Bioavailability and Evidence of Protective Effects Against Human Chronic Diseases. *Curr Med Chem* 2013;20:621–38. <https://doi.org/10.2174/092986713804999358>.
23. Bose D, Padmavati M. Honey Authentication: A review of the issues and challenges associated with honey adulteration. *Food Biosci* 2024;61:105004. <https://doi.org/10.1016/J.FBIO.2024.105004>.
24. Bukulmez O. Diminished Ovarian Reserve and Assisted Reproductive Technologies: Current Research and Clinical Management. 2019. <https://doi.org/10.1007/978-3-030-23235-1.PDF>.
25. Kumar R. Historical and Religious Perspective of Honey. *Honey: Nutraceutical and Therapeutic Significance* 2024:1–16. <https://doi.org/10.1201/9781003490180-1/HISTORICAL-RELIGIOUS-PERSPECTIVE-HONEY-RAJESH-KUMAR>.
26. Boukraâ L. Honey in traditional and modern medicine. CRC Press; 2023. <https://doi.org/10.1201/B15608>.
27. Her L, Kanjanasilp J. Efficacy and safety of herbal medicines for relief cough symptom in national list of essential medicines of Thailand and Lao PDR: A systematic review and Meta 2021.
28. Wang Z, Ran J, Wang R, Huang B, Wang L, Zhou Y, et al. Evolutionary pathway of TCM in allergic diseases: A Fusion from ancient wisdom to modern science. *Allergy Medicine* 2025;5:100029. <https://doi.org/10.1016/J.ALLMED.2025.100029>.
29. Kumar K, Bhowmik D, ... CB-JChemP, 2010 undefined. Medicinal uses and health benefits of honey: an overview. *RevenanmaarssevenNIKS Kumar, D Bhowmik, C Biswajit, MR ChandiraJ Chem Pharm Res, 2010•revenanmaarssevenNI 2010;2:385–95*.
30. Rajagopal H, Kumari R, Deenadayalan PP, Viyakappan B. A Study to Assess the Effectiveness of Honey in the Reduction of Constipation and Insomnia among Antenatal Mothers during the Third Trimester of Pregnancy. *J Pharm Bioallied Sci* 2024;16:S2901–3. https://doi.org/10.4103/JPBS.JPBS_563_24.
31. Yu G, Gao J, Gu J, Li H, Wang X, Bian H. Efficacy of honey suppositories in treating paediatric functional constipation: A comparative study. *J Paediatr Child Health* 2025;61:100–5. <https://doi.org/10.1111/JPC.16722;SUBPAGE:STRING:FULL>.
32. Sabalingam S, Banukie WJA, Jayasuriya N. Pharmaceutical excipients of marine and animal origin: A review. *Science Stays True Here" Biological and Chemical Research* 2019;6:184–96.
33. Yaghoobi R, Kazerouni A, kazerouni O, Yaghoobi R, Kazerouni A, kazerouni O, et al. Evidence for Clinical Use of Honey in Wound Healing as an Anti-bacterial, Anti-inflammatory Anti-oxidant and Anti-viral Agent: A Review. *Jundishapur Journal of Natural Pharmaceutical Products* 2013 8:3 2013;8:100–4. <https://doi.org/10.17795/JJNPP-9487>.
34. Tashkandi H. Honey in wound healing: An updated review. *Open Life Sci* 2021;16:1091–100. https://doi.org/10.1515/BIOL-2021-0084/ASSET/GRAPHIC/J_BIOL-2021-0084_FIG_002.JPG.
35. Amaan Zahid S, Deshmukh R, Khan G, Safwan Salim M, Hamza Ilyas A. A review on herbal drug excipient used in NDDS. *IdealpublicationInSA Zahid, R Deshmukh, G Khan, MS Salim, AH IlyasInt J Res Pharm Allied Sci, 2023•idealpublicationIn n.d.;2:124–35*.
36. Saraiva A, Carrascosa C, Raheem D, Ramos F, Raposo A. Natural Sweeteners: The Relevance of Food Naturalness for Consumers, Food Security Aspects, Sustainability and Health Impacts. *International Journal of Environmental Research and Public Health* 2020, Vol 17, Page 6285 2020;17:6285. <https://doi.org/10.3390/IJERPH17176285>.
37. Zhang S, Kumari S, Gu Y, Li X, Meng G, Zhang Q, et al. Honey consumption is inversely associated with prediabetes among Chinese adults: results from the Tianjin Chronic Low-Grade Systemic

- Inflammation and Health. CambridgeOrgS Zhang, S Kumari, Y Gu, X Li, G Meng, Q Zhang, L Liu, H Wu, Y Wang, T Zhang, X WangBritish Journal of Nutrition, 2020•cambridgeOrg 2020. <https://doi.org/10.1017/S0007114520000835>.
38. Talebi M, Talebi M, Farkhondeh T, Samarghandian S. Molecular mechanism-based therapeutic properties of honey. *Biomedicine & Pharmacotherapy* 2020;130:110590. <https://doi.org/10.1016/J.BIOPHA.2020.110590>.
 39. Ahmed S, Sulaiman SA, Baig AA, Ibrahim M, Liaqat S, Fatima S, et al. Honey as a Potential Natural Antioxidant Medicine: An Insight into Its Molecular Mechanisms of Action. *Oxid Med Cell Longev* 2018;2018:8367846. <https://doi.org/10.1155/2018/8367846>.
 40. Hussein SZ, Mohd Yusoff K, Makpol S, Mohd Yusof YA. Gelam Honey Attenuates Carrageenan-Induced Rat Paw Inflammation via NF- κ B Pathway. *PLoS One* 2013;8:e72365. <https://doi.org/10.1371/JOURNAL.PONE.0072365>.
 41. Kim H, Son K, Jeong H, Park S, ... JK-KJ of P, 2018 undefined. Anti-inflammatory activity of Acacia honey through inhibition of NF- κ B and MAPK/ATF2 signaling pathway in LPS-stimulated RAW264.7 cells. *KjprKrHN Kim, KH Son, HJ Jeong, SB Park, JD Kim, JB JeongKorean Journal of Plant Resources*, 2018•kjprKr n.d. <https://doi.org/10.7732/kjpr.2018.31.6.612>.
 42. Erejuwa OO, Sulaiman SA, Ab Wahab MS. Effects of Honey and Its Mechanisms of Action on the Development and Progression of Cancer. *Molecules* 2014;19:2497. <https://doi.org/10.3390/MOLECULES19022497>.
 43. Lobo V, Patil A, Phatak A, Chandra N. Free Radicals, Antioxidants and Functional Foods: Impact on Human Health. *Pharmacogn Rev* 2010;4:118–26. <https://doi.org/10.4103/0973-7847.70902>.
 44. Rudrapal M, Khairnar SJ, Khan J, Dukhyil A Bin, Ansari MA, Alomary MN, et al. Dietary Polyphenols and Their Role in Oxidative Stress-Induced Human Diseases: Insights Into Protective Effects, Antioxidant Potentials and Mechanism(s) of Action. *Front Pharmacol* 2022;13. <https://doi.org/10.3389/FPHAR.2022.806470>.
 45. Gorjanović SŽ, Alvarez-Suarez JM, Novaković MM, Pastor FT, Pezo L, Battino M, et al. Comparative analysis of antioxidant activity of honey of different floral sources using recently developed polarographic and various spectrophotometric assays. *Journal of Food Composition and Analysis* 2013;30:13–8. <https://doi.org/10.1016/J.JFCA.2012.12.004>.
 46. Sun LP, Shi FF, Zhang WW, Zhang ZH, Wang K. Antioxidant and Anti-Inflammatory Activities of Safflower (*Carthamus tinctorius* L.) Honey Extract. *Foods* 2020, Vol 9, Page 1039 2020;9:1039. <https://doi.org/10.3390/FOODS9081039>.
 47. Erejuwa OO, Sulaiman SA, Ab Wahab MS. Honey: A Novel Antioxidant. *Molecules* 2012, Vol 17, Pages 4400-4423 2012;17:4400–23. <https://doi.org/10.3390/MOLECULES17044400>.
 48. Biluca FC, de Gois JS, Schulz M, Braghini F, Gonzaga LV, Maltez HF, et al. Phenolic compounds, antioxidant capacity and bioaccessibility of minerals of stingless bee honey (Meliponinae). *Journal of Food Composition and Analysis* 2017;63:89–97. <https://doi.org/10.1016/J.JFCA.2017.07.039>.
 49. Sun LP, Shi FF, Zhang WW, Zhang ZH, Wang K. Antioxidant and Anti-Inflammatory Activities of Safflower (*Carthamus tinctorius* L.) Honey Extract. *Foods* 2020, Vol 9, Page 1039 2020;9:1039. <https://doi.org/10.3390/FOODS9081039>.
 50. [50] Alvarez-Suarez J. Bee products-chemical and biological properties. 2017. <https://doi.org/10.1007/978-3-031-89049-9.PDF>.
 51. Heim KE, Tagliaferro AR, Bobilya DJ. Flavonoid antioxidants: chemistry, metabolism and structure-activity relationships. *J Nutr Biochem* 2002;13:572–84. [https://doi.org/10.1016/S0955-2863\(02\)00208-5](https://doi.org/10.1016/S0955-2863(02)00208-5).

52. Bridi R, Montenegro G. Honey analysis. Rijeka, Croatia: IntechOpen 2017.
53. Mărgăoan R, Topal E, Balkanska R, Yücel B, Oravec T, Cornea-Cipcigan M, et al. Monofloral Honeys as a Potential Source of Natural Antioxidants, Minerals and Medicine. *Antioxidants* 2021, Vol 10, Page 1023 2021;10:1023. <https://doi.org/10.3390/ANTIOX10071023>.
54. Charlton NC, Mastuyugin M, Török B, Török M. Structural Features of Small Molecule Antioxidants and Strategic Modifications to Improve Potential Bioactivity. *Molecules* 2023, Vol 28, Page 1057 2023;28:1057. <https://doi.org/10.3390/MOLECULES28031057>.
55. Kumar R, Kumar S, Herbal SK-BP of, 2024 undefined. Pharmacological properties of honey. SpringerR Kumar, S Kumar, SS KanwarBiomedical Perspectives of Herbal Honey, 2024•Springer 2024:19–33. https://doi.org/10.1007/978-981-97-1529-9_2.
56. Krishnakumar GS, Mahendiran B, Gopalakrishnan S, Muthusamy S, Malarkodi Elangovan S. Honey based treatment strategies for infected wounds and burns: A systematic review of recent pre-clinical research. *Wound Medicine* 2020;30:100188. <https://doi.org/10.1016/J.WNDM.2020.100188>.
57. Israili ZH. Antimicrobial properties of honey. *Am J Ther* 2014;21:304–23. <https://doi.org/10.1097/MJT.0B013E318293B09B>.
58. Aurongzeb M, Biol MA-PakJBiochemMol, 2011 undefined. Antimicrobial properties of natural honey: a review of literature. *PjbmbOrgPkM Aurongzeb, MK AzimPak J Biochem Mol Biol, 2011•pjbmbOrgPk* 2011;44:118–24.
59. Proaño A, Coello D, Villacrés-Granda I, Ballesteros I, Debut A, Vizúete K, et al. The osmotic action of sugar combined with hydrogen peroxide and bee-derived antibacterial peptide Defensin-1 is crucial for the antibiofilm activity of eucalyptus honey. *LWT* 2021;136:110379. <https://doi.org/10.1016/J.LWT.2020.110379>.
60. Saikaly SK, Khachemoune A. Honey and Wound Healing: An Update. *Am J Clin Dermatol* 2017;18:237–51. <https://doi.org/10.1007/S40257-016-0247-8/METRICS>.
61. Robson V, Dodd S, Thomas S. Standardized antibacterial honey (Medihoney™) with standard therapy in wound care: randomized clinical trial. *J Adv Nurs* 2009;65:565–75. <https://doi.org/10.1111/J.1365-2648.2008.04923.X>.
62. Masalha M, Abu-Lafi S, Abu-Farich B, Rayan M, Issa N, Zeidan M, et al. A New Approach for Indexing Honey for Its Health/Medicinal Benefits: Visualization of the Concept by Indexing Based on Antioxidant and Antibacterial Activities. *Medicines* 2018, Vol 5, Page 135 2018;5:135. <https://doi.org/10.3390/MEDICINES5040135>.
63. Battino M, Forbes-Hernández TY, Gasparrini M, Afrin S, Cianciosi D, Zhang J, et al. Relevance of functional foods in the Mediterranean diet: the role of olive oil, berries and honey in the prevention of cancer and cardiovascular diseases. *Crit Rev Food Sci Nutr* 2019;59:893–920. <https://doi.org/10.1080/10408398.2018.1526165;SUBPAGE:STRING:ACCESS>.
64. Idrus RBH, Sainik NQAV, Nordin A, Bin Saim A, Sulaiman N. Cardioprotective effects of honey and its constituent: An evidence-based review of laboratory studies and clinical trials. *Int J Environ Res Public Health* 2020;17. <https://doi.org/10.3390/IJERPH17103613>.
65. Idrus RBH, Sainik NQAV, Nordin A, Bin Saim A, Sulaiman N. Cardioprotective effects of honey and its constituent: An evidence-based review of laboratory studies and clinical trials. *Int J Environ Res Public Health* 2020;17. <https://doi.org/10.3390/IJERPH17103613>.
66. Khalil M, Traditional SS-AJ of, Complementary undefined, 2010 undefined. The potential role of honey and its polyphenols in preventing heart disease: a review. *AjolInfoML Khalil, SA SulaimanAfrican Journal of Traditional, Complementary and Alternative Medicines, 2010•ajolInfo* 2010;7:315–21.

67. Khalil M, Traditional SS-AJ of, Complementary undefined, 2010 undefined. The potential role of honey and its polyphenols in preventing heart disease: a review. *AjolInfoML Khalil, SA SulaimanAfrican Journal of Traditional, Complementary and Alternative Medicines*, 2010•*ajolInfo* 2010;7:315–21.
68. Nguyen HTL, Panyoyai N, Kasapis S, Pang E, Mantri N. Honey and its role in relieving multiple facets of atherosclerosis. *Nutrients* 2019;11. <https://doi.org/10.3390/NU11010167>.
69. Saheera S, Krishnamurthy P. Cardiovascular Changes Associated with Hypertensive Heart Disease and Aging. *Cell Transplant* 2020;29. <https://doi.org/10.1177/0963689720920830>.
70. Erejuwa OO, Sulaiman SA, Ab Wahab MS, Sirajudeen KNS, Salleh S, Gurtu S. Honey supplementation in spontaneously hypertensive rats elicits antihypertensive effect via amelioration of renal oxidative stress. *Oxid Med Cell Longev* 2012. <https://doi.org/10.1155/2012/374037>.
71. Erejuwa OO, Sulaiman SA, Wahab MSA, Sirajudeen KNS, Salleh MSM, Gurtu S. Differential Responses to Blood Pressure and Oxidative Stress in Streptozotocin-Induced Diabetic Wistar-Kyoto Rats and Spontaneously Hypertensive Rats: Effects of Antioxidant (Honey) Treatment. *International Journal of Molecular Sciences* 2011, Vol 12, Pages 1888-1907 2011;12:1888–907. <https://doi.org/10.3390/IJMS12031888>.
72. Houston MC. The role of cellular micronutrient analysis, nutraceuticals, vitamins, antioxidants and minerals in the prevention and treatment of hypertension and cardiovascular disease. *Ther Adv Cardiovasc Dis* 2010;4:165–83. <https://doi.org/10.1177/1753944710368205>.
73. Metabolism SB-I journal of D and, 2005 undefined. Diabetes mellitus and its treatment. *KargerComS BastakiInternational Journal of Diabetes and Metabolism*, 2005•*kargerCom* 2005;13:111–34.
74. El-Seedi HR, Eid N, Abd El-Wahed AA, Rateb ME, Afifi HS, Algethami AF, et al. Honey bee products: preclinical and clinical studies of their anti-inflammatory and immunomodulatory properties. *FrontiersinOrg* El-Seedi, N Eid, AA Abd El-Wahed, ME Rateb, HS Afifi, AF Algethami, C ZhaoFrontiers in Nutrition, 2022•*frontiersinOrg* 2022;8:761267. <https://doi.org/10.3389/FNUT.2021.761267/FULL>.
75. Ahmed S, Sulaiman SA, Baig AA, Ibrahim M, Liaqat S, Fatima S, et al. Honey as a Potential Natural Antioxidant Medicine: An Insight into Its Molecular Mechanisms of Action. *Oxid Med Cell Longev* 2018;2018. <https://doi.org/10.1155/2018/8367846>.
76. Kumari A, Yadav SK, Yadav SC. Biodegradable polymeric nanoparticles based drug delivery systems. *Colloids Surf B Biointerfaces* 2010;75:1–18. <https://doi.org/10.1016/J.COLSURFB.2009.09.001>.
77. Schultz BG, Patten DK, Berlau DJ. The role of statins in both cognitive impairment and protection against dementia: a tale of two mechanisms. *Transl Neurodegener* 2018;7. <https://doi.org/10.1186/S40035-018-0110-3>.
78. Mackin C, Dahiya D, Nigam PS. Honey as a Natural Nutraceutical: Its Combinational Therapeutic Strategies Applicable to Blood Infections—Septicemia, HIV, SARS-CoV-2, Malaria. *Pharmaceuticals* 2023, Vol 16, Page 1154 2023;16:1154. <https://doi.org/10.3390/PH16081154>.
79. journal NA-W-M science monitor: international medical, 2004 undefined. Topical honey application vs. acyclovir for the treatment of recurrent herpes simplex lesions. *EuropepmcOrg* n.d.
80. Shahzad A, biomedicine RC-T, 2012 undefined. In vitro antiviral activity of honey against varicella zoster virus (VZV): A translational medicine study for potential remedy for shingles. *PmcNcbiNlmNihGovA Shahzad, RJ CohrsTranslational Biomedicine*, 2012•*pmcNcbiNlmNihGov* n.d.
81. Watanabe K, Rahmasari R, Matsunaga A, Haruyama T, Kobayashi N. Anti-influenza Viral Effects of Honey In Vitro: Potent High Activity of Manuka Honey. *Arch Med Res* 2014;45:359–65. <https://doi.org/10.1016/J.ARCMED.2014.05.006>.

82. Al-Hatamleh MAI, Hatmal MM, Sattar K, Ahmad S, Mustafa MZ, Bittencourt MDC, et al. Antiviral and Immunomodulatory Effects of Phytochemicals from Honey against COVID-19: Potential Mechanisms of Action and Future Directions. *Molecules* 2020, Vol 25, Page 5017 2020;25:5017. <https://doi.org/10.3390/MOLECULES25215017>.
83. Jacoby DB, Choi AMK. Influenza virus induces expression of antioxidant genes in human epithelial cells. *Free Radic Biol Med* 1994;16:821–4. [https://doi.org/10.1016/0891-5849\(94\)90198-8](https://doi.org/10.1016/0891-5849(94)90198-8).
84. Hossain KS, Hossain MG, Moni A, Rahman MM, Rahman UH, Alam M, et al. Prospects of honey in fighting against COVID-19: pharmacological insights and therapeutic promises. *Heliyon* 2020;6:e05798. <https://doi.org/10.1016/J.HELIYON.2020.E05798>.
85. Jaganathan S, Balaji A, Vellayappan M, Asokan M, Subramanian A, John A, et al. A Review on Antiproliferative and Apoptotic Activities of Natural Honey. *Anticancer Agents Med Chem* 2014;15:48–56. <https://doi.org/10.2174/1871520614666140722084747>.
86. Bouacha M, Boudiar I, Abdi A, Al-Kafaween MA, Khallef M. THE ANTIMUTAGENIC EFFECT OF MULTIFLORAL HONEY IN SALMONELLA/ MICROSOMAL ASSAY AND ITS CORRELATION WITH THE TOTAL POLYPHENOLIC CONTENT. *Journal of Microbiology, Biotechnology and Food Sciences* 2022;11:e5557–e5557. <https://doi.org/10.55251/JMBFS.5557>.
87. Rehman M, Majid S. Therapeutic applications of honey and its phytochemicals. 2020. <https://doi.org/10.1007/978-981-15-7305-7.PDF>.
88. Mohan A, Quek SY, Gutierrez-Maddox N, Gao Y, Shu Q. Effect of honey in improving the gut microbial balance. *Food Quality and Safety* 2017;1:107–15. <https://doi.org/10.1093/FQSAFE/FYX015>.
89. Williams BA, Grant LJ, Gidley MJ, Mikkelsen D. Gut Fermentation of Dietary Fibres: Physico-Chemistry of Plant Cell Walls and Implications for Health. *International Journal of Molecular Sciences* 2017, Vol 18, Page 2203 2017;18:2203. <https://doi.org/10.3390/IJMS18102203>.
90. Rosendale DI, Maddox IS, Miles MC, Rodier M, Skinner M, Sutherland J. High-throughput microbial bioassays to screen potential New Zealand functional food ingredients intended to manage the growth of probiotic and pathogenic gut bacteria. *Int J Food Sci Technol* 2008;43:2257–67. <https://doi.org/10.1111/J.1365-2621.2008.01863.X>.
91. Favarin L, Laureano-Melo R, Luchese RH. Survival of free and microencapsulated Bifidobacterium: effect of honey addition. *J Microencapsul* 2015;32:329–35. <https://doi.org/10.3109/02652048.2015.1017620>.
92. Sanz ML, Polemis N, Morales V, Corzo N, Drakoularakou A, Gibson GR, et al. In vitro investigation into the potential prebiotic activity of honey oligosaccharides. *J Agric Food Chem* 2005;53:2914–21. <https://doi.org/10.1021/JF0500684;WGROU:STRING:ACHS>.
93. Haddadin MSY, Nazer I, Raddad JA, Robinson RK. Effect of honey on the growth and metabolism of two bacterial species of intestinal origin. *Pakistan Journal of Nutrition* 2007;6:693–7. <https://doi.org/10.3923/PJN.2007.693.697>.
94. Agarwal SP, Khanna R, Karmarkar R, Anwer MK, Khar RK. Shilajit: a review. *Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives* 2007;21:401–5.
95. Aladi PC, Vikhe SR. SHILAJIT: A WONDER DRUG OF AYURVEDA. vol. 8. 2022.
96. Ali SM, Iqbal N, Ishaq W, Shabbir R, Afzal A, Amjad M, et al. SYSTEMATIC REVIEW OF SHILAJIT: CLINICAL EFFICACY AND SAFETY. *Journal of Population Therapeutics and Clinical Pharmacology* 2024;31:1464–71. <https://doi.org/10.53555/JPTCP.V31I6.6677>.
97. Ghosal S. Shilajit in perspective. Alpha Science International Limited Oxford; 2006.

98. Williamson EM. Shilajit in Perspective 2009.
99. Ali SM, Iqbal N, Ishaq W, Shabbir R, Afzal A, Amjad M, et al. SYSTEMATIC REVIEW OF SHILAJIT: CLINICAL EFFICACY AND SAFETY. *Journal of Population Therapeutics and Clinical Pharmacology* 2024. <https://doi.org/10.53555/jptcp.v31i6.6677>.
100. Kamgar E, Kaykhaii M, Zembrzuska J. A comprehensive review on Shilajit: what we know about its chemical composition. *Crit Rev Anal Chem* 2025;55:461–73.
101. Çetin E, Sancak T, Keleş ÖF, Ünlü İ, Akyol ME, Arabacı Ö. Histopathological and immunohistochemical investigation of the effect of Shilajit in rats with experimental spinal cord injury. *Turkish Journal of Trauma & Emergency Surgery* 2023;29:1329. <https://doi.org/10.14744/TJTES.2023.60621>.
102. Musthafa MS, Jawahar Ali AR, Hyder Ali AR, Mohamed MJ, War M, Naveed MS, et al. Effect of Shilajit enriched diet on immunity, antioxidants, and disease resistance in *Macrobrachium rosenbergii* (de Man) against *Aeromonas hydrophila*. *Fish Shellfish Immunol* 2016;57:293–300. <https://doi.org/10.1016/J.FSI.2016.08.033>.
103. Yadav SC, Govindasamy J, Ramnani R. Antioxidant and hepatoprotective activity of Shilajit (asphaltum punjabinum) against alcohol induced liver injury in wistar rats. *International Journal of Ayurveda and Pharma Research* 2020:1–8.
104. Elahi S, Mohamadi Sani A, Sarabi-Jamab M. Physicochemical, antioxidant and antimicrobial characteristics of two types of mumies(Shilajit). *Journal of Food Measurement and Characterization* 2024;18:4137–46. <https://doi.org/10.1007/S11694-024-02481-2/METRICS>.
105. Ali DQ. Evaluation of the Antibacterial Activity of Shilajit Aqueous Extract on Clinically Isolated Bacteria in Kalar District, Iraq. *Thi-Qar Medical Journal* 2024;28:320–9.
106. AlShubaily F, Jambi E. LC/MS profiling of Shilajit Extract for Antimicrobial & Antifungal and cytotoxic activities. *Int Trans J Eng Manag Appl Sci Technol* 2022;13:1–13.
107. Acharya SB, Frotan MH, Goel RK, Tripathi SK, Das PK. Pharmacological actions of Shilajit. *Indian J Exp Biol* 1988;26:775–7.
108. Cagno V, Donalisio M, Civra A, Cagliero C, Rubiolo P, Lembo D. In vitro evaluation of the antiviral properties of Shilajit and investigation of its mechanisms of action. *J Ethnopharmacol* 2015;166:129–34. <https://doi.org/10.1016/J.JEP.2015.03.019>.
109. Carlos CG, Leonardo G, Ricardo BM. Shilajit: a natural phytocomplex with potential procognitive activity. *Int J Alzheimer's Dis* 2012;10:1–4.
110. Andrade V, Wong-Guerra M, Cortés N, Pastor G, González A, Calfío C, et al. Scaling the andean Shilajit: a novel neuroprotective agent for alzheimer's disease. *Pharmaceuticals* 2023;16:960.
111. Mirza MA, Hamdard J, Mustafa G, Aamir Mirza M, Alam MN, Faiyazuddin M, et al. Shilajit: An Ancient Panacea *International Journal of Current Pharmaceutical Review and Research Shilajit: An Ancient Panacea*. 2010.
112. Pingali U, Nutalapati C. Shilajit extract reduces oxidative stress, inflammation, and bone loss to dose-dependently preserve bone mineral density in postmenopausal women with osteopenia: A randomized, double-blind, placebo-controlled trial. *Phytomedicine* 2022;105:154334. <https://doi.org/10.1016/J.PHYMED.2022.154334>.
113. Rajpoot A, Pandey AK, Roy VK, Mishra RK. Therapeutic potential of fulvic acid in chronic inflammatory diseases and diabetes. *Wiley Online Library* 2018;2018. <https://doi.org/10.1155/2018/5391014>.

114. Rajpoot A, Pandey AK, Roy VK, Mishra RK. Shilajit Mitigates Diabetes-Induced Testicular Dysfunction in Mice: A Modulation in Insulin Sensitivity, Germ Cell-Junctional Dynamics, and Oxidative-Apoptotic Status. *Wiley Online Library* 2025;2025. <https://doi.org/10.1155/AND/5517176>.
115. Shahrokhi N, Amiresmaili S, Afshar RM, Shahrokhi M. Comparing the Effects of Sulfasalazine and Shilajit on Liver Damage Caused by Acetic Acid-Induced Ulcerative Colitis in Male Rats. *Journal of Babol University of Medical Sciences* 2023;25.
116. Pandit S, Biswas S, Jana U, De RK, Mukhopadhyay SC, Biswas TK. Clinical evaluation of purified Shilajit on testosterone levels in healthy volunteers. *Wiley Online Library* 2016;48:570–5. <https://doi.org/10.1111/AND.12482>.
117. Joukar S, Najafipour H, Dabiri S, Sheibani M, Sharokhi N. Cardioprotective effect of mumie (Shilajit) on experimentally induced myocardial injury. *Cardiovasc Toxicol* 2014;14:214–21. <https://doi.org/10.1007/S12012-014-9245-3>.
118. Iqubal A, Qadir A. Cardioprotective effect of *Asphaltum punjabianum* (Shilajit): An evidence-based review. *Int J Herb Med* 2025;13:43–52. <https://doi.org/10.22271/FLORA.2025.V13.I3A.987>.
119. Surapaneni DK, Adapa SRSS, Preeti K, Teja GR, Veeraragavan M, Krishnamurthy S. Shilajit attenuates behavioral symptoms of chronic fatigue syndrome by modulating the hypothalamic–pituitary–adrenal axis and mitochondrial bioenergetics in rats. *J Ethnopharmacol* 2012;143:91–9. <https://doi.org/10.1016/j.jep.2012.06.002>.
120. Dargan PI, Gawarammana IB, Archer JRH, House IM, Shaw D, Wood DM. Heavy metal poisoning from Ayurvedic traditional medicines: an emerging problem? *IJEH* 2008;2:463–74. <https://doi.org/10.1504/IJENVH.2008.020936>.
121. Gour R, Patel Ambalal B. The Concept of Herb-Herb Combination over Single Herb. *International Journal of Pharmaceutical Research and Applications* 2008;5:114. <https://doi.org/10.35629/7781-0501114118>.
122. None A, S S. Evaluation of physicochemical and phytochemical properties of Safoof-E-Sana, a Unani polyherbal formulation. *Pharmacognosy Res* 2010;2:318. <https://doi.org/10.4103/0974-8490.72332>.
123. Jain DP, Pancholi SS, Patel R. Synergistic antioxidant activity of green tea with some herbs. *J Adv Pharm Technol Res* 2011;2:177. <https://doi.org/10.4103/2231-4040.85538>.
124. Jain DP, Pancholi SS, Patel R. Synergistic antioxidant activity of green tea with some herbs. *J Adv Pharm Technol Res* 2011;2:177. <https://doi.org/10.4103/2231-4040.85538>.
125. Viswanathan V, Kesavan R, Kavitha K V., Kumpatla S. A pilot study on the effects of a polyherbal formulation cream on diabetic foot ulcers. *Indian J Med Res* 2011;134:168.
126. Singh YN. Potential for interaction of kava and St. John's wort with drugs. *J Ethnopharmacol* 2005;100:108–13. <https://doi.org/10.1016/j.jep.2005.05.014>.
127. Bhope SG, Nagore DH, Kuber V V., Gupta PK, Patil MJ. Design and development of a stable polyherbal formulation based on the results of compatibility studies. *Pharmacognosy Res* 2011;3:122–9. <https://doi.org/10.4103/0974-8490.81960>.
128. Spinella M. The importance of pharmacological synergy in psychoactive herbal medicines. *Alternative Medicine Review* 2002;7:130–7.
129. Benzie IFF, Wachtel-Galor S. *Herbal medicine: biomolecular and clinical aspects* 2011.
130. Kavitha AN, Deepthi V. Design, formulation and evaluation of a polyherbal ointment for its wound healing activity. *Pharmacophore* 2013;4:175–80.
131. Saraf S. Evaluation of physicochemical and phytochemical properties of Safoof-E-Sana, a Unani polyherbal formulation. *Pharmacognosy Res* 2010;2:318.

132. Rastogi S, Chiappelli F, Ramchandani MH, Singh RH. Evidence-based practice in complementary and alternative medicine: Perspectives, protocols, problems and potential in Ayurveda. Springer Science & Business Media; 2012.
133. Wagner H. Multitarget therapy—the future of treatment for more than just functional dyspepsia. *Phytomedicine* 2006;13:122–9.
134. Tang J, Wennerberg K, Aittokallio T. What is synergy? The Saariselkä agreement revisited. *Front Pharmacol* 2015;6:181.
135. Sarris J, Ng CH, Schweitzer I. ‘Omic’ genetic technologies for herbal medicines in psychiatry. *Phytotherapy Research* 2012;26:522–7.
136. Sofowora A, Ogunbodede E, Onayade A. The role and place of medicinal plants in the strategies for disease prevention. *African Journal of Traditional, Complementary and Alternative Medicines* 2013;10:210–29.
137. Atpadkar KD, Mote AN, Pawar VH, Patil KS. Formulation and Evaluation of Poly Herbal Syrup. *Int J Res Appl Sci Eng Technol [Internet]* 2025;13:1014–21.
138. Wilson E, Rajamanickam GV, Dubey GP, Klose P, Musial F, Saha FJ, et al. Review on Shilajit used in traditional Indian medicine. *J Ethnopharmacol* 2011;136:1–9. <https://doi.org/10.1016/J.JEP.2011.04.033>.
- El-Soud N. Honey between traditional uses and recent medicine. 2012.
139. Aparna AR, Rajalakshmi D. Honey—its characteristics, sensory aspects, and applications. *Food Reviews International* 1999;15:455–71. <https://doi.org/10.1080/87559129909541199>.
140. Ghosal S, Reddy JP, Lal VK. Shilajit I: chemical constituents. *J Pharm Sci* 1976;65:772–3.
141. Bahrami M, Ataie-Jafari A, Hosseini S, Foruzanfar MH, Rahmani M, Pajouhi M. Effects of natural honey consumption in diabetic patients: an 8-week randomized clinical trial. *Int J Food Sci Nutr* 2009;60:618–26. <https://doi.org/10.3109/09637480801990389>.
142. Carrasco-Gallardo C, Guzmán L, Maccioni RB. *Shilajit*: A Natural Phytocomplex with Potential Procognitive Activity. *Int J Alzheimers Dis* 2012;2012:1–4. <https://doi.org/10.1155/2012/674142>.
143. Lee S, Ryu H, Whang W. Development of simultaneous analysis method for multi-compounds content of new Shilajit using HPLC-UV and the cognitive enhancing effect: Mongolian Shilajit. *Nat Prod Commun* 2021;16:1934578X211030433.
144. Keller JL, Housh TJ, Hill EC, Smith CM, Schmidt RJ, Johnson GO. The effects of Shilajit supplementation on fatigue-induced decreases in muscular strength and serum hydroxyproline levels. *J Int Soc Sports Nutr* 2019;16:3. <https://doi.org/10.1186/S12970-019-0270-2>.
145. Sumitra M, Manikandan P, Gayathri VS, Suguna L. Influence of Honey on Energy Metabolism during Wound Healing in Rats. *Scholarly Research Exchange* 2009;2009:1–6. <https://doi.org/10.3814/2009/715320>.
146. Honey Market Size, Share, Future Growth, 2032 | Bee Maid Honey n.d. <https://www.openpr.com/news/3674517/honey-market-size-share-future-growth-2032-bee-maid-honey> (accessed August 2, 2025).
147. Shilajit Market Size, Share & Growth Analysis Report, 2030 n.d. <https://www.grandviewresearch.com/industry-analysis/Shilajit-market-report> (accessed August 2, 2025).
148. Kordestani Z, Melki E, Vahidi R, Shideh R, Ghorbani N, Rouholamini SEY, et al. Modulation of IKK/NF- κ B Signaling: A Therapeutic Mechanism of Shilajit in Breast Cancer Cells. *Journal of Kerman University of Medical Sciences* 2024;31:66–71. <https://doi.org/10.34172/jkmu.2024.12>.

149. Hussein SZ, Mohd Yusoff K, Makpol S, Mohd Yusof YA. Gelam Honey Attenuates Carrageenan-Induced Rat Paw Inflammation via NF- κ B Pathway. *PLoS One* 2013;8:e72365. <https://doi.org/10.1371/JOURNAL.PONE.0072365>.
150. Kim HN, Son KH, Jeong HJ, Park S Bin, Kim JD, Jeong JB. Anti-inflammatory activity of Acacia honey through inhibition of NF- κ B and MAPK/ATF2 signaling pathway in LPS-stimulated RAW264.7 cells. *Korean Journal of Plant Resources* 2018;31:612–21.
151. Rajpoot A, Yadav K, Yadav A, Mishra RK. Shilajit mitigates chemotherapeutic drug-induced testicular toxicity: Study on testicular germ cell dynamics, steroidogenesis modulation, and Nrf-2/Keap-1 signaling. *J Ayurveda Integr Med* 2024;15:100930. <https://doi.org/10.1016/J.JAIM.2024.100930>.
152. Ogawa T, Ishitsuka Y, Nakamura Y, Okiyama N, Watanabe R, Fujisawa Y, et al. Honey and Chamomile Activate Keratinocyte Antioxidative Responses via the KEAP1/NRF2 System. *Clin Cosmet Investig Dermatol* 2020;13:657. <https://doi.org/10.2147/CCID.S270602>.
153. Kangari P, Roshangar L, Iraj A, Talaei-Khozani T, Razmkhah M. Accelerating effect of Shilajit on osteogenic property of adipose-derived mesenchymal stem cells (ASCs). *J Orthop Surg Res* 2022;17:424. <https://doi.org/10.1186/S13018-022-03305-Z>.