nutraceuticals

Review

Medicinal Properties of Honey and *Cordyceps* Mushrooms

Theodor-Ioan Badea and Emanuel Vamanu *

Faculty of Biotechnology, University of Agricultural Sciences and Veterinary Medicine, 011464 Bucharest, Romania; teodor.badea131@gmail.com
* Correspondence: emanuel.vamanu@gmail.com; Tel.: +40-742-218-240

Abstract: In a world still recovering after the COVID-19 pandemic, the consequences of which are still not entirely known, the attention of scientists worldwide is drawn to natural products with positive effects on immunity. The starting point for tackling such a subject is proper documentation of substances used in traditional medicine, which usually have significant nutritional and functional values. Among the most well-known of these substances are mushrooms and honey, both of which have been used for thousands of years all around the globe. The following work aims to gather information about the properties of honey and *Cordyceps* sp. mushrooms by studying the scientific literature available at this point. With the proper use of this information, it will be possible to develop products that incorporate the studied ingredients to increase their functional and medicinal value.

Keywords: *Cordyceps*; honey; antioxidants; polyphenols; supplements

check for updates

Citation: Badea, T.-I.; Vamanu, E. Medicinal Properties of Honey and *Cordyceps* Mushrooms. *Nutraceuticals* **2023**, *3*, 499–512. https://doi.org/10.3390/nutraceuticals3040036

Academic Editor: Ana María Gomez-Caravaca

Received: 16 August 2023
Revised: 5 October 2023
Accepted: 7 October 2023
Published: 10 October 2023

1. Introduction

In recent years, medicine has turned its attention to natural products with positive effects on human health. Due to the abundance of biologically active compounds found in such products, it is expected that these could bring more health benefits compared to regular medicine.

Honey is one of the most well-known natural substances to show health benefits. Its medicinal value has been known for thousands of years. The antioxidant, antibacterial, and antiviral properties make it a valuable tool for treatment or recovery after infectious diseases [1–4]. Honey has also shown effects as a neuroprotector and aid in wound healing [5,6].

Mushrooms have also been known to exhibit medicinal properties, and as such, they have been used in traditional medicine worldwide. Recently, scientists have turned their attention to *Cordyceps* (C.) sp. mushrooms in search of a natural product with high medicinal value. The study of *C.* mushrooms has shown they have anti-oxidant, anti-inflammatory, hypoglycemic, and anti-tumoral effects [7–10]. It has also been shown that they can help improve the gut microbiota [11–13].

This review should give a more thorough understanding of honey and *C.* and can serve as the basis for developing new products with significant nutritional and pharmaceutical values. We will discuss potential future research directions in the field of honey's medicinal properties. This addition highlights the emerging areas of interest and sets the stage for further exploration.

2. The *Cordyceps* Mushrooms

2.1. General Aspects

The *Cordyceps* genus contains over 400 species, amongst which the best known are *C. sinensis* and *C. militaris*. *C. sinensis* grows at high altitudes, typically in pastures over 3000 m above sea level in the Himalaya region (Nepal and India) and the Tibetan plateau (China) [14].

Most of the *Cordyceps* genus members are endoparasites, using arthropods as hosts. *C. sinensis* starts growing inside a living host, then it kills and mummifies its host. The fruiting growths then grow outside of the host's body. Recently, *C. sinensis* was renamed *Ophiocordyceps sinensis* [15]. For a very long time, this mushroom has been known to have medicinal properties. In the Tibet region, it is often known as "winter worm, summer grass" or " caterpillar mushroom" [8,16].

The parasitic nature of Cordyceps is a really intriguing characteristic. These organisms can infect various insects and arthropods, resulting in elongated and thin protrusions from the host's body. These protrusions serve as structures for producing fungal spores [17]. Parasitic *Cordyceps* have attracted considerable interest due to their possible therapeutic effects in traditional Chinese medicine and contemporary herbal supplements. In addition to their parasitic forms, certain species of *Cordyceps* also exhibit saprophytic growth, obtaining nutrients from decomposing organic material. The latest scientific investigations have revealed these organisms' intricate chemical makeup, encompassing several bioactive substances such as cordycepin and polysaccharides [18]. These findings have generated considerable attention due to the possible health advantages associated with these compounds, which encompass a wide range of benefits, including bolstering the immune system and enhancing athletic performance. Due to their varied ecological functions and potential in pharmacology, *Cordyceps* species remain a topic of scientific investigation and cultural importance [19].

Because of the environmental limitations and their parasitic nature, significant amounts of *Cordyceps* mushrooms are rarely found in nature. To solve this issue, efforts are made to allow cultivation on artificial media or submerged fermentation [20].

2.2. Composition

Various constituents have been detected in *Cordyceps* sp. mushrooms, encompassing proteins, polyamines, peptides, polysaccharides, nucleosides, sterols, and fatty acids. Through gas chromatography–mass spectrometry analysis, four distinct free sterols have been identified: cholesterol, ergosterol, beta-sitosterol, and campesterol. While many bioactive compounds have been pinpointed, it is suggested that *Cordyceps* may contain other additional compounds [14]. In other investigations, researchers aimed to unravel the structural attributes of the polysaccharides present in *C. sinensis*, including parameters such as molecular mass, monosaccharide composition, glycosidic bond configuration, and molecular chain conformation. Employing techniques such as chromatography, mass spectrometry, infrared spectroscopy, and nuclear magnetic resonance, these studies delved into the intricate characteristics of the polysaccharides [21].

Cordyceps polysaccharides are typically large, complex molecules composed of multiple sugar units linked together. They often have branched structures, making them more intricate than simple sugars. Many of the polysaccharides in *Cordyceps* are beta-glucans. Beta-glucans are a type of polysaccharide known for their immunomodulatory properties and ability to support the immune system. *Cordyceps* polysaccharides can have a high molecular weight, which may contribute to their bioactivity and potential health benefits [22]. These polysaccharides comprise various monosaccharides, including glucose, mannose, and galactose. The specific composition can vary depending on the *Cordyceps* species and extraction methods. Researchers have investigated the glycosidic bond configuration within *Cordyceps* polysaccharides. The arrangement of these chemical bonds can influence their biological activity [23].

2.3. Beneficial Effects, Pharmacological Properties and Bioactive Compounds

A large number of specialist studies described the pharmacological properties of *Cordyceps* mushrooms. The constituents of *Cordyceps* are associated with multiple pharmacological properties, such as anti-tumoral, anti-metastasis, immunomodulating, antioxidant, anti-inflammatory, hypoglycemic, hyperlipidemic, prebiotic, and anti-aging properties [21,24]. *Cordyceps* has also been effective in preventing viral infections [25].

Multiple studies have demonstrated the hypoglycemic effects of *C. sinensis* extracts, with a reduction of blood glucose concentration observed in vitro [26] and in vivo [27].

In traditional Chinese medicine, *Cordyceps* sp. mushrooms are used in preparing a natural medicine for multiple health problems such as lung or kidney dysfunction and generalized fatigue [28].

C. sinensis is used as an immunosuppressant in the maintenance treatment of kidney transplant recipients in China, but there is no consensus regarding its use [29].

Treatment with *C. militaris* extract inhibited metabolic disorders induced by obesity caused by fat-rich diets, mainly by improving metabolic parameters. As active constituents, pyrrolic alkaloids and nucleotide derivatives were characterized. These results suggest *C. militaris* could be used to treat obesity via the metabolic effects of its constituents [30].

In studies examining the properties of *C. sinensis* polysaccharides, the polysaccharide CS-F70 (composed of 62% galactose, 28% glucose, and 10% mannose), obtained from alkaline mycelium extract, was proven to have hypoglycemic effects. The extract showed powerful hypoglycemic activity in normal mice and those with induced diabetes. In parallel, the effects of the extract on cholesterol and triglycerides were also studied on the same two types of mice. The results showed a reduction in the triglycerides in both types of mice, which confirms the medicinal properties of the polysaccharide CS-F70 [31].

Mannitol and cordycepin are two of the most important pharmacologically active components of *C. sinensis* [32]. Mannitol has beneficial effects, such as diuretic or anti-coughing properties and inhibition of free radicals [33].

Cordycepin (3′-deoxyadenosine), one of the nucleosidic analogs, was first isolated from *C. militaris*. The difference between cordycepin and adenosine is the lack of the 3′-hydroxyl group in cordycepin [24].

Studies have shown that average levels of adenosine and cordycepin were significantly higher in cultivated *Cordyceps* compared to mushrooms harvested from wild flora. On the other hand, the levels of mannitol and polysaccharides were lower in the cultivated mushrooms [34].

Among the aspects studied was data regarding the effect of *Cordyceps* spp. and cordycepin in bones and associated processes. The impact of *Cordyceps* spp. and cordycepin on bones, teeth, and tooth pulp was described as the result of the interaction of AMPK (adenosine monophosphate-activated protein kinase) and ATP (adenosine-5′-triphosphate). This way, it is possible to obtain medicine with regenerative effects that can be used in trauma recovery or the terminal stages of some diseases [35].

Because it has been used for centuries in traditional Chinese medicine, *C. sinensis* was intensely studied for its anti-oxidative, anti-tumoral, anti-hyperglycemic, and immunomodulating properties [14].

In a study conducted by Cho et al. (2003), the researchers examined and evaluated the impacts of Cordyceps sp. extract (CME) and Sweet Potato Anthocyanin (SPA) on lipid peroxidation, DPPH radicals, and cognitive impairments. The two extracts exhibited comparable efficacy in their capacity to scavenge free radicals. The study's results indicate that only SPA demonstrated the ability to suppress the process of lipid peroxidation, which was induced by the presence of Fe2+ ions and ascorbic acid in rat brain tissue samples. The administration of SPA was found to enhance cognitive performance in mice that were subjected to ethanol treatment. The combined effects of SPA and CME were statistically similar to those observed with SPA alone [36]. Polysaccharides represent the most important biologically active compound in *C. sinensis* and *C. militaris*. The components of these compounds include rhamnose, ribose, arabinose, xylose, mannose, glucose, galactose, mannitol, fructose, and sorbose. The exopolysaccharide fraction has pharmacological properties, the most important of which are the immunomodulatory and anti-tumoral effects. Mannoglucan is also among the polysaccharides found in *Cordyceps*, its notable effect being mild cytotoxic effects on the cancer lineage SPC-I1. Various nucleosides and their corresponding compounds, including adenine, adenosine, inosine, cytidine, cytosine, guanine, uridine, thymidine, uracil, hypoxanthine, and guanosine, have been extracted from *C. sinensis*. These compounds contain amino acids and polypeptides that positively affect the cardiovascular system. They also exhibit sedative and hypnotic effects, with tryptophane being the most effective component in this regard [37].

C. sinensis mycelium extract helps reduce the growth and dissemination of bacteria, increasing the survival rate in mice inoculated with streptococci. The macrophages' phagocytosis activity was increased after the treatment with *C. sinensis* [38].

2.4. Effects on the Microbiota

The research targeted to evaluate the impact of *Cordyceps militaris* on the function of the intestinal barrier and the composition of the gut intestinal microbiota in a porcine model. Usage of *C. militaris* improved the number of goblet cells, increased the lymphocyte number, and improved intestinal morphology. *Cordyceps militaris* was found to downregulate pro-inflammatory cytokines and upregulate anti-inflammatory cytokines at the mucosal level. The use of *Cordyceps* can potentially achieve the modulation of intestinal microbiota and the intestinal barrier, hence offering potential avenues for the enhancement of intestinal health. [11,13,39,40].

The low molecular weight exopolysaccharides of *C. militaris* have an antioxidant effect. They are observed to be excellent prebiotics, which increases the proliferation of the probiotics and the increase of phenolic acid [9,10].

After elucidating the structural characteristics of the alkali-extracted polysaccharide CM3-SII obtained from *C. militaris*, the amelioration of hyperlipemia in hamsters with a heterozygous model of hyperlipidemia with low-density lipoprotein receptor (LDLR) deficiency was studied using this polysaccharide. The study demonstrated that CM3-SII significantly decreased plasma total cholesterol, high-density lipoprotein cholesterol, and triglyceride levels in LDLR-deficient heterozygous hamsters. Increased plasma concentration of polylipoprotein A1, abundance of Actinobacteria, and Bacteroidetes/Firmicutes ratio were observed [41].

A similar study was conducted on mice fed a high-fat, high-sucrose diet. Polysaccharides derived from *C. militaris* decreased blood sugar and serum lipid levels in these mice. In addition, *C. militaris* polysaccharide treatment ameliorated intestinal dysbiosis by promoting the next-generation probiotic *Akkermansia muciniphila* population in the intestine of mice fed the high-fat, high-sucrose diet. Polysaccharides derived from *C. militaris* have the potential to alter gut microbiota to increase metabolic syndrome. The cordycepin-rich solution obtained from *C. militaris* had different efficacies in regulating hyperglycemia and gut microbiota in studied mice [42]. Polysaccharides from *C. militaris* may be a potential prebiotic agent to modulate specific gut microbes [43,44].

Modulation of gut microbiota dysbiosis was studied in rats with diabetic nephropathy. The health benefits of *C. cicadae* polysaccharides (CCP) on renal injury and renal interstitial fibrosis in rats with induced diabetic nephropathy were studied. Rats that received CCP showed improved insulin resistance and glucose tolerance. It has also been observed to suppress inflammation and renal dysfunction, slowing the progression of renal intestinal fibrosis and modulating gut microbiota dysbiosis [40,45].

The theoretical background of the hypoglycemic effect of *C. cicadae* research was described in 2023. Bacterium substance polysaccharides (BSP), spore powder polysaccharides (SPP), and pure powder polysaccharides (PPP) were separated, purified, and collected from sclerotia, spores and fruiting bodies of *C. cicadae*, respectively, and chosen as study material. The basis of the hypoglycemic effect of SPP is the mechanism that regulates the mRNA expression of key PI3K/Akt genes involved in the insulin signaling pathway to alleviate insulin resistance, contributing to the development of functional products [46].

The protective efficacy of extracellular polysaccharides from *C. militaris* against toxicity and their regulatory effect on gut microbiota against Pb^{2+}-induced toxicity in vivo was demonstrated in lead-poisoned mice [39].

Special attention is paid to the relationship between the gut microbiota and type 2 diabetes. The hypoglycemic activity of the purified fraction obtained from the polysaccharides of *C. militaris* was investigated, together with its mechanisms, in mice with induced type 2 diabetes. The results indicated that the symptomatic improvement of diabetes could be related to the polysaccharide extracted from *C. militaris*, which regulates the intestinal microbiota against the TLR4/NF-κB pathway to protect the intestinal barrier [12,47].

The activity of cordycepin extracted from *C. militaris* was described in a study on mice, which demonstrated its influence on type 2 diabetes, improving the abundance of *Firmicutes/Bacteroides* that promote the growth of beneficial bacteria by regulation of the intestinal flora, enhancing the metabolites and metabolic pathways associated with the diabetes type 2 modifications [7].

Until now, the study's results have revealed the mechanisms involved in the reduction of blood sugar and lipids using *Cordyceps* and the way forward for the establishment of new anti-obesity and anti-inflammatory therapies would involve *Enterococcus cecorum* along with *Cordyceps* [47].

Considering the need to bring solutions as effective as possible and with as few side effects, polysaccharides from *C. cicadae* were studied for cervical cancer. There are few studies on the anti-cancer activity of *C. cicadae* artificially cultivated by the bionic method. Several studies have shown that the appearance and development of cervical cancer are linked to abnormal cell proliferation and differentiation alongside abnormal cell apoptosis [48]. This study provides the necessary support for further clinical applications, which observed polysaccharides on cell proliferation and apoptosis and the molecular mechanism [49,50].

2.5. Side Effects

There needs to be more information regarding the long-term effects of *Cordyceps* mushrooms, as severe side effects have yet to be reported. Despite this, one case of excessive bleeding has been documented in a patient after a dental intervention. Patients who require insulin must be aware of the hypoglycemic effects of *Cordyceps* sp. mushrooms and derivate products. Women are not recommended to consume *Cordyceps* products during pregnancy or breastfeeding as the effects on the newborn are not yet known. As a blood-diluting agent and immunostimulant, care must be taken when administering alongside immunosuppressants, blood dilutants, or coagulants [25].

3. Honey

3.1. General Aspects

Honey is one of the healthiest foods, known for its many benefits to the human body. Bees produce this as a food; it has the aspect of a sweet, viscous liquid [51].

According to the Codex Alimentarius (1981), honey is officially described as a "natural sweet substance that is produced by honey bees through the collection and transformation of nectar from plants, secretions from living parts of plants, or excretions from plant-sucking insects on living parts of plants. The bees then combine these substances with specific components of their own, deposit the resulting mixture, dehydrate it, store it, and allow it to ripen and mature within the honeycomb." [52].

The process of obtaining honey is complex and begins with collecting the pollen and honeydew from trees and flowers. The bees travel hundreds of kilometers daily to bring the raw materials to the hive. These are then mixed with the saliva of the harvester bee and other substances (enzymes and amino acids). Other bees then process the resulting mix, the honey becoming more viscous. This product is then stored in the honeycomb and left to dry to reduce the water content of the honey. Later, the honeycomb cells are capped with wax [53].

Honey can be classified by origin and the flowers from which the nectar was gathered. It can also be classified by its extraction method. Depending on its origin, honey can be split into floral honey (made by bees by processing nectar and pollen from flowers) and honeydew honey (extrafloral honey, made from other substances from plants or insects). Honeydew honey is darker in color compared to floral honey.

Honey can also be classified depending on the type of flowers from which the nectar was gathered (ex., rapeseed honey, manuka honey, coriander honey, sunflower honey, etc.). Honey can be extracted by removing pieces of honeycomb, draining the honeycomb, centrifugation, pressing, or melting the honeycomb [54].

Currently, beekeepers name the variety of the honey based on the moment of nectar appearance and the availability of individual nectar sources [55].

3.2. Composition

Honey is a substance characterized by its high concentration of sugars, primarily consisting of glucose (31%) and fructose (38%). Additional examples of disaccharides and trisaccharides encompass maltose, sucrose, isomaltose, gentiobiose, and maltotriose.

The antibacterial effect of honey comes from its high sugar content, low acidity, presence of flavonoids and phenolic acids, and methylglyoxal and defensin-1 from bees [3].

The pronounced effects of manuka honey on planktonic bacteria can be attributed to methylglyoxal [56].

Polyphenolic compounds (phenolic acids and flavonoids), vitamins C and E, enzymes (catalase, peroxidase, superoxide dismutase), and trace elements [2,57] are responsible for the antioxidant activity. Flavonoid content is associated with antioxidant activities in vitro. The phenolic compound content is influenced by several factors, including geographical location, botanical origin, type of phenolic compounds, storage time, and processing method [2].

The high content of polyphenols (quercetin and gallic acid) imparts neuroprotective properties to honey [5].

In nutritional science, honey consumption and its association with the gut microbiome has been studied recently, as it plays a key role in chronic diseases. Polyphenols in honey may enhance the balance changes between pathogenic and beneficial microbial populations in the gut microbiome, providing a beneficial effect [58].

Honey composition depends on floral source, season, and environmental factors [59].

3.3. Beneficial Effects and Pharmacological Properties

Since ancient times, honey has been known to have therapeutic properties and has been included in medical practice relatively recently [6].

Honey exhibits antibacterial characteristics, which contribute to its capacity for wound healing. Maintaining a moist wound condition and the high viscosity of the substance contribute to establishing a protective barrier, thereby preventing the occurrence of infections. The antibacterial action is derived from the enzymatic synthesis of hydrogen peroxide. Nevertheless, one alternative type of honey, known as peroxide-free honey, exhibits noteworthy antibacterial properties even without hydrogen peroxide activity (such as manuka honey). The potential mechanism underlying the observed effects could be attributed to the acidic nature of honey, characterized by a low pH and its high sugar content, resulting in elevated osmolarity. These properties collectively contribute to the antimicrobial activity of honey by effectively inhibiting microbial development. The efficacy of therapeutic honey in eradicating antibiotic-resistant bacteria responsible for several life-threatening diseases has been demonstrated in vitro [60]. Honey possesses therapeutic attributes that contribute to wound healing, such as promoting tissue proliferation, enhancing epithelialization, and mitigating scar formation. The utilization of honey does not elicit any allergic reactions [6]. Honey is a good source of natural antioxidants that play an important role in nutrition and health maintenance by combating the harmful effects caused by oxidants (risk of heart disease, cancer, immune system decline, cataracts, and various inflammatory processes) [55].

Honey has been extensively researched for its neuroprotective qualities, making it a notable natural product and functional food. In the realm of honey research, Tualang and thyme honey have exhibited notable attributes in terms of their antioxidant effect, anti-inflammatory properties, and anticholinesterase activity. These characteristics have been associated with the potential to mitigate and control various neurodegenerative ailments, including Alzheimer's disease [5].

A summary of the beneficial effects of honey can be found in Table 1.

Table 1. Beneficial and therapeutic properties of honey.

Effect	Works that Describe the Effect
Antioxidant	D'zugan et al., 2018 [55] Gheldof et al., 2002 [57] Stefanis et al., 2023 [1] Zawawi et al., 2021 [2]
Antibacterial	Kwakman and Zaat, 2012 [3] Eick et al., 2014 [56] Hbibi et al., 2020 [61] Kwakman et al., 2008 [62] Stefanis et al., 2023 [1] Vázquez-Quinones et al., 2018 [63] Mandal and Mandal, 2011 [60]
Antiviral	Hossain et al., 2020 [4]
Neuroprotector	Fadzil et al., 2023 [5]
Wound healing	Al-Waili et al., 2011 [6]

3.4. Effects on the Microbiota

The gut microbiota plays a vital role in human health. Disturbances in the balance of these organisms are linked to intestinal inflammation and the development and progression of numerous conditions, such as colon cancer, irritable bowel syndrome, obesity, and mental health problems. There is currently major interest in manipulating the gut microbiota to a more favorable balance to improve health through diet [64].

Relevant evidence of the effect of honey intake on the human gut microbiota and its relation to the amelioration of various chronic diseases has been presented in recent times [58].

Various animal models were chosen to understand the microbiota. The honeybee was also selected for animal modeling studies, providing a particularly good opportunity to study interactions between host biology and gut microbiota. All community core members are exclusive to this gut system and are important for host metabolism, endocrine signaling, and the immune system, as is known in other animal-microbe symbioses. Like other relatively simple insect model organisms that have been widely used for human disease, bees have homologous or analogous organs: the brain, fat body, oenocytes, gastrointestinal tract, and circulatory system, thus highlighting the bee as a promising subject for human disease modeling, particularly for understanding the role of the microbiome in human health and disease [65].

A study on buckwheat honey investigated the phenolic and carbohydrate composition of eight buckwheat honey samples using high-performance liquid and ion chromatography. Human gut microbes were cultured in a medium supplemented with eight buckwheat honey samples or the same concentration of fructooligosaccharides. Twelve phenolic compounds and four oligosaccharides were identified in most buckwheat honey samples, namely, protocatechuic acid, 4-hydroxybenzoic acid, vanillin, gallic acid, p-coumaric acid, benzoic acid, isoferulic acid, methyl syringate, trans-trans ascorbic acid, cis-trans ascorbic acid, ferulic acid, 4-hydroxybenzaldehyde, ketosis, isomaltose, isomaltotriose, and panose. This study was the first to report the presence of 4-hydroxybenzaldehyde in buckwheat honey. 4-Hydroxybenzaldehyde appears to be a field marker of buckwheat honey. The results indicated that buckwheat honey may benefit human gut health by selectively supporting the growth of indigenous bifidobacteria and restricting pathogenic bacteria in the intestinal tract. Hence, we infer that buckwheat honey may be a natural product that benefits gut health [66].

Most studies only focus on one aspect of anti-inflammatory activity, pathogen inhibition, or changes in gut microbiota [67].

Polyphenols can impede the proliferation and attachment of pathogenic gut microflora, including Alistipes, Helicobacter, and Oscillibacter, known to induce inflammation within the gastrointestinal system. Introducing phenolic compounds through administration has been observed to enhance the prevalence of beneficial species, such as Lactobacillus and Bifidobacterium, within gut microbial communities. Simultaneously, this intervention has been found to reduce the number of pathogenic species, such as Clostridium. The bioavailability and bioaccessibility of polyphenols play a crucial role in determining their favorable bioactivities, as the fast metabolism of many polyphenols occurs upon oral intake. Encapsulation technology has been investigated as a potential solution to address the challenges associated with polyphenols' solubility, stability, and bioavailability. This technique aims to facilitate the transportation of polyphenols through the gastrointestinal tract and enhance the delivery of phenolic chemicals. Starch demonstrates efficacy as a potential agent for regulating the release of polyphenols within the upper gastrointestinal tract, thereby safeguarding these compounds from reaching the lower regions of the digestive system and modulating the diversity and makeup of the gut microbiota [68].

Starch can influence the release of polyphenols in the digestive tract through several mechanisms. Starch can also physically encase polyphenols, acting as a protective barrier [69]. This limits the immediate release of polyphenols in the stomach and upper digestive tract. In the large intestine, certain starches that escape digestion in the small intestine can be fermented by gut bacteria. This fermentation process can create a more acidic environment in the colon, which may influence the release of polyphenols [70]. Starches may interact with other nutrients in the digestive tract, altering the solubility and absorption of polyphenols. For example, the presence of fats may enhance the absorption of certain polyphenols, and starches can affect how fats are emulsified and digested [71].

Honey polyphenols improve gut inflammation and resistance to oxidative stress by modulating gut microbiota, which is favorable to unraveling host–microbe interactions demonstrated in rats [72]. Ulcerative colitis is a recurrent immune disorder that requires long-term drug treatment. The alternative studied was honey and the effects of various honey constituents in dextran sulfate sodium salt (DSS)-induced colitis in rats. The findings indicate that the administration of honey polyphenols before treatment leads to a notable enhancement in the levels of superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), nitric oxide (NO), and myeloperoxidase (MPO). Additionally, it results in a reduction in colonic apoptosis induced by dextran sulfate sodium (DSS), as well as a decrease in the levels of inflammatory cytokines interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and transforming growth factor-beta 1 (TGF-β1) in the colon. The expression levels of the IL-1β, IL-6, TNF-α, and IFN-γ genes are decreased, while the expression level of the IκB-α gene is increased. Furthermore, it is worth noting that there are comparable alterations in microbial community structure and the preferential enrichment of crucial species seen in both honey and SASP polyphenols. The presence of honey polyphenols resulted in a notable decrease in the abundance of *Bacteroides*, *Corynebacterium*, and *Proteus* species. The study's findings demonstrate a significant correlation between the regulation of colonic gene expression by honey polyphenols and the presence of important species within the gut microbiota [72,73].

Current research suggests that certain types of honey may reduce the presence of gut infection-causing bacteria, including *Salmonella*, *Escherichia coli*, and *Clostridiodes difficile*, while stimulating the growth of potentially beneficial species such as *Lactobacillus* and *Bifidobacteria* [64].

One of the more common functional disorders is constipation, usually accompanied by intestinal dysbiosis. The antimicrobial and bifidogenic effects of compounds in honey have been studied in mice. Constipation was induced with loperamide in mice by altering the gut microbiota. The impact of honey treatment on the microbiota was analyzed using 16S rRNA gene sequencing of fecal material. Honey showed an obvious improvement in fecal water content and alleviated constipation by modulating the microbiota's microbial composition, indicating that honey could be considered a parameter to evaluate in strategies for constipation therapy [74].

3.5. Secondary Effects

Honey is a health benefit for the body but can also bring unwanted side effects.

Honey consumed for a long period in excess leads to weight gain. Daily sugar intake is recommended to be 10% of total calories, according to WHO recommendations.

Honey can also cause allergies if consumed in excess. Allergies to honey are not common; those susceptible are people allergic to pollen. Although honey allergies are rare, increased intake of foods containing honey as a basic ingredient can cause allergies. A honey allergy is considered to be a contact allergy and is caused by propolis or propolis-enriched honey [75,76].

The sugar content can cause blood sugar levels to rise. As a result, an increased level of glycosylated hemoglobin in the blood (HbA1c) has been observed in people who have been long-term honey consumers. Some studies have demonstrated the anti-diabetic properties of honey. Because honey contains fructose, it can cause diarrhea in sensitive people [77].

Because honey naturally contains bacteria, it can cause food poisoning and the growth of yeast, mold, and pollen or can be secondarily contaminated during processing. Poisoning is manifested by low blood pressure and bradycardia [78].

4. Conclusions

Honey and Cordyceps are two food items that provide potential health benefits and can be included more regularly in an individual's dietary regimen owing to their documented therapeutic properties in addressing many health ailments. Honey has garnered recognition for its potential to mitigate various health conditions, including colon cancer, irritable bowel syndrome, obesity, and mental health disorders. Cordyceps has garnered growing interest because of its possible advantages, namely about the gut microbiota and its potential implications for illnesses such as type 2 diabetes, obesity, poisonings, and hyperlipidemia. The regulation and manipulation of the gut microbiota have emerged as a focal point in the quest for improved human health. Current research is focused on investigating various approaches to enhance the equilibrium of gut microbiota using dietary interventions, acknowledging the considerable potential for enhancing overall health.

5. Further Developments

Both honey and *Cordyceps* have ample opportunities to be used in developing functional products. Future research can be dedicated to analyzing the best candidates from the human health point of view, analyzing and selecting the most efficient type of honey for treating different human diseases, including regulating the gut microbiota. On the other hand, the *Cordyceps* genus is already well known for its effects on the gut microbiota. An interesting proposition for future research would be to study the combined effects of honey and *Cordyceps* mushrooms on the human body. Such studies would allow for functional products containing honey and *Cordyceps* to be developed safely and effectively.

Initial data on honey's multiple applications need to be more, and much remains to be learned, such as how to most effectively combine various extracts. Despite the obvious importance of this topic, our knowledge of the present level of research in this area has surprising gaps. When it comes to antioxidant activity as a biomarker of honey variety, for instance, there do not appear to be any current studies comparable to those conducted by Prof. Dzugan and his team. There is still much to prove about the bioactive qualities of honey because of the need for more recent research into the topic. More research into honey and its prospective applications, especially after it has been fortified with various extracts, would greatly benefit the honey's functional characteristics [55,79].

A workflow for developing such a product is proposed in Figure 1.

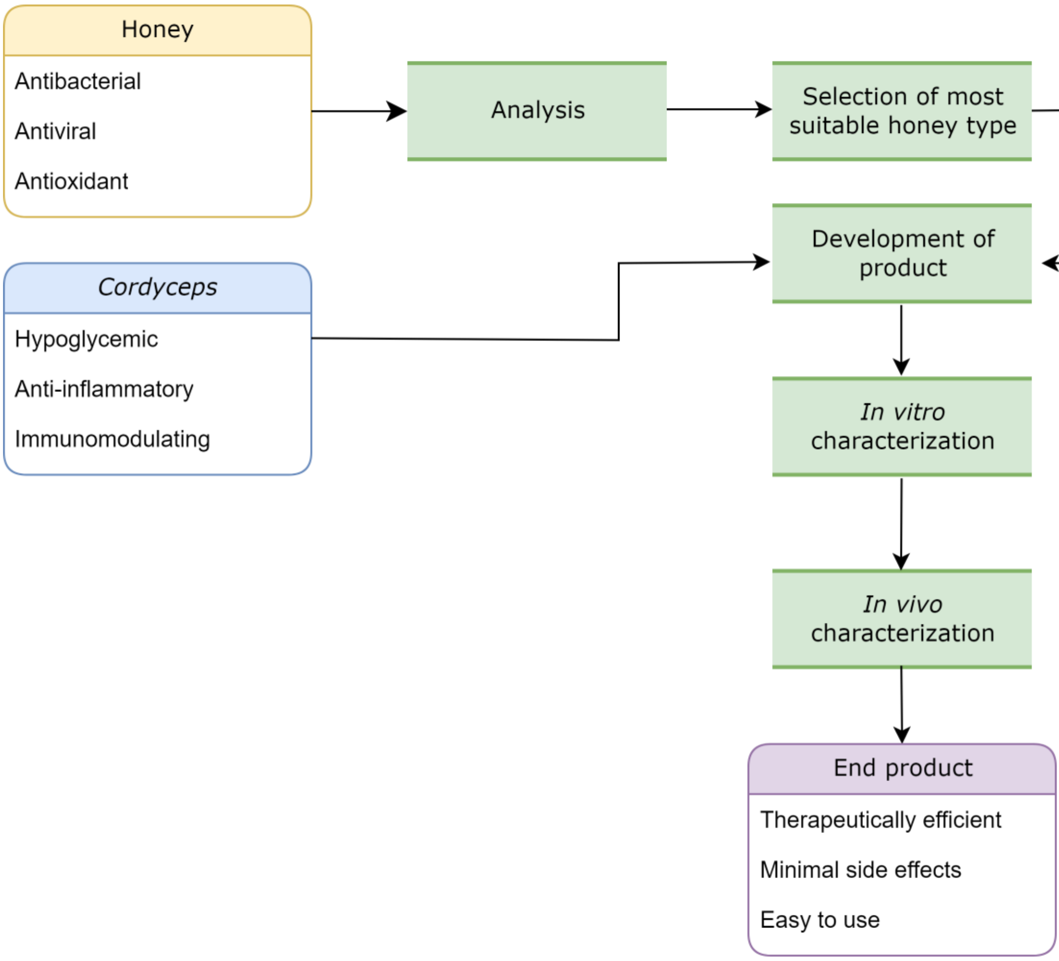

Figure 1. A method of obtaining functional products based on honey and *Cordyceps*.

Incorporating plant extracts and medicinal mushrooms into honey has been shown to enhance its nutritional composition substantially. Various plant extracts, like ginseng, echinacea, and turmeric, include a substantial content of vitamins, minerals, and antioxidants, which can potentially increase honey's nutritional composition [80]. Medicinal mushrooms such as Reishi, Chaga, and Cordyceps provide immune-enhancing and adaptogenic qualities, further enhancing honey's nutritional composition. The potential synergistic impact resulting from the combination of antioxidants derived from honey, plant extracts, and medicinal mushrooms can potent the fortified honey's total antioxidant capacity. Antioxidants play a vital role in neutralizing detrimental free radicals and mitigating the effects of oxidative stress, which has been associated with a range of chronic illnesses and the aging process. There is a growing trend among consumers to use healthier options instead of conventional sweeteners actively. Consequently, goods that can provide both palatability and health advantages are expected to garner a wider range of interest.

Author Contributions: Conceptualization, T.-I.B. and E.V. writing—original draft preparation, T.-I.B.; writing—review and editing, T.-I.B.; supervision, E.V.; project administration, E.V. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Data are contained within the article.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Stefanis, C.; Stavropoulou, E.; Giorgi, E.; Voidarou, C.; Constantinidis, T.C.; Vrioni, G.; Tsakris, A. Honey's Antioxidant and Antimicrobial Properties: A Bibliometric Study. *Antioxidants* **2023**, *12*, 414. [CrossRef] [PubMed]
2. Zawawi, N.; Chong, P.J.; Mohd Tom, N.N.; Saiful Anuar, N.S.; Mohammad, S.M.; Ismail, N.; Jusoh, A.Z. Establishing Relationship between Vitamins, Total Phenolic and Total Flavonoid Content and Antioxidant Activities in Various Honey Types. *Molecules* **2021**, *26*, 4399. [CrossRef] [PubMed]
3. Kwakman, P.H.; Zaat, S.A. Antibacterial Components of Honey. *IUBMB Life* **2012**, *64*, 48–55. [CrossRef] [PubMed]
4. Hossain, K.S.; Hossain, M.G.; Moni, A.; Rahman, M.M.; Rahman, U.H.; Alam, M.; Kundu, S.; Rahman, M.M.; Hannan, M.A.; Uddin, M.J. Prospects of Honey in Fighting against COVID-19: Pharmacological Insights and Therapeutic Promises. *Heliyon* **2020**, *6*, e05798. [CrossRef] [PubMed]
5. Fadzil, M.A.M.; Mustar, S.; Rashed, A.A. The Potential Use of Honey as a Neuroprotective Agent for the Management of Neurodegenerative Diseases. *Nutrients* **2023**, *15*, 1558. [CrossRef] [PubMed]
6. Al-Waili, N.; Salom, K.; Al-Ghamdi, A.A. Honey for Wound Healing, Ulcers, and Burns; Data Supporting Its Use in Clinical Practice. *Sci. World J.* **2011**, *11*, 766–787. [CrossRef] [PubMed]
7. Liu, X.; Dun, M.; Jian, T.; Sun, Y.; Wang, M.; Zhang, G.; Ling, J. *Cordyceps militaris* Extracts and Cordycepin Ameliorate Type 2 Diabetes Mellitus by Modulating the Gut Microbiota and Metabolites. *Front. Pharmacol.* **2023**, *14*, 1134429. [CrossRef]
8. Shashidhar, M.G.; Giridhar, P.; Udaya Sankar, K.; Manohar, B. Bioactive Principles from Cordyceps Sinensis: A Potent Food Supplement—A Review. *J. Funct. Foods* **2013**, *5*, 1013–1030. [CrossRef]
9. Nguyen, Q.-V.; Vu, T.-T.; Tran, M.-T.; Ho Thi, P.T.; Thu, H.; Le Thi, T.H.; Chuyen, H.V.; Dinh, M.-H. Antioxidant Activity and Hepatoprotective Effect of Exopolysaccharides from Cultivated Ophiocordyceps Sinensis against CCl4-Induced Liver Damages. *Nat. Prod. Commun.* **2021**, *16*, 1934578X21997670. [CrossRef]
10. Kang, J.Y.; Lee, B.; Kim, C.H.; Choi, J.H.; Kim, M.-S. Enhancing the Prebiotic and Antioxidant Effects of Exopolysaccharides Derived from *Cordyceps militaris* by Enzyme-Digestion. *LWT* **2022**, *167*, 113830. [CrossRef]
11. Zheng, H.; Cao, H.; Zhang, D.; Huang, J.; Li, J.; Wang, S.; Lu, J.; Li, X.; Yang, G.; Shi, X. *Cordyceps militaris* Modulates Intestinal Barrier Function and Gut Microbiota in a Pig Model. *Front. Microbiol.* **2022**, *13*, 810230. [CrossRef]
12. Zhao, H.; Li, M.; Liu, L.; Li, D.; Zhao, L.; Wu, Z.; Zhou, M.; Jia, L.; Yang, F. *Cordyceps militaris* Polysaccharide Alleviates Diabetic Symptoms by Regulating Gut Microbiota against TLR4/NF-KB Pathway. *Int. J. Biol. Macromol.* **2023**, *230*, 123241. [CrossRef]
13. Ying, M.; Yu, Q.; Zheng, B.; Wang, H.; Wang, J.; Chen, S.; Nie, S.; Xie, M. Cultured Cordyceps Sinensis Polysaccharides Modulate Intestinal Mucosal Immunity and Gut Microbiota in Cyclophosphamide-Treated Mice. *Carbohydr. Polym.* **2020**, *235*, 115957. [CrossRef] [PubMed]
14. Prasain, J.K. Pharmacological Effects of Cordyceps and Its Bioactive Compounds. *Stud. Nat. Prod. Chem.* **2013**, *40*, 453–468.
15. Lo, H.C.; Hsieh, C.; Lin, F.Y.; Hsu, T.H. A Systematic Review of the Mysterious Caterpillar Fungus Ophiocordyceps sinensis in Dong-ChongXiaCao (Dōng Chóng Xià Cǎo) and Related Bioactive Ingredients. *J. Tradit. Complement. Med.* **2013**, *3*, 16–32. [CrossRef]
16. Dworecka-Kaszak, B. Cordyceps Fungi as Natural Killers, New Hopes for Medicine and Biological Control Factors. *Ann. Parasitol.* **2014**, *60*, 151–158. [PubMed]
17. Baral, B. Entomopathogenicity and Biological Attributes of Himalayan Treasured Fungus *Ophiocordyceps sinensis* (Yarsagumba). *J. Fungi* **2017**, *3*, 4. [CrossRef]
18. Paterson, R.R. Cordyceps: A traditional Chinese medicine and another fungal therapeutic biofactory? *Phytochemistry.* **2008**, *69*, 1469–1495. [CrossRef]
19. Das, G.; Shin, H.S.; Leyva-Gómez, G.; Prado-Audelo, M.L.D.; Cortes, H.; Singh, Y.D.; Panda, M.K.; Mishra, A.P.; Nigam, M.; Saklani, S.; et al. *Cordyceps* spp.: A Review on Its Immune-Stimulatory and Other Biological Potentials. *Front. Pharmacol.* **2021**, *11*, 602364. [CrossRef]
20. Liang, Y.-L.; Liu, Y.; Yang, J.-W.; Liu, C.-X. Studies on Pharmacological Activities of Cultivated Cordyceps Sinensis. *Phytother. Res. Int. J. Devoted Med. Sci. Res. Plants Plant Prod.* **1997**, *11*, 237–239.
21. Yuan, Q.; Xie, F.; Tan, J.; Yuan, Y.; Mei, H.; Zheng, Y.; Sheng, R. Extraction, Structure and Pharmacological Effects of the Polysaccharides from Cordyceps Sinensis: A Review. *J. Funct. Foods* **2022**, *89*, 104909. [CrossRef]
22. Friedman, M. Mushroom Polysaccharides: Chemistry and Antiobesity, Antidiabetes, Anticancer, and Antibiotic Properties in Cells, Rodents, and Humans. *Foods* **2016**, *5*, 80. [CrossRef] [PubMed]
23. Miao, M.; Yu, W.Q.; Li, Y.; Sun, Y.L.; Guo, S.D. Structural Elucidation and Activities of *Cordyceps militaris*-Derived Polysaccharides: A Review. *Front. Nutr.* **2022**, *9*, 898674. [CrossRef] [PubMed]
24. Tuli, H.S.; Sandhu, S.S.; Sharma, A.K. Pharmacological and Therapeutic Potential of Cordyceps with Special Reference to Cordycepin. *3 Biotech* **2014**, *4*, 1–12. [CrossRef]
25. Mulcahy, L. Cordyceps: Benefits, Side Effects and Dosage. Available online: https://www.goodhousekeeping.com/health/diet-nutrition/a43236254/cordyceps-benefits/ (accessed on 13 May 2023).

26. Uddin, N.; Hasan, M.R.; Hossain, M.M.; Sarker, A.; Hasan, A.H.; Islam, A.F.; Chowdhury, M.M.; Rana, M.S. In vitro α-amylase inhibitory activity and in vivo hypoglycemic effect of methanol extract of *Citrus macroptera* Montr. fruit. *Asian Pac. J. Trop. Biomed.* **2014**, *4*, 473–479. [CrossRef]
27. Al-Aboudi, A.; Afifi, F.U. Plants used for the treatment of diabetes in Jordan: A review of scientific evidence. *Pharm. Biol.* **2011**, *49*, 221–239. [CrossRef]
28. Benzie, I.F.F.; Wachtel-Galor, S. (Eds.) *Herbal Medicine: Biomolecular and Clinical Aspects*, 2nd ed.; CRC Press/Taylor & Francis: Boca Raton, FL, USA, 2011.
29. Hong, T.; Zhang, M.; Fan, J. *Cordyceps sinensis* (a Traditional Chinese Medicine) for Kidney Transplant Recipients. *Cochrane Database Syst. Rev.* **2015**, *2015*. [CrossRef]
30. Kim, S.B.; Ahn, B.; Kim, M.; Ji, H.-J.; Shin, S.-K.; Hong, I.P.; Kim, C.Y.; Hwang, B.Y.; Lee, M.K. Effect of *Cordyceps militaris* Extract and Active Constituents on Metabolic Parameters of Obesity Induced by High-Fat Diet in C58BL/6J Mice. *J. Ethnopharmacol.* **2014**, *151*, 478–484. [CrossRef]
31. Kiho, T.; YAMANE, A.; HUI, J.; USUI, S.; UKAI, S. Polysaccharides in Fungi. XXXVI. Hypoglycemic Activity of a Polysaccharide (CS-F30) from the Cultural Mycelium of Cordyceps Sinensis and Its Effect on Glucose Metabolism in Mouse Liver. *Biol. Pharm. Bull.* **1996**, *19*, 294–296. [CrossRef]
32. Li, Z.; Noriaki, S.; Sun, S. TOF-SIMS Study of Mannitol and Cordycepin in Cordyceps Sinensis. *Guang Pu Xue Yu Guang Pu Fen Xi* **2016**, *36*, 1230–1234.
33. Reis, F.S.; Barros, L.; Calhelha, R.C.; Ćirić, A.; Van Griensven, L.J.; Soković, M.; Ferreira, I.C. The Methanolic Extract of *Cordyceps militaris* (L.) Link Fruiting Body Shows Antioxidant, Antibacterial, Antifungal and Antihuman Tumor Cell Lines Properties. *Food Chem. Toxicol.* **2013**, *62*, 91–98. [CrossRef] [PubMed]
34. Zhou, Y.; Wang, M.; Zhang, H.; Huang, Z.; Ma, J. Comparative Study of the Composition of Cultivated, Naturally Grown Cordyceps Sinensis, and Stiff Worms across Different Sampling Years. *PLoS ONE* **2019**, *14*, e0225750. [CrossRef] [PubMed]
35. Jędrejko, K.; Kała, K.; Sułkowska-Ziaja, K.; Krakowska, A.; Zięba, P.; Marzec, K.; Szewczyk, A.; Sękara, A.; Pytko-Polończyk, J.; Muszyńska, B. Cordyceps Militaris—Fruiting Bodies, Mycelium, and Supplements: Valuable Component of Daily Diet. *Antioxidants* **2022**, *11*, 1861. [CrossRef]
36. Cho, J.; Kang, J.S.; Long, P.H.; Jing, J.; Back, Y.; Chung, K.-S. Antioxidant and Memory Enhancing Effects of Purple Sweet Potato Anthocyanin and Cordyceps Mushroom Extract. *Arch. Pharm. Res.* **2003**, *26*, 821–825. [CrossRef] [PubMed]
37. Mal'učká, L.U.; Uhrinová, A.; Lysinová, P. Medicinal Mushrooms Ophiocordyceps Sinensis and Cordyceps Militaris. *Ceska Slov. Farm.* **2022**, *71*, 259–265. [CrossRef]
38. Kuo, C.-F.; Chen, C.-C.; Luo, Y.-H.; Huang, R.Y.; Chuang, W.-J.; Sheu, C.-C.; Lin, Y.-S. Cordyceps Sinensis Mycelium Protects Mice from Group A Streptococcal Infection. *J. Med. Microbiol.* **2005**, *54*, 795–802. [CrossRef]
39. Song, Q.; Zhu, Z. Using *Cordyceps militaris* Extracellular Polysaccharides to Prevent Pb^{2+}-Induced Liver and Kidney Toxicity by Activating Nrf2 Signals and Modulating Gut Microbiota. *Food Funct.* **2020**, *11*, 9226–9239. [CrossRef]
40. Yu, M.; Yue, J.; Hui, N.; Zhi, Y.; Hayat, K.; Yang, X.; Zhang, D.; Chu, S.; Zhou, P. Anti-Hyperlipidemia and Gut Microbiota Community Regulation Effects of Selenium-Rich *Cordyceps militaris* Polysaccharides on the High-Fat Diet-Fed Mice Model. *Foods* **2021**, *10*, 2252. [CrossRef]
41. Yu, W.-Q.; Wang, X.-L.; Ji, H.-H.; Miao, M.; Zhang, B.-H.; Li, H.; Zhang, Z.-Y.; Ji, C.-F.; Guo, S.-D. CM3-SII Polysaccharide Obtained from *Cordyceps militaris* Ameliorates Hyperlipidemia in Heterozygous LDLR-Deficient Hamsters by Modulating Gut Microbiota and NPC1L1 and PPARα Levels. *Int. J. Biol. Macromol.* **2023**, *239*, 124293. [CrossRef]
42. Lee, B.-H.; Chen, C.-H.; Hsu, Y.-Y.; Chuang, P.-T.; Shih, M.-K.; Hsu, W.-H. Polysaccharides Obtained from *Cordyceps militaris* Alleviate Hyperglycemia by Regulating Gut Microbiota in Mice Fed a High-Fat/Sucrose Diet. *Foods* **2021**, *10*, 1870. [CrossRef]
43. Chen, S.; Wang, J.; Fang, Q.; Dong, N.; Fang, Q.; Cui, S.W.; Nie, S. A Polysaccharide from Natural Cordyceps Sinensis Regulates the Intestinal Immunity and Gut Microbiota in Mice with Cyclophosphamide-Induced Intestinal Injury. *Food Funct.* **2021**, *12*, 6271–6282. [CrossRef] [PubMed]
44. Huang, S.; Zou, Y.; Tang, H.; Zhuang, J.; Ye, Z.; Wei, T.; Lin, J.; Zheng, Q. *Cordyceps militaris* Polysaccharides Modulate Gut Microbiota and Improve Metabolic Disorders in Mice with Diet-Induced Obesity. *J. Sci. Food Agric.* **2023**, *103*, 1885–1894. [CrossRef] [PubMed]
45. Yang, J.; Dong, H.; Wang, Y.; Jiang, Y.; Zhang, W.; Lu, Y.; Chen, Y.; Chen, L. Cordyceps Cicadae Polysaccharides Ameliorated Renal Interstitial Fibrosis in Diabetic Nephropathy Rats by Repressing Inflammation and Modulating Gut Microbiota Dysbiosis. *Int. J. Biol. Macromol.* **2020**, *163*, 442–456. [CrossRef] [PubMed]
46. Wang, Y.; Zeng, T.; Li, H.; Wang, Y.; Wang, J.; Yuan, H. Structural Characterization and Hypoglycemic Function of Polysaccharides from Cordyceps Cicadae. *Molecules* **2023**, *28*, 526. [CrossRef]
47. Wu, G.-D.; Pan, A.; Zhang, X.; Cai, Y.-Y.; Wang, Q.; Huang, F.-Q.; Alolga, R.N.; Li, J.; Qi, L.-W.; Liu, Q. Cordyceps Improves Obesity and Its Related Inflammation via Modulation of Enterococcus Cecorum Abundance and Bile Acid Metabolism. *Am. J. Chin. Med.* **2022**, *50*, 817–838. [CrossRef]
48. Pessôa, M.T.C.; Valadares, J.M.M.; Rocha, S.C.; Silva, S.C.; McDermott, J.P.; Sánchez, G.; Varotti, F.P.; Scavone, C.; Ribeiro, R.I.M.A.; Villar, J.A.F.P.; et al. 21-Benzylidene Digoxin Decreases Proliferation by Inhibiting the EGFR/ERK Signaling Pathway and Induces Apoptosis in HeLa Cells. *Steroids* **2020**, *155*, 108551. [CrossRef]

49. Chang, M.-M.; Hong, S.-Y.; Yang, S.-H.; Wu, C.-C.; Wang, C.-Y.; Huang, B.-M. Anti-Cancer Effect of Cordycepin on FGF9-Induced Testicular Tumorigenesis. *IJMS* **2020**, *21*, 8336. [CrossRef]
50. Xu, J.; Tan, Z.-C.; Shen, Z.-Y.; Shen, X.-J.; Tang, S.-M. Cordyceps Cicadae Polysaccharides Inhibit Human Cervical Cancer Hela Cells Proliferation via Apoptosis and Cell Cycle Arrest. *Food Chem. Toxicol.* **2021**, *148*, 111971. [CrossRef]
51. Baker, M.T.; Lu, P.; Parrella, J.A.; Leggette, H.R. Consumer Acceptance toward Functional Foods: A Scoping Review. *Int. J. Environ. Res. Public Health* **2022**, *19*, 1217. [CrossRef]
52. Alimentarius, C. Standard for Honey CXS 12-1981. Adopted in 1981. Available online: https://www.fao.org/fao-who-codexalimentarius/sh-proxy/fr/?lnk=1&url=https%253A%252F%252Fworkspace.fao.org%252Fsites%252Fcodex%252FStandards%252FCXS%2B12-1981%252FCXS_012e.pdf (accessed on 9 October 2023).
53. How Bees Make Honey Is Complex Process. Available online: https://www.dispatch.com/story/news/technology/2014/08/31/how-bees-make-honey-is/23975471007/ (accessed on 27 July 2023).
54. Sortimente de miere—Proprietăți și recomandări terapeutice. *Fagurele Cu Miere*, 10 August 2019.
55. Dżugan, M.; Tomczyk, M.; Sowa, P.; Grabek-Lejko, D. Antioxidant Activity as Biomarker of Honey Variety. *Molecules* **2018**, *23*, 2069. [CrossRef]
56. Eick, S.; Schäfer, G.; Kwieciński, J.; Atrott, J.; Henle, T.; Pfister, W. Honey—A Potential Agent against Porphyromonas Gingivalis: An in Vitro Study. *BMC Oral Health* **2014**, *14*, 24. [CrossRef] [PubMed]
57. Gheldof, N.; Wang, X.-H.; Engeseth, N.J. Identification and Quantification of Antioxidant Components of Honeys from Various Floral Sources. *J. Agric. Food Chem.* **2002**, *50*, 5870–5877. [CrossRef] [PubMed]
58. Cárdenas-Escudero, J.; Mármol-Rojas, C.; Escribano-Pintor, S.; Galán-Madruga, D.; Caceres, J.O. Honey Polyphenols: Regulators of Human Microbiota and Health. *Food Funct.* **2023**, *14*, 602–620. [CrossRef]
59. Manyi-Loh, C.E.; Ndip, R.N.; Clarke, A.M. Volatile Compounds in Honey: A Review on Their Involvement in Aroma, Botanical Origin Determination and Potential Biomedical Activities. *Int. J. Mol. Sci.* **2011**, *12*, 9514–9532. [CrossRef] [PubMed]
60. Mandal, M.D.; Mandal, S. Honey: Its Medicinal Property and Antibacterial Activity. *Asian Pac. J. Trop. Biomed.* **2011**, *1*, 154–160. [CrossRef] [PubMed]
61. Hbibi, A.; Sikkou, K.; Khedid, K.; El Hamzaoui, S.; Bouziane, A.; Benazza, D. Antimicrobial Activity of Honey in Periodontal Disease: A Systematic Review. *J. Antimicrob. Chemother.* **2020**, *75*, 807–826. [CrossRef]
62. Kwakman, P.H.; Van den Akker, J.P.; Güçlü, A.; Aslami, H.; Binnekade, J.M.; de Boer, L.; Boszhard, L.; Paulus, F.; Middelhoek, P.; te Velde, A.A. Medical-Grade Honey Kills Antibiotic-Resistant Bacteria in Vitro and Eradicates Skin Colonization. *Clin. Infect. Dis.* **2008**, *46*, 1677–1682. [CrossRef]
63. Vázquez-Quiñones, C.R.; Moreno-Terrazas, R.; Natividad-Bonifacio, I.; Quiñones-Ramírez, E.I.; Vázquez-Salinas, C. Microbiological Assessment of Honey in México. *Rev. Argent. Microbiol.* **2018**, *50*, 75–80. [CrossRef]
64. Schell, K.R.; Fernandes, K.E.; Shanahan, E.; Wilson, I.; Blair, S.E.; Carter, D.A.; Cokcetin, N.N. The Potential of Honey as a Prebiotic Food to Re-Engineer the Gut Microbiome Toward a Healthy State. *Front. Nutr.* **2022**, *9*, 957932. [CrossRef]
65. Wang, X.; Zhang, X.; Zhang, Z.; Lang, H.; Zheng, H. Honey Bee as a Model Organism to Study Gut Microbiota and Diseases. *Drug Discov. Today Dis. Models* **2018**, *28*, 35–42. [CrossRef]
66. Jiang, L.; Xie, M.; Chen, G.; Qiao, J.; Zhang, H.; Zeng, X. Phenolics and Carbohydrates in Buckwheat Honey Regulate the Human Intestinal Microbiota. *Evid.-Based Complement. Altern. Med.* **2020**, *2020*, 6432942. [CrossRef] [PubMed]
67. Ranneh, Y.; Akim, A.M.; Hamid, H.A.; Khazaai, H.; Fadel, A.; Zakaria, Z.A.; Albujja, M.; Bakar, M.F.A. Honey and Its Nutritional and Anti-Inflammatory Value. *BMC Complement. Med. Ther.* **2021**, *21*, 30. [CrossRef] [PubMed]
68. Shi, Y.; Zhou, S.; Fan, S.; Ma, Y.; Li, D.; Tao, Y.; Han, Y. Encapsulation of Bioactive Polyphenols by Starch and Their Impacts on Gut Microbiota. *Curr. Opin. Food Sci.* **2021**, *38*, 102–111. [CrossRef]
69. Ngo, T.V.; Kusumawardani, S.; Kunyanee, K.; Luangsakul, N. Polyphenol-Modified Starches and Their Applications in the Food Industry: Recent Updates and Future Directions. *Foods* **2022**, *11*, 3384. [CrossRef] [PubMed]
70. DeMartino, P.; Cockburn, D.W. Resistant starch: Impact on the gut microbiome and health. *Curr. Opin. Biotechnol.* **2020**, *61*, 66–71. [CrossRef]
71. Acevedo-Fani, A.; Singh, H. Biophysical insights into modulating lipid digestion in food emulsions. *Prog. Lipid Res.* **2022**, *85*, 101129. [CrossRef]
72. Zhao, H.; Cheng, N.; Zhou, W.; Chen, S.; Wang, Q.; Gao, H.; Xue, X.; Wu, L.; Cao, W. Honey Polyphenols Ameliorate DSS-Induced Ulcerative Colitis via Modulating Gut Microbiota in Rats. *Mol. Nutr. Food Res.* **2019**, *63*, 1900638. [CrossRef]
73. Wu, D.; Chen, L.; Teh, J.; Sim, E.; Schlundt, J.; Conway, P.L. Honeys with Anti-Inflammatory Capacity Can Alter the Elderly Gut Microbiota in an Ex Vivo Gut Model. *Food Chem.* **2022**, *392*, 133229. [CrossRef]
74. Li, Y.; Long, S.; Liu, Q.; Ma, H.; Li, J.; Xiaoqing, W.; Yuan, J.; Li, M.; Hou, B. Gut Microbiota Is Involved in the Alleviation of Loperamide-induced Constipation by Honey Supplementation in Mice. *Food Sci. Nutr.* **2020**, *8*, 4388–4398. [CrossRef]
75. Pasolini, G.; Semenza, D.; Capezzera, R.; Sala, R.; Zane, C.; Rodella, R.; Calzavara-Pinton, P. Allergic Contact Cheilitis Induced by Repeated Contact with Propolis-Enriched Honey. *Contact Dermat.* **2004**, *50*, 322–323. [CrossRef]
76. Matos, D.; Serrano, P. A Case of Allergic Contact Dermatitis Caused by Propolis-Enriched Honey. *Contact Dermat.* **2015**, *72*, 59–60. [CrossRef] [PubMed]
77. Erejuwa, O.O.; Sulaiman, S.A.; Wahab, M.S. Honey—A novel antidiabetic agent. *Int. J. Biol. Sci.* **2012**, *8*, 913–934. [CrossRef] [PubMed]

78. Inagaki, T.; Hagiwara, A.; Nagashima, A.; Kimura, A. Case of Honey Intoxication in Japan. *Chudoku Kenkyu Chudoku Kenkyukai Jun Kikanshi Jpn. J. Toxicol.* **2013**, *26*, 310–313.
79. Nicewicz, A.W.; Nicewicz, Ł.; Pawłowska, P. Antioxidant capacity of honey from the urban apiary: A comparison with honey from the rural apiary. *Sci. Rep.* **2021**, *11*, 9695. [CrossRef] [PubMed]
80. Available online: https://premiumbeautynews.xyz/benefits-of-using-vegan-beauty-products.html (accessed on 5 October 2023).