

Review

Honeybees and the One Health Approach

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Abstract: The One Health approach recognizes the interconnectedness between human, animal, and environmental health. Honeybees (*Apis mellifera*) embody this framework due to their crucial role in ecosystems, food production, and susceptibility to contaminants. Despite their suitability for a One Health approach, there is a lack of research showcasing the multidisciplinary impacts and contributions of bees. The objective of this work is to explore the application of the One Health approach to bees through a narrative review. This work highlights the contribution of bees to history and culture, economy, medicine, nutrition, food security, and the functioning of ecosystems. It also demonstrates that bee health is affected by land management, agricultural practices, environmental contaminants, nutritional resource availability, predators and diseases, weather, climate patterns, and beekeeping practices. This complex system is highly influenced by policy and beekeeping practices, which will benefit animal health directly and environmental and human health indirectly. Thus, the protection of bees should be prioritized.

Keywords: *Apis mellifera*; pollinators; One Health; beekeeping



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1. Introduction

The One Health concept is a transdisciplinary and collaborative approach to health, recognizing the interconnectedness between humans, animals, and the environment [1]. This transdisciplinary approach combines multiple areas of expertise and fosters improved communication among professionals [1]. Integrating transdisciplinary surveillance and mitigation strategies is crucial for managing the complex changes that pose new public health threats, including intricate environmental problems [2]. For instance, livestock farming can be associated with increasing exposure of neighboring communities to particulate matter and infectious agents [3], while, conversely, animals can act as sentinels for environmental contaminants [4].

Honeybees (*Apis mellifera*) embody the One Health framework due to their vital role in ecosystems, food production, and susceptibility to anthropogenic stressors. The current 20,000 species of bees evolved originally from carnivore wasps in the Cretaceous period, about 120 million years ago, around the same time that flowering plants began to spread [5]. Species of solitary bees generally produce a single generation of adults per year (during the flowering season), whereas social bees produce several generations per year (with annual cycles) [5]. The best-known species of social bee is the honeybee, domesticated for the production of honey, wax, and pollination. Social colonies of honeybees are divided into 30,000–60,000 workers and a single reproductive queen bee [6].

Bees provide ecosystem services as pollinators, which directly influences food security and ecosystem stability [7]. Besides beekeeping practices, the health of the beehives is

closely linked to environmental conditions, such as land use, agriculture practices, the presence of pathogens, and environmental contaminants [8]. Bees are key species for monitoring ecosystem health and potential human health risks [9]. Their products, such as honey, also enter the human food chain, potentially leading to human exposure [10]. Therefore, the objective of this work was to conduct a narrative review to explore the application of the One Health approach to honeybees (*Apis mellifera*), integrating findings from various disciplines and enhancing understanding of the interconnectedness between honeybees, ecosystems, and human health. Beyond the integration of human, animal, and environmental health, there is no clear framework on how to apply a One Health approach [11]. Thus, this work is divided into the following sections: (i) bees' contributions, addressing the contribution to ecosystems, food safety, health, and culture; (ii) anthropogenic stressors affecting bees, addressing beekeeping practices, environmental changes, and pesticide exposure; and (iii) applying a One Health approach to bees, integrating the previous sections, exploring their intersections, and applying a transdisciplinary perspective.

2. Bees' Contributions

2.1. Ecosystem Services of Bees

Bees play an important ecological role as pollinators [12]. Pollination is part of the reproductive cycle of certain plants and consists of the transfer of pollen from male structures (anthers) to female structures (stigmata) [12]. It is estimated that 87.5% of flowering plants depend on animal pollination services [13]. These services are often provided by bee species, which represent the most frequent flower visitors (e.g., 75% of flower visits) [12].

Honeybees are responsible for 13% of total visits to plants and for the exclusive pollination of 5% of plant species [14]. Additionally, they are a species with a high geographic distribution, generalist in the plants they visit, and highly competent as pollinators, being irreplaceable in ecosystems [15]. The introduction of domesticated bees can also change ecosystems by favoring certain plant species (e.g., invasive plants), competing with other pollinator species, and contributing to the dispersion of pathogens [14]. It appears that the introduction of domestic bees may not harm native pollinators in ecosystems with high plant diversity and that wild species tend to be more resistant to pathogens [14]. However, high-density beekeeping can compete and reduce the occurrence of wild bees (e.g., by 55%) and the productivity of honeybees themselves, based on a study of rosemary plants in Europe [16]. In that case, densities of 7.8 and 3.9 honeybee colonies km⁻² were recommended for "saturation" (i.e., most efficient resource use by honeybees) and "half-saturation" (i.e., half-resource use by honeybees for wild bee conservation), respectively [16]. Moreover, there is a positive association between the prevalence of viral infections in wild bees and their prevalence in honeybees and a negative effect from extreme climatic events (e.g., temperature and precipitation) [17]. Yet, these capabilities emphasized the role of domesticated bees in crop pollination, resulting in their global dissemination, improvements in beekeeping technology, and transhumance beekeeping (moving hives to increase access to nectar and/or provide pollination services).

2.2. Bees and Food Security

The activity of pollinators, including domestic bees, is worth approximately EUR 22 billion to the European agricultural sector [18]. It is estimated that the agricultural pollination service has a value 15 to 20 times higher than the products obtained from bees, such as honey and wax [18]. Moreover, pollination by animals contributes to 30% of global food production, and a third of the human diet depends directly on bees [19]. The presence of honeybees also improves agricultural yields, increasing it up to 84% in Ethiopia [20]. Losing 50% of pollination services could translate into 700,000 additional human deaths per year from malnutrition [21].

The importance of honeybees in agriculture likely stems from a growing demand from pollinator services as a result of economic and political decisions, namely the loss of wild pollinators (e.g., habitat loss, pesticide use), the intensification of agricultural production,

and the increasing demand for pollinator-dependent crops [22]. Indeed, a study on the United States found evidence of pollinator limitation in most sampled areas (64–94%), while attesting that most visits were performed by bees (74%, varying with plant species), which translated into an estimate USD 6.4 billion in crop yields just for highbush blueberry, apple, sweet cherry, tart cherry, almond, watermelon, and pumpkin [23]. Moreover, the vibration of bee wings during flight (similar to that of predatory wasps) can activate defense mechanisms and restrict feeding in caterpillars, preventing the destruction of foliage and agricultural losses [24]. However, intensive farming creates an adverse environment for pollinators.

2.3. Bee Products and Human Health

Besides pollinator services, bees produce honey, which is the primary reason for their domestication [25]. Honey is produced from nectar or plant secretions, collected up to 10 km from the hive, subjected to cycles of regurgitation and evaporation, resulting in water concentration <20% and the breakdown of sucrose into fructose and glucose [26]. It is mainly composed of monosaccharides (fructose, glucose) and trace amount compounds which are responsible for the organoleptic (e.g., taste), medicinal properties, and shelf-stability of honey, such as amino acids, proteins, enzymes, minerals, and polyphenols [27].

Demand for honey was high until the 17th century, decreasing due to the availability of sugar, but recovering recently due to the recognition of its unique health benefits. Its growing demand has led to an approximately 45% rise in the global number of honeybee colonies over the past 50 years, mostly for honey production [22]. However, up to 46% of imports and 14% of honey on the market in the European Union (EU) are suspected of adulteration [28]. The rapid increase in demand motivates adulteration with cheaper sweeteners, which may reduce financial returns of beekeepers, change honey's natural properties, and introduce harmful contaminants (e.g., metals) [29,30].

Honey has remarkable nutritional and pharmacological properties [31]. For instance, it can be used to treat upper respiratory tract infections, acute diarrhea, and applied topically on burns and wounds [32]. It is also prebiotic due to the presence of oligo and polysaccharides, used by the gastrointestinal flora, and probiotic, containing lactic acid bacteria, such as *Lactobacillus* [33]. As summarized in Table 1, honey has low toxicity and presents multiple medical applications, including as an antitumoral, anti-inflammatory, antimicrobial, and complementary therapy agent.

Bees also produce wax, propolis, bee pollen, bee bread, bee venom, and royal jelly, which also have antioxidant, anti-inflammatory, antitumoral, antimicrobial, immunomodulatory, analgesic, and neuroprotective functions, being used in the production of cosmetics, pharmaceuticals, and nutritional supplements [34]. In nutrition, bee pollen can be used as a source of protein (21%), omega-3 fatty acids, minerals, B-complex vitamins, and polyphenols [35]. Therefore, it has long been recognized as a food supplement, with a recommended daily intake of 30 g [36]. Propolis is a gluey mixture mostly composed of resin (50%) and rich in bioactive phytochemicals, which are highly dependent on the available botanical sources [37]. Propolis has shown broad-spectrum antiviral and antibacterial activities, while being simultaneously an immune stimulator and modulator (i.e., protecting against infection but preventing excessive inflammation) [38]. Remarkably, there is moderate evidence of its topical use in the clinical management of herpes labialis [38].

These products are applied in human medicine and in veterinary medicine, when allergies to bee venom, glandular secretions, or pollen are not present [39] (it is estimated that allergy to bee stings affects up to 7.5% of adults [40]). Conversely, honey seems to relieve symptoms and inflammation of other allergic diseases [41]. The use of honeybee products as therapy is known as apitherapy [26]. However, the variation in composition and the lack of data on safety and therapeutic effectiveness currently hinder the use of bee products in medicine [42].

Table 1. A summary of original articles addressing honey’s therapeutical properties published in 2023 and 2024 based on a search for “honey AND medicine” on Web of Science in May 2024 (20 selected from 126 results).

Type	Application	Effects	Reference
In vitro	Antitumoral agent	60 kDa protein in Pakistani Sidr honey inhibited angiogenesis in umbilical vein endothelial cells, suggesting its use as a cancer treatment.	[43]
		Sidr honey has shown antiproliferation activity in cancer cells due to aggregation in G1 phase, increase in apoptosis and necrotic cell death, showing its potential use as an antitumoral agent.	[44]
		Thyme and chestnut honey had little to no effect on the apoptosis of human cancer cells, which was increased through its mixture (10%) with royal jelly or propolis, suggesting its use as a supplement to conventional cancer treatments.	[45]
In vitro	Antimicrobial agent	Stingless bee honey (<i>Hymenoptera, Apidae, Meliponini</i>) has antimicrobial activity against Gram-positive, Gram-negative bacteria and fungi, with some cases showing stronger activity than the standard antibiotic (ciprofloxacin).	[46]
		Honey has antimicrobial activity, but it may vary depending on botanical origins and season.	[47]
		Latvian monofloral honey presented antimicrobial activity, higher against Gram-positive than Gram-negative bacteria, with some cases exceeding Manuka honey’s inhibition.	[48]
		Pre-exposure to Sumra and Sidr honey increase antibiotic sensitivity of bacteria and reduced biofilm formation.	[49]
		Manuka honey (rich in methylglyoxal) has a broad-spectrum antimicrobial activity, with both varieties inhibiting bacterial growth but only one having bactericidal and antibiofilm properties.	[50]
		<i>Castanea crenata</i> honey treatment in vitro prevented influenza virus infection in mouse macrophages by inhibiting the expression of viral proteins and increasing the expression in proinflammatory cytokines, while in vivo increase survival, reduced body weight loss, decreased viral replication, reduced inflammatory response, stimulated antiviral response, and prevented infection, presenting protective effects on influenza virus infection in mice.	[51]

Table 1. Cont.

Type	Application	Effects	Reference
In vitro	Anti-inflammatory agent	Manuka honey natural pteridine derivative 3,6,7-trimethylumazine (Lepteridine™) shows partial inhibition of a metalloproteinase (MMP) involved in non-healing chronic wounds through a dysregulated proteolytic activity (MMP-9); this activity is not lost during simulated gastrointestinal digestion, which may explain the beneficial anti-inflammatory effects of oral consumption or topical applications.	[52]
		Honey applied to in vitro cultures of canine, equine, and chicken peripheral blood lymphocytes stimulate proliferation (i.e., moderate stimulant) but also increased cytotoxicity.	[53]
		Stingless bees honey (<i>Melipona, Trigona</i>) inhibits the release of inflammatory mediators from human mast cells, including tumor necrosis factor- α , interleukin-4, and histamine, depending on the botanical origins (for bamboo and rubber tree but not mango and noni honey), which could help treat allergic diseases.	[54]
In vivo		Isolation and purification of an Alhagi honey polysaccharide (AHPN50-1a), which was shown to reduce colon tissue damage, reduce inflammation, and restore intestinal microbiota in mice, presenting a potential treatment for inflammatory bowel disease.	[55]
		Isolation and purification of an Alhagi honey polysaccharide (AHPN80), which was shown to improve liver parameters, repair the intestinal barriers, and reduce oxidative stress in mice with alcohol-induced acute liver injury.	[56]
Case study	Complementary therapy	Postoperative treatment of synovial sepsis in three horses with intraarticular or intrathecal medical-grade honey instillation led to good recoveries (free from lameness in all gaits).	[57]
Randomized controlled trial		Gargling with silk-cotton tree or kapok tree honey every 6 h for 10 days after a tonsillectomy reduced pain and the need for analgesics, suggesting its use as a complementary therapy in postoperative patients.	[58]

Table 1. Cont.

Type	Application	Effects	Reference
In vitro		Treatment of peripheral blood lymphocytes with strawberry tree honey reveals low genotoxic potential, not impairing in vitro proliferation and offering geno- and cytoprotection against a cytotoxic agent damage, showing in vitro safety.	[59]
In vivo	Low toxicity	Evaluation of repeated dose oral toxicity of <i>Apis cerana</i> honey in Winstar mice testing concentrations of 3–24 g kg ⁻¹ body weight/day of honey for 28 days only found decrease in food consumption and body weight in the highest tested concentration and determined the no-observed-adverse-effect level at 12 g kg ⁻¹ body weight day.	[60]
In vivo	Negative results	Supplementation of rats undergoing forced swimming tests as a proxy for physical stress with wild bee honey did not result in a significant reduction in antioxidative stress in ovarian follicles. Manuka honey was applied on clean surgical wounds every day for 15 days on 12 beagle dogs and 12 shorthaired cats, showing no significant different healing than control in cosmetic and histologic evaluations, but showing higher skin thickening and smaller wound area (antimicrobial activity benefits may not be evident in clean surgical wounds).	[61] [62]

2.4. Bees as Indicators and Sentinels

Bees are indicator organisms, as they translate the risk to ecosystems, and sentinels, as they act as an early alert system for human health. Bees and their products are good indicators of toxic substances such as metals, pesticides, radioactive elements, and persistent organic pollutants [9,10]. These compounds tend to deposit on plants and thus be transported to the hive. They accumulate in colony products and lead to changes in behavior and mortality (i.e., toxicity).

Assessing the presence of contaminants in honey is relevant to food safety and as an indicator of environmental problems. These contaminants are generally present in low concentrations, but in mixtures that can have synergistic adverse effects [63]. Human beings are exposed through water and food (orally) but also through environmental exposure through inhalation or skin contact [64]. For example, in archipelagos in the South Pacific, bees from hives close to smelters had high concentrations of nickel in their internal tissues, revealing a potential risk for neighboring human populations [65]. Therefore, environmental monitoring can be conducted through bees, which act as passive environmental samplers.

2.5. Bees in Culture, Science, and Technology

The production of honey led to the domestication of bees and development of beekeeping. During this period of coexistence, beekeeping also influenced the development of culture and religion, including the arts (e.g., statues originally carved in wax), local legends, rituals (e.g., honey used in funeral and religious rituals, wax candles in Christianity), and

traditional medicine [66]. Moreover, it is believed that the development of eusociality (i.e., higher levels of altruism and cooperation) in insects, such as bees, is similar to the evolution of human societies [67]. Eusociality is characterized by colonies composed of overlapping generations, cooperation, and division between reproductive and nonreproductive castes [68]. Honeybees live in hives consisting of multiple generations, where they care for their brood, have a division of labor, and rely on a single reproductive queen [68]. Moreover, their behavior (e.g., learning capacity) is dependent on social interactions [69]. In addition to helping us understand our evolutionary history, bees currently contribute to our collective bond. Indeed, beekeeping fosters community ties through local food production, social cohesion, and sustainability, while also enhancing understanding of ecosystems [70].

Bees are also used as model organisms in scientific research. Their complex social behavior, navigational skills, and capacity for mathematical operations (including understanding the concept of zero) is controlled by a brain with only 1 million neurons [71,72]. Their repertoire of behaviors also includes societal responses to disease known as social immunity, which mostly consist of segregation between casts (e.g., of foragers highly exposed to pathogens) and hygienic response (e.g., by eliminating infected bees) [73]. Moreover, bees present an alternative developmental model, complementary to *Drosophila* and with higher plasticity [74]. The microbiome influences metabolism, immune response, and pathogen defense, but its study is complicated by interactions between the host's phenotype, environment, and diet [75]. The microbiome of bees also provides resistance to stressors, such as pathogens and pesticides, which can be exploited through the use of probiotics (i.e., administration of beneficial live microorganisms) [76]. Besides its value to beekeeping, the microbiome of bees also offers a simpler model to study its development and health impacts on social insects of lower complexity than mammals [77,78]. Therefore, bees are great models for research in areas such as development, neurosciences, and the gut microbiome. Compared to other organisms, bees offer several advantages as model organisms: (i) they have a basic body plan; (ii) their genome has been sequenced; (iii) they exhibit higher brain functions; (iv) they are social animals; (v) their hives have low maintenance costs; and (vi) they meet ethical requirements (i.e., invertebrates are not covered by animal experimentation laws, e.g., Directive 2010/63/EU) [79].

The study of bees also supports technological development. Studies on bees' visual perception and navigation could allow the development of autonomous navigation systems [80]. Knowledge of their anatomy could inspire the creation of lighter, more maneuverable and cheaper aerial robots [81]. Bee-inspired flight control and sensory abilities can also provide technology for the exploration of Mars [82]. The decentralized organization of tasks by several agents is also of interest for modeling systems with self-organization [83]. The hive social system is based on horizontal information exchange (i.e., "swarm intelligence"), which can prove a useful alternative to traditional vertical human organization [79]. For instance, the Hewlett Packard Enterprise is drawing on the decentralized learning and decision-making of hives and applying it to networks as a form of artificial intelligence, which can be used, for instance, in self-driving vehicles [84]. Technology can also involve bees, such as their use for drug screening in airports following conditioning [79], or be used to modulate their behavior, such as through "dancing" robots that communicate with the hive to artificially modify feeding areas [85].

3. Anthropogenic Stressors Affecting Bees

3.1. Detrimental Beekeeping Practices

Honey and wax were first harvested from wild hives, followed by the likely beginning of beekeeping in Egypt in 2400 BC, which spread to other Mediterranean populations [86]. Stingless bees (*Melipona beecheii*) were simultaneously domesticated by the Mayan civilization in the Yucatan peninsula [87]. Beekeeping began by maintaining hives in logs, ceramic pots, and straw baskets in ancient times, followed by recesses in stones in the medieval period, and finally the recent and progressive development of the modern commercial beehive [66]. Its developments began in the 17th century in Greece by introducing bars on

top of vertical hives that would serve as anchors for honeycombs. It was followed by the invention of the removable frame in 1838 in Poland, the current Langstroth hive in 1851 in the United States, completed by the addition of molded sheets of wax to frames (i.e., foundations) in 1857 in Germany. The development is still ongoing, with the introduction of new materials (e.g., plastics). For instance, plastic foundations are being introduced as a cost-effective alternative to wax foundations, but they are less accepted by bees and difficult to clean [88]. However, the impact of changing to synthetic materials has not yet been researched.

Modern beekeeping practices encompass high densities of hives, which can facilitate the transmission of diseases. More spaced hives, at different heights, painted with different colors and symbols favor honey production, reduce disease transmission, and reduce mortality [89]. Practices involving prophylactic use of antibiotics increase the susceptibility to opportunistic agents of disease through the depletion of the honeybee's gut microbiome [90]. Transhumance may also harm bees when conducted as an intensive beekeeping practice, which involves moving the hive to provide pollinator services to agriculture, exposing bees to large nectar yields limited in time and diversity (i.e., mass flowerings), favoring pathogen exchange by concentrating colonies from different places, and increasing the risk of exposure to pesticides [91]. Moreover, most winter mortality in the EU has been found in colonies kept by inexperienced hobbyist beekeepers, which also suffered most from bacterial infections and *Varroa* infestation [92].

Colony collapse disorder occurs when worker bees disappear, leaving a condemned hive with food, immature bees, and the queen. It is thought to have a multifactorial origin due to habitat changes, nutritional deficiencies, immune suppression, exposure to contaminants and pesticides, infestations and infections, and increased stress due to transhumance beekeeping [93,94]. An investigation conducted in 2012 and 2013 in the European Union estimated that bee winter mortality could reach 30% in some Member States [95]. Moreover, the global spread of the invasive Asian yellow-legged hornet (*Vespa velutina*) in the last decades (2000s and 2010s) has also contributed to colony losses, as they pillage from hives and predate on bees (especially foraging bees, reducing food intake) [96]. Similarly, the parasitic mite *Varroa* can lead to colony loss within one or two seasons as a result of weakened worker bees and as a vector of diseases (e.g., deformed wing virus) [97].

3.2. Environmental Changes

Hives have an increased vulnerability to disease due to a compromised immune function resulting from environmental factors [98], which are largely dependent on habitat management [99]. Honeybees' immunity is influenced by ambient temperature, suppression caused by anthropogenic chemicals (e.g., pesticides), availability of floral nutritional resources, and existing plant species to provide beneficial phytochemicals and bioactive compounds [98,99]. For instance, abscisic acid and nitric oxide are two molecules involved in bee immunity synthesized, directly or indirectly, from the amino acid L-arginine, which depends on available nutritional resources [100]. Intensive agriculture generally consists of monocultures (i.e., single crop agriculture), which may cause nutritional deficiencies due to the crops producing pollen and/or nectar in poor quantity, of poor quality (e.g., low diversity), or only during a short time [101–103]. Natural landscapes rich in wildflowers (e.g., hedgerows) can supplement the diets of bees in intensive agriculture settings [102]. Climate change can also lead to a decline of hive population and food reserves due to changes in flowering resulting from a higher frequency of extreme events such as droughts and high temperatures [104]. Environment and diet also influence the honeybee's gut microbiome, which has an important role in digestive functions, health, and detoxification of environmental pollutants (e.g., pesticides) [105].

3.3. Exposure to Pesticides

Exposure to pesticides and other environmental contaminants also contributes to increased stress [101,103]. Due to the importance of pollinators for food production, the

EU is evaluating toxicity and regulating or banning pesticides that have an impact on this species. Moreover, exposure to pesticides is higher when bees' diets are more reliant on treated crops [106]. The use of three neonicotinoids pesticides (clothianidin, thiamethoxam, imidacloprid) was severely restricted in the EU following Regulation No. 485/2013. These three pesticides do not elicit an avoidance response from bees, leading to continued feeding or even preference to solutions containing thiamethoxam and imidacloprid, which can result in adverse effects to individuals and colonies [107]. Nonetheless, measures to protect pollinators from plant protection products were hindered due to the lack of consensus between Member States [108]. In 2019, a revision of guidelines defined risk assessment targets more clearly, including the Specific Protection Goal (i.e., a standard that translates the maximum impact tolerated by the legislator based on risk assessment) for honeybees as a maximum of 10% colony size reduction [108]. Other pesticides may also have adverse effects on bee colonies. For instance, field-relevant concentrations of the fungicide pyraclostrobin and the insecticide fipronil compromised the production of brood-food in the glands of nurse honeybees [109]. The herbicide glyphosate also changes the bees' microbiome, increasing susceptibility to infection [110]. Pesticides may also enter the human food chain through honeybee products such as honey and pollen. Yet, a study from Greece spanning from 2015 to 2020 found pesticide concentrations ranging from 1.3 to 785.0 ng g⁻¹ of honey (26% positive), which were considered of low risk for bee and human risk assessment [111].

4. Applying a One Health Approach to Bees

The concept of One Health refers to growing recognition of the interdependence between human, animal, and environmental health. As previously shown throughout this work, bees clearly integrate the One Health concept as an agent of a multidisciplinary system integrated in an ecosystem and closely linked to human health.

Bees can have a direct influence on human health through the nutritional and pharmacological properties of their products (Table 1). These properties are dependent on available plant species (and respective phytochemicals) [98,99], which result in high variations in composition and biological activity [42]. Yet, there are currently no low-cost, high-throughput methods of chemical characterization of honey [112]. The availability of diverse plant species depends on land management, which often reflects political decisions.

Bees also pollinate agricultural crops, which contributes to human food security. Loss of half of pollination services by animals, responsible for 30% of global food production [19], could lead to 0.7 million additional human deaths per year due to malnutrition [21]. This is concerning, considering that 9.2% of the world population already suffers from hunger [113] and that agricultural environments are averse to pollinators due to nutritional deficiencies (i.e., low plant diversity) and pesticide use [102]. Yet, most crops in the United States suffer from pollinator limitation [23], which also can stem from political decisions on land management and agricultural production (e.g., higher demand for pollinator-dependent crops) [22].

Bees have a dynamic relationship with the environment. Pollinator services are relevant not only for agricultural crops but also for the reproduction of plants, and therefore the productivity of ecosystems [14]. However, domesticated bees can have negative impacts on ecosystems by favoring certain plant species and/or outcompeting wild pollinators [14,16]. Bees are also victim to invasive species, such as the predator Asian yellow-legged hornet (*Vespa velutina*) [96] and the parasitic mite *Varroa* [97]. Conversely, anthropogenic stressors (e.g., pesticides, habitat loss) can have a negative impact on bees' health. Monitoring these negative impacts can prove useful, as bees can provide an early alert system for environmental degradation and/or the presence of risks to human health [9].

Bees' health is also influenced by environmental properties, such as temperature, contamination, habitat, nutritional resources, and available phytochemicals [98,99]. Land management policies, such as the preservation of natural landscapes, can prove favorable to bees' health [102]. Indeed, measures aimed at protecting bees (e.g., habitat conservation,

pesticide restrictions) also contribute to a greater protection of environmental health, food security, and, consequently, human health.

Humans also have a dynamic relationship with bees. Besides sharing eusociality, culture has been highly influenced by bees (e.g., use of bee products in art, medicine, and religion) [66]. Presently, beekeeping still contributes to sustainability and community ties while stimulating local food production and a better understanding of ecosystems [70]. Beekeeping practices have also evolved alongside culture and have a high impact on the survival of hives. For instance, most colony losses are attributed to inexperienced hobbyist beekeepers [92], while highly intensive beekeeping practices can overexploit environmental resources [16], facilitate the transmission of diseases, and deplete natural hive defenses, including their protective gut microbiome [77]. Restoring balance often involves using antibiotics prophylactically and therapeutically. However, antibiotic resistance persists and amplifies in the bee gut, potentially becoming vectors for the spread of resistance genes [114]. Moreover, many countries have banned their use in beekeeping due to concerns about antibiotic resistance, ineffectiveness against infectious spores, suppression of symptoms without cure, residues in honey, and negative impacts on the hive's brood [115]. Nonetheless, 4% of beekeepers in the EU admit to using antibiotics, even though there are no approved pharmaceuticals for honeybees [116]. Moreover, exposure to environmental contaminants can contribute to the loss of the gut microbiome, upregulate transporters that reduce the effectiveness of antimicrobials, and increase the prevalence and transmission of pathogens [98].

Good beekeeping practices should focus on managing hives to promote health, while conscious of their role in a complex social-ecological system [117]. Veterinarians should have more active participation in bee protection, which also requires increased dissemination of honeybee veterinary medicine [118]. Moreover, bees continue to contribute to human development through their use as model organisms and their study as an inspiration for technological development. In summary, bees are integrated in a complex system that represents the interaction between animals, humans, and the environment, being easily integrated in the One Health concept.

The stock and flow diagram represented in Figure 1 summarizes these dynamics between human, animal, and environmental health, aiming to clarify their relationship with bees. Therefore, the principal stocks are "animal health" (i.e., bee health), "human health", and "environmental health", complemented by secondary stocks that represent practices or status (e.g., transhumance, natural landscapes). Arrows represent the relationships between stocks, based on the information previously summarized.

The diagram reveals that the system is highly interconnected due to the interdependence between bees and the environment, ecosystems, and food production. Many factors can indirectly impact bee health. For instance, intensive agriculture reduces plant diversity, hindering balanced nutrition for bees, thus reducing their resilience. Moreover, factors having a negative impact on bees generally also have indirect negative impacts on human and animal health.

Overall, the system seems to be influenced by two key factors: (i) policy, which controls land management, agricultural practices, and contamination (e.g., pesticide use); and (ii) beekeeping and veterinary practices, which should have a preventive mission by catering to the bees' needs and enhancing their natural defense mechanisms. Because of the system's interdependency, measures to protect bees will also safeguard environmental and human health. Therefore, protecting bees is of utmost importance and offers high cost-benefit advantages.

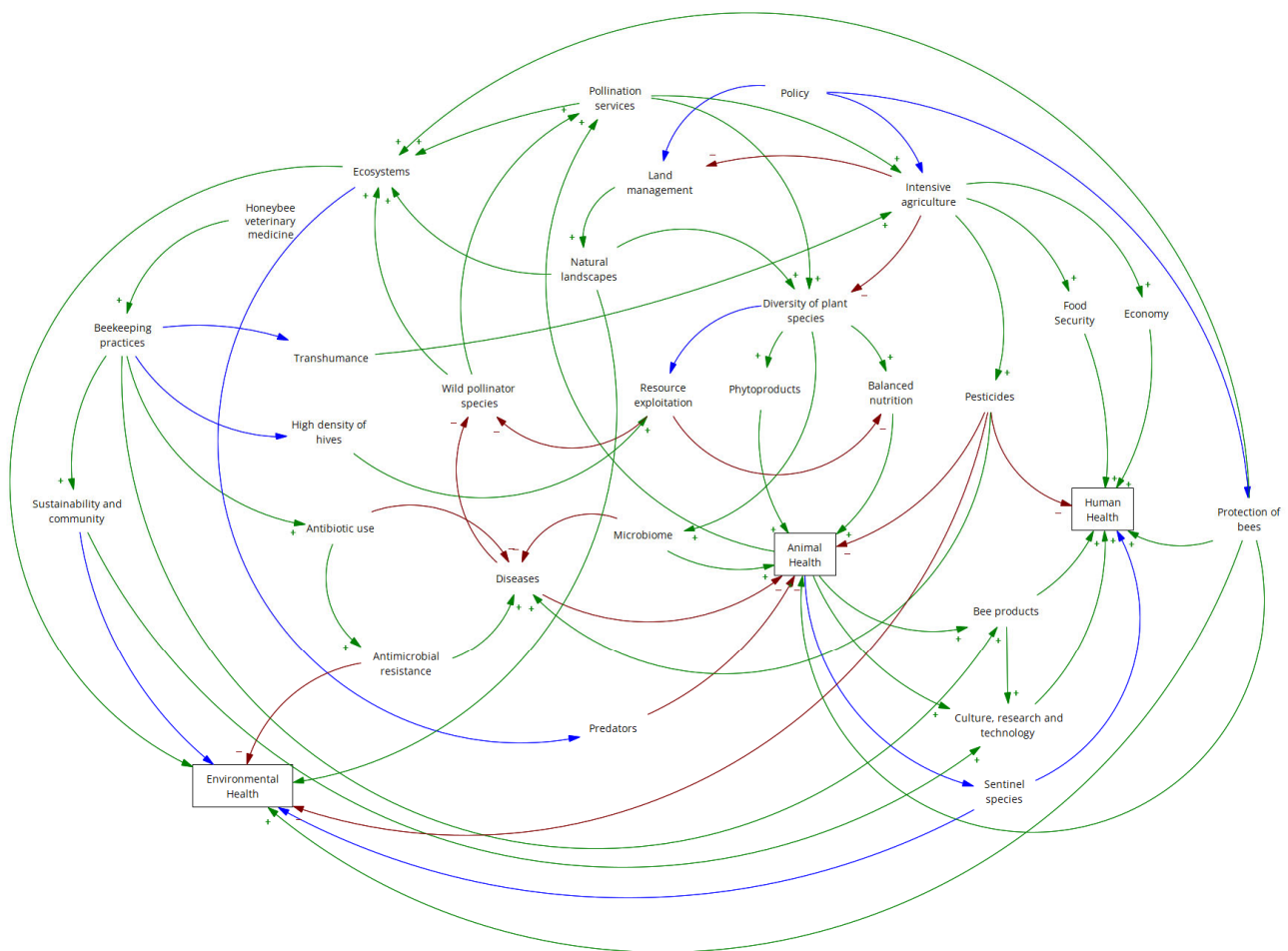


Figure 1. Stocks and flow diagram representing the One Health concept applied to honeybees (*Apis mellifera*). Arrows represent relationships, namely neutral (blue), positive (green), and negative (red). Created on Vensim PLE.

5. Conclusions

This narrative review highlights the interconnections between bees, ecosystems, and human health, integrated into a One Health framework. By incorporating findings from multiple disciplines, this work demonstrates the multifaceted impacts of bees on environmental and public health. Bees have significantly contributed to history and culture, economy, medicine and health, nutrition and food security, ecosystems (e.g., through pollination), and scientific and technological development. Conversely, bees are impacted by land management, agriculture practices, environmental contaminants, availability of nutritional resources, presence of predators and diseases, weather and climate patterns, and beekeeping practices. The study of these interactions reveals two main meeting points that highly influence this complex system: (i) policy aiming to protect bees, especially regarding land management, agriculture practices, and contaminant control (e.g., pesticide use); and (ii) beekeeping and veterinary practices, which can increase the resilience of bees by respecting their needs and boosting their natural defense mechanisms. Finally, measures undertaken to protect bees will have a high cost–benefit ratio considering they will indirectly lead to the protection of the environment and human health.

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References

1. Prata, J.C.; Ribeiro, A.I.; Rocha-Santos, T. An Introduction to the Concept of One Health. In *One Health*; Elsevier: Amsterdam, The Netherlands, 2022; pp. 1–31.
2. Zinsstag, J.; Crump, L.; Schelling, E.; Hattendorf, J.; Maidane, Y.O.; Ali, K.O.; Muhummed, A.; Umer, A.A.; Aliyi, F.; Nooh, F.; et al. Climate Change and One Health. *FEMS Microbiol. Lett.* **2018**, *365*, fny085. [[CrossRef](#)]
3. Heederik, D. The One Health Approach. *Environ. Epidemiol.* **2019**, *3*, 157. [[CrossRef](#)]
4. Rabinowitz, P.M.; Gordon, Z.; Holmes, R.; Taylor, B.; Wilcox, M.; Chudnov, D.; Nadkarni, P.; Dein, F.J. Animals as Sentinels of Human Environmental Health Hazards: An Evidence-Based Analysis. *Ecohealth* **2005**, *2*, 26–37. [[CrossRef](#)]
5. Murray, E.A.; Bossert, S.; Danforth, B.N. Pollinivory and the Diversification Dynamics of Bees. *Biol. Lett.* **2018**, *14*, 20180530. [[CrossRef](#)] [[PubMed](#)]
6. Evans, J.D.; Chen, Y. Colony Collapse Disorder and Honey Bee Health. In *Honey Bee Medicine for the Veterinary Practitioner*; Wiley: Hoboken, NJ, USA, 2021; pp. 229–234.
7. Papa, G.; Maier, R.; Durazzo, A.; Lucarini, M.; Karabagias, I.K.; Plutino, M.; Bianchetto, E.; Aromolo, R.; Pignatti, G.; Ambrogio, A.; et al. The Honey Bee *Apis Mellifera*: An Insect at the Interface between Human and Ecosystem Health. *Biology* **2022**, *11*, 233. [[CrossRef](#)] [[PubMed](#)]
8. Klein, S.; Cabriol, A.; Devaud, J.-M.; Barron, A.B.; Lihoreau, M. Why Bees Are So Vulnerable to Environmental Stressors. *Trends Ecol. Evol.* **2017**, *32*, 268–278. [[CrossRef](#)] [[PubMed](#)]
9. Salkova, D.; Panayotova-Pencheva, M. Honey Bees and Their Products as Indicators of Environmental Pollution: A Review. *Agric. Sci. Technol.* **2016**, *8*, 175–182. [[CrossRef](#)]
10. Cunningham, M.M.; Tran, L.; McKee, C.G.; Ortega Polo, R.; Newman, T.; Lansing, L.; Griffiths, J.S.; Bilodeau, G.J.; Rott, M.; Marta Guarna, M. Honey Bees as Biomonitors of Environmental Contaminants, Pathogens, and Climate Change. *Ecol. Indic.* **2022**, *134*, 108457. [[CrossRef](#)]
11. Muhammad-Bashir, B.; Halimah, B.A. Challenges and Future Perspectives for the Application of One Health. In *One Health*; Elsevier: Amsterdam, The Netherlands, 2022; pp. 329–343.
12. Willmer, P.G.; Cunnold, H.; Ballantyne, G. Insights from Measuring Pollen Deposition: Quantifying the Pre-Eminence of Bees as Flower Visitors and Effective Pollinators. *Arthropod. Plant Interact.* **2017**, *11*, 411–425. [[CrossRef](#)]
13. Ollerton, J.; Winfree, R.; Tarrant, S. How Many Flowering Plants Are Pollinated by Animals? *Oikos* **2011**, *120*, 321–326. [[CrossRef](#)]
14. Hung, K.-L.J.; Kingston, J.M.; Albrecht, M.; Holway, D.A.; Kohn, J.R. The Worldwide Importance of Honey Bees as Pollinators in Natural Habitats. *Proc. R. Soc. B Biol. Sci.* **2018**, *285*, 20172140. [[CrossRef](#)]
15. Aslan, C.E.; Liang, C.T.; Galindo, B.; Kimberly, H.; Topete, W. The Role of Honey Bees as Pollinators in Natural Areas. *Nat. Areas J.* **2016**, *36*, 478–488. [[CrossRef](#)]
16. Henry, M.; Rodet, G. Controlling the Impact of the Managed Honeybee on Wild Bees in Protected Areas. *Sci. Rep.* **2018**, *8*, 9308. [[CrossRef](#)] [[PubMed](#)]
17. Piot, N.; Schweiger, O.; Meeus, I.; Yañez, O.; Straub, L.; Villamar-Bouza, L.; De la Rúa, P.; Jara, L.; Ruiz, C.; Malmstrøm, M.; et al. Honey Bees and Climate Explain Viral Prevalence in Wild Bee Communities on a Continental Scale. *Sci. Rep.* **2022**, *12*, 1904. [[CrossRef](#)] [[PubMed](#)]
18. European Commission. Honey Bees. Available online: https://food.ec.europa.eu/animals/live-animal-movements/honey-bees_en (accessed on 18 June 2024).
19. Khalifa, S.A.M.; Elshafiey, E.H.; Shetaia, A.A.; El-Wahed, A.A.A.; Algethami, A.F.; Musharraf, S.G.; AlAjmi, M.F.; Zhao, C.; Masry, S.H.D.; Abdel-Daim, M.M.; et al. Overview of Bee Pollination and Its Economic Value for Crop Production. *Insects* **2021**, *12*, 688. [[CrossRef](#)]
20. Bareke, T.; Addi, A. Effect of Honeybee Pollination on Seed and Fruit Yield of Agricultural Crops in Ethiopia. *MOJ Ecol. Environ. Sci.* **2019**, *4*, 205–209. [[CrossRef](#)]
21. Smith, M.R.; Singh, G.M.; Mozaffarian, D.; Myers, S.S. Effects of Decreases of Animal Pollinators on Human Nutrition and Global Health: A Modelling Analysis. *Lancet* **2015**, *386*, 1964–1972. [[CrossRef](#)]
22. Aizen, M.A.; Harder, L.D. The Global Stock of Domesticated Honey Bees Is Growing Slower Than Agricultural Demand for Pollination. *Curr. Biol.* **2009**, *19*, 915–918. [[CrossRef](#)]

23. Reilly, J.R.; Artz, D.R.; Biddinger, D.; Bobiwash, K.; Boyle, N.K.; Brittain, C.; Brokaw, J.; Campbell, J.W.; Daniels, J.; Elle, E.; et al. Crop Production in the USA Is Frequently Limited by a Lack of Pollinators. *Proc. R. Soc. B Biol. Sci.* **2020**, *287*, 20200922. [CrossRef]
24. Tautz, J.; Rostás, M. Honeybee Buzz Attenuates Plant Damage by Caterpillars. *Curr. Biol.* **2008**, *18*, R1125–R1126. [CrossRef]
25. Noiset, P.; Cabirol, N.; Rojas-Oropeza, M.; Warrit, N.; Nkoba, K.; Vereecken, N.J. Honey Compositional Convergence and the Parallel Domestication of Social Bees. *Sci. Rep.* **2022**, *12*, 18280. [CrossRef] [PubMed]
26. Beekman, M.; Ratnieks, F.L.W. Long-range Foraging by the Honey-bee, *Apis mellifera* L. *Funct. Ecol.* **2000**, *14*, 490–496. [CrossRef]
27. Cengiz, M.F.; Durak, M.Z. Rapid Detection of Sucrose Adulteration in Honey Using Fourier Transform Infrared Spectroscopy. *Spectrosc. Lett.* **2019**, *52*, 267–273. [CrossRef]
28. European Commission. EU Coordinated Action “From the Hives” (Honey 2021–2022). Available online: https://food.ec.europa.eu/safety/eu-agri-food-fraud-network/eu-coordinated-actions/honey-2021-2022_en (accessed on 18 June 2024).
29. Kumar, N.; Ranjan, R.; Kumar, Y.; Patel, S.S.; Sai Krishna, V.; Appaiah, A.; Gupta, K.; Panchariya, P. Discrimination of Various Pure Honey Samples and Its Adulterants Using FTIR Spectroscopy Coupled with Chemometrics. In Proceedings of the 2021 7th International Conference on Advanced Computing and Communication Systems (ICACCS), Coimbatore, India, 19–20 March 2021; IEEE: New York, NY, USA, 2021; pp. 808–811.
30. Pauliuc, D.; Dranca, F.; Ropciuc, S.; Oroian, M. Advanced Characterization of Monofloral Honeys from Romania. *Agriculture* **2022**, *12*, 526. [CrossRef]
31. Israili, Z.H. Antimicrobial Properties of Honey. *Am. J. Ther.* **2014**, *21*, 304–323. [CrossRef] [PubMed]
32. Majtan, J.; Bucekova, M.; Kafantaris, I.; Szweda, P.; Hammer, K.; Mossialos, D. Honey Antibacterial Activity: A Neglected Aspect of Honey Quality Assurance as Functional Food. *Trends Food Sci. Technol.* **2021**, *118*, 870–886. [CrossRef]
33. Mustar, S.; Ibrahim, N. A Sweeter Pill to Swallow: A Review of Honey Bees and Honey as a Source of Probiotic and Prebiotic Products. *Foods* **2022**, *11*, 2102. [CrossRef] [PubMed]
34. Hills, S.P.; Mitchell, P.; Wells, C.; Russell, M. Honey Supplementation and Exercise: A Systematic Review. *Nutrients* **2019**, *11*, 1586. [CrossRef]
35. Thakur, M.; Nanda, V. Composition and Functionality of Bee Pollen: A Review. *Trends Food Sci. Technol.* **2020**, *98*, 82–106. [CrossRef]
36. Chézeries, J.-F. *A Saúde Pelo Mel e Produtos Da Colmeia*; Litexa Editora: Lisbon, Portugal, 1984; ISBN 9789725781029.
37. Zullkiflee, N.; Taha, H.; Usman, A. Propolis: Its Role and Efficacy in Human Health and Diseases. *Molecules* **2022**, *27*, 6120. [CrossRef]
38. Magnavacca, A.; Sangiovanni, E.; Racagni, G.; Dell’Agli, M. The Antiviral and Immunomodulatory Activities of Propolis: An Update and Future Perspectives for Respiratory Diseases. *Med. Res. Rev.* **2022**, *42*, 897–945. [CrossRef] [PubMed]
39. Weis, W.A.; Ripari, N.; Conte, F.L.; Honorio, M.d.S.; Sartori, A.A.; Matucci, R.H.; Sforzin, J.M. An Overview about Apitherapy and Its Clinical Applications. *Phytomed. Plus* **2022**, *2*, 100239. [CrossRef]
40. Bilò, B.M.; Bonifazi, F. Epidemiology of Insect-Venom Anaphylaxis. *Curr. Opin. Allergy Clin. Immunol.* **2008**, *8*, 330–337. [CrossRef] [PubMed]
41. Aw Yong, P.Y.; Islam, F.; Harith, H.H.; Israf, D.A.; Tan, J.W.; Tham, C.L. The Potential Use of Honey as a Remedy for Allergic Diseases: A Mini Review. *Front. Pharmacol.* **2021**, *11*, 599080. [CrossRef] [PubMed]
42. Giampieri, F.; Quiles, J.L.; Cianciosi, D.; Forbes-Hernández, T.Y.; Orantes-Bermejo, F.J.; Alvarez-Suarez, J.M.; Battino, M. Bee Products: An Emblematic Example of Underutilized Sources of Bioactive Compounds. *J. Agric. Food Chem.* **2022**, *70*, 6833–6848. [CrossRef]
43. Wahid, M.; Nazeer, M.; Qadir, A.; Azmi, M.B. Investigating the Protein-Based Therapeutic Relationship between Honey Protein SHP-60 and Bevacizumab on Angiogenesis: Exploring the Synergistic Effect through In Vitro and in Silico Analysis. *ACS Omega* **2024**, *9*, 17143–17153. [CrossRef]
44. Qanash, H.; Bazaid, A.S.; Binsaleh, N.K.; Patel, M.; Althomali, O.W.; Sheeha, B. Bin In Vitro Antiproliferative Apoptosis Induction and Cell Cycle Arrest Potential of Saudi Sidr Honey against Colorectal Cancer. *Nutrients* **2023**, *15*, 3448. [CrossRef]
45. Sánchez-Martín, V.; Morales, P.; Iriondo-DeHond, A.; Hospital, X.F.; Fernández, M.; Hierro, E.; Haza, A.I. Differential Apoptotic Effects of Bee Product Mixtures on Normal and Cancer Hepatic Cells. *Antioxidants* **2023**, *12*, 615. [CrossRef]
46. Mduda, C.A.; Muruke, M.H.; Hussein, J.M. Antimicrobial Properties of Honeys Produced by Stingless Bees (*Hymenoptera, Apidae, Meliponini*) from Different Vegetation Zones of Tanzania. *Int. J. Trop. Insect Sci.* **2023**, *43*, 1563–1581. [CrossRef]
47. Rikohe, I.F.; Mlozi, S.H.; Ngondya, I.B. Seasons and Bee Foraging Plant Species Strongly Influence Honey Antimicrobial Activity. *J. Agric. Food Res.* **2023**, *12*, 100622. [CrossRef]
48. Skadiņš, I.; Labsvārds, K.D.; Grava, A.; Amirian, J.; Tomson, L.E.; Ruško, J.; Viksna, A.; Bandere, D.; Brangule, A. Antimicrobial and Antibiofilm Properties of Latvian Honey against Causative Agents of Wound Infections. *Antibiotics* **2023**, *12*, 816. [CrossRef] [PubMed]
49. Aldarhami, A.; Bazaid, A.S.; Qanash, H.; Ahmad, I.; Alshammari, F.H.; Alshammari, A.M.; Alshammari, A.H.; Aljanfawe, F.M.; Aldamiri, B.; Aldawood, E.; et al. Effects of Repeated In-Vitro Exposure to Saudi Honey on Bacterial Resistance to Antibiotics and Biofilm Formation. *Infect. Drug Resist.* **2023**, *16*, 4273–4283. [CrossRef]
50. Clare, J.; Lindley, M.R.; Ratcliffe, E. The Antimicrobial and Antibiofilm Abilities of Fish Oil Derived Polyunsaturated Fatty Acids and Manuka Honey. *Microorganisms* **2024**, *12*, 778. [CrossRef] [PubMed]

51. Kwon, E.-B.; Kim, S.-G.; Kim, Y.S.; Kim, B.; Han, S.M.; Lee, H.J.; Choi, H.M.; Choi, J.-G. Castanea Crenata Honey Reduces Influenza Infection by Activating the Innate Immune Response. *Front. Immunol.* **2023**, *14*, 1157506. [[CrossRef](#)]
52. Lin, B.; Nair, S.; Fellner, D.M.J.; Nasef, N.A.; Singh, H.; Negron, L.; Goldstone, D.C.; Brimble, M.A.; Gerrard, J.A.; Domigan, L.; et al. The Leptospermum Scoparium (Mānuka)-Specific Nectar and Honey Compound 3,6,7-Trimethylumazine (LepteridineTM) That Inhibits Matrix Metalloproteinase 9 (MMP-9) Activity. *Foods* **2023**, *12*, 4072. [[CrossRef](#)] [[PubMed](#)]
53. Turn, J.T.; Mayer, J.; Nagata, K.; Banovic, F.; Meichner, K.; Hurley, D.J.; Koslowski, E.; Gogal, R.M., Jr. Impact of Apitherapy on Canine, Equine, and Chicken Lymphocytes, In Vitro. *Vet. Immunol. Immunopathol.* **2024**, *268*, 110700. [[CrossRef](#)]
54. Yong, P.Y.A.; Yip, A.J.W.; Islam, F.; Hong, H.J.; Teh, Y.E.; Tham, C.L.; Tan, J.W. The Anti-Allergic Potential of Stingless Bee Honey from Different Botanical Sources via Modulation of Mast Cell Degranulation. *BMC Complement Med. Ther.* **2023**, *23*, 307. [[CrossRef](#)] [[PubMed](#)]
55. Song, J.; Chen, Y.; Lv, Z.; Taoerdahong, H.; Li, G.; Li, J.; Zhao, X.; Jin, X.; Chang, J. Structural Characterization of a Polysaccharide from Alhagi Honey and Its Protective Effect against Inflammatory Bowel Disease by Modulating Gut Microbiota Dysbiosis. *Int. J. Biol. Macromol.* **2024**, *259*, 128937. [[CrossRef](#)]
56. Song, J.; Zhao, X.; Bo, J.; Lv, Z.; Li, G.; Chen, Y.; Liang, J.; Zhang, C.; Jin, X.; Liu, C.; et al. A Polysaccharide from Alhagi Honey Protects the Intestinal Barrier and Regulates the Nrf2/HO-1-TLR4/MAPK Signaling Pathway to Treat Alcoholic Liver Disease in Mice. *J. Ethnopharmacol.* **2024**, *321*, 117552. [[CrossRef](#)]
57. Terschuur, J.A.; Coomer, R.P.C.; McKane, S.A. Administration Safety of Medical-Grade Honey (MGH) in Septic Synovial Structures in Horses: 3 Cases. *Can. J. Vet. Res.* **2023**, *87*, 153–156.
58. Lubis, A.S.; Herwanto, H.R.Y.; Rambe, A.Y.M.; Munir, D.; Asroel, H.A.; Ashar, T.; Lelo, A. The Effect of Honey on Post-Tonsillectomy Pain Relief: A Randomized Clinical Trial. *Braz. J. Otorhinolaryngol.* **2023**, *89*, 60–65. [[CrossRef](#)] [[PubMed](#)]
59. Jurič, A.; Brčić Karačoni, I.; Gašić, U.; Milojković Opsenica, D.; Prđun, S.; Bubalo, D.; Lušić, D.; Vahčić, N.; Kopjar, N. Protective Effects of *Arbutus unedo* L. Honey in the Alleviation of Irinotecan-Induced Cytogenetic Damage in Human Lymphocytes—An In Vitro Study. *Int. J. Mol. Sci.* **2023**, *24*, 1903. [[CrossRef](#)] [[PubMed](#)]
60. Du, H.; Zhang, P.; Zheng, S.; Nie, Y.; Zhang, W.; Feng, Y.; Ning, J.; Li, G.; Gao, S. A 28-Day Subacute Oral Toxicity Study of *Apis cerana* (Fabricius) Honey in Wistar Rats. *Int. Food Res. J.* **2023**, *30*, 1481–1494. [[CrossRef](#)]
61. Plumeriastuti, H.; Widjiati; Proboningrat, A.; Sajida, M.V.P. SOD2 and HIF-1 α Expression in Rat Ovaries (*Rattus norvegicus*) Administered with Forest Bee Honey (*Apis dorsata*) Following Physical Stress. *Bali Med. J.* **2023**, *12*, 1835–1839.
62. Gouletsou, P.G.; Zacharopoulou, T.; Skampardonis, V.; Georgiou, S.G.; Doukas, D.; Galatos, A.D.; Flouraki, E.; Dermisiadou, E.; Margeti, C.; Barbagianni, M.; et al. First-Intention Incisional Wound Healing in Dogs and Cats: A Controlled Trial of Dermapliq and Manuka Honey. *Vet. Sci.* **2024**, *11*, 64. [[CrossRef](#)] [[PubMed](#)]
63. Di Noi, A.; Casini, S.; Campani, T.; Cai, G.; Caliani, I. Review on Sublethal Effects of Environmental Contaminants in Honey Bees (*Apis mellifera*), Knowledge Gaps and Future Perspectives. *Int. J. Environ. Res. Public Health* **2021**, *18*, 1863. [[CrossRef](#)] [[PubMed](#)]
64. Martinello, M.; Manzinello, C.; Dainese, N.; Giuliano, I.; Gallina, A.; Mutinelli, F. The Honey Bee: An Active Biosampler of Environmental Pollution and a Possible Warning Biomarker for Human Health. *Appl. Sci.* **2021**, *11*, 6481. [[CrossRef](#)]
65. Taylor, M.P.; Gillings, M.M.; Fry, K.L.; Barlow, C.F.; Gunkel-Grillion, P.; Gueyte, R.; Camoin, M. Tracing Nickel Smelter Emissions Using European Honey Bees. *Environ. Pollut.* **2023**, *335*, 122257. [[CrossRef](#)]
66. Kritsky, G. Beekeeping from Antiquity through the Middle Ages. *Annu. Rev. Entomol.* **2017**, *62*, 249–264. [[CrossRef](#)]
67. Turner, J.H.; Maryanski, A. The Deep Origins of Society: An Assessment of E.O. Wilson’s Genesis. *Int. Sociol.* **2019**, *34*, 536–551. [[CrossRef](#)]
68. Wilson, E.O.; Hölldobler, B. Eusociality: Origin and Consequences. *Proc. Natl. Acad. Sci. USA* **2005**, *102*, 13367–13371. [[CrossRef](#)] [[PubMed](#)]
69. Tsvetkov, N.; Cook, C.N.; Zayed, A. Effects of Group Size on Learning and Memory in the Honey Bee *Apis mellifera*. *J. Exp. Biol.* **2019**, *222*, jeb193888. [[CrossRef](#)] [[PubMed](#)]
70. Sponsler, D.B.; Bratman, E.Z. Beekeeping in, or for the City? A Socioecological Perspective on Urban Apiculture. *People Nat.* **2021**, *3*, 550–559. [[CrossRef](#)]
71. Menzel, R. The Honeybee as a Model for Understanding the Basis of Cognition. *Nat. Rev. Neurosci.* **2012**, *13*, 758–768. [[CrossRef](#)] [[PubMed](#)]
72. Howard, S.R.; Avarguès-Weber, A.; Garcia, J.E.; Greentree, A.D.; Dyer, A.G. Numerical Ordering of Zero in Honey Bees. *Science* **2018**, *360*, 1124–1126. [[CrossRef](#)]
73. Laomettachit, T.; Liangruksa, M.; Termsaithong, T.; Tangthanawatsakul, A.; Duangphakdee, O. A Model of Infection in Honeybee Colonies with Social Immunity. *PLoS ONE* **2021**, *16*, e0247294. [[CrossRef](#)] [[PubMed](#)]
74. Cridge, A.G.; Lovegrove, M.R.; Skelly, J.G.; Taylor, S.E.; Petersen, G.E.L.; Cameron, R.C.; Dearden, P.K. The Honeybee as a Model Insect for Developmental Genetics. *Genesis* **2017**, *55*, e23019. [[CrossRef](#)] [[PubMed](#)]
75. Vijay, A.; Valdes, A.M. Role of the Gut Microbiome in Chronic Diseases: A Narrative Review. *Eur. J. Clin. Nutr.* **2022**, *76*, 489–501. [[CrossRef](#)] [[PubMed](#)]
76. Chmiel, J.A.; Daisley, B.A.; Pitek, A.P.; Thompson, G.J.; Reid, G. Understanding the Effects of Sublethal Pesticide Exposure on Honey Bees: A Role for Probiotics as Mediators of Environmental Stress. *Front. Ecol. Evol.* **2020**, *8*, 22. [[CrossRef](#)]

77. Engel, P.; Kwong, W.K.; McFrederick, Q.; Anderson, K.E.; Barribeau, S.M.; Chandler, J.A.; Cornman, R.S.; Dainat, J.; de Miranda, J.R.; Doublet, V.; et al. The Bee Microbiome: Impact on Bee Health and Model for Evolution and Ecology of Host-Microbe Interactions. *mBio* **2016**, *7*, e02164. [[CrossRef](#)]
78. Zheng, H.; Steele, M.I.; Leonard, S.P.; Motta, E.V.S.; Moran, N.A. Honey Bees as Models for Gut Microbiota Research. *Lab. Anim.* **2018**, *47*, 317–325. [[CrossRef](#)] [[PubMed](#)]
79. Hoshihara, H.; Sasaki, M. Perspectives of Multi-modal Contribution of Honeybee Resources to Our Life. *Entomol. Res.* **2008**, *38*, S15–S21. [[CrossRef](#)]
80. Srinivasan, M.V. Honeybees as a Model for the Study of Visually Guided Flight, Navigation, and Biologically Inspired Robotics. *Physiol. Rev.* **2011**, *91*, 413–460. [[CrossRef](#)] [[PubMed](#)]
81. Sabo, C.; Yavuz, E.; Cope, A.; Gurney, K.; Vasilaki, E.; Nowotny, T.; Marshall, J.A.R. An Inexpensive Flying Robot Design for Embodied Robotics Research. In Proceedings of the 2017 International Joint Conference on Neural Networks (IJCNN), Anchorage, AK, USA, 14–19 May 2017; IEEE: New York, NY, USA, 2017; pp. 4171–4178.
82. Thakoor, S.; Moro, J.M.; Chahl, J.; Hine, B.; Zornetzer, S. BEES: Exploring Mars with Bioinspired Technologies. *Computer* **2004**, *37*, 38–47. [[CrossRef](#)]
83. Hoogendoorn, M.; Schut, M.C.; Treur, J. Modeling Decentralized Organizational Change in Honeybee Societies. In *Advances in Artificial Life*; Springer: Berlin/Heidelberg, Germany, 2007; pp. 615–624.
84. Hewlett Packard Enterprise. Swarm Intelligence. Available online: <https://www.hpe.com/pt/en/what-is/swarm-intelligence.html> (accessed on 18 June 2024).
85. Landgraf, T.; Rojas, R.; Nguyen, H.; Kriegel, F.; Stettin, K. Analysis of the Waggle Dance Motion of Honeybees for the Design of a Biomimetic Honeybee Robot. *PLoS ONE* **2011**, *6*, e21354. [[CrossRef](#)] [[PubMed](#)]
86. Crane, E. Recent Research on the World History of Beekeeping. *Bee World* **1999**, *80*, 174–186. [[CrossRef](#)]
87. Paris, E.H.; Castrejon, V.B.; Walker, D.S.; Lope, C.P. The Origins of Maya Stingless Beekeeping. *J. Ethnobiol.* **2020**, *40*, 386–405. [[CrossRef](#)]
88. Weiss, K. Experiences with Plastic Combs and Foundation. *Bee World* **1983**, *64*, 56–62. [[CrossRef](#)]
89. Dynes, T.L.; Berry, J.A.; Delaplane, K.S.; Brosi, B.J.; de Roode, J.C. Reduced Density and Visually Complex Apiaries Reduce Parasite Load and Promote Honey Production and Overwintering Survival in Honey Bees. *PLoS ONE* **2019**, *14*, e0216286. [[CrossRef](#)]
90. Raymann, K.; Shaffer, Z.; Moran, N.A. Antibiotic Exposure Perturbs the Gut Microbiota and Elevates Mortality in Honeybees. *PLoS Biol.* **2017**, *15*, e2001861. [[CrossRef](#)]
91. Rodet, G. The Man and the Bees: A Coviability Issue—Beekeeping Can It Be Intensively Farmed? In *Coviability of Social and Ecological Systems: Reconnecting Mankind to the Biosphere in an Era of Global Change*; Springer International Publishing: Cham, Switzerland, 2019; pp. 305–327.
92. Jacques, A.; Laurent, M.; Ribière-Chabert, M.; Saussac, M.; Bougeard, S.; Budge, G.E.; Hendrikx, P.; Chauzat, M.-P. A Pan-European Epidemiological Study Reveals Honey Bee Colony Survival Depends on Beekeeper Education and Disease Control. *PLoS ONE* **2017**, *12*, e0172591. [[CrossRef](#)] [[PubMed](#)]
93. Sonmez Oskay, G.; Uygur, G.S.; Oskay, D.; Arda, N. Impact of Stress Factors Internal and External to the Hive on Honey Bees and Their Reflection on Honey Bee Products: A Review. *J. Apic. Res.* **2023**, 1–16. [[CrossRef](#)]
94. Hristov, P.; Shumkova, R.; Palova, N.; Neov, B. Factors Associated with Honey Bee Colony Losses: A Mini-Review. *Vet. Sci.* **2020**, *7*, 166. [[CrossRef](#)]
95. Chauzat, M.-P.; Laurent, M.; Riviere, M.-P.; Saugeon, C.; Hendrikx, P.; Ribiere-Chabert, M. A Pan-European Epidemiological Study on Honeybee Colony Losses 2012–2013. Available online: https://food.ec.europa.eu/system/files/2017-04/la_bees_epilo_bee-report_2012-2013.pdf (accessed on 18 June 2024).
96. Laurino, D.; Liroy, S.; Carisio, L.; Manino, A.; Porporato, M. *Vespa Velutina*: An Alien Driver of Honey Bee Colony Losses. *Diversity* **2019**, *12*, 5. [[CrossRef](#)]
97. Peck, D.T. The Parasitic Mite *Varroa destructor*. In *Honey Bee Medicine for the Veterinary Practitioner*; Wiley: Hoboken, NJ, USA, 2021; pp. 235–251.
98. de Jongh, E.J.; Harper, S.L.; Yamamoto, S.S.; Wright, C.J.; Wilkinson, C.W.; Ghosh, S.; Otto, S.J.G. One Health, One Hive: A Scoping Review of Honey Bees, Climate Change, Pollutants, and Antimicrobial Resistance. *PLoS ONE* **2022**, *17*, e0242393. [[CrossRef](#)] [[PubMed](#)]
99. Wilfert, L.; Brown, M.J.F.; Doublet, V. One Health Implications of Infectious Diseases of Wild and Managed Bees. *J. Invertebr. Pathol.* **2021**, *186*, 107506. [[CrossRef](#)]
100. Negri, P.; Villalobos, E.; Szawarski, N.; Damiani, N.; Gende, L.; Garrido, M.; Maggi, M.; Quintana, S.; Lamattina, L.; Eguaras, M. Towards Precision Nutrition: A Novel Concept Linking Phytochemicals, Immune Response and Honey Bee Health. *Insects* **2019**, *10*, 401. [[CrossRef](#)]
101. Castelli, L.; Branchiccela, B.; Garrido, M.; Invernizzi, C.; Porrini, M.; Romero, H.; Santos, E.; Zunino, P.; Antúnez, K. Impact of Nutritional Stress on Honeybee Gut Microbiota, Immunity, and *Nosema Ceranae* Infection. *Microb. Ecol.* **2020**, *80*, 908–919. [[CrossRef](#)] [[PubMed](#)]
102. Bretagnolle, V.; Gaba, S. Weeds for Bees? A Review. *Agron. Sustain. Dev.* **2015**, *35*, 891–909. [[CrossRef](#)]

103. Alberoni, D.; Favaro, R.; Baffoni, L.; Angeli, S.; Di Gioia, D. Neonicotinoids in the Agroecosystem: In-Field Long-Term Assessment on Honeybee Colony Strength and Microbiome. *Sci. Total Environ.* **2021**, *762*, 144116. [CrossRef]
104. Flores, J.M.; Gil-Lebrero, S.; Gámiz, V.; Rodríguez, M.I.; Ortiz, M.A.; Quiles, F.J. Effect of the Climate Change on Honey Bee Colonies in a Temperate Mediterranean Zone Assessed through Remote Hive Weight Monitoring System in Conjunction with Exhaustive Colonies Assessment. *Sci. Total Environ.* **2019**, *653*, 1111–1119. [CrossRef] [PubMed]
105. Tilocca, B.; Greco, V.; Piras, C.; Ceniti, C.; Paonessa, M.; Musella, V.; Bava, R.; Palma, E.; Morittu, V.M.; Spina, A.A.; et al. The Bee Gut Microbiota: Bridging Infective Agents Potential in the One Health Context. *Int. J. Mol. Sci.* **2024**, *25*, 3739. [CrossRef] [PubMed]
106. Wood, T.J.; Goulson, D. The Environmental Risks of Neonicotinoid Pesticides: A Review of the Evidence Post 2013. *Environ. Sci. Pollut. Res.* **2017**, *24*, 17285–17325. [CrossRef] [PubMed]
107. Kessler, S.C.; Tiedecken, E.J.; Simcock, K.L.; Derveau, S.; Mitchell, J.; Softley, S.; Radcliffe, A.; Stout, J.C.; Wright, G.A. Bees Prefer Foods Containing Neonicotinoid Pesticides. *Nature* **2015**, *521*, 74–76. [CrossRef] [PubMed]
108. Adriaanse, P.; Arce, A.; Focks, A.; Ingels, B.; Jölli, D.; Lambin, S.; Rundlöf, M.; Süßenbach, D.; Del Aguila, M.; Ercolano, V.; et al. Revised Guidance on the Risk Assessment of Plant Protection Products on Bees (*Apis mellifera*, *Bombus* spp. and *Solitary bees*). *EFSA J.* **2023**, *21*, 3295. [CrossRef]
109. Zaluski, R.; Justulin, L.A.; Orsi, R.d.O. Field-Relevant Doses of the Systemic Insecticide Fipronil and Fungicide Pyraclostrobin Impair Mandibular and Hypopharyngeal Glands in Nurse Honeybees (*Apis mellifera*). *Sci. Rep.* **2017**, *7*, 15217. [CrossRef] [PubMed]
110. Motta, E.V.S.; Raymann, K.; Moran, N.A. Glyphosate Perturbs the Gut Microbiota of Honey Bees. *Proc. Natl. Acad. Sci. USA* **2018**, *115*, 10305–10310. [CrossRef]
111. Kasiotis, K.M.; Zafeiraki, E.; Manea-Karga, E.; Anastasiadou, P.; Machera, K. Pesticide Residues and Metabolites in Greek Honey and Pollen: Bees and Human Health Risk Assessment. *Foods* **2023**, *12*, 706. [CrossRef]
112. Siddiqui, A.J.; Musharraf, S.G.; Choudhary, M.I.; Rahman, A. Application of Analytical Methods in Authentication and Adulteration of Honey. *Food Chem.* **2017**, *217*, 687–698. [CrossRef]
113. Food and Agriculture Organization of the United Nations. SDG Indicators Data Portal. Available online: <https://www.fao.org/sustainable-development-goals-data-portal/data/indicators/2.1.1-prevalence-of-undernourishment/en#:~:text=Global%20hunger%20remained%20relatively%20unchanged,world%20faced%20hunger%20in%202022> (accessed on 18 June 2024).
114. Sun, H.; Li, H.; Zhang, X.; Liu, Y.; Chen, H.; Zheng, L.; Zhai, Y.; Zheng, H. The Honeybee Gut Resistome and Its Role in Antibiotic Resistance Dissemination. *Integr. Zool.* **2023**, *18*, 1014–1026. [CrossRef]
115. Rodrigues, H.; Leite, M.; Oliveira, B.; Freitas, A. Antibiotics in Honey: A Comprehensive Review on Occurrence and Analytical Methodologies. *Open Res. Eur.* **2024**, *4*, 125. [CrossRef]
116. Croppi, S.; Yu, L.; Robinette, C.S.; Hassler, E.E.; Newmark, A.J.; Scott, A.; Cazier, J.; Song, J.; Formato, G. Impact of Legislation on Antibiotic Use and Awareness of Beekeepers. *J. Apic. Sci.* **2021**, *65*, 265–277. [CrossRef]
117. Donkersley, P.; Elsner-Adams, E.; Maderson, S. A One-Health Model for Reversing Honeybee (*Apis mellifera* L.) Decline. *Vet. Sci.* **2020**, *7*, 119. [CrossRef] [PubMed]
118. Tlak Gajger, I.; Mañes, A.M.; Formato, G.; Mortarino, M.; Toporcak, J. Veterinarians and Beekeeping: What Roles, Expectations and Future Perspectives?—A Review Paper. *Vet. Arh.* **2021**, *91*, 437–443. [CrossRef]

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