

Review

Significance of Apoidea as Main Pollinators. Ecological and Economic Impact and Implications for Human Nutrition

Peter Hristov ^{1,*} , Boyko Neov ¹, Rositsa Shumkova ² and Nadezhda Palova ³

¹ Department of Animal Diversity and Resources, Institute of Biodiversity and Ecosystem Research, Bulgarian Academy of Sciences, 1113 Sofia, Bulgaria; boikoneov@gmail.com

² Research Center of Stockbreeding and Agriculture, Agricultural Academy, 4700 Smolyan, Bulgaria; rositsa6z@abv.bg

³ Scientific Center of Agriculture, Agricultural Academy, 8300 Sredets, Bulgaria; nadejda_palova@abv.bg

* Correspondence: peter_hristoff@abv.bg; Tel.: +35-92-979-2327

Received: 16 June 2020; Accepted: 13 July 2020; Published: 15 July 2020



Abstract: Wild and managed bees provide pollination services to crops and wild plants, as well as a variety of other services beneficial to humans. Honey bees are the most economically valuable pollinator worldwide. It has been calculated that 9.5% of the total economic value of agricultural production comes from insect pollination, thus amounting to just under USD 200 billion globally. More than 100 important crops depend on pollination by honey bees. The latter pollinate not only a wide number of commercial crops but also many wild plants, some of which are threatened by extinction and constitute a valuable genetic resource. Moreover, as pollinators, honey bees play a significant role in every aspect of the ecosystem by facilitating the growth of trees, flowers, and other plants that serve as food and shelter for many large and small creatures. In this paper, we describe how the reduction in honey bee populations affects various economic sectors, as well as human health.

Keywords: *Apis mellifera*; honey bee products; medicinal impact; human nutrition

1. Introduction

The honey bee plays a significant role as a pollinator of a wide range of agricultural and wild plant species [1,2]. Furthermore, wasps, flies, butterflies, moths, and beetles also contribute to the pollination of a variety of plants [3]. Since the beginning of the 21st century, there has been a growing trend of decreases in the diversity of both managed and non-managed animal pollinators—some birds (hummingbirds, sunbirds, spider hunters, etc.) and mammals (bats, rodents, etc.) [4]. Numerous studies have documented a significant decline in the diversity and range of non-managed wild pollinators over the past three decades worldwide [5]. Additionally, many animal pollinators (birds and mammals) are going extinct and have been narrowing their habitats globally over the past 25 years [6].

This review provides data about the vital role of the honey bee as the main pollinator. It also surveys data regarding the essential role of honey bees in ecosystem services and human nutrition, as well as the medicinal significance of honey bee products.

2. Some Factors Leading to Honey Bee Colony Decline

Colony collapse disorder (CCD) is an abnormal phenomenon occurring when the majority of worker honey bees in a colony disappear, whereas the queen is left behind with plenty of food and a few nurse honey bees to care for the remaining immature honey bees [7]. It was described for the first time in the late 2006, when 30–40% of the managed honey bee colonies in the United States declined [8].

Beekeepers, mainly in some European countries, have been observing a similar phenomenon since the end of the 20th century, particularly in Southern and Western Europe [9,10]. Moreover, the Northern Ireland Assembly received reports of a decline of over 50% in honey bee colonies [11]. Hypotheses regarding the causes of the syndrome mentioned above have taken into consideration various factors, including the consequences of traditional honey bee diseases inflicted by parasites, such as varroa mites, the excessive use of pesticides in agricultural production, genetically modified plants, electromagnetic radiation, inadequate honey bee nutrition, crops growing in monoculture, and biodiversity loss [12–15].

The other form of decline involves a multi-annual, permanent reduction in the number of honey bee colonies in separate, specific regions. For example, since the mid-1980s, honey bee colonies in Europe have decreased by 25% and in the USA by 50–60% [16]. Meanwhile, despite sporadic cases of local extinction, the number of honey bee colonies worldwide has increased by about 45% in the past 50 years and particularly since 1961 [17,18]. The latter seems hopeful, but these findings must be interpreted with care, as there is often a lack of objectively collected data about the status of honey bees in individual countries and about population changes over the years and by region.

The loss and fragmentation of natural habitats resulting from the urbanization or intensification of agriculture leads to the reduction of sources of alternative foraging for the honey bee and nesting places for wild bees—tree hollows, bushes, cavities and holes, caves, and others [18,19]. The process of reducing and degrading the terrain occupied by natural vegetation—grassy or trees—escalated in the 20th century and is still ongoing today. Growing honey bees in an urban environment is considered to have its advantages—alternative food sources throughout the season (parks, alleys, etc.) and a lower risk of pesticide intoxication. However, if the environment is highly urbanized, flowering vegetation may not be sufficient for honey production. In addition, there is a risk of man-made pollution, as well as the collision of flying honey bees with moving vehicles [6]. Industrial agriculture has various and massive impacts on managed and wild pollinators due to the narrowing natural ranges of these pollinators [20,21].

Factors that have to be taken into account include the fragmentation of natural and semi-natural habitats, the expansion of monocultures, and the lack of diversity [22,23]. Globally, industrial agriculture has been one of the most crucial threats to pollinator communities due to the destructive practices that restrict the possibility of honey bee nesting and also due to the spraying of herbicides and pesticides. It should be noted, however, that agricultural systems working with biodiversity and without chemicals, e.g., ecological farming systems, can be beneficial both to managed and to wild pollinator communities [24,25]. For example, by increasing habitat heterogeneity for honey bees, ecological mixed-cropping systems can provide additional flower resources for pollinators. This highlights the potential benefits of ecological and organic agriculture methods.

Recent studies on wild pollinators have shown that the latter are more significant contributors to global crop pollination than previously assumed [26]. Many insects besides bees are also effective pollinators, with 39% of visits to crop flowers [3]. Wild insect pollinator species are considered to be the most efficient pollinators of fruit crops [27].

Many reports have confirmed the decreasing biodiversity in wild pollinators. For example, cases of declines in wild bees, especially in bumblebees (*Bombus* spp.), have been recorded worldwide [28]. Most of these losses were observed in the second half of the 20th century, which coincided with the general timeframe of the global industrialization of agriculture and the ensuing conversion and degradation of bee habitats [5]. Changes in climate and land use may also have contributed to the losses of northeastern bumblebees due to the continued alterations of precipitation patterns, temperature, phenology, and the availability of native flora; however, the effects of the listed factors have not been fully determined yet [29].

There is strong evidence for decreases in the populations and ranges of the native solitary bee, resulting in a general loss of pollinator species richness in many areas [30]. Several interrelated factors have been implicated in this decline, e.g., pathogens, climate change, and increased pesticide use, yet habitat loss is definitely one of the primary drivers [21,31,32].

Additional pollinator taxa, besides honey bees, have been the subject of monitoring concerns: several local and national level butterflies (Lepidoptera) have been recorded, mainly in the USA. Based on the intensive long-term monitoring of individual butterfly species, rigorous quantitative estimates of declines have been established. It should be noted that the eastern North American monarch has declined by over 85% [33] and the western North American monarch by over 95% [34] over the last two decades. Butterfly populations in Europe have also decreased drastically in recent decades. In England and in the Netherlands, respectively, 42% and 24% of the resident breeding species became extinct in the late 19th and the 20th centuries [35]. There have been reports of similar declines in Japan, and in hotspots of butterfly endemism such as Brazil, South Africa, and Australia [36–39]. The intensification of human land use, for the purposes of agriculture, in particular, remains the major cause of butterfly declines and of the changes in community composition [40].

There has been strong evidence of declines in mammalian and bird pollinators as well. The latter include larger and more visible species, and thus are more often included in monitoring schemes. At least 45 species of bats, 36 species of non-flying mammals, 26 species of hummingbirds, seven species of sunbirds, and 70 species of passerine birds—all of which are known pollinators—are of global conservation concern [41].

3. Negative Impact of Monocultures on Beehives

Poor honey bee management is associated with specific peculiarities in beekeeping practices and directly adds to the combination of stressors that can contribute to honey bee population decline. These stressors include artificial substances and unilateral feeding, antibiotics, acaricides, and insecticides applied to the hive, exposure to adverse temperatures and temperature fluctuations, infections and parasites, the overexploitation of honey bee products, and unreliable sources of honey bees and honey bee queens [16,42]. The one-sided selection of honey bees results in genetic erosion in the species population and a lack of resistance to infectious diseases, mites, acaricides applied by beekeepers in hives, etc. [17,18].

Studies on the arrival of honey bees to pollinate almond flowers in California orchards—primarily in five counties between the San Francisco Bay Area and Los Angeles—have reported the start of a brief frenzy of activity. According to researchers, this is the world's largest pollination event. Depending on where a farm is located, certain pollination strategies may be more appropriate than others, because wild bees are more often found in orchards near natural habitats [5,25]. In such areas, it is important to maintain the natural habitat. Growers whose orchards are far from the habitat can diversify their pollination strategies by using alternatively managed honey bees, such as the blue orchard bee (*Osmia lignaria*), in addition to honey bees, and by adding flowering resources to support these managed honey bees and to attract wild species. The feeding of honey bees is often insufficient, be it due to the overcrowding of hives or irregular grazing, and in the conditions of prolonged cold and rainy weather, it is lacking [43,44]. Feeding is considered to be deficient in areas with intensive agricultural production where the so-called stress from a monotonous or “monocultural” diet is evidenced [6]. The latter refers to the continuous grazing of honey bees on crops in mass flower, and which are grown over large areas, such as sunflower or rapeseed, as well as acacia, where the purpose is to produce honey, or just to pollinate the plants.

Some investigations have revealed that the monocultural diet may be increasing pollinators' visits to defended plants [45]. Such is the case with the presence of cyanogenic glycoside amygdalin in almond pollen. The authors of the relevant study established that the amygdalin levels in the nectar and in the honey were below the lethal threshold for honey bees, as no unusual levels of bee mortality were detected. Additionally, the authors suggested that amygdalin deters honey bees, and that these concentrations are high enough to account for the preference for white mustard flowers over almond in almond orchards. It was hypothesized that the presence of secondary compounds in nectar and/or pollen may enhance plant fitness by attracting more specialized pollinators.

Similarly, Stephenson [46] found that the iridoid glycosides of *Catalpa speciosa* increase floral constancy by inhibiting nectar “thieves” but not legitimate pollinators. These data suggest that the presence of cyanogenic glycosides in the nectar and pollen of almond flowers might inhibit inefficient pollinators or nectar “thieves”. Honey bees, as the most effective pollinators of almonds, can probably tolerate the toxicity of amygdalin, up to a certain level.

The African continent is characterized by a significant number of managed honey bee subspecies, which are exposed to a plethora of factors attributing to colony losses in other biogeographic realms. Data about Africa show that, with the exception of the bacterial American foulbrood epidemic in the Western Cape, there has been an insignificant decline in honey bee populations [47]. There are some preconditions for this picture: (1) Honey bee populations in some countries in Africa (South Africa) may have a natural immunity to pathogens and diseases coming from other continents [48]; (2) as mentioned earlier, African populations are more genetically diverse than their European counterparts (due to a large wild population), and are less commercialized [49,50]; (3) the African honey bees are known to exhibit specific behavior in response to unfavorable climatic conditions and the presence of various pests or predators [51]. All of the listed factors may have contributed to the reduced impact of stressors on honey bee health in Africa. Thus, the honey bee colony losses observed in Africa have been lower than those on other continents [47,48].

As far as Europe is concerned, honey bee population declines vary in different parts of the continent. In central Europe, the observed losses since 1985 have amounted to a quarter of the honey bee colonies, with a 54% loss in the United Kingdom [5]. Since 1998, weakening and mortality in colonies have been recorded in Europe, especially in France, Belgium, Switzerland, Germany, the UK, the Netherlands, Italy, and Spain. Lethality is the highest at the end of the winter and at the beginning of the spring [23]. During the last several winters, honey bee colony mortality in Europe averaged about 20% (with a wide range of 1.8% to 53% among European countries). Over the winter of September 2008, honey bee losses in Europe ranged between 7% and 22%, and over the winter of October 2009, between 7% and 30% [37]. In addition to the decline in managed bee colonies, a global decrease in native wild pollinators has been reported as well [5,52]. Typical examples in this regard are the UK and the Netherlands [53].

All these data have led to suggestions that honey bee declines are localized in specific regions, mostly in Europe and North America, whereas in other parts of the world, honey bee population declines seem to be of lower values. Thus, the declines seem to be compensated by increases in the major honey-producing countries (Argentina, China, and Spain) [17].

4. Impacts of Pollinator Declines on Crop Production

Despite the considerable number of existing pollinators, the honey bee plays a significant role for many agricultural plants. It has been suggested that 75% of all crops that are used for human consumption depend on insect pollination [54]. Plenty of the world’s most important crop plants are wind pollinated (wheat, rice, corn, rye, barley, and oats) [55]. Moreover, fruits constitute a substantial part of human diet, as they provide high amounts of essential nutrients such as vitamins, antioxidants, and fiber [56,57]. The most significant pollinator-dependent crops are vegetables and fruits, representing about €50 billion each, followed by edible oil crops, stimulants (e.g., coffee, cocoa, etc.), nuts, and spices [58]. The authors calculated the world value for the contribution of pollinators to the production of crops used directly for human food to be as much as €153 billion, which is about 9.5% of the total value of the production of human food worldwide. In case of the total loss of pollinator services, the average global fruit supplies could drop by 22.9%, vegetables by 16.3%, and nuts and seeds by 22.1% [59]. Such a decline in these valuable resources may have a radical impact on global human health [60].

The expansion of pollinator-dependent crops in certain regions has been analyzed in the paper of Aizen et al. [61]. The authors conclude that if pollinator-dependent agriculture continues to grow, there will be an increasing global demand for pollination services and a risk of pollination shortfall

caused by reduced biodiversity in both managed and wild pollinators. The consequences of this trend may vary at regional and country levels. It is necessary to identify which countries and regions are particularly vulnerable, because the steep increase in their agricultural pollinator dependence involves a potentially high environmental cost and may not be compensated by the economic and social benefits associated with more diverse agricultural practices.

It is well known that urban areas are growing globally and this has consequently been affecting biodiversity and ecosystem services, such as pollination [62]. The influence of urbanization on pollinators depends on the urban sprawl, and positive responses were observed with moderate levels of urbanization of rural, mostly agricultural, land of below 50% impervious surface. Additionally, urbanization generally reduces pollinator diversity in comparison with natural or semi-natural areas, but enhances it in comparison with intensified agricultural landscapes. As a whole, it seems that urban pollinator communities still provide enough pollination services to crops and wild vegetation.

Overall, pollinator diversity depends on the amount of urban green spaces at the landscape scale. Urbanization also increases the competition between managed and wild pollinator with regard to certain flowering sources [63]. It has been established that the pollinating activity of large solitary bees, bumblebees, and beetles is negatively related to the density of honey bee colonies in the surrounding landscape.

Agriculture and land-use intensification also have a negative effect on bee nutrition and health [64]. For example, it is well known that pollen quality has numerous positive effects on honey bee health. Due to primary human activity, most landscapes are characterized by a mix of different habitat types with varying proportions of natural, semi-natural, agricultural, and urban areas. An important consequence of this process is the provision of additional resources, such as pollen and nectar, for pollinators [65]. The influence of pollen diet quality and diversity on the physiology of young nurse honey bees has been investigated [64]. The authors found that pollen quality affected both nurse bee physiology and the tolerance to the parasite. Pollen diet diversity had no impact on the physiology of nurse bees and the survival of healthy honey bees. However, when parasitized, honey bees fed with the polyfloral blend survived longer than honey bees fed with monofloral pollens, with the exception of the most protein-rich monofloral pollen. These results have come to support the perception that both the quality and diversity of pollen can influence honey bee physiology and might help to better understand the impacts of agriculture and land-use intensification on honey bee nutrition and health.

Although the complete disappearance of all pollinators is impossible, it is of great importance to calculate the relative importance of insect pollination as an important agricultural input [66,67]. It should be noted that this calculation takes into consideration the fact that most crops only partially decline in production in the absence of insect pollinators, and this fact is utilized to calculate the economic value [48]. Different crop varieties may have different yield responses to major changes in animal pollination; however, only a little data about these differences are available. With this connection, it is necessary to calculate the global economic value of pollination in accordance with each variety, as well as the area cultivated per variety.

5. Ecosystem Service Benefits

Estimates of flowering plant dependence on animal pollination vary between 78% and 94% in temperate and tropical ecosystems, respectively [68]. As can be expected, it has been proven that plants which require pollination by animals decline in tandem with their pollinators, although further studies are needed in order to elucidate a more complete picture [53,69–71]. Ashman et al. [70] suggest that pollen limitation may have profound effects on certain species (like obligate outcrossing animal-pollinated annual plants), and this can, in turn, cause additional profound changes to the whole ecosystem. It is not unreasonable to extrapolate the effects of the reduced production of crops caused by pollinator decline to such a decline in wild plants. Allen-Wardell et al. [41] list several cases of decline in certain plant populations or even extinction related to the reduction in pollinator abundance, also highlighting the possibility of an extinction chain within an ecosystem if key species are affected.

Since it has been proven that honey bee health is related to floral diversity, and, correspondingly, honey bee health and growth improve with a diverse diet, it may therefore be expected that plant declines driven by honey bee declines may exacerbate the problem by forming a positive feedback loop [72]. Although plant–pollinator networks are generally characterized by a certain robustness and ability to compensate both for the decline and extinction of a pollinator or a pollinated species, we can reasonably presume that these networks have a limited compensation reserve and may reach a tipping point, leading to an ecosystem collapse and profound species composition reshift [73].

As we mentioned above, honey bees are a significant pollinator not only for many crops, but for many other plants in their natural habitats. What are the benefits of this pollination? Directly or indirectly, pollinators provide ecosystem services in addition to pollination. These contributions include (but are not limited to): carbon sequestration, the water cycle and water purification, biodiversity preservation, organic matter degradation, and others. The first significant benefit is associated with carbon sequestration: no less than 80% of all flowering plants need pollination in order to reproduce [68]. Flowering plants use the carbon dioxide from the atmosphere for growing through the process of photosynthesis, during which they release oxygen as a waste product of their metabolism [74]. A second, very important, issue is related to the water cycle. The latter is a combination of physical processes, one of which is transpiration, through which plants return moisture from the soil into the atmosphere [75]. Plant transpiration contributes to 10% of the total moisture content in the atmosphere, while the other 90% comes from evaporation from water surfaces [76]. A fully grown tree can transpire as much as 760 liters (200 gallons) of water annually. Third, pollination by honey bees plays a crucial role for sustaining many endangered plant species (e.g., in the USA these include American ginseng, Hawaiian sandalwood, rosy periwinkle, and wild yam) [77]. These species serve as valuable genetic resources in many countries, and their disappearance will have an adverse impact on the biodiversity in the respective countries. Furthermore, the loss of endemic plant species will negatively affect the ecosystem equilibrium within the geographical area [78].

Thus, the global decline in honey bee populations, as well as the fact that managing honey bees is more difficult than it used to be, will negatively influence the reproduction and population dynamics of plants in natural areas [79], and, consequently, the ecosystem services provided by such plants, e.g., carbon sequestration and soil retention. Different populations of *A. mellifera* have recently been introduced to overcome the problem in many regions [80]. However, this activity may have certain negative consequences, such as: competition for floral resources with native pollinators; competition for nest sites; the co-introduction of natural enemies, especially pathogens, or compromised plant reproductive success [81]. These phenomena are of major ecological, evolutionary, and conservation significance, but until now there have been limited data about the importance of honey bees as a pollinator in their native natural ecosystems or as an introduced species in some regions.

6. Honey Bee Products and Their Medicinal Value

Honey bee products, such as honey, pollen, royal jelly, propolis, bee venom, wax, and bee bread, are important sources for human nutrition and the production of pharmaceuticals and food additives. This makes honey and pollen suitable for the treatment of a plethora of diseases and infections [82].

Honey, the definitive honey bee product, is a natural substance produced by honey bees, mainly from the nectar of blossoming plants. It can also be derived from the secretions of living parts of plants or the excretions of plant sucking insects (e.g., aphids) on the living parts of plants, which honey bees collect, transform, and combine with specific substances of their own metabolism, then store and leave in the honey comb to ripen and mature [83].

The usage of honey as a medicine has been well known since ancient times [84]. It has been found that honey has numerous properties, e.g., antimicrobial and anti-inflammatory. Its wound-healing property is due to the fact that it maintains the moisture of the wound while at the same time its high viscosity provides a protective barrier to prevent bacterial infection [85,86]. Honey is also proven to

have an antibacterial property due to the enzymatic production of free radicals and other reactive oxygen species, including hydrogen peroxide [87,88].

In the light of the rising issue of antibiotic resistance, which poses a very serious threat to public health, different antibacterial agents are essential in the fight against many infectious diseases. Therefore, more and more attention is being paid to alternative antimicrobial strategies, and honey fully meets these requirements [84,89,90]. Thus, as well as a nutrient, honey may be used successfully as an alternative medicine therapy, thus replacing antibiotic treatment [91].

Another typical honey bee product with a possible medicinal application is pollen. Pollen pellets are stored in comb cells and are combined with honey, nectar, or glandular secretions. These conditions are favorable for the pollen bolus to undergo a lactic acid fermentation and become what is called “bee bread” (composed of proteins, monosaccharides, organic acids, minerals, fatty acids, tocopherols, and polyphenols), which also has antioxidant and antimicrobial properties [92–94].

Propolis is probably the most popular honey bee product with a primarily medicinal application, having its own antimicrobial, antifungal, antiviral, anti-inflammatory, and anesthetic activities [95]. Propolis is a resinous substance and is used for honey bees’ protection, disinfection, and isolation of beehives [96,97]. Based on analysis, it has been established that there are at least 149 compounds and 22 minerals in propolis [82].

Royal jelly is known as a valuable source of energy nutrients and essential amino acids, as well as vitamins, minerals, and hormone-like substances [98,99]. Thus, royal jelly improves general wellbeing and brain function, increases appetite, stimulates and controls endocrine function, etc. [100]. Since it can mitigate unfavorable conditions and inconveniences related to ageing, which, among other things, include a deficient diet, royal jelly has proven to be an excellent dietary supplement, particularly for the elderly.

Bee venom is also used as an alternative therapy, most importantly for the treatment of many human diseases [101]. Bee venom contains several active biomolecules, such as peptides and enzymes, which are potentially beneficial in treating inflammation and central nervous system diseases like Alzheimer’s disease, Parkinson’s disease, and amyotrophic lateral sclerosis [102,103]. Furthermore, it has been shown that bee venom has promising benefits against different types of cancer, as well as anti-viral activity, even against the highly challenging human immunodeficiency virus (HIV) [104,105].

Bee bread is the result of the lactic fermentation of pollen collected by honey bees and mixed by their digestive enzymes, then carried into the hive and kept with a thin layer of honey and beeswax. Bee bread is the main food in the hive, particularly for larvae and young honey bees producing royal jelly [106]. Research on the chemical composition of bee bread has shown that it usually consists of water, proteins, free amino acids, carbohydrates, fatty acids, and other bioactive molecules [107,108]. It is known that bee bread definitely has antioxidant activities and effectiveness against all bacteria and fungi [109,110].

7. The Beneficial Role of Honey Bee Products on Individual Honey Bees’ Health and Their Impact on Social Immunity

Honey bees suffer from various, often interrelated, unfavorable factors, such as parasites, pathogens, pesticides, and poor nutrition and management [111]. In this regard, it is particularly important to understand the effects of individual stressors and the interactions among stressors in order to provide solutions to improve colony health and survival. Moreover, it is important to understand how honey bees’ natural immune responses (individual immunity) and collective behavioral defenses (social immunity) can increase and maintain honey bee health and counteract stressors without human intervention. One form of social immunity in honey bee colonies is the formation of a propolis envelope within the nest, which acts as an important antimicrobial layer. It is believed that certain types of social immunity behavior, such as the collection of plant resins and their deposition in the nest as an antimicrobial propolis envelope, have evolved to compensate for deficiencies in innate or physiological immunity [112]. These facts have been supported by evidence that propolis may reduce

the effects of mycotoxins produced by fungi [113]. There are multiple honey bee products, such as nectar and pollen, that contribute to social immunity and have a direct influence on colony health [114]. In addition, collecting the antimicrobial secondary metabolites of plants can also be beneficial to honey bees [115]. This defense from microbes is conferred to individual honey bees when they ingest the secondary metabolites, as is true for all pollinators that do so. Furthermore, pollinators can counteract pathogens by collecting and storing non-edible plant materials, such as resin. Honey bees also store these antimicrobial molecules within the edible and non-edible substances that they create from these plant materials, thus preserving the antimicrobial properties in the products they make [115].

8. Impact of Pollination on Human Nutrition

Apart from its impact on crop production, the loss of pollination may also affect not only the macronutrient aspect of human nutrition, but also the micronutrient one. Pollinator-dependent crops are the main sources of a number of micronutrients, such as vitamins A and C, calcium, fluoride, and folic acid [116]. Where the deficiency of such vitamins is observed depends mainly on the geographical region. For example, according to Chaplin-Kramer et al. [117], the production of vitamin A, which is highly pollinator-dependent, reaches a 50% dependence on pollination in North–Central and Southeastern India, Thailand, Western Iran, Romania, Eastern and Southwestern Australia, Argentina, Mexico, and parts of the USA. Vitamin A is important for human growth and development, and folic acid, which is essential for body functions, cannot be synthesized by humans. Thus, the loss of pollinators can further threaten the health of human populations.

Changes in food and nutrient intake due to the reduction in animal pollinators and pollination have been linked to the risk of three groups of diseases: non-communicable (non-infectious, chronic diseases such as cancer, diabetes, and heart disease), communicable (transmissible diseases such as TB and influenza) and malnutrition-related diseases (e.g., vitamin deficiencies such as rickets) [118]. If all pollinators were eliminated, 71 million people in low-income countries could develop a deficiency of vitamin A and another 2.2 billion, whose consumption is already below the average, would experience further declines in supply [119]. As for folic acid, 173 million people may become newly deficient in the vitamin and another 1.23 billion, who are already deficient, would experience further declines [120]. According to published data, about 74% of all lipids produced worldwide are present in oils from plants that are promoted by animal pollination, and these plants are also primary sources of the fat-soluble vitamins [57]. Regarding the water-soluble vitamins, it should be noted that 98% of the available vitamin C comes from animal-pollinated plants, primarily citrus plants, as well as other fruits and vegetables [121]. Plants are also valuable sources of the B vitamins, particularly folic acid. The human body's requirements for folic acid are higher during pregnancy, which is related to the prevention of neural tube defects in infants [122]. Nowadays, another considerable human health concern on a global scale is vitamin A deficiency. Insect-pollinated crops provide about 70% of this vitamin, and pollination increases the yields of these crops by about 43% [57]. The loss of pollinators and the related services could thus create problems for human nutrition, although the magnitudes of the problems might often depend on the geographical location and the degree of social development. Thus, the consequences related to human health generally affect to a greater extent the developing countries where people are poor and often more dependent on their local insect-pollinated crops [57]. The influence of pollinator losses on human health may be less notable in more developed countries, yet it still has the potential to adversely affect the quality of human diets or deepen the dependence on synthetic micronutrients, such as vitamin supplements. An interesting study has been carried out, using a bioeconomic approach, to calculate a world value for the contribution of pollinators to the production of crops that are used directly for human food. This value has been estimated to be \$166 billion, which is about 9.5% of the total value of the production of human food worldwide [58].

The authors have established the most vulnerable crop categories—namely, stimulant crops, nuts, and fruits, as well as the categories that stand for the largest part of the economic vulnerability—fruits, vegetables, and edible oil crops. Furthermore, crop vulnerability varies in different geographical

regions. The most affected region turns out to be East Asia (15%), followed by Central Asia (14%), South Asia (12%), and non-EU countries (12%). On a global scale, the vulnerability of the northern countries appears higher than that of the southern ones. This suggests that the decrease in insect pollinators may significantly affect North–South agro-food production [58].

9. Conclusions

Today, there is growing evidence related to significant pollinator losses in many regions of the world. Further studies are needed in order to map the ubiquity of the phenomenon. Integrating the existing national and local monitoring schemes and the establishment of a global program may provide much needed data in order to help and improve direct policy decisions on pollinators. Not only are pollution threats diverse, but they can also interact. Currently, the main challenge is to better determine the relative importance of a number of drivers, and their synergistic effects in particular. Due to the persistent pressure from well-known drivers, such as habitat loss and pathogens, combined with the environmental and economic risks that have been clearly associated with pollinator loss, there is still a continuing need to improve our understanding of the nature, causes, and consequences of the declines in pollinator services locally, nationally, and globally.

Author Contributions: All authors have equally contributed to the idea of this review. P.H. and B.N. prepared the original draft with considerable contributions from R.S. All authors have substantially contributed to the writing of the final text. Moreover, all authors have read and agreed to the published version of the manuscript.

Funding: This work was funded by the National Scientific Fund of the Bulgarian Ministry of Education and Science [grant numbers 06/10 17.12.2016]. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Acknowledgments: We thank to Maya Marinova (IBPhBME-BAS, Bulgaria) for the English editing.

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

References

1. Van der Sluijs, J.P.; Vaage, N.S. Pollinators and global food security: The need for holistic global stewardship. *Food Ethics* **2016**, *1*, 75–91. [\[CrossRef\]](#)
2. Hung, K.J.; Kingston, J.M.; Albrecht, M.; Holway, D.A.; Kohn, J.R. The worldwide importance of honey bees as pollinators in natural habitats. *Proc. Biol. Sci.* **2018**, *285*, 20172140. [\[CrossRef\]](#) [\[PubMed\]](#)
3. Rader, R.; Bartomeus, I.; Garibaldi, L.A.; Garratt, M.P.; Howlett, B.G.; Winfree, R.; Cunningham, S.A.; Mayfield, M.M.; Arthur, A.D.; Andersson, G.K.; et al. Non-bee insects are important contributors to global crop pollination. *Proc. Natl. Acad. Sci. USA* **2016**, *113*, 146–151. [\[CrossRef\]](#) [\[PubMed\]](#)
4. Potts, S.G.; Biesmeijer, J.C.; Kremen, C.; Neumann, P.; Schweiger, O.; Kunin, W.E. Global pollinator declines: Trends, impacts and drivers. *Trends Ecol. Evol.* **2010**, *25*, 345–353. [\[CrossRef\]](#)
5. Goulson, D.; Nicholls, E.; Botias, C.; Rotheray, E.L. Bee declines driven by combined stress from parasites, pesticides, and lack of flowers. *Science* **2015**, *347*, 1255957. [\[CrossRef\]](#)
6. Regan, E.C.; Santini, L.; Ingwall-King, L.; Hoffmann, M.; Rondinini, C.; Symes, A.; Taylor, J.; Butchart, S.H.M. Global trends in the status of bird and mammal pollinators. *Conserv. Lett.* **2015**, *8*, 397–403. [\[CrossRef\]](#)
7. Oldroyd, B.P. What's Killing American Honey Bees? *PLoS. Biol.* **2007**, *5*, e168. [\[CrossRef\]](#)
8. Van Engelsdorp, D.; Underwood, R.; Caron, D.; Hayes, J., Jr. An estimate of managed colony losses in the winter of 2006–2007: A report commissioned by the apiary inspectors of America. *Am. Bee J.* **2007**, *147*, 599–603.
9. Bacandritsos, N.; Granato, A.; Budge, G.; Papanastasiou, I.; Roinioti, E.; Caldon, M.; Mutinelli, F. Sudden deaths and colony population decline in Greek honey bee colonies. *J. Invertebr. Pathol.* **2010**, *105*, 335–340. [\[CrossRef\]](#)
10. Dainat, B.; Van Engelsdorp, D.; Neumann, P. Colony collapse disorder in Europe. *Environ. Microbiol. Rep.* **2012**, *4*, 123–125. [\[CrossRef\]](#)
11. Breeze, T.; Roberts, S.P.M.; Potts, S.G. Decline of England's bees: Policy review and recommendations. In *Friends of the Earth Report*; University of Reading: Reading, UK, 2012.

12. Kang, Y.; Blanco, K.; Davis, T.; Wang, Y.; DeGrandi-Hoffman, G. Disease dynamics of honeybees with *Varroa destructor* as parasite and virus vector. *Math. Biosci.* **2016**, *275*, 71–92. [[CrossRef](#)] [[PubMed](#)]
13. Barbosa, W.F.; Smagghe, G.; Guedes, R.N.C. Pesticides and reduced-risk insecticides, native bees and pantropical stingless bees: Pitfalls and perspectives. *Pest. Manag. Sci.* **2015**, *71*, 1049–1053. [[CrossRef](#)] [[PubMed](#)]
14. Bekić, B.; Jeločnik, M.; Subić, J. Honey bee colony collapse disorder (*Apis mellifera* L.)—Possible causes. Scientific Papers. Series. *Manag. Econ. Eng. Agric. Rural Dev.* **2014**, *14*, 13–88.
15. Van Engelsdorp, D.; Traynor, K.S.; Andree, M.; Lichtenberg, E.M.; Chen, Y.; Saegerman, C.; Cox-Foster, D.L. Colony Collapse Disorder (CCD) and bee age impact honey bee pathophysiology. *PLoS ONE* **2017**, *12*, e0179535. [[CrossRef](#)]
16. Smith, K.M.; Loh, E.H.; Rostal, M.K.; Zambrana-Torrel, C.M.; Mendiola, L.; Daszak, P. Pathogens, pests, and Economics: Drivers of Honey Bee Colony Declines and Losses. *EcoHealth* **2014**, *10*, 434–445. [[CrossRef](#)]
17. 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](#)]
18. Goulson, D.; Lye, G.C.; Darvill, B. Decline and conservation of bumble bees. *Annu. Rev. Entomol.* **2008**, *53*, 191–208. [[CrossRef](#)]
19. Brown, M.J.; Paxton, R.J. The conservation of bees: A global perspective. *Apidologie* **2009**, *40*, 410–416. [[CrossRef](#)]
20. Kovács-Hostyánszki, A.; Espíndola, A.; Vanbergen, A.J.; Settele, J.; Kremen, C.; Dicks, L.V. Ecological intensification to mitigate impacts of conventional intensive land use on pollinators and pollination. *Ecol. Lett.* **2017**, *20*, 673–689. [[CrossRef](#)]
21. Belsky, J.; Joshi, N.K. Impact of biotic and abiotic stressors on managed and feral bees. *Insects* **2019**, *10*, 233. [[CrossRef](#)]
22. Patrício-Roberto, G.B.; Campos, M.J. Aspects of landscape and pollinators—What is important to bee conservation? *Diversity* **2014**, *6*, 158–175. [[CrossRef](#)]
23. Rollin, O.; Pérez-Méndez, N.; Bretagnolle, V.; Henry, M. Preserving habitat quality at local and landscape scales increases wild bee diversity in intensive farming systems. *Agric. Ecosyst. Environ.* **2019**, *275*, 73–80. [[CrossRef](#)]
24. Földesi, R.; Kovács-Hostyánszki, A.; Kőrösi, Á.; Somay, L.; Elek, Z.; Markó, V.; Báldi, A. Relationships between wild bees, hoverflies and pollination success in apple orchards with different landscape contexts. *Agric. For. Entomol.* **2016**, *18*, 68–75. [[CrossRef](#)]
25. Sponsler, D.B.; Grozinger, C.M.; Hitaj, C.; Rundlöf, M.; Botías, C.; Code, A.; Thogmartin, W.E. Pesticides and pollinators: A socioecological synthesis. *Sci. Total Environ.* **2019**, *662*, 1012–1027. [[CrossRef](#)] [[PubMed](#)]
26. Breeze, T.D.; Bailey, A.P.; Balcombe, K.G.; Potts, S.G. Pollination services in the UK: How important are honeybees? *Agric. Ecosyst. Environ.* **2011**, *142*, 137–143. [[CrossRef](#)]
27. Chagnon, M.; Kreutzweiser, D.; Mitchell, E.A.; Morrissey, C.A.; Noome, D.A.; Van der Sluijs, J.P. Risks of large-scale use of systemic insecticides to ecosystem functioning and services. *Environ. Sci. Pollut. Res.* **2015**, *22*, 119–134. [[CrossRef](#)]
28. Senapathi, D.; Carvalheiro, L.G.; Biesmeijer, J.C.; Dodson, C.A.; Evans, R.L.; McKerchar, M.; Morton, R.D.; Moss, E.D.; Roberts, S.P.M.; Kunin, W.E.; et al. The impact of over 80 years of land cover changes on bee and wasp pollinator communities in England. *Proc. R. Soc. B* **2015**, *282*, 1806. [[CrossRef](#)]
29. Jacobson, M.M.; Tucker, E.M.; Mathiasson, M.E.; Rehan, S.M. Decline of bumble bees in northeastern North America, with special focus on *Bombus terricola*. *Biol. Conserv.* **2018**, *217*, 437–445. [[CrossRef](#)]
30. Kline, O.; Joshi, N.K. Mitigating the Effects of Habitat Loss on Solitary Bees in Agricultural Ecosystems. *Agriculture* **2020**, *10*, 115. [[CrossRef](#)]
31. Woodcock, B.A.; Bullock, J.M.; Shore, R.F.; Heard, M.S.; Pereira, M.G.; Redhead, J.; Ridding, L.; Dean, H.; Sleep, D.; Henrys, P.; et al. Country-specific effects of neonicotinoid pesticides on honey bees and wild bees. *Science* **2017**, *356*, 1393–1395. [[CrossRef](#)]
32. Hladik, M.L.; Vandever, M.; Smallegang, K.L. Exposure of native bees foraging in an agricultural landscape to current-use pesticides. *Sci. Total Environ.* **2016**, *542*, 469–477. [[CrossRef](#)]
33. Agrawal, A.A.; Inamine, H. Mechanisms behind the monarch’s decline. *Science* **2018**, *360*, 1294–1296. [[CrossRef](#)] [[PubMed](#)]

34. Schultz, C.B.; Brown, L.M.; Pelton, E.; Crone, E.E. Citizen science monitoring demonstrates dramatic declines of monarch butterflies in western North America. *Biol. Conserv.* **2017**, *214*, 343–346. [[CrossRef](#)]
35. Van Strien, A.J.; Van Swaay, C.A.; Van Strien-van Liempt, W.T.; Poot, M.J.; WallisDeVries, M.F. Over a century of data reveal more than 80% decline in butterflies in the Netherlands. *Biol. Conserv.* **2019**, *234*, 116–122. [[CrossRef](#)]
36. Nakahama, N.; Uchida, K.; Ushimaru, A.; Isagi, Y. Historical changes in grassland area determined the demography of semi-natural grassland butterflies in Japan. *Heredity* **2018**, *121*, 155–168. [[CrossRef](#)] [[PubMed](#)]
37. Shuey, J.; Labus, P.; Carneiro, E.; Dias, F.M.S.; Leite, L.A.R.; Mielke, O.H. Butterfly communities respond to structural changes in forest restorations and regeneration in lowland Atlantic Forest, Paraná, Brazil. *J. Insect Conserv.* **2017**, *21*, 545–557. [[CrossRef](#)]
38. Topp, E.N.; Loos, J. Local and landscape level variables influence butterfly diversity in critically endangered South African renosterveld. *J. Insect Conserv.* **2019**, *23*, 225–237. [[CrossRef](#)]
39. New, T.R.; Sands, D.P. Management of threatened insect species in Australia, with particular reference to butterflies. *Aust. J. Entomol.* **2004**, *43*, 258–270. [[CrossRef](#)]
40. Thomas, J.A. Butterfly communities under threat. *Science* **2016**, *353*, 216–218. [[CrossRef](#)]
41. Allen-Wardell, G.; Berhardt, P.; Bitner, R.; Burquez, A.; Buchmann, S.; Cane, J.; Cox, P.A.; Dalton, V.; Feinsinger, P.; Ingram, M.; et al. The potential consequences of pollinator declines on the conservation of biodiversity and stability of food crop yields. *Conserv. Biol.* **1998**, *12*, 8–17.
42. Johnson, R.; Corn, M.L. Bee Health: The Role of Pesticides. In *Congressional Research Service (CRS) Reports*; CreateSpace: Scotts Valley, CA, USA, 2015; p. 47.
43. Van Engelsdorp, D.; Evans, J.D.; Saegerman, C.; Mullin, C.; Haubruge, E.; Nguyen, B.K.; Frazier, M.; Frazier, J.; Cox-Foster, D.; Chen, Y.P.; et al. Colony collapse disorder: A descriptive study. *PLoS ONE* **2009**, *4*, e6481. [[CrossRef](#)] [[PubMed](#)]
44. Van Engelsdorp, D.; Evans, J.D.; Donovall, L.; Mullin, C.; Frazier, M.; Frazier, J.; Tarpy, D.R.; Hayes, J.; Pettis, J.S. Entombed pollen: A new condition in honey bee colonies associated with increased risk of colony mortality. *J. Invertebr. Pathol.* **2009**, *101*, 147–149. [[CrossRef](#)] [[PubMed](#)]
45. London-Shafir, I.; Shafir, S.; Eisikowitch, D. Amygdalin in almond nectar and pollen—facts and possible roles. *Plant. Syst. Evol.* **2003**, *238*, 87–95. [[CrossRef](#)]
46. Stephenson, A.G. Iridoid glycosides in the nectar of *Catalpa speciosa* are unpalatable to nectar thieves. *J. Chem. Ecol.* **1982**, *8*, 1025–1034. [[CrossRef](#)]
47. Pirk, C.W.W.; Strauss, U.; Yusuf, A.A.; Démares, F.; Human, H. Honeybee health in Africa—A review. *Apidologie* **2016**, *47*, 276–300. [[CrossRef](#)]
48. Pirk, C.W.W.; Human, H.; Crewe, R.M.; Van Engelsdorp, D. A survey of managed honey bee colony losses in the Republic of South Africa—2009 to 2011. *J. Apic. Res.* **2014**, *53*, 35–42. [[CrossRef](#)]
49. Dietemann, V.; Pirk, C.W.W.; Crewe, R.M. Is there a need for conservation of honey bees in Africa? *Apidologie* **2009**, *40*, 285–295. [[CrossRef](#)]
50. Wallberg, A.; Han, F.; Wellhagen, G.; Dahle, B.; Kawata, M.; Haddad, N.; Simoes, Z.L.; Allsopp, M.H.; Kandemir, I.; De la Rúa, P.; et al. A worldwide survey of genome sequence variation provides insight into the evolutionary history of the honey bee *Apis mellifera*. *Nat. Genet.* **2014**, *46*, 1081–1088. [[CrossRef](#)] [[PubMed](#)]
51. Scott Schneider, S.; DeGrandi-Hoffman, G.; Smith, D.R. The African honey bee: Factors contributing to a successful biological invasion. *Annu. Rev. Entomol.* **2004**, *49*, 351–376. [[CrossRef](#)]
52. Cameron, S.A.; Lozier, J.D.; Strange, J.P.; Koch, J.B.; Cordes, N.; Solter, L.F.; Griswold, T.L. Patterns of widespread decline in North American bumble bees. *Proc. Natl. Acad. Sci. USA* **2011**, *108*, 662–667. [[CrossRef](#)]
53. Biesmeijer, J.C.; Roberts, S.P.M.; Reemer, M.; Ohlemuller, R.; Edwards, M.; Peeters, T.; Schaffers, A.P.; Potts, S.G.; Kleukers, R.; Thomas, C.D.; et al. Parallel declines in pollinators and insect-pollinated plants in Britain and the Netherlands. *Science* **2006**, *313*, 351–354. [[CrossRef](#)]
54. Bartomeus, I.; Potts, S.G.; Steffan-Dewenter, I.; Vaissière, B.E.; Woyciechowski, M.; Krewenka, K.M.; Tscheulin, T.; Roberts, S.P.; Szentgyörgyi, H.; Westphal, C.; et al. Contribution of insect pollinators to crop yield and quality varies with agricultural intensification. *PeerJ* **2014**, *2*, e328. [[CrossRef](#)] [[PubMed](#)]
55. Ghazoul, J. Buzziness as usual? Questioning the global pollination crisis. *Trends Ecol. Evol.* **2005**, *20*, 367–373. [[CrossRef](#)] [[PubMed](#)]

56. Seeram, N.P. Berry fruits: Compositional elements, biochemical activities, and the impact of their intake on human health, performance, and disease. *J. Agric. Food Chem.* **2008**, *56*, 627–629. [[CrossRef](#)]
57. Eilers, E.J.; Kremen, C.; Smith Greenleaf, S.; Garber, A.K.; Klein, A.M. Contribution of pollinator-mediated crops to nutrients in the human food supply. *PLoS ONE* **2011**, *6*, e21363. [[CrossRef](#)]
58. Gallai, N.; Salles, J.M.; Settele, J.; Vaissiere, B.E. Economic valuation of the vulnerability of world agriculture confronted with pollinator decline. *Ecol. Econom.* **2009**, *68*, 810–821. [[CrossRef](#)]
59. Das, A.; Sau, S.; Pandit, M.K.; Saha, K. A review on: Importance of pollinators in fruit and vegetable production and their collateral jeopardy from agro-chemicals. *J. Entomol. Zool. Stud.* **2018**, *6*, 1586–1591.
60. Mason-D’Croz, D.; Bogard, J.R.; Sulser, T.B.; Cenacchi, N.; Dunston, S.; Herrero, M.; Wiebe, K. Gaps between fruit and vegetable production, demand, and recommended consumption at global and national levels: An integrated modelling study. *Lancet Planet. Health* **2019**, *3*, e318–e329. [[CrossRef](#)]
61. Aizen, M.A.; Aguiar, S.; Biesmeijer, J.C.; Garibaldi, L.A.; Inouye, D.W.; Jung, C.; Martins, D.J.; Medel Medel, R.; Morales, C.L.; Ngo, H.; et al. Global agricultural productivity is threatened by increasing pollinator dependence without a parallel increase in crop diversification. *Glob. Chang. Biol.* **2019**, *25*, 3516–3527. [[CrossRef](#)]
62. Wenzel, A.; Grass, I.; Belavadi, V.V.; Tschardtke, T. How urbanization is driving pollinator diversity and pollination—A systematic review. *Biol. Conserv.* **2020**, *241*, 108321. [[CrossRef](#)]
63. Ropars, L.; Dajoz, I.; Fontaine, C.; Muratet, A.; Geslin, B. Wild pollinator activity negatively related to honey bee colony densities in urban context. *PLoS ONE* **2019**, *14*, e0222316. [[CrossRef](#)] [[PubMed](#)]
64. Di Pasquale, G.; Salignon, M.; Le Conte, Y.; Belzunces, L.P.; Decourtye, A.; Kretzschmar, A.; Suchail, S.; Brunet, J.-L.; Alaux, C. Influence of pollen nutrition on honey bee health: Do pollen quality and diversity matter? *PLoS ONE* **2013**, *8*, e72016. [[CrossRef](#)]
65. Härtel, S.; Steffan-Dewenter, I. Ecology: Honey bee foraging in human-modified landscapes. *Curr. Biol.* **2014**, *24*, R524–R526. [[CrossRef](#)] [[PubMed](#)]
66. Fijen, T.P.; Scheper, J.A.; Boom, T.M.; Janssen, N.; Raemakers, I.; Kleijn, D. Insect pollination is at least as important for marketable crop yield as plant quality in a seed crop. *Ecol. Lett.* **2018**, *21*, 1704–1713. [[CrossRef](#)] [[PubMed](#)]
67. Marini, L.; Tamburini, G.; Petrucco-Toffolo, E.; Lindström, S.A.; Zanetti, F.; Mosca, G.; Bommarco, R. Crop management modifies the benefits of insect pollination in oilseed rape. *Agric. Ecosyst. Environ.* **2015**, *207*, 61–66. [[CrossRef](#)]
68. Ollerton, J.; Winfree, R.; Tarrant, S. How many flowering plants are pollinated by animals? *Oikos* **2011**, *120*, 321–326. [[CrossRef](#)]
69. Donaldson, J.; Nanni, I.; Zachariades, C.; Kemper, J. Effects of habitat fragmentation on pollinator diversity and plant reproductive success in *Renosterveld shrublands* of South Africa. *Conserv. Biol.* **2002**, *16*, 1267–1276. [[CrossRef](#)]
70. Ashman, T.L.; Knight, T.M.; Steets, J.A.; Amarasekare, P.; Burd, M.; Campbell, D.R.; Dudash, M.R.; Johnston, M.O.; Mazer, S.J.; Mitchell, R.J.; et al. Pollen limitation of plant reproduction: Ecological and evolutionary causes and consequences. *Ecology* **2004**, *85*, 2408–2421. [[CrossRef](#)]
71. Aguilar, R.; Ashworth, L.; Galetto, L.; Aizen, M. Plant reproductive susceptibility to habitat fragmentation: Review and synthesis through a meta-analysis. *Ecol. Lett.* **2006**, *9*, 968–980. [[CrossRef](#)]
72. Alaux, C.; Allier, F.; Decourtye, A.; Odoux, J.F.; Tamic, T.; Chabirand, M.; Delestra, E.; Decugis, F.; Le Conte, Y.; Henry, M. A Landscape physiology approach for assessing bee health highlights the benefits of floral landscape enrichment and semi-natural habitats. *Sci. Rep.* **2017**, *7*, 40568. [[CrossRef](#)]
73. Memmott, J.; Waser, N.M.; Price, M.V. Tolerance of pollination networks to species extinctions. *Proc. R. Soc. Lond. B Biol. Sci.* **2004**, *271*, 2605–2611. [[CrossRef](#)] [[PubMed](#)]
74. De Gara, L.; Locato, V.; Dipierro, S.; De Pinto, M.C. Redox homeostasis in plants. The challenge of living with endogenous oxygen production. *Respir. Physiol. Neurobiol.* **2010**, *173*, S13–S19. [[CrossRef](#)]
75. Tabacchi, E.; Lambs, L.; Guilloy, H.; Planty-Tabacchi, A.M.; Muller, E.; Decamps, H. Impacts of riparian vegetation on hydrological processes. *Hydrol. Process.* **2000**, *14*, 2959–2976. [[CrossRef](#)]
76. Dawson, T.E.; Burgess, S.S.; Tu, K.P.; Oliveira, R.S.; Santiago, L.S.; Fisher, J.B.; Simonin, K.A.; Ambrose, A.R. Nighttime transpiration in woody plants from contrasting ecosystems. *Tree Physiol.* **2007**, *27*, 561–575. [[CrossRef](#)]

77. Lennartsson, T. Extinction thresholds and disrupted plant–pollinator interactions in fragmented plant populations. *Ecology* **2002**, *83*, 3060–3072.
78. Kaluza, B.F.; Wallace, H.M.; Heard, T.A.; Minden, V.; Klein, A.; Leonhardt, S.D. Social bees are fitter in more biodiverse environments. *Sci. Rep.* **2018**, *8*, 12353. [[CrossRef](#)]
79. Potts, S.G.; Imperatriz-Fonseca, V.; Ngo, H.T.; Aizen, M.A.; Biesmeijer, J.C.; Breeze, T.D.; Dicks, L.V.; Garibaldi, L.A.; Hill, R.; Settele, J.; et al. Safeguarding pollinators and their values to human well-being. *Nature* **2016**, *540*, 220–229. [[CrossRef](#)] [[PubMed](#)]
80. Goulson, D. Effects of introduced bees on native ecosystems. *Annu. Rev. Ecol. Evol. Syst.* **2003**, *34*, 1–26. [[CrossRef](#)]
81. Landry, C.L. Pollinator-mediated competition between two co-flowering Neotropical mangrove species, *Avicennia germinans* (Avicenniaceae) and *Laguncularia racemosa* (Combretaceae). *Ann. Bot.* **2013**, *111*, 207–214. [[CrossRef](#)]
82. Sahinler, N.; Kaftanoglu, O. Natural product propolis: Chemical composition. *Nat. Prod. Res.* **2005**, *19*, 183–188. [[CrossRef](#)]
83. El Sohaimy, S.A.; Masry, S.H.D.; Shehata, M.G. Physicochemical characteristics of honey from different origins. *Ann. Agric. Sci.* **2015**, *60*, 279–287. [[CrossRef](#)]
84. Mandal, M.D.; Mandal, S. Honey: Its medicinal property and antibacterial activity. *Asian Pac. J. Trop. Biomed.* **2011**, *1*, 154–160. [[CrossRef](#)]
85. Minden-Birkenmaier, B.A.; Bowlin, G.L. Honey-Based Templates in Wound Healing and Tissue Engineering. *Bioengineering* **2018**, *5*, 46. [[CrossRef](#)]
86. Nolan, V.C.; Harrison, J.; Cox, J.A.G. Dissecting the Antimicrobial Composition of Honey. *Antibiotics* **2019**, *8*, 251. [[CrossRef](#)]
87. Majtan, J.; Bohova, J.; Prochazka, E.; Klaudiny, J. Methylglyoxal may affect hydrogen peroxide accumulation in manuka honey through the inhibition of glucose oxidase. *J. Med. Food.* **2014**, *17*, 290–293. [[CrossRef](#)]
88. Bucekova, M.; Buriova, M.; Pekarik, L.; Majtan, V.; Majtan, J. Phytochemicals-mediated production of hydrogen peroxide is crucial for high antibacterial activity of honeydew honey. *Sci. Rep.* **2018**, *8*, 9061. [[CrossRef](#)]
89. Morroni, G.; Alvarez-Suarez, J.M.; Brenciani, A.; Simoni, S.; Fioriti, S.; Pugnali, A.; Giampieri, F.; Mazzoni, L.; Gasparrini, M.; Marini, E.; et al. Comparison of the Antimicrobial Activities of Four Honeys From Three Countries (New Zealand, Cuba, and Kenya). *Front. Microbiol.* **2018**, *9*, 1378. [[CrossRef](#)]
90. Wasihun, A.G.; Kasa, B.G. Evaluation of antibacterial activity of honey against multidrug resistant bacteria in Ayder Referral and Teaching Hospital, Northern Ethiopia. *SpringerPlus* **2016**, *5*, 842. [[CrossRef](#)]
91. Wijesinghe, M.; Weatherall, M.; Perrin, K.; Beasley, R. Honey in the treatment of burns: A systematic review and meta-analysis of its efficacy. *N. Z. Med. J.* **2009**, *122*, 47–60. [[PubMed](#)]
92. Mattila, H.R.; Rios, D.; Walker-Sperling, V.E.; Roeselers, G.; Newton, I.L. Characterization of the active microbiotas associated with honey bees reveals healthier and broader communities when colonies are genetically diverse. *PLoS ONE* **2012**, *7*, e32962. [[CrossRef](#)]
93. Kaškonienė, V.; Adaškevičiūtė, V.; Kaškonas, P.; Mickienė, R.; Maruška, A. Antimicrobial and antioxidant activities of natural and fermented bee pollen. *Food Biosci.* **2020**, *34*, 100532. [[CrossRef](#)]
94. Bridi, R.; Atala, E.; Pizarro, P.N.; Montenegro, G. Honeybee pollen load: Phenolic composition and antimicrobial activity and antioxidant capacity. *J. Nat. Prod.* **2019**, *82*, 559–565. [[CrossRef](#)] [[PubMed](#)]
95. Wagh, V.D.; Borkar, R.D. Indian propolis: A potential natural antimicrobial and antifungal agent. *Int. J. Pharm. Pharm. Sci.* **2012**, *4*, 12–17.
96. Viuda-Martos, M.; Ruiz-Navajas, Y.; Fernández-López, J.; Pérez-Álvarez, J.A. Functional properties of honey, propolis, and royal jelly. *J. Food Sci.* **2008**, *73*, R117–R124. [[CrossRef](#)]
97. Bankova, V.; Bertelli, D.; Borba, R.; Conti, B.J.; Da Silva Cunha, I.B.; Danert, C.; Eberlin, M.N.; Falcão, S.I.; Isla, M.I.; Moreno, M.I.N.; et al. Standard methods for *Apis mellifera* propolis research. *J. Apic. Res.* **2019**, *58*, 1–49. [[CrossRef](#)]
98. Silva-Carvalho, R.; Baltazar, F.; Almeida-Aguiar, C. Propolis: A complex natural product with a plethora of biological activities that can be explored for drug development. *Evid. Based Complement. Alternat. Med.* **2015**, *2015*, 206439. [[CrossRef](#)]
99. Kunugi, H.; Mohammed, A.A. Royal jelly and its components promote healthy aging and longevity: From animal models to humans. *Int. J. Mol. Sci.* **2019**, *20*, 4662. [[CrossRef](#)]

100. Fujita, T.; Kozuka-Hata, H.; Ao-Kondo, H.; Kunieda, T.; Oyama, M.; Kubo, T. Proteomic analysis of the royal jelly and characterization of the functions of its derivation glands in the honeybee. *Proteome Res.* **2013**, *12*, 404–411. [[CrossRef](#)]
101. Wehbe, R.; Frangieh, J.; Rima, M.; El Obeid, D.; Sabatier, J.M.; Fajloun, Z. Bee Venom: Overview of Main Compounds and Bioactivities for Therapeutic Interests. *Molecules* **2019**, *24*, 2997. [[CrossRef](#)]
102. Baek, H.; Lee, C.; Choi, D.B.; Kim, N.-S.; Kim, Y.-S.; Ye, Y.J.; Kim, Y.-S.; Kim, J.S.; Shim, I.; Bae, H. Bee venom phospholipase A2 ameliorates Alzheimer's disease pathology in A β vaccination treatment without inducing neuro-inflammation in a 3xTg-AD mouse model. *Sci. Rep.* **2018**, *8*, 17369. [[CrossRef](#)]
103. Awad, K.; Abushouk, A.I.; AbdelKarim, A.H.; Mohammed, M.; Negida, A.; Shalash, A.S. Bee venom for the treatment of Parkinson's disease: How far is it possible? *Biomed. Pharmacother.* **2017**, *91*, 295–302. [[CrossRef](#)] [[PubMed](#)]
104. Jung, G.B.; Huh, J.E.; Lee, H.J.; Kim, D.; Lee, G.J.; Park, H.K.; Lee, J.D. Anti-cancer effect of bee venom on human MDA-MB-231 breast cancer cells using Raman spectroscopy. *Biomed. Opt. Express* **2018**, *9*, 5703–5718. [[CrossRef](#)] [[PubMed](#)]
105. Rady, I.; Siddiqui, I.A.; Rady, M.; Mukhtar, H. Melittin, a major peptide component of bee venom, and its conjugates in cancer therapy. *Cancer Lett.* **2017**, *402*, 16–31. [[CrossRef](#)]
106. Kieliszek, M.; Piwowarek, K.; Kot, A.M.; Błażej, S.; Chlebowska-Śmigiel, A.; Wolska, I. Pollen and bee bread as new health-oriented products: A review. *Trends. Food. Sci. Technol.* **2018**, *71*, 170–180. [[CrossRef](#)]
107. Bakour, M.; Fernandes, Â.; Barros, L.; Sokovic, M.; Ferreira, I.C. Bee bread as a functional product: Chemical composition and bioactive properties. *LWT* **2019**, *109*, 276–282. [[CrossRef](#)]
108. Bakour, M.; Al-Waili, N.S.; El Meniy, N.; Imtara, H.; Figuera, A.C.; Al-Waili, T.; Lyoussi, B. Antioxidant activity and protective effect of bee bread (honey and pollen) in aluminum-induced anemia, elevation of inflammatory makers and hepato-renal toxicity. *J. Food Sci. Technol.* **2017**, *54*, 4205–4212. [[CrossRef](#)] [[PubMed](#)]
109. Disayathanoowat, T.; Li, H.; Supapimon, N.; Suwannarach, N.; Lumyong, S.; Chantawannakul, P.; Guo, J. Different Dynamics of Bacterial and Fungal Communities in Hive-Stored Bee Bread and Their Possible Roles: A Case Study from Two Commercial Honey Bees in China. *Microorganisms* **2020**, *8*, 264. [[CrossRef](#)]
110. Urcan, A.; Criste, A.; Dezmirean, D.; Bobiş, O.; Mărghitaş, L.; Mărgăoan, R.; Hrinca, A. Antimicrobial Activity of Bee Bread Extracts Against Different Bacterial Strains. Bulletin of University of Agricultural Sciences and Veterinary Medicine Cluj-Napoca. *Anim. Sci. Biotechnol.* **2018**, *75*, 85–91.
111. Sánchez-Bayo, F.; Goulson, D.; Pennacchio, F.; Nazzi, F.; Goka, K.; Desneux, N. Are bee diseases linked to pesticides?—A brief review. *Environ. Int.* **2016**, *89–90*, 7–11. [[CrossRef](#)]
112. Simone-Finstrom, M.; Borba, R.S.; Wilson, M.; Spivak, M. Propolis Counteracts Some Threats to Honey Bee Health. *Insects* **2017**, *8*, 46. [[CrossRef](#)]
113. Mahmoodzadeh Hosseini, H.; Hamzeh Pour, S.; Amani, J.; Jabbarzadeh, S.; Hosseinabadi, M.; Mirhosseini, S.A. The effect of Propolis on inhibition of *Aspergillus parasiticus* growth, aflatoxin production and expression of aflatoxin biosynthesis pathway genes. *J. Environ. Health Sci. Eng.* **2020**, *18*, 297–302. [[CrossRef](#)]
114. Colwell, M.J.; Williams, G.R.; Evans, R.C.; Shutler, D. Honey bee-collected pollen in agro-ecosystems reveals diet diversity, diet quality, and pesticide exposure. *Ecol. Evol.* **2017**, *7*, 7243–7253. [[CrossRef](#)] [[PubMed](#)]
115. Erler, S.; Moritz, R.F. Pharmacophagy and pharmacophory: Mechanisms of self-medication and disease prevention in the honeybee colony (*Apis mellifera*). *Apidologie* **2016**, *47*, 389–411. [[CrossRef](#)]
116. 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](#)]
117. Chaplin-Kramer, R.; Dombek, E.; Gerber, J.; Knuth, K.A.; Mueller, N.D.; Mueller, M.; Ziv, G.; Klein, A.M. Global malnutrition overlaps with pollinator-dependent micronutrient production. *Proc. Biol. Sci.* **2014**, *281*, 20141799. [[CrossRef](#)]
118. Lim, S.S.; Vos, T.; Flaxman, A.D.; Danaei, G.; Shibuya, K.; Adair-Rohani, H.; Amann, M.; Anderson, H.R.; Andrews, K.G.; Aryee, M.; et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: A systematic analysis for the Global Burden of Disease Study 2010. *Lancet* **2012**, *380*, 2224–2260. [[CrossRef](#)]
119. Ellis, A.M.; Myers, S.S.; Ricketts, T.H. Do pollinators contribute to nutritional health? *PLoS ONE* **2015**, *10*, e114805. [[CrossRef](#)]
120. Nicole, W. Pollinator power: Nutrition security benefits of an ecosystem service. *Environ. Health Perspect.* **2015**, *123*, A210–A215. [[CrossRef](#)]

121. Pinke, M. How far is world agricultural production likely to be threatened by pollinator declines? *J. Sustain.* **2013**, *1*, 1–9.
122. Poletti, S.; Gruissem, W.; Sautter, C. The nutritional fortification of cereals. *Curr. Opin. Biotech.* **2004**, *15*, 162–165. [[CrossRef](#)]



© 2020 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<http://creativecommons.org/licenses/by/4.0/>).