Review

Potential Existence of Heavy Metal Pollution and Pesticide in Honey-based Products

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Simple Summary: Honey bees provide nutritious honey that helps in maintaining our good health. Besides honey, honey bees also produce several honey-based products such as pollen, beeswax, beebread and propolis. Honey bees also help humans in agriculture field because they are an excellent pollinator for plants. Honey contains approximately 45 minerals in general. Some of them are useful when used in the proper dosage, while others can cause serious toxicity in humans. This toxicity can happen if the honey is exposed to heavy metals pollution. Anthropogenic pollution, such as industrial and agricultural wastes is the factor that causes toxic effects to bees and their products. Therefore, the aim of this paper is to review the potential existence of heavy metal pollution as well as pesticide in honey-based products from the available literature. However, to not endanger consumers, more detailed studies are needed to maintain the quality of bee products so that the nutrients contained in the products are unperturbed.

Abstract: Over the centuries, honey is known for its superior usage in culinary, and for its rich nutrition and therapeutic values which are scientifically proven in the medical field. The chemical composition of honey varies depending on its botanical sources and environment. Therefore, the nutrition content in honey is highly likely to be affected by contaminants, such as heavy metals and pesticides. To ensure the quality of honey, parameters such as the heavy metal content should be within the safe range of total standard mineral and trace elements as defined by the International Food Standard (Codex Alimentarius), and pesticides should not be present at all. The high concentration of heavy metal and pesticides not only deteriorates the quality and quantity of honey, but also causes harm to the bee colony itself. In the agriculture sector, the excessive usage of pesticides and fertilizer negatively impacts the overall honey production process. Bees, a pollinating agent, bring the polluted nectar back to their beehives, eventually contaminating the honey and depreciating its value. Hence, this article will comprehensively review the activities that contribute to heavy metal and pesticide contamination, the interactions of bees as a pollinating agent, the impact of the pollutant to the colonies, and subsequently to the honey production.

Keywords: heavy metal; pesticides; honey bee; trace elements

1. Introduction

Since time immemorial, honey was widely used not only as a natural sweetener but also traditionally utilised as a remedy for diseases like stomach-ache, cough, and disinfectant [1]. In terms of modern medicine, it has been confirmed that the existence of several compounds and elements in honey are capable of treating many other diseases like asthma, wound, neurological diseases, diabetes, cardiovascular diseases, gastrointestinal problems and cancer [1; 2; 3]. Moreover, previous studies have proved that honey has its virucidal effect on enveloped viruses like HIV, herpes simplex, influenza virus, and varicella-zoster virus [4; 5; 6] and the current study shows that honey can treat novel coronavirus (COVID-19) and reduce the severity of pulmonary inflammation for COVID-19 patients [7; 8].

Bees produce nutritious honey that is beneficial to the human body by supplying various nutrients needed in the body's metabolism, strengthening the body's immunity, and helps in production of antibodies. Honey is rich in antioxidants that help maintain cell function and cell activity [9]. Antioxidants plays an important role in repairing and stabilizing chemical bonds by releasing electrons to free radicals. In addition, the phytochemical compounds present in honey also has medicinal properties that can act as anti-microbial, anti-parasitic, anti-diabetic (which helps reduce glucose in the blood), anti-inflammatory, wound healing agent, anti-cancer, and can also prevent cardiovascular diseases [2; 10]. Honey is also often used in cosmetics and skincare products because the nutrients found in honey may help repair the skin barrier structure and inhibit the formation of excessive oxidative stress. Usually, honey and beeswax are two bee products used in the beauty industry in the skin and cosmetics products as toners and softeners to treat skin tissues, facial cleansers, facial scrubs, and masks. [10;11]. Besides that, propolis is one of the honey products studied by many scientists due to its active compounds. This is because propolis has pharmacological properties, such as anti-hepatotoxic, anti-tumor, anti-oxidative, anti-microbial, and anti-inflammatory.

Besides nutritious honey, bees help in forest sustainability through environmental conservation by pollination activities, which also helps the agricultural sector to increase agricultural products that can contribute to ecotourism development [12] and maintain the ecosystem. They can carry many pollen grains on their hairy bodies and rely on flowering plant species that make bees effective pollinators even though bees are not the most diverse group of pollinators [13]. Bees are included in the social group of Hymenoptera insects. In Malaysia, there are several types of bee species that catch the attention of beekeepers or producers in honey production. They belong to the genus Apis spp, such as *A. dorsata*, *A. mellifera*, and *A. cerana*, which were known as honey bees. At the same time, the stingless bee from the tribe Meliponin also increased in terms of sales popularity.

The bioactive compounds, minerals and trace elements that constitute honey products can be contaminated by heavy metals occurring in the environment, directly affecting the quality of bee products. Heavy metals contamination may disrupt the activity of the bee colony. Thus, bees can be used as a subject for various studies related to the environment, and considered as an ideal bioindicator to determine the level of environmental quality.

2. The importance of chemical elements in the human body

In general, the human body has at least 60 chemical elements. Nevertheless, only 25 of them play an important role in human health [14,15]. These chemical elements can be classified into three groups based on the body's needs: macroelements, trace elements, and ultra-trace elements. Macroelements or also known as macrominerals are needed in large quantities while elements required in small quantities are known as microminerals. Excess intake of microminerals may be toxic to the human body. Other than that, there are also unnecessary elements which are toxic and unbeneficial to humans. Table 1 shows the concentration of elements required in the human body.

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Table 1. The concentration of mineral required in the human body.

Mineral	Elements	The concentration required by human body per day
Major elements	Sodium, potassium, calcium, magnesium, phosphorus, chlorine	>50 mg/day
Trace elements	Iron, iodin, fluorine, zinc, selenium, copper, manganese, chromium, molybdenum, cobalt and nickel	<50 mg/day
Ultra-trace elements	Aluminum, arsenic, barium, bismuth, boron, bromine, cadmium, lithium, cesium, germanium, mercury, lead, tin, samarium, rubidium, antimony, silicon, strontium, thallium, titanium, tungsten	< 1μg/day

Trace elements are needed as catalysts in enzyme systems. Some of metal ions like iron and copper are involved in oxidation-reduction reactions in energy metabolism. For example, iron constitutes haemoglobin and myoglobin that are critical in oxygen transport. In comparison, copper is required to carry out biochemical and physiological functions. Copper has unique abilities in several different redox reactions, such as oxidation (Cu^{2+}) and reduction (Cu^{+}). Copper also functions as a cofactor in enzyme reaction associated with oxidative stress.

The low copper concentration in the human body can interfere in the biochemical function of the body. In pregnant women, its deficiency can cause neurological and immunological ailment, increased risk of osteoporosis, disruption of melanin synthesis, weak immune system that increases the rate of infection, cardiovascular disease that leads to changes in the cholesterol metabolism, and iron mobilization disturbance; and affect the bone formation during the development of the baby [16,17]. However, an excessive amount of copper in the body can also negatively impact the body, causing severe toxicity at the biomolecular and cellular levels, eventually leading to death. This copper toxicity occurs due to copper contamination in water and food sources [18]. Based on nutrient intake recommendations or RDA (Recommended Dietary Allowance), ultra-trace elements also benefit human health, including iodine, selenium, manganese, molybdenum, chromium, boron, and cobalt.

3. The concentration of elements in honey

By searching for publications on honey published in the last 10 years in PubMed and ScienceDirect database, 45 minerals are found in honey. (Table 2).

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Table 2. Minerals found in honey by countries as searched in PubMed and ScienceDirect database using "trace elements honey" as keywords [19 – 33].

Location	Minerals found in honey
Algeria [19]	K, Mg, Na, Zn, Fe, Mn, Cu, Cr, Ni, Se, As, Pb, Cd, Sb, Ti, V, Co, Hg
Argentina [20]	Br, Ce, Co, Cr, Cs, Eu, Fe, La, Rb, Sb, Sc, Sm, Th, Zn
Australian (*Apis mellifera*) [21]	Co, Cu, Cr, Fe, Mn, Mo, Zn, Ca, K, Mg, Na, P, B, Sr, Ni
Croatia [22]	As, Cu, Cd, Pb, Se, Ca, Fe, K, Mg, Na, Zn, Hg
Egypt [23]	Al, As, B, Ba, Be, Ca, Cd, Co, Cr, Cu, Fe, Hg, Mg, Mn, Mo, Ni, P, Pb, Sb, Si, Ti, Tl, V, Zn
Hungary [24]	Al, Ca, Cu, Fe, K, Mg, Mn, P, S, Zn, As, Cd, Cr, Mo, Pb, Se
Jordanian [25]	Na, K, Mg, Ca, Fe, Ni, Cu, Hg, Pb, Ag
Malaysia [26]	Ca, Mg, Fe, Zn, Na, K, As, Pb, Cd, Cu, Co
New Zealand [27]	K, P, Ca, Cd, Pb, Zn
NS [28]	Ag, Al, As, B, Ba, Be, Ca, Cd, Co, Cr, Cu, Fe, Hg, Mg, Mn, Mo, Ni, Pb, Sb, Se, Si, Ti, Tl, V, Zn
NS [29]	K, Ca, Mg, Na, Fe, Li, Zn
Portugal [30]	Ag, As, Br, Ca, Cl, Cs, Cu, Fe, K, La, Mg, Mn, Na, Rb, Sb, Sc, U, V and Zn
Poland [31]	Al, B, Ba, Ca,Cd, Cr, Cu, K, Mg, Mn, Na, Ni, Pb, Sr, Zn
Turkey [32]	Al, Ba, Ca, Cd, Cr, Co, Fe, Cu, K, Mg, Mn, Ni, Na, Pb, Sr,Ag, Bi, Ga, In, Li, Ti, Zn
Turkey [33]	K, Na, Ca, Fe, Zn, Cd, Cu, Mn, Pb, Ni, Cr, Al, Se

Note: NS=Not state.

Trace elements found in honey determine the level of honey quality. Based on the study by Bogdanove et al. [34], minerals content in honey vary with the estimated range of 0.04% (for pale yellowish honey) to 0.20% (for dark-colored honey). The trace elements content in honey is used as the standards to ensure that the honey is safe to be consumed and absorbed by the human body. The ash content is a parameter used to determine the number of minerals present in honey. Referring to the Codex Alimentarius (International Food Standard), the ash content in honey should not be more than 0.6%. The major mineral content in honey is commonly obtained from soil and nectar-producing plants, such as fruit trees and flowering plants. The content of minerals and heavy metals is also influenced by the environment, geographic area, and anthropogenic factors [35,36].

Mineral elements, such as K, Na, Ca, Fe, Zn, Cd, Cu, Mn, Pb, Ni, Cr, Al, and Se may be present in unifloral honey and polyfloral honey, and it has become the objective of the researchers to study the level of these elements. In order to determine their concentration in honey samples, instruments like the Plasma Coupling Induced Mass Spectrometer (ICP-MS) [30] or the Plasma Coupling Induced-Optical Emission Spectrometer (ICP-OES) will be used to analyzed them. The most abundant elements found in bee honey and kelulut honey were K, Na, Ca and Mg [37 – 40]. Table 3 shows the concentrations of the elements analyzed through laboratory studies in different countries.

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Table 3. Elements and their concentration in honey by location based on four different studies [34, 38, 40, 41].

Elements	Concentration	Location
Potassium (K)	880.73 mg/kg	Malaysia
	761.22 mg/kg	Malaysia
Iron (Fe)	35.6 µg/l	Switzerland
	10.26 mg/kg	Thailand
	781 mg/kg	Malaysia
Sodium (Na)	589.46 mg/kg	Malaysia
Calcium (Ca)	292.67 mg/kg	Malaysia
	205.98 mg/kg	Malaysia
Magnesium (Mg)	41.06 mg/kg	Malaysia
Chromium (Cr)	36.2 µg/l	Switzerland
	0.489 mg/kg	Thailand
Zinc (Zn)	54.5 µg/l	Switzerland
	4.37 mg/kg	Malaysia
	9.461 mg/kg	Thailand
	3.03 mg/kg	Malaysia
Mangan (Mn)	123.0 µg/l	Switzerland
	8.16 mg/kg	Thailand
Copper (Cu)	88.8 µg/l	Switzerland
	2.482 mg/kg	Thailand
Lead (Pb)	28.5 µg/l	Switzerland
Nickel (Ni)	27.3 µg/l	Switzerland
Cadmium (Cd)	23.7 µg/l	Switzerland

4. Sources of heavy metal pollution

Heavy metals and metalloids in the soil can occur naturally or by pollution activities. Anthropogenic pollutions, such as industrial and agricultural wastes may produce lethal and sublethal toxic effects on bees [42]. Consequently, bees can act as bioindicator or biosensor agents that can detect polluted area due to the presence of high heavy metals concentration (Figure 2).

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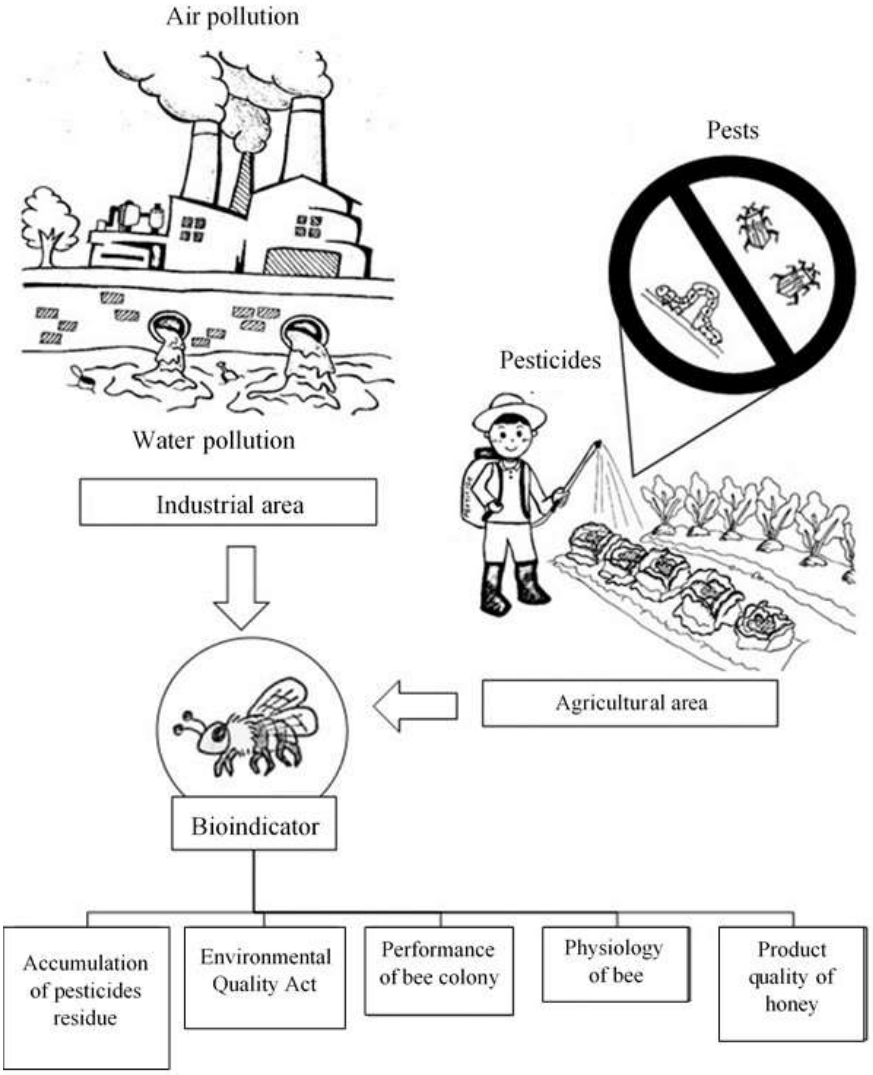

Figure 2. Heavy metals discharged from industrial and agricultural wastes are highly toxic, polluting the environment when they accumulate in high concentration. Bees act as bioindicators through the abnormalities in their performance colony, physiology changes and the quality honey products.

The industries that can lead to heavy metals pollution are the mining and ore processing industry, metallurgy and plating, chemicals industry, dye and pigment industry and petroleum refinery [43]. Besides that, heavy metals also occur due to soil erosion, industrial effluent discharge, sewage disposal and pesticide usage in agriculture either through the air, water and soil [44]. The heavy metals released such as As, Cd, Hg, Pb, Cr, Cu, Ni and Zn can jeopardize human health as well as animal habitats [45]. According to Kováčik et al. [46], there are carcinogenic and cytotoxic elements like Pb, Cd, Ni and Cr found in honey at high concentrations, especially those located close to the industrial and urban areas.

4.1. The exposure of agrochemical to bees

Agrochemical is a chemical used in agriculture, such as pesticides and fertilizers. Pesticide is used to control the growth of pests while fertilizer supplies nutrients to plants. In general, pesticide is made from chemical compounds used to kill crops-damaging pests, like insects, rodents, and unwanted plants (weeds). However,

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excessive and uncontrolled use of these pesticides will negatively impact non-target organisms and biodiversity. There are various groups of pesticides available in the market, such acaricides, organic acids, insecticides, fungicides, herbicides and bactericides [47]. Each of these pesticides is meant to be effective against specific pests.

Pesticides can be produced from natural or synthetic compounds. Organochlorine, carbamate, organophosphates, pyrethroids and neonicotinoids are types of pesticides widely chosen and used by farmers to protect their crops. Pesticides are volatile and easy to dissolve in water, thus leaching into water sources like rivers, ponds or oceans [48]. If the pesticide has a high solubility in water, it will remain soluble in water and may end up in a nearby stream due to runoff. Other than that, the chemicals released from the pesticides will be absorbed into the soil too. Consequently, it will pollute surface water and groundwater (by leaching process), and impact soil fertility which adversely affects the beneficial soil microorganisms. Soil microorganisms are important to plants because they help in the process of turning the atmospheric nitrogen into nitrate [49].

The effects of using pesticides depend on the types of pesticides used. For example, neonicotinoids can contaminate soil and waterways and attack nontarget crops. The effects may be prolonged because the lifespan of neonicotinoids in the soil can exceed 1000 days, and it potentially accumulates in the soil if used repeatedly [50]. According to Botías et al. [51], the higher residue of neonicotinoid is found in pollen and nectar of wild plants growing around farm areas than that found in farm crops.

Within 10 years (between 2009 and 2019), based on the literature search within ScienceDirect database, the pesticide and toxic elements found in honey across the country showed an increasing trend (Figure 3). Research showing honey contaminated by pesticides was relatively high with 1796 publications while 74 publications showed toxic elements in honey. However, this topic will keep increasing year after year due to urbanization and development in many countries, which eventually requires the production of agricultural products quickly to support their residents. Thus, they will need chemicals to help speed up the rate of production in agriculture, like fertilizers and pesticides.

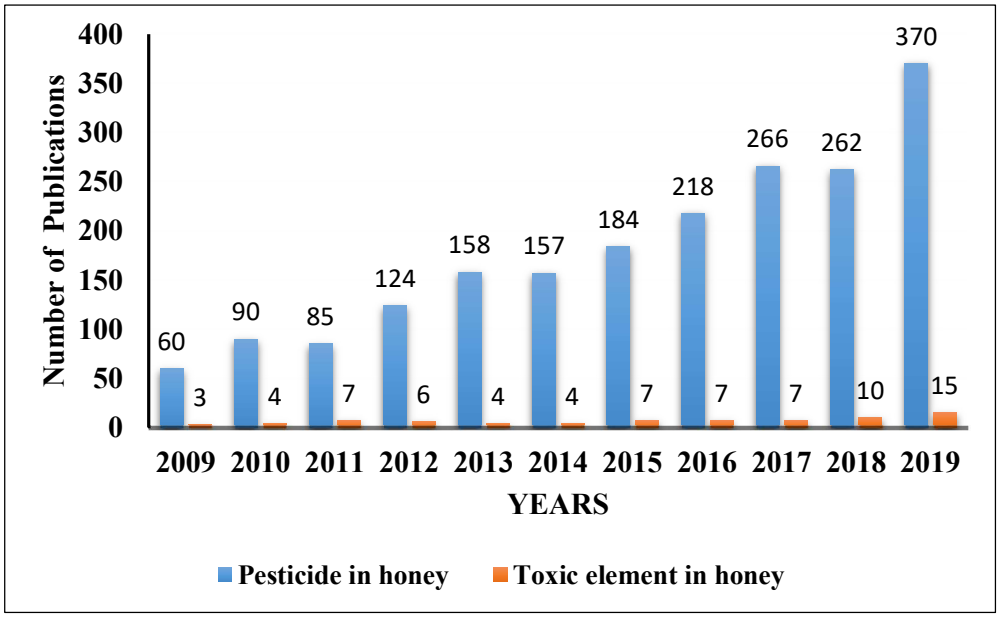

Figure 3. Number of publications in a period of 10 years. Information was taken from the ScienceDirect database using two research queries, "Pesticide in Honey" and "Toxic elements in honey" (Search conducted in June 2020).

Some pesticides are carcinogenic, potentially causing chromosomal abrasions [52], and the pesticide residue can harm humans, leading to genetic mutations and cellular defects [47].

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Table 4. List of types of pesticides that have been identified in honey and pollen products from several locations [53 – 57].

Honey	Location	Type of pesticide
Honey bee	Belgium	Fungicide, pyrimethanil and insecticide detected. [53]
Honey bee	Ghana	Organophosphorus and pyrethroids detected in very low concentration. [54]
Honey bee	Hawaii Island	118 ppb glyphosate in 0.5 g honey [55]
Honey bee	Mexico Southern	Organochlorine has been identified in concentration range between 0.51 to 370.56 ug/kg honey. [56]
Honey bee (pollen)	Poland	Fungicide and prothioconazole were detected where prothioconazale showed high concentration with 356 μg kg^{-1}. [57]

5. The interaction of bees with environment

Bees are important in the agriculture as the most effective pollinating agents. Pollination is the primary key to global biodiversity, providing important ecosystem services to wild crops and plants [58]. Bees are indirectly involved in producing seeds and fruits, and increasing the success rate of reproduction of plants around them. Bees have a high chance of being exposed to heavy metals via water sources, and nectar and pollens accumulated with heavy metals [42].

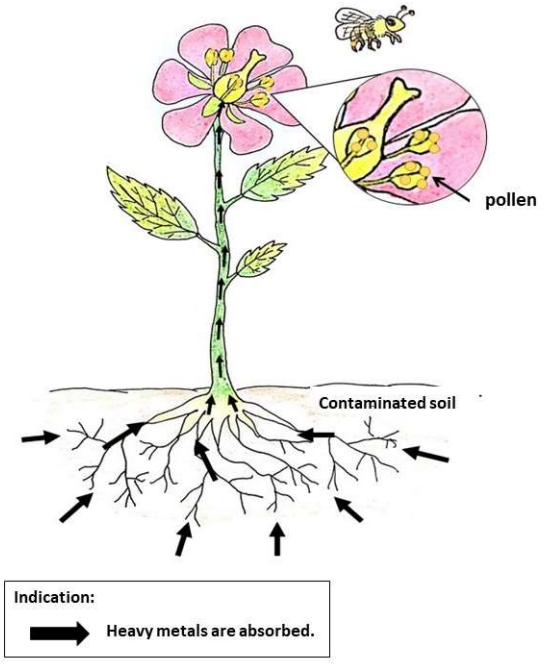

Figure 4. Heavy metals will be actively absorbed by root hairs in the form of dissolved ions from contaminated soil and then transported along with water through the vascular system to the rest of the plant cells. The pollen is easily contaminated by exposure to air pollution that contains heavy metal particles in the air.

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The number of heavy metals contained in a plant will keep increasing as the amount of heavy metals present in the soil increases. Meanwhile, air pollution also pollutes pollen by causing heavy metals like lead present in the air to stick to the pollen. Bees alighting on flowers will collect both contaminated pollen and nectar, and carry them to the hive (Figure 4). However, different plant species have different rates of assimilating heavy metals. Previous studies found that the presence and the accumulation of heavy metals such as Cr, Cd, Pb and Ni in the beehives depend on atmospheric particulate matter, and they caused the death of bee colonies [59,60].

The pesticide residues in pollen, and nectar are also carried by bees to their hive, and these residues will remain in the bee bread and honey for some period before being fed to the larvae and queen [61]. Based on the studies that have been conducted in the U.S, there was pesticide residue present in honey samples collected from 23 states where they used honeybees as a pollinator agent [62]. Moreover, previous research studies have shown that honey, propolis and wax in bees' colonies worldwide contain various toxins, including pesticides, herbicides, and some heavy metals [63].

6. The effect of heavy metals towards bees

Bees can potentially detect some chemical toxins through the receptors on their antenna and proboscis. They also have the ability to recognize harmful substances by the malaise reaction that arises after ingestion, and this can be attributed to the taste of the substance. Then, the bees will avoid it in the future [64]. However, not all toxic compounds can give a malaise effect to bees. It depends on how many bees that have been exposed to them. Moreover, heavy metals like selenium, a toxic metalloid, at high concentrations cannot be detected through the antenna and proboscis of the bees [65].

A high concentration of heavy metals will directly interfere with the bees' nerve pathways. Damaging in bee brains' affect their cognitive capacity lead them fail to navigate properly. The worker bees which cooperate in food collection needs to have a high cognitive capacity in order to allocate the radius of the nectar source, determine the location of high-quality feeding sites, and efficiently navigate back to the brood nest for nectar and pollen reservation [66].

6.1. The effect of pesticide towards bees

Neonicotinoid insecticides, such as imidacloprid, thiacloprid, and guadipyr are popular pesticides used by farmers around the world. These pesticides act systematically and move through plant tissues, and are highly toxic to most arthropod insects. These pesticides affect bee's behaviour, making them abnormal. Previous research studies prove that imidacloprid leads to sublethal damage like cellular damage including severe lesions in the midgut wall [67,68].

Imidacloprid is a systemic insecticide that acts as a neurotoxin to insects, disrupting the central nervous system. It is absorbed by plants, spreading to all tissues including pollen and nectar through the vascular system and indirectly transmitting to the hive during pollen and nectar delivery [68,69]. Imidacloprid negatively affects the development of bee brain as detected through the immunolabelling of the synaptic units of the petals of the corpora pedunculate [67], and increases the mortality of bees [69].

6.2. The effect on bee product

Pollution of heavy metals and pesticides affects bees and bee colonies. It affects the quality of bees' productivity in the hive, such as the production of honey, propolis, beeswax, bee pollen and bee bread. The presence of heavy metals, like Pb, Cd, Cu, Zn, Mn, Hg, As and insecticides, like organochlorine, organophosphates, pyhrethrins and pyrethroids in honey samples have been identified by several studies [70 – 72]. Authors [73-75], detected the presence of heavy metals, such as Cd, Pb, Fe, Mg, Zn and As in samples of propolis, beeswax and bee pollen. Nascimento et al. [76] also detected some

heavy metals present in the pollen stored by the stingless bees that live near mining activities.

Furthermore, there is poison honey produced by bees derived from poisonous plants, resulting in toxicity towards humans. For example, honey produced from the leaves of plants belonging to the family Ericaceae, such as *Rhododendron ponticum* and *Andromeda* contains alkaloids and grayanotoxins that can cause paralysis in human limbs and can lead to death [77]. This occurrence requires more scientific research to prevent these toxic bee honey sales by beekeepers.

7. Conclusion

Bee colonies and bee products are critical as monitoring agents to determine the quality of the environment and thus, identify the environment contaminated with heavy metals and pesticides. However, more detailed studies are needed to maintain the quality of bee products so that the nutrients contained in the products are not affected and a danger to consumers. In addition, a similar study should be developed for stingless bee or kelulut species because kelulut honey is gaining attention not only in Malaysia, but also around the world. Consequently, areas that may be potentially exposed to contaminants should be identified and monitored. Through this monitoring method, the quality of honey-based products will be guaranteed, as well as maintaining the title of Superfood Malaysia, thus helping entrepreneurs generate income and promoting environmental sustainability.

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