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Research Article

Honey Bee Products: Honey And Royal Jelly And Their Nutritional And Medicinal Values To Humans

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ABSTRACT

Being one of the most important insect pollinators, honey bee plays a great role in the livelihood of mankind. It pollinates flowers during foraging and shares a great contribution in agriculture and horticulture towards the yield of fruits and crops. Interestingly, this tiny insect has very sophisticated machines hidden inside its' body that produce honey, royal jelly, wax and propolis etc. Considering the great number of exocrine glands present in their bodies, honey bee body may be considered as a chemical factory. Honey bees produce these products through a sophisticated machinery mechanism involving regurgitation, enzymatic activity and water evaporation. Honey bees prepared these products for various purposes such as to feed queens/workers/drones, making honey combs, hive construction and colony maintenance etc. On the other hand these bee products are highly benefited to human as nutritional food supplements and medicine. This article narrates the summary of honey and royal jelly and their medicinal benefits to human.

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INTRODUCTION

Among the social insects honey bee is one of the most widely studied animals. Their well ordained social features had been the central attraction for several behavioral scientists and neuroscientists. Over the years, study on the dynamic behaviors of honey bees dominated the research on honey bees. In 1973, the Nobel Prize in Physiology or Medicine was awarded to Karl Ritter von Frisch along with Nikolaas Tinbergen and Konrad Lorenz [1-3]. Karl Ritter von Frisch was one of the first persons to translate honey bee waggle dance. With the help of waggle dance foraging bees communicate and share information about the direction and distance to the source of nectar and pollen yielding flowering plants, sources of water, and new nest site locations etc. [4-5]. In the recent years, research in honey bees has been expanding at the cellular and molecular levels for understanding the mechanisms or channels underlying the dymamics of honey behavior which in turn can help better understanding the highly complex sensory and motor neuron circuits of the human brain [6-9]. On the other hand, there is limited data on the scientific understanding and application on the honey bee products such as honey, royal jelly, bee wax and propolis. These naturally available products are results of tireless works of bees in order to supply food for their colony, build the hive and maintain their colony. On the other hand, humans use these products as nutritional supplement and medicines since the ancient times. The current research trends on honey bees also move towards the scientific understanding of bee products as the need arises for more precise understanding in the use of these products. Since these sophisticated products are manufactured inside their tiny bodies, it won't be wrong to state that honey bees have "chemical factories" inside their bodies which present a great number of exocrine glands [10]. More interestingly, bees of different ages are categorically involved with different tasks in making these products. This article intends to bring the summary on upto date research reports available on honey bee products, primarily emphasizing on honey and royal jelly for their common uses by human for nutritional values and medical purposes.

Honey:

Honey is a sticky viscous substance which is sweet in taste and a widely used delicious food ingredient of human. Honey bees prepare honey as their food of the colony using nectar from flowers through a well organized intelligent machinery system and corporation. During foraging, bees extract nectar from flowers and stored it into their honey sac or abdomen which has glandular system containing *invertase* enzymes [11-13]. This enzyme breaks the sucrose present in the nectar into fructose and glucose [14-15]. When the honey sac is filled with nectar, the bees return to the hive and release the nectar to the honey comb cells. Then young bees concentrate nectar removing water from it. This is done using two intelligent laborious methods by the young bees. First, the young bees pass the nectar from bee to bee and 'drink' the water out of the nectar by absorbing it through their stomach wall [14-15]. Secondly, they generate heat and air flow in the hive, vibrating their wings and flight muscles, allowing the nectar in the cells to evaporate [14-15]. After the bees prepared fully matured honey which contain about 17.8% water, the bees stored it by sealing the cells with a thin layer of beewax [15-18]. A sealed honey is not spoiled even after thousands of years as most microorganisms do not grow in honey [11,19-20].

Nutrients present in honey:

Honey primarily contains carbohydrates and traces of vitamins, minerals and antioxidants. The carbohydrates include fructose (38%), glucose (31%), water (17%), maltose (7%), and traces of trisaccharides and sucrose [21-22]. The traces of vitamin include Thiamin, Riboflavin, Niacin, Pantothenic acid, Vitamin B-6, Vitamin B-12, Folate, Vitamin C, Vitamin A, Vitamin D, Vitamin E and Vitamin K. Minerals contain Calcium, Copper, Iron, Magnesium, Manganese, Phosphorous, Potassium, Sodium and Zinc [23]. The

antioxidants are made up of enzymatic (Catalase) and non-enzymatic (ascorbic acid) and flavonoids components [11-12].

Extraction of honey for human use:

On average, a wild or natural beehive may produce about 29 kilograms of honey per year [24]. Long time ago, beekeepers used to crush honeycomb to extract honey [24]. However, the current trend is changed to centrifugal extraction which produces more honey quantity. In this method, beekeepers scratch or slice off a thin layer of wax from the surface of the comb and spin it; by doing this allows honey to be released from the comb by centrifugal force [25]. This procedure maintains the integrity of the comb and the bees have much lesser work to repair any cracks or shallow the spots in the comb. The earlier method yields less amount of honey because the method causes the bees to spend lots of time, labor and resources in making new combs for replacement rather than making more honey. It may be well noted that honeybees consume 7 kilograms of honey in order to prepare 1 kilogram of beeswax [26]. Freshly extracted honey contains traces of wax and the odd bee knee and elbow which can be removed by allowing it to settle in a hanging tank for a day or two, or by pumping the honey through a filter [25].

***Figure 1**: Honey bee Apis mellifera live in the artificial hive: (A) Modern Beehive figure: Three Langstroth hives adjacent to a water source. Figure source By Thomas Zimmermann (THWZ) - Own work, CC BY-SA 3.0 de, https://commons.wikimedia.org/w/index.php?curid=25892624; (B) A comb frame covered with honey bees in the hive: original photograph taken by the authors; (C) Honey bee feeding larvae and larvae floating in jelly- source: Fat Bees – Part 1 by Randy Oliver at ScientificBeekeeping.com available at http://scientificbeekeeping.com/fat-bees-part-1/; (D) Nurse bees consuming pollen (yellow) and beebread (orange) for converting into jelly- source: Fat Bees – Part 1 by Randy Oliver at ScientificBeekeeping.com available at http://scientificbee keeping. com/fat-bees-part-1/.*

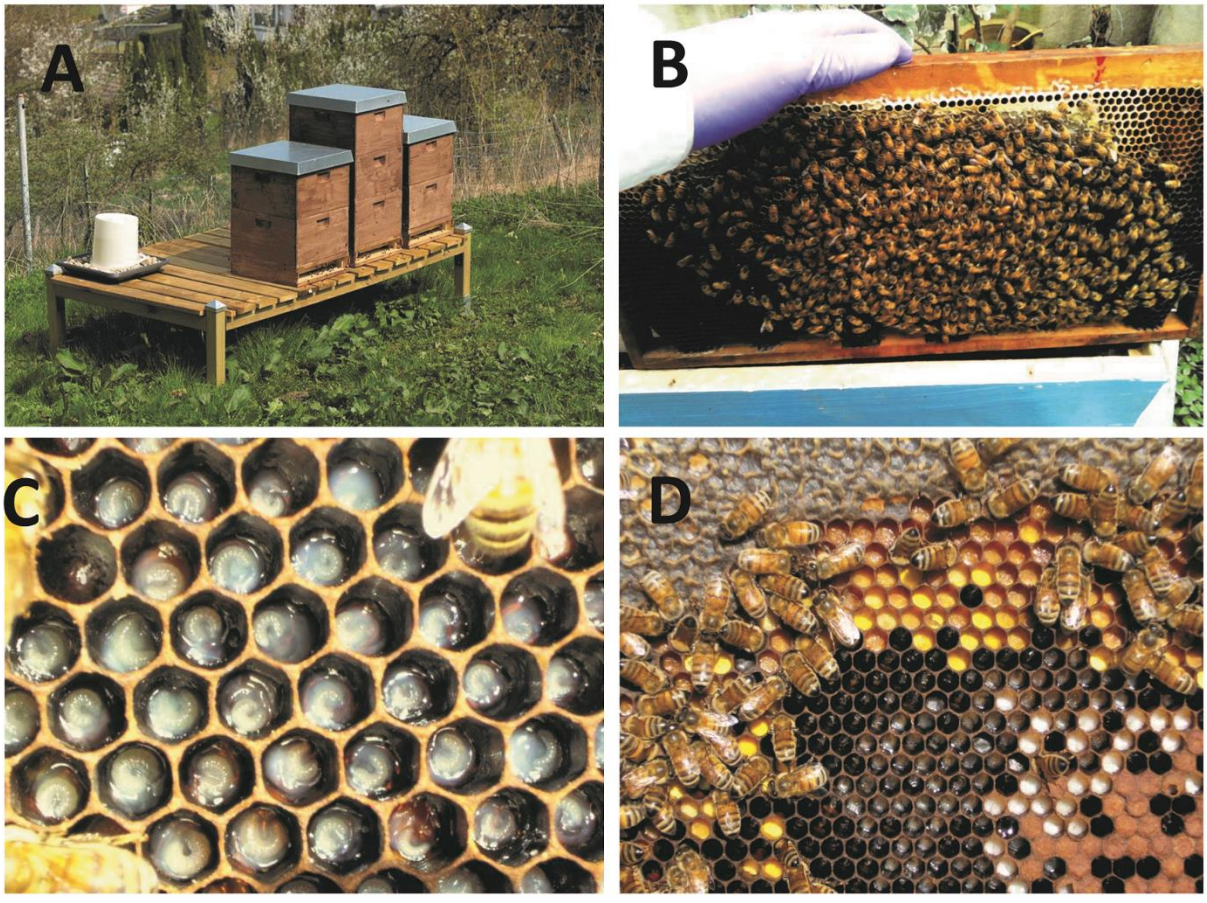

Figure 2: Honey bee Apis mellifera foraging: (A) Honeybee collecting pollen- source: photographed by John Sullivan: http://www.public-domain-image.com/public-domain-images-pictures-free-stock-photos/fauna-animals-public-domain-images-pictures/insects-and-bugs-public-domain-images-pictures/bees-insects-pictures/honeybee-apis-mellifera-bees-collecting-pollen.jpg; (B) Pollen foragers returning to their hive carrying pollen in their pollen bags- source: Fat Bees – Part 1 by Randy Oliver at ScientificBeekeeping.com available at http://scientificbee keeping. com/fat-bees-part-1/; (C) A bee foraging for nectar on rose flower- source: Photo by Dorin Gheorghe published in Sihag RS and Kaur G (2018) Patterns of short-and long-term responses of honey bee (Apis mellifera L.) colony to changes in its internal environment. Journal of Eco and the Nat Envr 10:108-128, DOI: 10.5897/JENE2017.0679. (D) A part of honey comb in showing bees storing nectar/honey in the comb-source: photographed by Apiculteur Miel published in Sihag RS and Kaur G (2018) Patterns of short-and long-term responses of honey bee (Apis mellifera L.) colony to changes in its internal environment. Journal of Eco and the Nat Envr 10:108-128, DOI: 10.5897/JENE2017.0679.

Medicinal benefits of honey:

Antimicrobial, antinflammetory and antioxidant properties of honey has been known since olden days and honey has been used for healing cuts, scapes, burns and even open wounds etc. for centuries [27-29]. During mid 1900 before the development of antibiotics, honey was the primary treatment for wounds in the battlefields [30-31], but declined drastically in the following 50 years, especially in western countries [32-33]. However, the interest of using honey for wound healing has been renewed in the last 20 years concerning of the rapid evolution of various antibiotic resistant strains of antibacteria [34-36]. In treating open wounds, honey helps to reduce inflamation, swelling and pain quickly and to cease unpleasant odours [29]. With honey, wound dressings can be changed without pain and damage to the re-growing tissues leading to minimal scarring and faster healing [27]. Natural honey has been found to have bactericidal activity against more than 60 species of bacteria including *Vibrio cholrae*, *Yersinia enterocolitica*, *Plesiomonas shigelloides*, *Aeromonas hydrophila*,

Salmonella typhi, *Shigella boydi* and *Clostridium jejuni*, *Salmonella*, *Shigella*, *Escherichia coli* and *Helicobacter pylori* etc. [37-43]. It also has been used in treating skin ulcers, chronic leg ulcers and diabetic foot ulcers etc. [29-31,44-45]. Honey prevents growth of bacteria in the wounds and protects the wound from infection [46]. By providing moist, nutrient rich environment to the wound area honey supports the natural process of healing in the body [47]. Some honey types that have been tested include Gelan, Medihoney, Tualang and Manuka honey and they were found to possess similar properties [29,39].

The choice of honey over antibiotics had been reported in many articles. Honey has multiple modes of action to attack bacteria through different routes, unlike the antibiotics which generally have a single mode of action against bacteria [29,37,48-55]. Not only it inhibits wide range of bacterial species, there are multiple properties honey possesses. 1) honey contains sugar more than 80% that leaves few water molecules available for micro-organisms, 2) acidic nature of honey with pH ranges between 3.2 to 4.5 is a intolerable environment for most wound bacteria, 3) glucose oxidase enzyme that enhances reactions for slow release of hydrogen peroxide is present in honey; with the low levels of hydrogen peroxides enables to kill bacteria without damaging body tissues, 4) Particular honey like Manuka honey contains other plant chemicals with anti-microbial properties.

Not all honey have same anti-microbial properties, the effect can vary upto 100 times. Moreover different honeys produced from different nectar sources also have different anti-microbial activities against various strains of wound bacteria [56]. Most extensively studied honey is the Manuka honey, for it revealed highly active antibacterial properties far more than the other honey types. Manuka honey is produced from the nectar of Manuka bush (*Leptospermum scoparium*), a member of the tea tree family commonly found in New Zealand and Australia [53]. This particular antibacterial property of Manuka honey is also called as Unique Manuka Factor (UMF) which is highly stable compared to the hydrogen peroxide antibacterial mode that deteriorates on high temperatures and over the span of 6-12 months. Presently, Manuka honey is the honey of choice for wound care dressings [57]. However, only medical grade honey is recommended for open wounds that ensure the honey has been sterilized and free from active pathogens. This honey is also widely used to assist in the treatment of gastrointestinal problems, such as peptic ulcers believing that the UMF antibacterial activity of the honey works against harmful bacteria in the digestive tract [58-59].

Royal Jelly:

Royal jelly is a white-yellowish gelatinous-viscous substance secreted by the hypopharyngeal and mandibular glands of 5 to 15 days old young nurse honey bees which has slight characteristic smell of phenol that gives its flavour [60-62]. Other names of royal jelly are Bee Saliva, Bee Spit, Gelée Royale, Honey Bee Milk, Honey Bee's Milk, Jalea Real, Lait des Abeilles and Royal Bee Jelly etc. Bees prepare Royal Jelly to feed all the larvae in the bee colony [63]. It is strongly believed that while all the bee larvae are fed with royal jelly, the duration of feeding a female larva with royal Jelly determines the development of the larva into a reproductive queen or a sterile worker. All the female larvae fed with royal jelly for 3 days (form hatching to the third day of life) during their larval development followed by jelly with honey and beebread causes to the development of sterile workers [62, 64-65]. Beebread is a ball or a pellet of flower pollen made by worker bees in which the bee secretions induce a fermentation process that causes biochemical transformations breaking down the walls of flower pollen grains rendering the nutrients more readily available [66]. On the other hand, the female larvae which have been selected to become queens by worker bees are fed with royal jelly until the 5^{th} day of the larval stage and the one that become queen is exclusively fed only with royal jelly throughout her life [64-65]. However, it is not

fully clear whether the different diet exclusively causes in the development of worker bees or queen and how the diet different diet components lead to the differentiation to worker or queen bee. However, it is significant that diet has great impact on the longevity of bee's lives as since the workers that fed with mix diet live about 45 days while the queen fed with only Royal Jelly lives upto 5 years [62]. A report states that Royalactin, a 57-kDa protein present in Royal Jelly induces the differentiation of honeybee larvae into queens [67]. This protein played a role to the increase body size and ovary development and shortened developmental time in honeybees through epidermal growth factor receptor (Egfr) signaling pathway. Royalactin activates p70 S6 kinase leading to body size increase and the increase activity of mitogen-activated protein kinase (MAPK) resulted in the decreased developmental time, and increased the titre of juvenile hormone essential for ovary development [67]. In another invitro experiment, it was also observed that addition of p-coumaric acid in the royal jelly, produced adults with less developed ovary [68]. Further RNA-seq analysis showed that p-coumaric acid which was found to be ubiquitous to honey and beebread differentially regulated the genes involved in caste development [68]. Silencing the DNA methyltransferase Dnmt3 expression (a key driver of epigenetic global reprogramming) in newly hatched larvae led to a royal jelly like effect on larval developmental trajectory [69]. The majority of Dnmt3 small interfering RNA-treated individuals emerged to queens with fully developed ovaries suggesting the role of DNA methylation in storing epigenetic information. Nutritional input can differentially alter the use of this stored information, that would lead to the flexibility of epigenetic modifications underpins, profound shifts in developmental fates with massive implications for reproductive and behavioral status [69]. It was also observed that, upon every feeding since the hatching of larva, the nurse bees first inspected and made sure that the location of the head of the larva before dropping the jelly near the larva [70-72]. This suggests that non-random selection of female larva to nourish and become queen. Moreover, mode of feeding for drone larvae is also different from the worker and queen larvae [70]. To this end the date available is insufficient for understanding the cast differentiation upon feeding and the mysterious behavior of dynamic honey bees remains and much further research is necessary to give clear answers. Nonetheless, even though non random selection of queen larva would be true, base on the above findings, the dietary role to the fate of female larvae into becoming whether to a worker or a queen bee cannot be rule out.

Discovery of Queen Bee **and Royal jelly:**

Jan Swammerdam (1637-1680), a 17th century Dutch naturalist, biologist, entomologist and microscopist who believed his scientific research as a tribute to the Creator was the first scientist to discover the chief of the bee hive to be queen bee (not a king bee) when he found the presence of eggs inside that chief bee's ovary [73-77]. It may be noted that the chief bee in the bee hive was believed to be a male king bee until 17th century [78]. Jan Swammerdam was also the first person to describe nourishment compounds in the royal cell [62] and further into his credit included of being the first person to observe red blood cells under the microscope [79]. However, it was René Antoine Ferchault de Réaumur, a French entomologist and writer (who contributed to many different fields, especially in the study of insects) who first coined the term "Royal Jelly" to this yellowish creamy product of bees and assumed of its exceptional role in the growth of queen [62,80-82]. He also discovered that all the hives have only one queen, even those ones very close to swarming. If introduced other queens, they will be rejected. If a colony is deprived of its queen, the colony must prepare a new queen by feeding royal jelly to a larva otherwise the colony will perish. He further discovered that under certain conditions, a hive without a queen may accept a queen from other colony [80].

Diet components of Royal Jelly:

About 60-70% (w/w) of royal jelly is made up of water and it is acidic in nature with pH ranging from 3.6 to 4.2 [83-84]. Carbohydrates contributes 7.5-15% of royal jelly, of which 90% is made up of fructose and glucose, whereas sucrose contributes 0.8-3.6%; the remaining carbohydrate portion comprises of traces of maltose, trehelose, melibios, ribose and erlose [85]. Lipids contribute 7-18% percent that comprises of short hydroxy fatty acids with 8-12 carbon atoms in the carbon chain and dicarboxylic acids; however 90% of the lipid components present in royal jelly are rare [86]. Royal jelly also contains proteins, vitamins, mineral, flavonoids, polythenols and several other biologically active substances. Notably 50% of dry matter royal jelly is made up of proteins, of which 90% of the protein components consist of Major Royal Jelly Proteins (MJRPs), 49-87 kDa and the rest are glycoproteins, royalisin, elleines and aspimin etc [83,87]. Among the vitamins (A, B1, B2, B5, B6, B8, B12, C and E), B5 is most the abundant one with 52.8 mg/100g [86,88]. Mineral constituents made up of 1.5% of royal jelly which include various elements such as potassium (K), sodium (Na), magnesium (Mg), calcium (Ca), phosphorous (P), sulphur (S), copper (Cu), iron (Fe), zinc (Zn), aluminum (Al), barium (Ba), strontium (Sr), bismuth (Bi), cdmium (Cd), mercury (Hg), lead (Pb), tin (Sn), tellurium (Te), thallium (Tl), tungsten (W), antimony (Sb), chromium (Cr), manganese (Mn), nickel (Ni), titanium (Ti), valium (V), cobalt (Co), and molybdenum (Mo) [83,86]. Flavonoids of royal jelly consists of flavonones (hesperetin, isosakuranetin, and naringenin), flavones (acacetin, apigenin and its glucoside, chrysin, and luteolin glucoside), flavonols (isorhamnetin and kaempferol glucosides) and soflavonoids (coumestrol, formononetin, and genistein) etc. [86,89]. And polyphenols are largely consists of pinobanksin, organic acids such as octanoic acids, dodecanoic acid, 1,2-benzenedicarboxylic acid as well as their esters [86,89]. Biologically active compounds such as acetylcholine, nitrogen bases (adenosine, uridine, guanosine, iridine and cytidine) and phosphates (AMP, ADP, ATP) are also richly present in royal jelly [85,90-91].

Human use of Royal Jelly in olden days:

During ancient days, humans used royal jelly for different purposes without proper scientific knowledge and the idea of specific functions. In Greeks' belief, the nectar is known as "ambrosia" and it gives immortal to the gods of Olympus containing a portion of royal jelly and according to historians, honeycombs shredded with honey, royal jelly, bee larvae, propolis and pollen, were eaten freshly [62,92-93]. Aristotle, the Greek philosopher and polymath who lived during Classical period in Ancient Greece (384–322 BC) was the first person to have discovered the function of Royal Jelly [94-95]. He regarded consumption of royal jelly could increase physical strength and intellectual capacity through the knowledge of the effect of royal jelly to the queen bees,; with this belief, ultimately his school breakfast was exclusively prepared with honey and royal jelly [95-96]. In ancient Egypt, royal jelly was used as cosmetic and moreover at that time it became a symbol of strength majesty of the Pharos [97-98]. In China, Royal jelly has been used as traditional medicine since ancient times and during the ancient dynasties of this country, the royal jelly which was exclusively produced in the sovereign garden was believed to be linked with the increase of sexual intensity and its longevity even at the old age [99-100].

In 1852, Reverend Lorenzo Lorraine first performed the chemical analysis of Royal jelly; however the method he used did not provide significant scientific information [98,101]. It may be noted that Reverend Lorenzo Lorraine was also considered to be the father of American beekeeping and he created modern day bee hive [102]. He further proposed royal jelly to be commercially available in the areas where the honey production was not profitable [74,103]. The use of royal jelly as staple food and health enhancer had been investigated since early 60s with the development of Apitherapy [62]. And the use of Apitherapy both for man and bee itself has been largely continued [74,100].

Medicinal benefits of Royal jelly:

Antibacterial function of royal jelly has been established as early as eight decades ago. In the year 1939, invitro experiments by Mccleskey and Mrlamp demonstrated antibacterial effect of royal jelly against four bacterial strains such as *Staphylococcus aureus*, *Eberthella typkosa (Rawlins strain)*, *Escherichia coli* and *Bacillus metiens* [104]. Their finding showed a greater bacteriostatic effect against the gram-positive *Staphylococcus aureus* and *Bacillus metiens* than the gram-negative *Escherichia coli* and *Eberthella typhosa*; whereas bactericidal effect was found to be the other way round. Further studies also reported antibacterial properties of royal jelly and one of its main fatty acid component 10-HDA (10-hydroxy-2decenoic acid) against several bacterial species that included *Escherichia coli* and *Micrococcus pyogenes* [105-109].

In another experiment by Suemaru et al. (2008) on hamsters with 5-fluorouracil induced oral mucositis showed improved significant recovery from 5-fluorouracil-induced damage in a dose-dependent manner when ointments with 3%, 10% and 30% royal jelly were applied [110]. Some studies have revealed anticancer effect of royal jelly and its major fatty acid component 10-HDA having protective role in therapy induced toxicities in malignancies [111-115]. Oral administration of royal jelly to mice model of breast cancer, prior to tumor cell transplantation, had significant inhibition of tumor growth, however the effect was not detected if the oral administration was performed after tumor cell transplantation to the mice [112]. This indicates the effect of royal jelly as prophylactic agent but not as therapeutic agent. As early as 60 years ago, 10-HDA which is so far not detected in any other natural row material except royal jelly was found to have function against leukemia and ascetic tumors [111,114-115]. In a recent clinical study on patients with malignancies showed protective effect of cisplastin (cis-diamminedichloroplatinum; CDDP) induced neurotoxin to those patients treated with royal jelly, but 40% of the patients showed remarkable reduction in kidney function [116]. However the study was inconclusive as the number of patients examined was too low (n=10). Other compound isolated from royal jelly that has been reported to have antibacterial function is the “royalisin” (5.5-kDa peptide) and this peptide was shown to be effective against *Bacillus sub-tilis* and *Paenibacillus larvae subsp. larvae* [117-118].

A prolong survival capacity was also reported on mice with Ehrlich ascites tumour (EAT) which may be due to preventive role of royal jelly to the myelosupression induced by the temporal evolution of the tumour and abrogation of splenic haematopoiesis in those mice [113]. Subsequently, mice treated with royal jelly were detected with low kidney DNA and serum levels of 8-hydroxy-2-deoxyguanosine which is considered as a marker for oxidative stress that increases with aging [119]. In another study, a long-term intragastric administration of royal jelly and protease treated royal jelly into d-galactose-induced aging mice resulted numerous anti-aging and health span effects such as preventing aging-related weight loss, improving memory and motor performance, and delaying aging-related atrophy of thymus; these effects were related to inhibition of lipid peroxidation and improvement of antioxidant enzymes level [120]. In vitro studies that examined on human cell lines also supported the finding. When photo aging was induced to normal human skin fibroblasts by exposing to ultraviolet-irradiated, then followed by treatment with royal jelly and 10-HAD, resulted protection to the cells against ultraviolet A- and B-induced ROS related oxidative damage, while cellular senescence were decreased and the production of pro collagen type I was stimulated and transforming growth factor-β1 [121-122]. In support to the role of royal jelly in the longevity of survival, it may be reminded that the worker bees which fed on honey and pollen live about 45 days while the queen bee which fed exclusively with royal jelly lived up to 5 years.

DISCUSSION AND CONCLUSION:

Honey bees share an indispensable part of human life since the time immemorial, as they are regarded to be one of the major contributors in crop pollination and humans' use of its products as delicious food ingredients and medicinal purposes. As many as of 20000 species of bees have been reported to exits on earth [123]. However, only eight species have been recognized so far, with which included a total of 43 subspecies; though historically seven to 11 species were recognized [124]. And several unrecognized species are regarded as wild pollinators [125]. While some other types of bees including the stingless bees also produce and store honey and kept by human for its products, only the members of the genus *Apis* are considered as true honey bees. The most domesticated honey bee is the western honey bee *Apis mellifera* and the other one is the eastern honey bee *Apis cerana* which is a native of South Asia. Notably only *Apis mellifera* species has been used extensively for commercial pollination of crops and honey production. The same bee species is used in most researches for understanding bee behavior and its molecular mechanism and for finding nutritious components in the products for food and medicinal remedies. This article has focused only on 'honey' and 'royal jelly'; however other products such as propolis and bee-wax also will be discussed in the near future.

Number of researches has reported that honey consists of least 181 components that include sugars, phenolic acids, flavonoids, glucose oxidase, catalase ascorbic acid, carotinoids, organic acids, amino acids, proteins and α-terpenoids [126-129]. However, the actual compositions may vary depending on pollen source, climate, environmental conditions and the processing methods [127-128]. Royal jelly also includes carbohydrates, lipids, proteins and vitamins but with a large number of bioactive components such as 10-hydroxy decanoic acid, several peptides and proteins (MRJPs-Major royal jelly proteins, Apismin, Royalactina, Roalisin, Jelleines, Glucose oxidase, Apolippophorin III like) [62,118,126,130-132]. Honey and royal jelly may be considered as functional foods because of having naturally high an-tioxidant potential in them [126]. Considering the presence of more bioactive components in royal jelly than honey, it is highly assumable that difference in the dietary mode has a substantial role in the development of queen. Even though both worker and queen have almost identical genes, the female larvae fed with honey and pollen develop into worker bees, whereas the larvae fed exclusively with royal jelly led to the development of queen bee with larger body size, intellectual capacity and reproductively. Taking this to account, the ancient use of royal jelly to gain more physical strength, intellectual capacity and sexual enhancement etc. [74,95-96,99] has valid ideas even though there is no proper scientific explanation, which may be done in the further researches. Even now, due of lack of deeper research the underling mechanisms are not clearly understood and the large amount of explanations are still remains based on the few studies. Much research is required to be tested in regard to the individual and combine effect of those components using invitro and invivo designed experiments, for gaining more scientific understanding in the use of honey and royal jelly by human. Subsequently the few reports on the role of honey and royal jelly on having antibacterial, anticancer properties and in longevity are highly promising. However it needs much more research in order to draw a conclusive remark. There has been suggestions to be cautious while eating honey assuming that possible containing of certain yeast, spore forming bacteria, heavy metals such as Sb, As, Cd(II) and Pb(II) that may cause illness to human at certain conditions [133]. From the reports to date, it is clear that research on honey bee products such as honey and royal jelly is very limited and much further research is required for proper scientific understanding with respect to their medicinal properties for specific treatment and nutritional values to human.

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