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Industrial products of honeybee and their therapeutic effects on human health

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Abstract
Honeybee products have traditionally been used as folk medicine for centuries by ancient nations such as Greeks, Chinese, Romans, Italians, and others. These honeybee products are honey, pollens, propolis, royal jelly, wax and bee venom and they exert incredible and uncountable therapeutic effects on human health such as they have antimicrobial, anti-inflammatory, antioxidative, antiviral, antidiabetic, and neurological properties. These honeybee products are also found to suppress tumor growth and metastasis and hence these are equally efficient in cancer therapy. Pollens are rich in essential amino acids, fatty acids, multiple vitamins (Vitamin A, B, C, D, and E), and protein. Propolis is a natural antibiotic, royal jelly is a food supplement (it improves normal functioning of the brain), whereas bee-wax has potential applications in cosmetic industry where it is used for good-looking and soft, wrinkled-free skin. Bee venom is another industrial product of honeybee and is used for desensitizing the bee sting. Honey is the most important and valued, natural, industrial honeybee product. Naturally, two types of honey are there; first one is produced by honeybees and second one is produced by stingless bees. Both types have distinct chemical composition and physical appearance. Honey is not just taken as nutritional rich product but has its clinical importance. In this literature review, detailed study has been on therapeutic effects of honeybee products such as their efficacies against gastrointestinal disorders, neurological disorders, fertility disorders, cardiac issues, and various others. Traditionally, for centuries, honey has been used to cure eye diseases, infections e.g., throat infection, chest infection, hiccups, hepatitis, constipation, fatigue, thirst, tuberculosis and various other. Honey has important biological components such as flavonoids, phytochemicals, various types of vitamins, trace elements and enzymes paly a role in the treatment of various disorders and unhealthy/uncomfortable conditions. Because of natural therapeutic agent, honey is recommended to be used on daily basis for both healthy, and normal people as well as in hospital wards.

Keywords: honeybee products, therapeutic effects, antioxidants, anti-inflammatory, anti-cancer, royal jelly, propolis, bee-wax, pollens, bee venom

Introduction
Honeybees are playing crucial role to maintain natural balance and in survival of human and other species. Their industrial products, being entirely a natural food source, are being used by humans since long time ago, approximately 5500 years (Adebolu, 2005) [1]. These products are perfect food source for this extravagant increasing population. Honey is the most important industrial product of honeybee along with some other such as wax, propolis, royal jelly pollen and bee venom (worldbeeday.org, 2015) [50]. These products are being used for both nutritional purposes as well as because of their medicinal properties (Adebolu, 2005; Ashrafi, Mastronikolas, & Wu, 2005) [1, 9]. *Apis mellifera* is one of those species (*Apis cerana, Apis floria, Apis andreniformis, Apis dorsata, and Apis koschevnikov*) of honeybees which are involved in the production of honey_ the natural product formed from flowers' nectar (Dashora, Sodde, Bhagat, S Prabhu, & Lobo, 2011) [19].
Being the most important industrial product, honey has nutritional as well as therapeutic and cosmetic values (Bansal, Medhi, & Pandhi, 2005; Mishra, Mishra, & Verma) [11]. There are no special condition required to store honey; it can be stored at room temperature, dry place; there is no need of refrigeration (Babacan & Rand, 2007; Hassapidou, Fotiadou, Maglara, & Papadopoulou, 2006) [10, 34].
Honey is a product that has religious values. '*Madhu Purnima'* is a festival celebrated by Buddhists in which they give honey to monks. This is in the commemoration of the happening when Lord Buddha departed to the jumble due to the dispute among his followers and there a monkey offered him honey (Ediriweera & Premarathna, 2012) [21]. In Hindu religion, honey is considered as elixir (*Panchamruta*). '*Madhu Abhisheka*' is a Hindu custom in which honey is spilled over deities' statues. 'Rosh Hashana'_ A Jews' custom to eat honey-dipped slices of apple to bring sweetness in the coming year. Prophet Muhammad (PBUH) strongly recommended honey for healing Honey is also recommended for healing purposes and as a nutritious and

healthy food in Islam by Prophet Muhammad (PBUH) as well as by Quran (Ediriweera & Premarathna, 2012) [21].

Honey is being extensively used for various purposes and almost 200 different chemical compounds are found in it (Ahmed & Othman, 2013) [2].

The composition of honey relies on the fact that which are those plants honeybee is extracting nectar. However, generally, 80-85% is glucose and fructose, 15-17% is water, 0.2 is ash, protein and amino acids are 0.1-0.4% and there are other trace elements such as enzymes, and vitamins. Among phenolic compounds, caffeic and ellagic acids are prominent. Apigenin, quercetin, hesperetin, galangin, chrysin, and pinocembrin are included among flavonoids that are present in honey. Superoxide dismutase (SOD), ascorbic acid, tocopherol, catalase (CAT) and reduced glutathione (GSH) are antioxidants. These compounds having unique properties act in a synergistic way which brings a broad range of medical applications to honey (Vargas & Maza, 2015) [48]. Physical and chemical properties of honey are greatly affected by the environmental conditions, what type of flora it is, and from where honeybees are taking nectar. Honey produced from sting bee and/or stingless bee is discriminated by applying different methods in a recent study (Vargas & Maza, 2015; Vit, Uddin, Zuccato, Maza, & Schievano, 2015) [48]. And nuclear magnetic resonance was used for the confirmation of commercial honeys.

Properties of honey such as antibacterial, anti-inflammatory, antioxidants, anticancer, antidiabetic, antihyperlipidemic and several other have been confirmed by many studies (O. Erejuwa *et al*., 2010; Kishore, Halim, Syazana, & Sirajudeen, 2011; Viuda-Martos) [24, 38]. Many therapeutic effects such as blood glucose level, cholesterol, blood lipids, triglycerides (TG) and homocysteine level have been investigated by administrating both natural and synthetic honey. Significantly improved consequences have been seen with natural honey like it has lowered risk of cardiovascular diseases (Al-Waili, 2004) [4].

A study by Othman et.al showed that "Tualang"_ a type of honey has a role in improving memory and learning by increasing neurotrophic factors and acetylcholine level in brain as well as by decreasing acetyl cholinesterase activity and oxidative stress on brain (Al-Himyari & Dementia, 2009; Othman *et al*., 2015) [5, 42]. Color, taste and viscosity of honey produced from stingless bee is different from the honey which produced from sting bee (genus *Apis*; honey bee) (de Almeida-Muradian, Stramm, Estevinho, & technology, 2014; Guerrini *et al*., 2009) [20, 31]. This precious honeybee product is being used directly or in different medical products. "Meliponary" is the modern and established way of harvesting honey directly from the forest or it can also be harvested by using traditional methods. In this literature review, it is going to be explained various therapeutic benefits of honey and other industrial products of honeybee.

Industrial products of honeybee

1. Honey_ bioactive components containing natural sweetener

For centuries, honey was only being taken as a natural sweetener but now with the advancements in science we came to know that honey is not only an excellent food source but also exerts various therapeutic effects on human health because of its antioxidants and antibacterial properties. Not being required special conditions for its storage makes it the cheapest natural sweetener with health benefits. The best condition for its storage is dry place at room temperature. Honey would remain unspoiled for more than two years at room temperature, dry, cool, and dark place. But if there is a need to store I for longer period, then different storage conditions are required (Castro-Vázquez *et al*., 2008) [15].

The quality honey is going to be crystalize sooner or later and it is a natural process. This does not affect the chemical composition of honey, but heating does. So, we should avoid mixing honey in a hot water or tea, but it can be added into well-cocked items such as vegetables and meats. Water bath is used to make crystalized honey liquefy but the temperature should not be more than 40°C. Overheating increases the risk of harm to biological compounds present in honey.

2. Pollens_ protein rich honeybee product

Pollens are loaded with various biological active components such as vitamin B, C, D, E, provitamin A and extremely good source of essential amino acids. When honeybees collect nectar from different flowers, they get loaded with pollens of those flowers. We can get these pollen balls out of the honeycomb; this is sometimes referred as a pollen bread. The easy way of extracting pollens is installing a trap-wires over the hive so that pollens fall off their legs when they enter the hive. The recommended way of using pollens is to soak in water or juice for few hours prior to use. Soaking makes pollens swell and increases their dissolution and digestibility. This also makes the beneficial substances in it to absorbed directly and easily into the blood stream. They can also be taken as such in dried form, but in this case, they need to be chewed properly so that they would have a chance to be mixed with saliva.

As far as storage of pollens is concerned, they are stored in refrigerator, so that beneficial components would remain as such. Dry pollens are stored in dark and cool place.

3. Royal jelly_ supplement for older people

Royal jelly is the honeybee product excreted from the glands of young bees on to which queen and larvae feed. This feed is the most important factor that decides, would it be a worker bee or a queen when larvae hatched. Royal jelly is found in the combs of hive and beekeepers extract it when a lot of it is in there.

Royal jelly is considered to improve conditions related to ageing and has proved itself a perfect nutritional supplement especially for elder people. That is the reason royal jelly is in demand. It also enhances normal glands and brain functioning. It can directly be ingested in natural form, or it can be taken as in the form of mixture of propolis, wax, honey, and royal jelly.

4. Propolis_ a natural antibiotic

While feeding larvae, honeybees mix resin collected from different plants, herbs and shrubs with pollen grains, this blend is called propolis and it is proved that it contains more than 360 different substances. Propolis being a natural antibiotic could be used in the form of mixture with water, honey or sour milk and tea. It is found in their because it coats inside of the hive to protect it from microbes.

5. Wax_ for softer skin

Honeycombs are made up of wax. And honey-filled cells are also topped with wax. It is produced by the glands of honeybees. A candy made by the fortification with honey and wax is a best chewing gum substitute. Wax is rich in fatty-acid esters and over 300 biological active components are found in it. Wax appearance turns into yellowish color some days later but the fresh one is of pure white color with a pleasant smell. Wax has antibiotic properties and makes the skin smooth, soft, and younger looking which makes it a potential product for cosmetic industry. It can also be used as chewing capping as well as for thermal therapies after massage.

6. Bee venom_ desensitizer against bee sting

There is always a good reason for bees to sting. This happens if they find their lives threatened. The story in front of beehive is different, guard bees usually secure the entrance to the hive by guarding not only the bountiful reserves of honey and pollens but also the larvae. So, one should avoid going in front of honeybee's hive and pointing it out without any reason.

Having allergic reaction in case of bee sting is normal but one should take precautions. Bee venom is used in the treatment of few diseases such as to desensitize the bee sting. It is considered as a potential substitute for Botox and gaining importance in cosmetics industry and is added in various types of creams and serums.

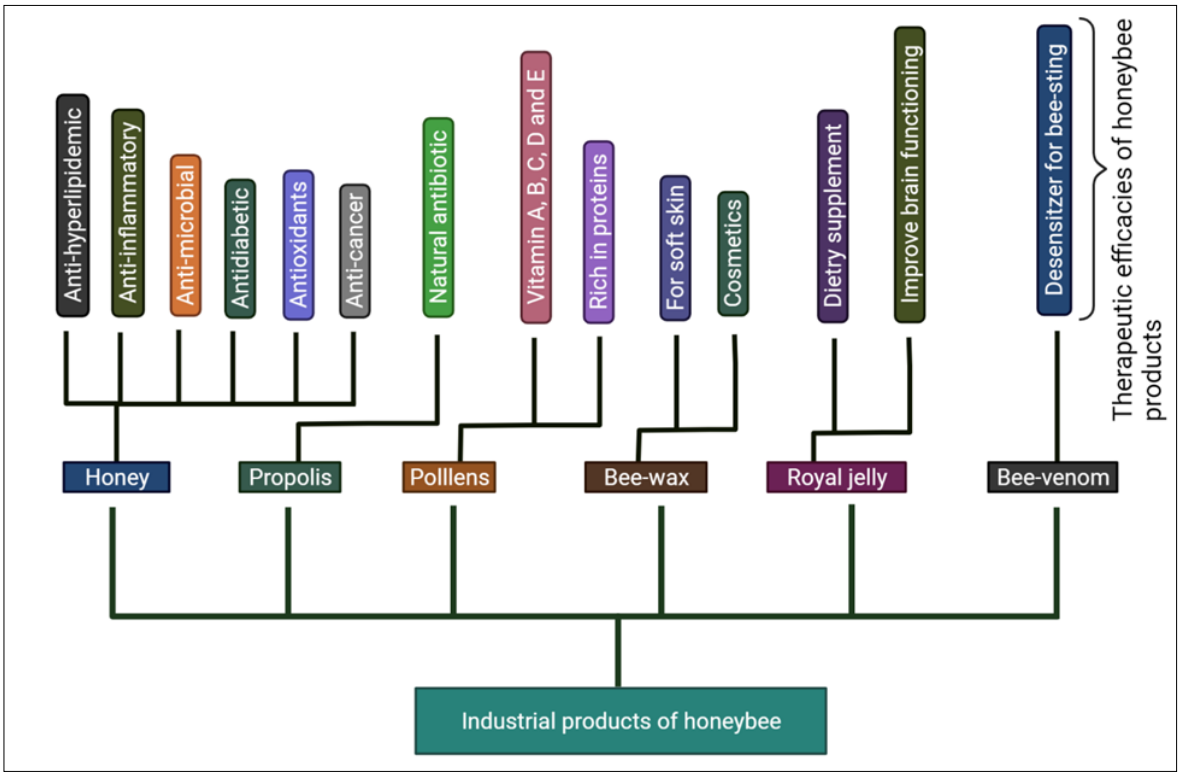

Fig 1: Graphical abstract

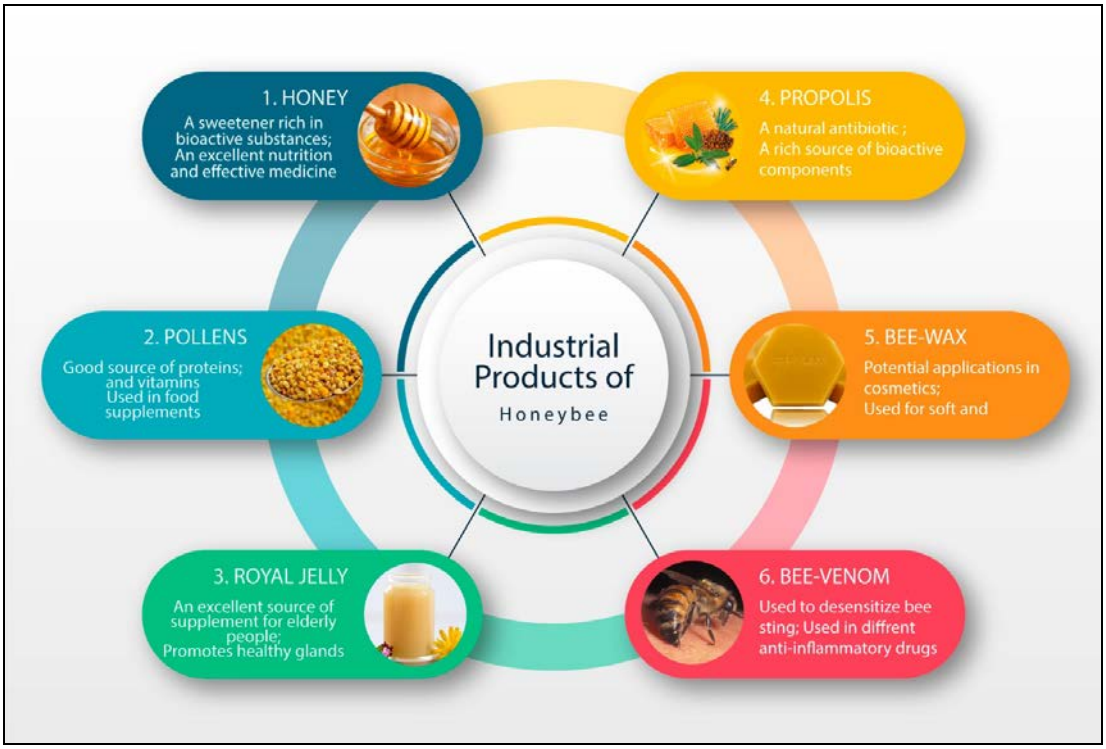

Fig 2: Industrial products of honeybee with their main properties highlighted

Chemical composition of honey

Over two hundred different chemical compounds and biological active substances such as vitamins, amino acids, organic acids, and enzymes are found in honey. 95-99% of the dried honey consists of sugars. 32- 38% of all sugar content is just fructose. Several other sugars such as sucrose, maltotriose, maltose, and panose are also found in honey.

Among vitamins, vitamin B1 (thiamine), B5 (pantothenic acid), B2 (riboflavin), B3 (nicotinic acid), B6 (pyridoxine), B8 (biotin), B9 (folic acid), B12 (cyanocobalamin), and vitamin C (ascorbic acid) are also found (Ciulu *et al*., 2011). There are other trace elements and minerals are also present in honey such as magnesium (Mg), copper (Cu), zinc (Zn), sulfur (S), iron (Fe), manganese (Mn), and phosphorus (P) can also be seen in honey. Though proteins and enzymes play a significant role in antimicrobial activities and help in calcium absorption, but not a very notable percentage is found in honey. Oxidative stress is ameliorated by honey due to the presence of not only phenolic compounds, but flavonoids are also there to enhance the antioxidant potential of honey and it has been shown by many studies (Escriche, Kadar, Juan-Borrás, & Domenech, 2014; Flores, Escuredo, & Seijo, 2015; Habib, Al Meqbali, Kamal, Souka, & Ibrahim, 2014) [26, 28, 33]. O-glycosil has been detected to be found with inter-glycosidic bonding by chromatographic techniques.

Among flavonoids and terpenoids, chrysin, kaempferol, sakuranetin, quercetin, magniferolic acid, pinocembrin, luteolin, isorhamnetin, galangin, and 3β-hydroxy-24-methylenecycloartan-26-oic acid are also found in honey (Truchado, Vit, Heard, Tomás-Barberán, & Ferreres, 2015) [46]. Therapeutic effects of honey are being shown in Fig 1.

Honey as a traditional medicine

Honey has been a traditional medicine since age. It has been used as an antioxidant and it plays a central role in the treatment of liver, heart, and gastrointestinal diseases (EL-Kholy, Hassan, Nour, Abe Elmageed, & Matrougui, 2009; El Denshary *et al*., 2012; O. O. Erejuwa *et al*., 2012). Honey, being the best natural wound healer available in the world has been used by ancient nations such as Chinese, Greeks, Egyptians, Romans etc. to treat intestinal diseases. Honey has antibacterial effects against *E. coli*, *Helicobacter pylori*, *Salmonella* spp., *Shigella* spp. etc. (Al Somal, Coley, Molan, & Hancock, 1994; McGovern, Abbas, Vivian, & Dalton, 1999) [6, 39]. Anti-inflammatory properties, anti- breast and cervical cancerous activities, anti-prostate cancerous and anti-osteosarcoma activities of honey have also been reported in several studies. In addition, honey has also been reported as an anti-diabetic, blood lipid lowering agent, and improves thyroid functioning (Kassim, Achoui, Mustafa, Mohd, & Yusoff, 2010; Nasuti, Gabbianelli, Falcioni, & Cantalamessa, 2006).

Therapeutic effects of honey on humans

1. Biological activities of honey

1.1 Honey as antioxidant

Antioxidants play an important role in preventing or slowing down the damage. Oxygen and other free radicals are oxidants while honey acts as an oxidant. Honey, being a natural antioxidant, has improved therapeutic effects

on ageing and it plays a role in processing of harmful oxygen derived substances and ROS (reactive oxygen species) which are produced during the metabolism. These highly reactive substances cause various diseases by reacting with proteins, lipids in cell membrane as well as with enzymes and affect the biochemical processes. These reactive substances are dealt by antioxidants before they do any damage, fortunately.

The amount antioxidants present in honey depends upon how much darker honey is. Brighter honey does not have plentiful antioxidants. The antioxidant activity of honey entirely depends upon phenolic compounds. Because higher level of phenolic compounds, higher would be the absorbance of free radicals. In another study, it was showed that antioxidant properties of honey are associated with how many biological active components are there in honey. This makes honey a dietary antioxidant. Oxidative stress can be ameliorated by taking honey directly or in combination with conventional approaches. This combination may have considered a new antioxidant therapy (Gheldof, Wang, Engeseth, & chemistry, 2003) [29].

1.2 Honey as an antimicrobial entity

Honey has its antimicrobial potential due to enzymatic oxidation reactions of glucose and some physiochemical conditions (Beretta, Orioli, & Facino, 2007; Cushnie & Lamb, 2005) [12, 18] but there other factors such as low pH and redox potential, low protein content, high viscosity, high osmotic pressure, high carbon to nitrogen ratio and various phytochemicals are actually responsible for antimicrobial activity of honey.

Yeast bacterial growth can be inhibited due to having underlined biologically important chemicals in honey such as glucose oxidases, peroxidases, and low water acidity. These chemical compounds increase the antimicrobial level of honey, but few other compounds are also found in honey which does not have role in increasing the antimicrobial level of honey such as synergic acid, pinocembrin, terpenes, methyl syringic acid, and some benzoic acid derivatives. Antimicrobial activity of honey is generated due the minimum concentration of these growth inhibitory compounds. Studies showed that antimicrobial efficacy of honey is implemented on many bacterial and fungus pathogens. *Manuka* honey has high antimicrobial activity and has been studied against both *Escherichia coli* and *Staphylococcus aureus* (Cushnie & Lamb, 2005; Snowdon & Cliver, 1996) [18, 45].

Fig 3: Therapeutic efficacies of honey and other industrial products of honeybee

1.3 Honey as anti-inflammatory agent:

Healing process could be halted by tissue damage due to inflammation. In clinical trials as well as in animal model studies, it was seen that honey significantly reduced the inflammatory responses (Bilsel *et al*., 2002; Candiracci *et al*., 2012; Fernandez-Cabezudo *et al*., 2013) [13, 14, 27]. And anti-inflammatory activity of honey is due to the presence of various phenolic compounds. The alleviation of inflammation occurs by suppressing the activities of enzymes such as cyclooxygenase (COX-2), ornithine decarboxylase, tyrosine kinase, and inducible nitric oxide synthase (iNOS) which in turn have a role in activation of inflammation causing cytokines. Against these pro-inflammatory cytokines, honey has been found to stimulate the production of tumor necrosis factors and interleukins (IL-1 *beta*, IL-6) (Araújo, Gonçalves, & Martel, 2011; Cho *et al*., 2004; Hussein, Mohd Yusoff, Makpol, Mohd Yusof, & Medicine, 2012) [8, 16]. *In vitro* studies on cell culture showed that honey is involved in the production of lymphocytes (T and B), macrophages, neutrophils, eosinophils, antibodies and kill T cells. Honey is also involved in the production of short chain fatty acids (SCFA) which reduce the risk of onset of inflammatory diseases and modulate the immune system. Due to having fermentable sugars such as nigerooligosacharides, honey has immune-potent effects. Immune system can also be modulated by non-sugar content in honey (Schley & Field, 2002) [43].

2. Medicinal values of honey

2. 1. Honey and wound

Honey is known to have wound-healing activities and it is known to be the oldest and efficient wound healer. In many studies, it is reported to be good wound healer because of its antibacterial, anti-inflammatory, antioxidants, and antiviral effects. Leukocytes, on induction by honey release cytokines which initiate the repair mechanism. In addition, it also modulates immune system against infection. Honey is used to control the acute wound by proliferation of lymphocytes and phagocytes and makes the skin thick where there is a burn. Studies also showed the use of honey in the treatment of leg ulcer but to support this claim more studies are required (Simon *et al*., 2009) [44].

2.2 Honey and diabetes

Honey has efficacies in the treatment of diabetes mellitus and many studies are available to support this clam. These studies describe the therapeutic advancement of honey as an adjunct to current diabetes therapies for treatment of diabetes mellitus. Those therapies which target the increased level of ROS are also used as an adjunct to available anti-diabetic drugs in the treatment of diabetes. In a clinical study done on type 1 and type 2 diabetes mellitus patients, significant reduction of glycemic index was observed when they were given honey as an adjunct to different available anti-diabetic drugs. In another study, it was noted that application of honey is associated with lowering blood plasma glucose level, but it did not affect dextran level so much.

Honey has also been associated with lowering blood lipid profile in hyperlipidemic patients as well as has a role in reduction homocysteine and C-reactive proteins. But there are studies which raise questions about the uncertainty in availability of such therapies which target both diabetic condition as well as oxidative stress. In addition, the application of honey is just not restricted to manage higher blood glucose level but it might also be used to improve other metabolic complexities (Günes, Eser, & Nursing, 2007) [32].

2.3 Honey and cancer

Honey in the treatment of cancer has been reported in many studies. And it exerts cancer-curing effects through cascade of mechanisms e.g., it interferes with cell-signaling pathways such as anti-inflammatory, anti-proliferative, antimutagenic, apoptotic pathways. It has also been found to modulate immune responses. In skin, epithelial and cervical, endometrial, colorectal, and prostate, and other type of cancer cells, it was shown that honey is involved in inhibition of proliferation of cancer cells, enhancing apoptosis, and depolarization of mitochondrial membrane.

Furthermore, to strengthen the claims, honey has also been found to inhibit many different forms of tumors such as carcinoma, hepatic cancer, bladder cancer, breast cancer and melanoma in animal modelling (Aliyu *et al*., 2013) [7].

2.4 Honey and cardiovascular diseases

The biological active components in honey such as antioxidants, vitamin C, polyphenols, flavonoids etc. can be used to reduce the risk of cardiovascular diseases. Flavonoids act as antithrombotic, antioxidant, vasorelaxant and anti-ischemic; these protective properties of flavonoids prevent cardiac arrest and other heart malfunctioning. And mechanisms through which these flavonoids prevent heart diseases are: a) coronary vasodilation, b) not letting the platelets to be clot and c) inhibit oxidation of low density lipoproteins.

Caffeic acid, kaempferol, galangin, phenethyl ester, quercetin and acacetin are some types of antioxidants which are varied in different forms of honey. Polyphenols in certain honey have also been found to reduce the cardiovascular disorder risks. However, there is a need to set *in vitro*, *in vivo*, and clinical trials to further validate these claims (Kamaruzaman, Sulaiman, Kaur, Yahaya, & medicine, 2014) [36].

2.5 Honey and neurological diseases

Honey is one the most efficient natural nutraceutical antioxidant and plenty of literature available on nutraceuticals and their use in neuroprotective drugs. In many studies, it was shown that polyphenols in honey have nootropic and neuroprotective properties such as it acts as anticonvulsant, antidepressant, anxiolytic, and antinociceptive. ROS (which cause neurotoxicity, aging and deposition of misfolded proteins e.g., amyloid beta) are ameliorated/quenched by polyphenols in honey (Akanmu *et al*., 2011) [3].

Oxidative stress is encountered by excitotoxins such as kainic acid, quinolinic acid as well as neurotoxins such as 1-methyl-4-phenyl-1, 2, 3, 6-tetrahydropyridine and 5-S-cysteinyl-dopamine. Methyl mercury, amyloid beta and retinoid are polyphenolic compounds which encounters apoptotic stress. Microglia-induced neuroinflammation in hippocampus_ memory developing structure of brain which is caused by immunogenic neurotoxins is treated by honey polyphenols. Furthermore, polyphenols also play their role in molecular-level memory production as well as they prevent memory related disorders. Several studies show that honey has neuropharmacological and memory improving effects on brain functioning in the form of neural circuit modifications (Ghosh & Playford, 2003) [30]. However, to know more therapeutic neurological effects of honey, further studies should be carried out.

2.6 Honey and gastrointestinal disorders:

Gastrointestinal tract disorders such as periodontal and various other conditions e.g., dyspepsia is treated by using honey. Helicobacter pylori infection is successfully treated by using honey which shows antibacterial activity when ingested *(Oyefuga, Ajani, Salau, Agboola, & Adebawo, 2012*. In clinical trials, *manuka* honey has been shown to eradicate *Helicobacter pylori.*

Honey is also effective in oral rehydration therapies. A clinical trial has been done on hospital-admitted infants and children with gastroenteritis, significantly reduction in the duration of diarrhea was seen when they were given honey (McGovern *et al*., 1999) [39].

Conclusion

Plenty of literature is available which explains us the potential therapeutic effects/benefits of using above-mentioned industrial products of honeybee. But studies are needed to validate these claims. It has been proven that therapeutic effects of honey and other honeybee products are due to their anti-inflammatory, antioxidative, antimicrobial, anti-proliferative, apoptosis promoting activities. This literature review has made us well-aware about the use of honey and other amazing products of honeybee in relation to their various disease eradicating properties. But more studies are still required to cover all aspects of honey as medicinal important product.

References

1. Adebolu TJAJoB. Effect of natural honey on local isolates of diarrhea-causing bacteria in southwestern Nigeria,2005:4(10):1172-1174.
2. Ahmed S, Othman NHJTMjomsM. Review of the medicinal effects of tualang honey and a comparison with manuka honey,2013:20(3):6.
3. Akanmu MA, Olowookere TA, Atunwa SA, Ibrahim BO, Lamidi OF, Adams PA *et al*. Neuro pharmacological effects of Nigerian honey in mice, 2011 8(3).
4. Al-Waili NSJJomf. Natural honey lowers plasma glucose, C-reactive protein, homocysteine, and blood lipids in healthy, diabetic, and hyperlipidemic subjects: comparison with dextrose and sucrose,2004:7(1):100-107.
5. Al-Himyari FAJAs, Dementia. P1-241: The use of honey as a natural preventive therapy of cognitive decline and dementia in the middle east. *5*(4S_Part_8), 2009, P247-P247.
6. Al Somal N, Coley K, Molan P, Hancock BJJotRSoM. Susceptibility of Helicobacter pylori to the antibacterial activity of manuka honey,1994:87(1):9.
7. Aliyu M, Odunola OA, Farooq AD, Rasheed H, Mesaik AM, Choudhary MI, Cancer. Molecular mechanism of antiproliferation potential of Acacia honey on NCI-H460 cell line,2013:65(2):296-304.
8. Araújo JR, Gonçalves P, Martel FJNr. Chemopreventive effect of dietary polyphenols in colorectal cancer cell lines,2011:31(2):77-87.
9. Ashrafi S, Mastronikolas S, Wu C. *Use of honey in treatment of aphthous ulcers.* Paper presented at the Abstract, 2005.
10. Babacan S, Rand AGJJofs. Characterization of honey amylase,2007:72(1):C050-C055.
11. Bansal V, Medhi B, Pandhi PJKUmj. Honey--a remedy rediscovered and its therapeutic utility,2005:3(3):305-309.
12. Beretta G, Orioli M, Facino RMJPM. Antioxidant and radical scavenging activity of honey in endothelial cell cultures (EA. hy926),2007:73(11):1182-1189.
13. Bilsel Y, Bugra D, Yamaner S, Bulut T, Cevikbas U, Turkoglu UJDS. Could honey have a place in colitis therapy? Effects of honey, prednisolone, and disulfiram on inflammation, nitric oxide, and free radical formation,2002:19(4):306-312.
14. Candiracci M, Piatti E, Dominguez-Barragán M, García-Antrás D, Morgado B, Ruano D. chemistry f. Anti-inflammatory activity of a honey flavonoid extract on lipopolysaccharide-activated N13 microglial cells,2012:60(50):12304-12311.

15. Castro-Vázquez L, Díaz-Maroto M, González-Viñas M, De La Fuente E, Pérez-Coello MJJoA, Chemistry F. Influence of storage conditions on chemical composition and sensory properties of citrus honey,2008:56(6):1999-2006.
16. Cho H, Yun C-W, Park W-K, Kong J-Y, Kim KS, Park Y, Kim B-K JPR. Modulation of the activity of pro-inflammatory enzymes, COX-2 and iNOS, by chrysin derivatives,2004:49(1):37-43.
17. Ciulu M, Solinas S, Floris I, Panzanelli A, Pilo MI, Piu PC. RP-HPLC determination of water-soluble vitamins in honey,2011:83(3):924-929.
18. Cushnie TT, Lamb AJJIjoaa. Antimicrobial activity of flavonoids,2005:26(5):343-356.
19. Dashora N, Sodde V, Bhagat J, S Prabhu K, Lobo RJPC. Antitumor activity of Dendrophthoe falcata against ehrlich ascites carcinoma in swiss albino mice, 2011, 2(1).
20. de Almeida-Muradian LB, Stramm KM, Estevinho LMJIjofs, technology. Efficiency of the FT-IR ATR spectrometry for the prediction of the physicochemical characteristics of M elipona subnitida honey and study of the temperature's effect on those properties,2014:49(1):188-195.
21. Ediriweera E, Premarathna NJA. Medicinal and cosmetic uses of Bee's Honey–A review,2012:33(2):178.
22. EL-Kholy WM, Hassan HA, Nour SE, Abe Elmageed ZE, Matrougui KJTFJ. Hepatoprotective effects of Nigella sativa and bees' honey on hepatotoxicity induced by administration of sodium nitrite and sunset yellow,2009:23:733:732-733.732.
23. El Denshary ES, Al-Gahazali MA, Mannaa FA, Salem HA, Hassan NS, Abdel-Wahhab MAJE *et al*. Dietary honey and ginseng protect against carbon tetrachloride-induced hepatonephrotoxicity in rats,2012:64(7-8):753-760.
24. Erejuwa O, Sulaiman S, Wahab M, Sirajudeen K, Salleh MM, Gurtu S. *Antioxidant protection of Malaysian tualang honey in pancreas of normal and streptozotocin-induced diabetic rats.* Paper presented at the Annales d'endocrinologie, 2010.
25. Erejuwa OO, Sulaiman SA, Wahab M, Sirajudeen K, Salleh M, Gurtu SJIJARNP. Hepatoprotective effect of tualang honey supplementation in streptozotocin-induced diabetic rats,2012*:*4(4):37-41.
26. Escriche I, Kadar M, Juan-Borrás M, Domenech EJFc. Suitability of antioxidant capacity, flavonoids and phenolic acids for floral authentication of honey. Impact of industrial thermal treatment,2014:142:135-143.
27. Fernandez-Cabezudo MJ, El-Kharrag R, Torab F, Bashir G, George JA, El-Taji H *et al*. Intravenous administration of manuka honey inhibits tumor growth and improves host survival when used in combination with chemotherapy in a melanoma mouse model,2013:8(2):e55993.
28. Flores MSR, Escuredo O, Seijo MCJFC. Assessment of physicochemical and antioxidant characteristics of Quercus pyrenaica honeydew honeys,2015:166:101-106.
29. Gheldof N, Wang X-H, Engeseth NJJJoa, chemistry f. Buckwheat honey increases serum antioxidant capacity in humans,2003:51(5):1500-1505.
30. Ghosh S, Playford RJJCs. Bioactive natural compounds for the treatment of gastrointestinal disorders,2003:104(6):547-556.
31. Guerrini A, Bruni R, Maietti S, Poli F, Rossi D, Paganetto G, Sacchetti GJFC. Ecuadorian stingless bee (Meliponinae) honey: A chemical and functional profile of an ancient health product,2009:114(4):1413-1420.
32. Günes ÜY, Eser IJJoWO, Nursing C. Effectiveness of a honey dressing for healing pressure ulcers,2007:34(2):184-190.
33. Habib HM, Al Meqbali FT, Kamal H, Souka UD, Ibrahim WHJFc. Bioactive components, antioxidant and DNA damage inhibitory activities of honeys from arid regions,2014:153:28-34.
34. Hassapidou M, Fotiadou E, Maglara E, Papadopoulou SKJO. Energy intake, diet composition, energy expenditure, and body fatness of adolescents in northern Greece,2006:14(5):855-862.
35. Hussein SZ, Mohd Yusoff K, Makpol S, Mohd Yusof YAJE-BC, Medicine A. Gelam honey inhibits the production of proinflammatory, mediators NO, PGE2, TNF-α, and IL-6 in carrageenan-induced acute paw edema in rats, 2012.
36. Kamaruzaman NA, Sulaiman SA, Kaur G, Yahaya BJBc, medicine a. Inhalation of honey reduces airway inflammation and histopathological changes in a rabbit model of ovalbumin-induced chronic asthma,201414(1):1-11.
37. Kassim M, Achoui M, Mustafa MR, Mohd MA, YusoffK MJNr. Ellagic acid, phenolic acids, and flavonoids in Malaysian honey extracts demonstrate *in vitro* anti-inflammatory activity,2010:30(9):650-659.
38. Kishore RK, Halim AS, Syazana MN, Sirajudeen KJNr. Tualang honey has higher phenolic content and greater radical scavenging activity compared with other honey sources,2011:31(4):322-325.
39. McGovern DP, Abbas SZ, Vivian G, Dalton HRJJotRSoM. Manuka honey against Helicobacter pylori,1999:92(8):439-439.
40. Mishra S, Mishra A, Verma TJJoAiP A Review of Honey and its Pharmacological Actions, 1(1).
41. Nasuti C, Gabbianelli R, Falcioni G, Cantalamessa FJNR. Antioxidative and gastroprotective activities of anti-inflammatory formulations derived from chestnut honey in rats,2006:26(3):130-137.
42. Othman Z, Zakaria R, Hussain NHN, Hassan A, Shafin N, Al-Rahbi B, Ahmad AHJMS. Potential role of honey in learning and memory,2015:3(2):3-15.
43. Schley P, Field CJBJoN. The immune-enhancing effects of dietary fibres and prebiotics,2002*:*87(S2):S221-S230.

44. Simon A, Traynor K, Santos K, Blaser G, Bode U, Molan PJE-bc. medicine, a. Medical honey for wound care—still the ‘latest resort’?,2009 6(2):165-173.
45. Snowdon JA, Cliver DOJIjofm. Microorganisms in honey,1996*:*31(1-3):1-26.
46. Truchado P, Vit P, Heard TA, Tomás-Barberán FA, Ferreres FJRCiMS. Determination of interglycosidic linkages in O-glycosyl flavones by high-performance liquid chromatography/photodiode-array detection coupled to electrospray ionization ion trap mass spectrometry. Its application to Tetragonula carbonaria honey from Australia,2015:29(10):948-954.
47. Vargas O, Maza F. Meliponini biodiversity and medicinal uses of the honey from El Oro province in Ecuador, 2015.
48. Vit P, Uddin J, Zuccato V, Maza F, Schievano EJIJBBAFBE. Entomological origin of honey discriminated by NMR chloroform extracts in Ecuadorian honey,2015:9(5):495-497.
49. Viuda-Martos MJJoFS. Col. Functional Properties of Honey, Propolis, and Royal Jelly, 2008, 73, 9.
50. worldbeeday.org. *Honey and other bee products* Retrieved from, 2015.