Composition and functional properties of propolis (bee glue): A review

Syed Ishtiaq Anjum, Amjad Ullaha, Khalid Ali Khan, Mohammad Attaullah, Hikmatullah Khan, Hussain Ali, Muhammad Amjad Bashir, Muhammad Tahir, Mohammad Javed Ansari, Hamed A. Ghram, Nuru Adgaba, Chandra Kanta Dash

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A B S T R A C T

Propolis is a natural substance collected by honey bees from various plants such as, poplar, palm, pine, conifer secretions, gums, resins, mucilage and leaf buds. It is collected and brought very painstakingly by honey bees to be used for sealing cracks and crevices occurring in their hives. Originally, it as an antiseptic meant for preventing bee-hive from microbial infections along with preventing decomposition of intruders. Additionally, propolis has been used in folk medicine for centuries. The biological characteristics of propolis depend upon its chemical composition, plant sources, geographical zone and seasons. More than 300 compounds have been identified in propolis such as, phenolic compounds, aromatic acids, essential oils, waxes and amino acids. Many scientific articles are published every year in different international journals, and several groups of researchers have focused their attention on the chemical compounds and biological activity of propolis.

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1. Introduction

The word propolis has been derived from Greek in which the morpheme ‘Pro’ means “in front of” or “at the entrance to”) and the morpheme ‘polis’ means ‘community’ or ‘city’ (Aminimoghadamfarouj and Nematoallah, 2017; Chadha et al., 2014; Yumnam et al., 2017) which means hive defensive substance (Al-Hariri, 2011; Aminimoghadamfarouj and Nematoallah, 2017). Bankova et al., 2000; Burdock, 1998; Castaldo and Capasso, 2002; Fokt et al., 2010; Ota et al., 2001; Parolia et al., 2010; Ramos and Miranda, 2007; Sabir, 2017; Sforcin, 2016; Toreti et al., 2013; Wagh, 2013) Propolis is collected by worker-bees, from numerous plant resins and secretions (Banskota et al., 2001b; Çiftci-Yılmaz et al., 2017) such as mucilage, gums, resins (Bankova et al., 1992) and lattices and also from leaf buds (Harfouch et al., 2016; Marcucci, 1995; Ozcan, 1999; Walker and Crane, 1987) of different plant species like palm, pine, alder, poplar, beech, conifer and birch (Zheng et al., 2017) and then mixed with salivary and enzymatic secretions (Sforcin, 2007). It is also called “Bee-glue” which is a natural resin (wax-like) substance (Abdulrahman et al., 2012; Tosi et al., 1996) present in bee hives and used by Honey bees as a cementing material to close open spaces and cracks occurring in their hives (Ahmed et al., 2017; Bankova et al., 2000; Bankova et al., 1999; Castaldo and Capasso, 2002; El Hady and Hegazi, 2002; Grange and Davey, 1990; Hegazi et al., 2000; Koo and Masry, 2014; Pasupuleti et al., 2017). Similarly, propolis not only to protect their hives, by blocking the cracks, sealing the spaces and smoothening the internal walls of their hives but they also use it as an antiseptic (Akbay et al., 2017; Al-Hariri, 2011; Alonso-Salces et al., 2017; Fernández et al., 2004; Greenaway et al., 1990; Kasiotis et al., 2017; Rajpara et al., 2009; Sabir and Sumidarti, 2017; Seidel et al., 2008; Shouqin et al., 2005; Uzel et al., 2001) to protect the bees larvae, honey stores and comb from microbial infections (Açıkgöz et al., 2005; Drescher et al., 2017; Omar et al., 2017; Rufatto et al., 2017; Sforcin, 2016; Simone-Finstrom et al., 2017). It is also applied to those areas of the hive where the comb is attached to an object so as to create germ-free, smooth surface (Sforcin, 2007; Simone-Finstrom and Spirvak, 2010). The reason is that honey bees live together, and therefore infection occurring in one bee can spread quickly in the whole colony (Aminimoghadamfarouj and Nematoallah, 2017; Kuropatnicki et al., 2013; Seeley and Morse, 1976; Simone-Finstrom et al., 2017; Vischer, 1980). In addition, it is also used by honey bees to prevent decomposition of the carcass of the intruder in the hives (Kumar et al., 2008; Shinohara and Miranda, 2014; Pasupuleti et al., 2017). Similarly, propolis prevents entry of water to the hive which maintains constant humidity and also serves as a control over the air flow towards the hive (Afroz et al., 2017; Kuropatnicki et al., 2013).

Propolis was identified and used by man since long (Kuropatnicki et al., 2013; Lotfy, 2006). Currently propolis is used as an anti-bacterial, anti-inflammatory, anti-viral (Sforcin et al., 2017), anti-oxidant, anti-protozoal, anesthetic, anti-tumoural, anti-cancer, anti-fungal (Rajpara et al., 2009; Sforcin, 2016), anti-septic, anti-mutagenic, anti-hepatotoxic in addition to being used for cytotoxic activity, etc. (Toreti et al., 2013).

2. History of propolis

Propolis was used by man as a traditional medicine since 300 BC (Ghisalberti, 1979; Seidel et al., 2008; Sung et al., 2017; Trusheva et al., 2007; Uzel et al., 2005; Veiga et al., 2017). Researchers stated that the healing activities of propolis were identified by Roman (Machado et al., 2017) and Greek doctors (Elmakady et al., 2017; Ferreira et al., 2017) as well as other scientists, such as Dioscorides, Galen, Aristoteles and Pliny (Castaldo and Capasso, 2002; Crane, 1997; Dobrowolski et al., 1991; Kuropatnicki et al., 2013). Similarly, physicians used propolis efficiently for the treatment of injuries during Anglo-Boer battle (De Castro, 2001; Sforcin, 2007) as well as in World War II (Lotfy, 2006; Ramos and Miranda, 2007). Early Egyptians used propolis to preserve their corpses from decomposition (Martinotti and Ranzaei, 2013; Sawicka et al., 2012; Zabaou et al., 2017) and to heal wounds (El Sahaimy and Masry, 2014; Parolia et al., 2010; Sforcin, 2007), because they were aware of the putrefactive properties of propolis (Ahuja and Ahuja, 2011; Castaldo and Capasso, 2002; Lotfy, 2006; Sforcin, 2016; Wagh, 2013). Furthermore, propolis was recognized as an anti-bacterial agent during 17th and 20th century in Europe (Toreti et al., 2013; Wagh, 2013). In England, Propolis was recognized as a better medicine for the treatment of wounds during 17th century (Kuropatnicki et al., 2013; Monti et al., 1983; Murray and Pizzorno Jr., 2005). Similarly in China, propolis was recognized as an anti-cancer and anti-infection medicine (Chen et al., 2013). The first scientific report about propolis, its composition and chemical actions was announced to the public in 1908 (Fokt et al., 2010; Helfenberg, 1908). In 17th century used as for varnishing (Fokt et al., 2010; Martinotti and Ranzaei, 2015).

3. Physical properties of propolis

The color of propolis varies according to area and the plant source (Ahmed et al., 2017; De Castro, 2001; Lotfy, 2006; Ozcan, 1999; Sawicka et al., 2012). It melts on 60°C to 70°C while some of its kinds melt on 100°C (Martinotti and Ranzaei, 2013; Ramos and Miranda, 2007; Wagh, 2013). Hard at low while soft at high temperature (Açıkgöz et al., 2005; Burdock, 1998; Fokt et al., 2010; Hausen et al., 1987; Kuropatnicki et al., 2013; Marcucci,
It is extracted commercially with suitable solvents i.e. ethanol, methanol, chloroform, ether and acetone but Ethanol is the best (Martinotti and Ranzato, 2015; Ramos and Miranda, 2007; Trusheva et al., 2007). The biological activity of propolis sample varies, due to its different geographical origin (Wagh, 2013). It is found commercially in the form of dentifrices, lozenges, mouth rinses, creams, gels, cough syrups, wine, cake, powder, soap, chewing gums and tablets (Chandna et al., 2014; Parolia et al., 2010; Rajpara et al., 2009; Wagh, 2013) as well as candies, shampoos, chocolate bars, skin lotions, toothpastes (Ferreira et al., 2017; Yumnam et al., 2017), antiseptic mixtures (Ramos and Miranda, 2007) and is also used for the preservation of flesh (Chan et al., 2013). The estimated colony collection per year is 150–200 g (Krell, 1996; Kuropatnicki et al., 2013; Martinotti and Ranzato, 2015).

### 4. Composition of propolis

Chemically propolis is composed of more than 180 different types of chemicals (Kuropatnicki et al., 2013) and season to season. Propolis is collected both in temperate zones and tropical zones and slightly different (Popova et al., 2004; Simone-Finstrom and Spivak, 2010).

As a result more than 300 different components have been identified in propolis (Ahuja and Ahuja, 2011; Al-Hariri, 2011; Banskota et al., 2001b; Chan et al., 2013; De Barros et al., 2008; De Castro, 2001; Drescher et al., 2017; El Sohaimy and Masry, 2014; Fokt et al., 2010; Kuropatnicki et al., 2013; Rajpara et al., 2009; Ramos and Miranda, 2007; Sforcin, 2007; Sforcin, 2016; Toreti et al., 2013; Uzel et al., 2005; Viuda-Martos et al., 2008; Wagh, 2013). The percentage of diverse material present in propolis depends upon the time of its collection and also on the geographical origin (Afrouzan et al., 2017; Bueno-Silva et al., 2017; Cuesta-Rubio et al., 2007; Kustiawan et al., 2017; Silva et al., 2017; Wagh, 2013).

#### 4.1. Gross composition of propolis

| Compounds                        | References                                      |
|----------------------------------|-------------------------------------------------|
| **Flavonoids, Flavanones, Flavones & Flavonols:** |                                                                 |
| Islapinin, Ermanin, Pectolinarinigenin, Sakuranetin, Isosakuranetin, Quercetin-3,3′-dimethyl ether, 3-acetyl pinobanksin, Betuletol, Isorhamnetin, Kaempferide, Rhamnazin, Rhamnetin, Alnusin, Alpinetin, Alnusitol, Pinostrobin, Pinocembrin, Chrysins, Tectochrysin, Acacetin, Rhamnocitrin, Quercetin, Galangin, Apigenin, Pinobanksin, Kaempferol, Rutin, Catechin, Luteolin, Naringenin | Walker and Crane (1987) |
| **Benzonic acid and derivatives:** |                                                                 |
| Benzoic acid, Salicylic acid, Genticis acid, Gallic acid, Phenylmethyl ester of benzoic acid, Phenylmethyl ester of salicylic acid, Trans-coniferyl benzoate, Trans-p-coumaryl benzoate, Protocatechuc acid | Lotfy (2006) |
| **Benzaldehyde derivatives:** |                                                                 |
| Vanillin, Caproic aldehydes, Isovanillin p-hydroxybenzaldehyde, Protocatechualdehyde | Walker and Crane (1987) |
| **Cinnamyl alcohol, cinnamic acid & its derivatives:** |                                                                 |
| Cinnamyl alcohol, Hydrocaeffic acid, Isoferulic acid, Cinnamic acid methyl ester, Cinnamylidene acetic acid, Cinnamic acid, Caffeic acid, Ferulic acid | Abdulkhan et al. (2017), Akbay et al. (2017), Marcucci (1995), Walker and Crane (1987) |
| **Aliphatic hydrocarbons:** |                                                                 |
| Eicosine, 1-octadecene, Tricosane, Pentacosane, Eicosane, Heneicosane | Kuropatnicki et al. (2013) |
| **Sugar:** |                                                                 |
| d-ribofuranose, d-fructose, d-glucitol, d-gulose, Talose, Sucrose, d-glucose |                                                                 |
| **Vitamins:** |                                                                 |
| B1, B2(complex), B6, C, E |                                                                 |
| **Nicotinic acid, Pantothenic acid** |                                                                 |
| Alpinetin chalcone, Naringinenine chalcone, Pinobanksin chalcones, Pinobanksin-3-acetate chalcone, Pinostrobin chalcone, Pinocembrin chalcones, Sakuranetin chalcone, 2′,6′,a-trihydroxy-4′-methoxy chalcone, 2′,6′,dihydroxy-4′-methoxydihydro chalcone, 2′,4′,6-trihydroxydihydro chalcone | Marcucci (1995) |
### Compounds

| **Compounds** | **References** |
|---------------|---------------|
| **Amino acids:** Alanine, β-alanine, α-amino butyric acid, δ-amino butyric acid, Arginine, Asparagine, Aspartic acid, Cystine, Cysteine, Glutamic acid, Glycine, Histidine, Hydroxyproline, Isoleucine, Leucine, Lysine, Methionine, Ornithine, Phenylalanine, Proline, Pyroglutamic acid, Sarcosine, Serine, Threonine, Tryptophane, Tyrosine, Valine | El Hady and Hegazi (2002) |
| **Esters:** Methyl palmitate, Cinnamyl-trans-4-coumarate, Ethyl palmitate, Stearic acid methyl ester, Phthalate ester, Benzyl benzoate, Benzyl-trans-4-coumarate, 3-Methyl-3-butenyl isofurulate, 3-Methyl-2-butenyl isofurulate, 3-Methyl-3-butenyl caffeate, 2-Methyl-2-butenyl caffeate, 3-Methyl-2-butenyl caffeate, Benzyl caffeate, Phenylethyl caffeate, Cinnamyl caffeate, Tetradecyl caffeate, Tetradecenyl caffeate (isomer), Tetradecanoyl caffeate, Hexadecyl caffeate | |
| **Other acids and derivatives** Phenylmethyl ester of 14-methylpentadecanoic acid, Ethyl ester of palmitic acid, Myristic acid, Sorbic acid, Butyl-2-methylpropyl ester of Phthalic acid, Stearic acid, Methyl ester of anulistic acid | Walker and Crane (1987) |
| **Alcohol, ketones, phenols and heteroaromatic compounds:** Benzyl alcohol, Hexadecanol acetate, Coumarine, Pterostilbene, Xanthorrhoeol, Scopoletol | |
| **Terpene, Sesquiterpene, alcohol & derivatives:** Geraniol, Nerol, β-bisabolol, Guaiol, Farnisol, Dihydrodeuesmol, α-acetoxybetulene | |
| **Sesquiterpene & Triterpene hydrocorbons:** β-patchoulene, β-bisabolene, Squalene, β-bourbonene, Copaene, Calarene, Calamenene, Caryophyllene, Patchouline, Selene, Aromadendrene | |
| **Sterols & steroid hydrocorbons:** Cholestrilene, Cholinasterol, Stigmasterol, β-dihydrofucosterol, Lanosterol, Cholesterol | |
| **Minerals:** Sr, Ba, Cd, Sn, Pb, Ti, Ag, Co, Mo, Al, Si, V, Ni, Mn, Cr Na, Mg, Cu, Ca, Zn, Fe, K | Lotfy (2006), Pasupuleti et al. (2017), Walker and Crane (1987) |
| **Enzymes:** Glucose-6-phosphatase, Acid phosphatase, Adenosine triphosphatase, Succinic dehydrogenase | Marcucci (1995) |
| **Ketones:** Acetophenone, p-acetophenolacetophenone, Dihydroxy-acetope9i9inone, Methylacetophenone, Hept-5-en-2-one, 6-methylketone Waxy acids: Archid acid, Behenic acid, Cerotic acid, Lauric acid, Linoleic acid, Lignoceric acid, Montanic acid | |
| **Aliphatic acids & aliphatic esters:** Acetic acid, Angelic acid, Butyric acid, Crotonic acid, Fumaric acid, Isobutyric acid, Methylbutyric acid, Isobutyl acetate, Isopentyl acetate, Isopentyl acetate Waxy acids: Archid acid, Behenic acid, Cerotic acid, Lauric acid, Linoleic acid, Lignoceric acid, Montanic acid | El Hady and Hegazi (2002) |
| **Alcohol:** Benzene methanol, Cinnamyl alcohol, Glycerol, α-glycerophosphate, Phenethyl alcohol, Isobutenol, Hydroquinone, Prenyl alcohol | |
| **Aliphatic acids:** Lactic acid, Hydroxyacetic acid, Malic acid, 5-Hydroxy-n-valeric acid, 2,3-Dihydroxypropanoic acid, Pentonic acid-2-deoxy-3,5-dihydroxy-γ-lactoneb, Pentonic acid-2-deoxy-3,5-dihydroxy-γ-lactone (isomer)β, Succinic acid, 2,3,4,5-Tetrahydroxypentanoic acid-1,4-lactone, 2,3,4,5-Tetrahydroxypentanoic acid-1,4-lactone (isomer)β, Nonanoic acid, Palmitic acid, Oleic acid, Decanoic acid, Dodecanoic acid, Tetradecanoic acid, Heptadecanoic acid, Octadecenoic acid, Tetrasanoic acid, Eicosanoic acid, Hexacosanoic acid, 2-Hydroxy hexacosanoic acid |
4.2. Geographical origin of propolis and composition

Poplar tree (Populus nigra), is found in North America, Europe, non-tropical regions of Asia as well as New Zealand. Propolis collected from Egypt was known to possess constituent of poplar tree as well as esters of caffeic acid and long-chain fatty alcohols including tetradecanol, hexadecanol and dodecanol (Bankova et al., 2009). Birch propolis collected from Russia in hold flavonoids and Flavones (distinct from poplar propolis) of Betula verrucosa (plant source). Similarly, the main source of Brazilian propolis is Baccharis dracunculifolia leaf resin, including constituents, such as diterpenes, lignans, prenylated derivatives of p-coumaric acid as well as of acetylphenone and flavonoids (distinct from poplar type). Brazilian propolis contains artepillin C in large amount as compared to CAPE (caffeic acid phenethyl ester) (Chan et al., 2013; Ferreira et al., 2017). There are some compounds, found only in tropical zones, e.g. sesquiterpenoids including germacrene d, ledol and spathulenol (Bankova et al., 2000). The main source of Cuban propolis is Clusia rosea, and contains polyisoprenylated benzophenone which is distinct from both European and Brazilian propolis (Awale et al., 2008; Bankova, 2005; Bankova et al., 2000).

5. Biomedical application of propolis

Propolis use has great effect on human health and is used for various purposes. Nowadays, it is used as an antioxidant, antifungal, anti-inflammatory, antiviral, anesthetic, antioxidant (Boukraà and Sulaiman, 2009; Omar et al., 2017), antitumoural, antiprotozoal, anticancer (Abdulrhman et al., 2012; Bankova et al., 2000; Bankova et al., 1992; Fokt et al., 2010; Koo and Park, 1997; Kuropatnicki et al., 2013; Popova et al., 2004; Rajpara et al., 2009; Ramos and Miranda, 2007; Sforcin, 2016) antihypertensive, anticarcinogenic and anti-hepatotoxic in addition to possessing cytotoxic activity, etc. (Toreti et al., 2013).

5.1. Anti-bacterial activity of propolis

Propolis has a significant effect against bacteria such as Enterococcus spp., Escherichia coli and Staphylococcus aureus (Al-Waili et al., 2012; Grange and Davey, 1990; Kasiotics et al., 2017; Kujumgiev et al., 1999; Kuropatnicki et al., 2013; Martin and Pileggi, 2004; Sforcin et al., 2000; Silici and Kutluca, 2005). It also surface that, ethanolic extracts of propolis were more effective against gram-positive bacteria and showed limited effect against gram-negative bacteria (Ahuja and Ahuja, 2011; De Castro, 2001; Fokt et al., 2010; Grange and Davey, 1990; Harfouch et al., 2016; Lotfy, 2006; Martinotti and Ranzato, 2015; Uzel et al., 2005; Wagh, 2013) but only stop growth by gram-negative bacteria due to high concentration of propolis (Sforcin et al., 2000). The mode of action of propolis is due to the interaction between physicochemical with other compounds such as pinocembrin, galangin, and pinobanksin (Castaldo and Capasso, 2002; Tosi et al., 1996; Wagh, 2013). Similarly, the antibacterial activity takes place due to its active compounds such as, aromatic compounds (caffeic acid) and flavonoids (Parolia et al., 2010). Moreover, propolis acts as a bactericidal agent, to stop division of bacterial cell, destroy cell wall, bacterial cytoplasm (Parolia et al., 2010) and stop protein synthesis (Lotfy, 2006; Machado et al., 2017). The component of propolis such as Pinocembrin shows antibacterial activity towards Streptococcus spp. artepillin C, p-Coumaric acid and 3-phenyl-4-di hydrocinnamylocinnamic acid towards Helicobacter pylori and Apigenin strongly restrain bacterial glycosyltransferase (Martinotti and Ranzato, 2015).

Brazilian propolis was more effective against Gram-positive bacteria as compared to Gram-negative ones (Salomao et al., 2008). Propolis show antibacterial activity against some aerobic bacteria such as, Bacillus cereus, B. subtilis, Enterococcus faecalis, Micrococcus luteus, Nocardia asteroides, Rhodococcus equi, Staphylococcus auricularis, S. epidermidis, S. capitis, S. haemolyticus, S. warneri, S. mutans, S. hominis, Streptococcus cricetus, St. faecalis, St. pyogenes, St. pneumoniae, St. sobrinus and St. viridians (Fokt et al., 2010).

5.2. Anti-fungal activity of propolis

Propolis showed activity against different fungi (Acikelli et al., 2013; Aghel et al., 2014; Al-Waili et al., 2012; Alvareda et al., 2015; Franchin et al., 2016; Kartal et al., 2003; Marcucci, 1995). It was investigated that propolis inhibit the aflatoxigenic fungi, and also decreases conidial growth in Aspergillus flavus. Propolis from different areas show activity against Candida guilliermondii, C. guilliermondii, C. krusei, C. albicans. In another investigation, a French propolis was effectively used against human fungal pathogen C. albicans, C. glabrata, Aspergillus fumigates. A constituent of propolis called pinocembrin shows activity against Penicillium italicum, which stops mycelial growth and acting on the pathogen respiration and energy homeostasis leading to the rupturing of cell membrane and metabolism disorder (Sforcin, 2016). Propolis also showed fungicidal effect against yeast (Sforcin et al., 2000). The presence of flavonoids in propolis shows fungicidal activity against C. pelliculosa, C. parapsilosis, and Pichia ohmeri, C. famata, C. glabrata (Wagh, 2013). Australian propolis showed antifungal activity towards C. albicans, due the greater amount of pinocembrin (Banksota et al., 2001b). It was reported that, constituents of propolis such as, 3-acetylpinobanksin, pinobanksin-3-acetate, pinocembrin, p-coumaric acid and caffeic acid out of 26 or more constituents show anti-fungal activity. Furthermore, caffeic acid showed antimycotic activity towards Helminthosporium carotovorum (Ozcan, 1999). Propolis showed good result against Mycobacteria, Candida, Trichophyton, Fusarium as well as other skin infecting fungi (Fokt et al., 2010).

5.3. Anti-tumoural activity of propolis

The components of propolis possess anti-tumoural property (Banksota et al., 2000; Callejo et al., 2001; Kim et al., 1998;...

5.4. Antioxidant activity of propolis

The major component of propolis is artepillin C, which acts as a... (Sforcin...

5.5. Antioxidant activity of propolis

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Komericki and Kränke, 2009; Su et al., 1995; Veiga et al., 2017) and components such as caffeic acid phenethyl ester (CAPE) (Castaldo and Capasso, 2002) and artepillin C were investigated, and found to possess anti-tumoural effects (Chan et al., 2013). These compounds of propolis are involved in the cell-cycle arrest, inhibition of matrix metalloproteinases, anti-angiogenesis effect and also inhibit disease transferring from one body part to another (Sforcin, 2016). Propolis has the ability to stop DNA synthesis in tumor cells, has the property to cause aging of tumor cells (Apoptosis) and possesses the capability to put into action the white blood cells for generating those agents which are able to regulate the function of B, T and natural killer cells respectively (Salomão et al., 2011; Wagh, 2013). Other compounds such as galangin, carnosol, nemerosone and chrysin are involved to prevent the rapid division of tumor cells (Sforcin, 2016). The cytotoxic activity of natural killer cell (NK) against murine lymphoma increased with the use of propolis for 3 days (Fokt et al., 2010; Sforcin, 2007). The presence of tumor suppressor proteins in Caffeic acid phenethyl ester causes the G0 gi lioma cells apoptosis (De Castro, 2001; Sforcin, 2016; Watanabe et al., 2011). Caffeic acid and esters as well as diterpenoids and phenolic compounds had the destructive capability against tumor cells. The anti-tumor effect of propolis is due to its polyphenolic constituents combined function (Sforcin, 2007). Decrease in the production of glutathione in tumor cell due to radiations, is consequently fulfilled by propolis, as the synthesis of glutathione in haemato poetic tissues (Chandna et al., 2014). Turkish propolis acts as an anti-tumor by enhancing program cell death it also showed retardation of leucine, thymidine and uridine from becoming cancer causing cells, by restraining the synthesis of DNA (Watanabe et al., 2011).

5.4. Anti-protozoal activity of propolis

Antiprotozoal activity of propolis against many protozoan that cause diseases in human and other animals such as, giardiasis (Freitas et al., 2006), chagas disease, leishmaniasis (Durán et al., 2008), trichomoniasis, toxoplasmosis (De Castro, 2001; Salomão et al., 2011; Torres et al., 1990) has been reported (Aghel et al., 2014). However propolis showed antiprotozoal activity against Leishmania donovani, Trypanosoma cruzi, Giardia lamblia, Trichomonas vaginalis, Toxoplasma gondii and G. duodenalis (Aminimoghadamfarouj and Nematollahi, 2017; Santos et al., 2002; Won Seo et al., 2003). It increases the glutathione level while stop lipid peroxidation and oxidized glutathione level. Consequently, propolis increase antioxidant activity against mercury induced-toxicity and acts as a hepatoprotective agent. Studies also showed that, extract of propolis possess protective role against CCL4-entice hepatoperal oxidative stress and resultant injury (Wagh, 2013). Propolis showed hepatoprotective effect toward liver damage in rats caused due to allyl alcohol CCL4 and paracetamol (Castaldo and Capasso, 2002; Tosi et al., 1996; Wagh, 2013). Banskota et al. (2001a) isolated phenolic components as well as diterpenic acids from Brazilian propolis, showing hepatoprotective property (Bankova, 2005; Banskota et al., 2001a).

5.5. Anti-inflammatory activity of propolis

Propolis possess the anti-inflammatory capability due to the presence of flavonoids (de Groot, 2013; Dobrowolski et al., 1991; El-Guendouz et al., 2017; Franchin et al., 2016; Khayyal et al., 1993; Machado et al., 2017; Castaldo and Capasso, 2002; Martinotti and Ranzato, 2015; Parolia et al., 2010; Ramos and Miranda, 2007; Viuda-Martos et al., 2008). It controls NADPH-oxidase ornithine decarboxylase, myeloperoxidase activity, hyaluronidase from guinea pig mast cells and tiro sine-protein kinase (Lotfy, 2006). The mode of action of these compounds is that, to restrain leukotrienes and prostaglandins production by white blood cells (Machado et al., 2017) and retarding myeloperoxidase activity, ornithine decarboxylase, tyrosine-protein-kinase and NADPH-oxidase (Ramos and Miranda, 2007). CAPE and galangin, both are components of propolar propolis demonstrated the anti-inflammatory property and inhibit carrageenan pleurisy, carrageenan oedema and helpful arthritis inflammations in rats (Wagh, 2013). The effect of Brazilian propolis and Chinese on the pathogenesis of collagen-induced arthritis in mice was also reported (Sforcin, 2016). Propolis regulate those inflammatory substances which are produced in the cell, as a result of pressures, poisonous material or pathogenicity (Kröl et al., 2013).

5.6. Hepatoprotective activity of propolis

Propolis acts as a hepatoprotective agent (Andrade et al., 2008; Banskota et al., 2001a; Khayyal et al., 1993; Peña, 2008; Prusotam and Four, 1996; Santos et al., 2002; Won Seo et al., 2003). It increases the glutathione level while stop lipid peroxidation and oxidized glutathione level. Consequently, propolis increase antioxidant activity against mercury induced-toxicity and acts as a hepatoprotective agent. Studies also showed that, extract of propolis possess protective role against CCL4-entice hepatoperal oxidative stress and resultant injury (Wagh, 2013). Propolis showed hepatoprotective effect toward liver damage in rats caused due to allyl alcohol CCL4 and paracetamol (Castaldo and Capasso, 2002; Tosi et al., 1996; Wagh, 2013). Banskota et al. (2001a) isolated phenolic components as well as diterpenic acids from Brazilian propolis, showing hepatoprotective property (Bankova, 2005; Banskota et al., 2001a).

5.7. Dental action of propolis

Ethanolic extract of propolis collected from four different regions of Brazil and Turkey, were used against different anaerobic bacterial strains, such as Actinomycyes naeslundii, Porphyromonas gingivalis, Fusobacterium nucleatum, Veillonella parvula, Lactobacillus acidophilus, Peptostreptococcus anaerobius, Peptostreptococcus micros, Prevotella oralis and Prevotella melaninogenica gave result of low inhibitive and also low bacterioidal activity through agar dilution method. Due to the presence of flavonoids, such as galangine, chrysin, pinobanksin, quercetin, naringenin, galangine and aromatic acids present in propolis are more effective against mouth abnormalities (especially dental diseases) (De Castro, 2001; Sforcin, 2016). It had significant role in dental pulp repairing (Chandna et al., 2014; Kuropatnicki et al., 2013). The combination of ethanolic extract of propolis with mouthwash and toothpastes enhanced the prevention of microbial infection as well as to treat inflammation of gums (De Castro, 2001; Pasupuleti et al., 2017).

5.8. Anti-oxidant activity of propolis

It was noted that, propolis had an antioxidant property due to its components galangin and pinocembrin (Ahn et al., 2004; Al-Hariri, 2011; El-Guendouz et al., 2017; Machado et al., 2017; Martinotti and Ranzato, 2015; Russo et al., 2002; Viuda-Martos et al., 2008). Due to higher polyphenols contents, the aqueous extract of propolis was more effective than ethanolic extracts. Galangin showed more activity in both extracts as compared to pinocembrin, due to structural difference in both (Wagh, 2013). The antioxidants had the ability to refuse free radical also prevent vitamin C, lipids and other compounds from destruction or oxidation. Because free radical and other factors are the primary cause of aging of cells and deterioration in such states as parkin-
ion in red blood cells of human (Zabaiou et al., 2017). Propolis had the antioxidant property and prevent lipid peroxidation due to radiations or before maturation of dermal cells aging (Król et al., 2013). The mechanism of anti-oxidant property of propolis is due to phenolic compounds which donate hydrogen ions to free radicals to protect cell from oxidation reactions and also food storage from oxidation and poisoning. Propolis had the capability to remove free radicals, which are the primary cause of lipids, nucleic acids and proteins oxidation (Chandna et al., 2014). Portuguese Propolis had the antioxidant property and prevent lipid peroxidation in red blood cells of human (Zabaiaou et al., 2017).

5.9. Anti-viral activity of propolis

It is known that, propolis showed antiviral activity (Amoros et al., 1992a; Amoros et al., 1992b), by inhibiting the virus entry into the cells, create disturbance in viral replication which cause destruction of RNA before or after its (RNA) release in the cells (Sforcin, 2016). Among other factors, propolis showed antiviral capability against genital herpes infection (HSV-2) (Kuropatnicki et al., 2013). Flavonoids which include kaempferol, acacetin, quer cetin, galangin and chrysin were reported as a cytotoxic (Marcucci, 1995). Some other researcher reported a compound, separated from poplar propolis called 3-methyl-buty-2-enyl caffeate inhibit titration and DNA synthesis of herpes simplex virus (type1) ex vivo. Another compound called isopentyl ferulated showed activity against influenza virus A1 Hong Kong (H3N2) ex vivo (Lofy, 2006). Propolis showed antiviral activity against avian influenza virus, rift valley fever virus, newcastle disease virus, herpes bursal disease virus and influenza virus (El Hady and Hegazi, 2002).

5.10. Wound healing activity of propolis

Propolis components also has therapeutic capability of propolis on tissue repairing and regeneration of injury (Kuropatnicki et al., 2013). These are due to its immunomodulatory, anti-inflammatory and antimicrobial features (Martinotti and Ranzato, 2015; Sforcin, 2016). It was also noted that, propolis lower the quantity of free radicals in inflammatory injury and to increase collagen and its constituents development (Król et al., 2013; Martinotti and Ranzato, 2015). It accelerate different enzymatic reactions, metabolism of cells, blood circulation and also formation of collagen fibers, due to the presence of bioflavonoids, arginine, vitamin C, provitamin A, B complex as well as some minerals (Parolia et al., 2010).

5.11. Anti-cancer activity of propolis

Due to its antioxidant activity, propolis (ethanolic extract) of Indian stingless bees had capability of anticancer against four various cancer cell lines at various concentrations; which gave result of apoptosis and cytotoxic of these cancer cells (Król et al., 2013). Flavonoids in propolis stop breast cancers, lung cancer, oral cancer as well as esophagus, stomach, colorectal, prostate, and skin cancer (Martinotti and Ranzato, 2015). Brazilian propolis had the property of angiogenesis as well as stops the increase number of human umbilical vein endothelial cells (Zabainou et al., 2017). Ethanolic extract of Brazilian propolis had the anti-cancer capability, examined upon 1.2 dimethylhydrazine which causing colon carcinogenesis in mice (Watanabe et al., 2011). The water extract of propolis from Thailand was examined by researchers, showed greater anti-cancer activity against colon carcinoma cell line SW620 as compared to methanolic extract of propolis (Watanabe et al., 2011). Ethanolic extract of propolis had the cytotoxicity against HT-29 colon adenocarcinoma cells as well as toward HT-1080 human fibrosarcoma, however demonstrate no cytotoxicity toward typical human skin fibroblasts (Watanabe et al., 2011).

6. Conclusion

Propolis; a honey-bee hive product, possesses a wide range of pharmacological potentials including anti-bacterial, anti-fungal, anti-protozoal, hepatoprotective, anti-oxidant, anti-inflammatory, anti-viral, anti-cancer and anti-tumor properties. Besides, the addition of ethanolic extract of propolis in the composition of mouthwashes and toothpastes enhances the prevention of microbial infection and is effective in the treatment of gums inflammation. Moreover, the presence of bioflavonoids, arginine, vitamin C, provitamin A, B complex along with some minerals possesses wound healing property and therefore enhances injury cure. Instead of individual component, there may be combined action, which leads propolis to have diverse biological performance. Finally, the development of new propolis compounds from propolis coming from diverse geographical origins is vital in controlling various pathogenic diseases. The current literature review suggests that propolis may be explored further for its potential properties against human pathogen.

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