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Production Status of Propolis in Ethiopia (Bee Glue) and its Medicinal Importance in Livestock

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Abstract

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. In Ethiopia its production is not reported in any part of the country.

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Propolis collection, bees, sprouts, flower-buds, trees.

Introduction

Honeybees collect resinous/waxy substances from exudates of plants to make a sticky material known as propolis (Parolia *et al.,* 2010). Propolis is a resinous substance with varying colors and consistencies, collected by Apismellifera bees from several vegetal sources. Propolis is a honeybee product with a very complex chemical composition, made by gummy and balsamic material collected by bees from sprouts, flower-buds, trees and other vegetal-tissue resinous exudates. During propolis collection, bees mix the beeswax and the collected propolis with the 13-glicosidase enzyme found in their saliva, hydrolyzing flavonoids glycosides into flavonoid aglycones (34). Afterwards, the collected material is augmented with enzymatic and salivary secretions (Park Y *et al.,* 1998). They utilize propolis to seal cracks in hives, encapsulate invader carcasses and protect their hives from infection by bacteria and fungi (Simone-Finstrom & Spivak 2010).

The term propolis comes from two Greek words, pro (which means for or in defence of) and polis (which means the city); thus propolis means in defence of the city or beehive (Ghisalberti 1979). Propolis is a sticky resinous substance, which is gathered from buds and the bark of trees. It is also known as “bee glue” as bees use it to cover surfaces, seal holes and close gaps in their hives, thus providing a sterile environment that protects them from microbes and spore-producing organisms, including fungi and molds (Wagh 2013). Flavonoids, aromatic acids, diterpenoid acids, triterpenoids, and phenolic compounds are the major components of propolis (Chen *et al.,* 2008; Daugsch *et al.,* 2008; Kumazawa *et al.,* 2008; Popova *et al.,* 2010). Propolis is typically composed of 50% resin and vegetable balsam, 30% wax, 10% essential and aromatic oils, 5% pollen and 5% other substances (Cirasino *et al.,* 1987; Monti *et al.,* 1983).

The ancient Greeks, Romans, and Egyptians were the first to use propolis, with applications in wound healing and as a disinfection substance (Sforcin 2007). According to Egyptian history, propolis was one of the main ingredients used in an embalming recipe for mummification, in which it serves as a preservative agent (Mejanelle *et al.,* 1997; Kuropatnicki *et al.,* 2013). Many other ancient civilizations, such as Chinese, Indian, and Arabian, all believed in the power of propolis to treat medical conditions like sores, ulcers, and some skin lesions, so it was used both internally and externally (Kuropatnicki *et al.,* 2013). Despite such early use, propolis is often still considered a "folk medicine" and remains an unofficial drug in the field of pharmacy (Valenzuela-Barra *et al.,* 2015; Kuropatnicki *et al.,* 2013; Toreti *et al.,* 2013).

Propolis for the last two decades, its use has begun to gain scientific backing. It is considered to be a promising natural source for the discovery of new pharmaceutical products to treat several types of diseases. Thus, it has been subjected to intensive studies investigating its antioxidant, antimicrobial, anti-inflammatory, immune-stimulating, and anticancer properties (Banskota *et al.,* 2001b). Nevertheless, propolis is still not considered an official conventional medicine in healthcare because of a lack of standardization of its composition due to the variability of its chemical components and thus its biological activity, which varies according to the different geographic locations of its collection (Silva-Carvalho *et al.,* 2015). In addition, there is presently inadequate data regarding therapeutic efficacy from clinical trial studies involving propolis. As a result, there are a few propolis products which have undergone FDA approval (Fitzmaurice *et al.,* 2011). Importance of propolis in the aspect of animal health is not compile in coordinated form so far in Ethiopia.

Therefore, the main objective of this study is to review the production status, the chemical compositions, and medicinal value of propolis in livestock in Ethiopia.

Propolis in History

The ancient Greeks, Romans, and Egyptians were the first to use propolis, with applications in wound healing and as a disinfection substance (Sforcin 2007). The long history of the use of propolis as a medicine is claimed to be as old as the use of other honeybee products, with the former being used from at least 300 BC (Ghisalberti 1979; Burdock 1998; Sforcin 2007).

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Physical Properties of Propolis

The color of propolis varies according to area and the plant source (Ahmed *et al.,* 2017; Lotfy, 2006; Sawicka *et al.,* 2012). It melts on 60 ^{0}C to 70 ^{0}C while some of its kinds melt on 100^{0}C (Martinotti and Ranzato, 2015;Wagh, 2013). Hard at low while soft at high temperature (Fokt *et al.,* 2010; Kuropatnicki *et al.,* 2013; Martinotti and Ranzato, 2015; Wagh, 2013). 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). 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;Wagh, 2013) as well as candies, shampoos, chocolate bars, skin lotions, toothpastes (Ferreira *et al.,* 2017; Yumnam *et al.,* 2017), antiseptic mixtures and is also used for the preservation of flesh. The estimated colony collection per year is 150–200 g (Martinotti and Ranzato, 2015).

Table.1 Composition of propolis

Compounds	References
Flavonoids, flavanones, flavones &flavonols: Islapinin, Ermanin, Pectolinarigenin, Sakuranetin, Isosakuranetin, Quercetin-3,3^0-dimethyl ether, 3-acetyl pinobanksin, Betuletol, Isorhamnetin, Kaempferide, Rhamnazin, Rhamnetin, Alnusin, Alpinetin, Alnusitol, Pinostrobin, Pinocembrin, Chrysin, Tectochrysin, Acacetin, Rhamnocitrin, Quercetin, Galangin, Apigenin, Pinobanksin, Kaempferol, Rutin, Catechin, Luteolin, Naringenin	Walker and Crane (1987) Lotfy (2006)
Benzoic acid and derivatives: Benzoic acid, Salicylic acid, Gentisic acid, Gallic acid, Phenylmethyl ester of benzoic acid, Phenylmethyl ester of salicylic acid, Trans-coniferyl benzoate, Trans-p-coumaryl benzoate, Protocatechuic acid	Walker and Crane (1987)
Benzaldehyde derivatives: Vanillin, Caproic aldehydes, Isovanillin p-hydroxybenzaldehyde, Protocatechualdehyde	Abdulkhani *et al.*, (2017),
Cinnamyl alcohol, cinnamic acid & its derivatives: Cinnamyl alcohol, Hydrocaeffic acid, Isoferulic acid, Cinnamic acid methyl ester, Cinnamic acid ethyl ester, Cinnamylidene acetic acid, Cinnamic acid, Caffeic acid, Ferulic acid	Walker and Crane (1987)
Aliphatic hydrocorbons: Eicosine, 1-octadecene, Tricosane, Pentacosane, Eicosane, Heneicosane	Walker and Crane (1987)
Sugar: d-ribofuranose, d-fructose, d-glucitol, d-gulose, Talose, Sucrose, d-glucose	Walker and Crane (1987)
Vitamins: B1, B2(complex), B6, C, E	Kuropatnicki *et al.*, (2013)
Nicotinic acid, Pantothenic acid Chalcones&dihydrochalcones: Alpinetinchalcone, Naringinenchalcone, Pinobanksinchalcones, Pinobanksin-3-acetate chalcone, Pinostrobinchalcone, Pinocembrin chalcones, Sakuranetinchalcone, 2,6,a-trihydroxy-4^0-methoxy chalcone, 2^0,6,dihy droxy-4^0-methoxydihydro chalcone, 2^0,4^0,6-trihydroxydihydro chalcone	Marcucci (1995)
Amino acids: Alanine, b-alanine, a-amino butyric acid, d-amino butyric acid, Arginine,Asparagine, Aspartic acid, Cystine, Cystein, Glutamic acid, Glycine, Histidine,Hydroxyproline, Isoleucine, Leucine, Lysine, Methionine, Ornithine,Phenylalanine, Proline, Pyroglutamic acid, Sarcosine, Serine, Threonine,Tryptophane, Tyrosine, Valine	Marcucci (1995)
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 isoferulate, 3-Methyl-2-butenyl isoferulate, 3-Methyl-3- butenylcaffeate, 2-Methyl-2-butenyl caffeate, 3-Methyl-2-butenyl caffeate, Benzyl caffeate, Phenylethylcaffeate, Cinnamylcaffeate, Tetradecylcaffeate, Tetradecenylcaffeate, Tetradecenylcaffeate (isomer)[b], Tetradecanylcaffeate[b], Hexadecylcaffeate	El Hady and Hegazi (2002)
Other acids and derivatives: Phenylmethyl ester of 14-methylpentadecanoic acid, Ethyl ester of palmitic acid, Myristic acid, Sorbic acid, Butyl-2-methylpropyle ester of Phthalic acid, Stearic acid, Methyl ester of alnustic acid	Walker and Crane (1987)

Alcohol, ketones, phenols and heteroaromatic compounds: Benzyl alcohol, Hexadecanol acetate, Coumarine, Pterostilbene, Xanthorrhoeol, Scopoletol	Walker and Crane (1987)
Terpene, Sesquiterpene, alcohol & derivatives: Geraniol, Neroledol, b-bisabolol, Guaiol, Farnisol, Dihydroeudesmol, a-acetoxybetulenol	Walker and Crane (1987)
Sesquiterpene& Triterpene hydrocorbons: b-patchoulene, b-bisabolene, Squalene, b-bourbonene, Copaene, Calarene, Calamenene, Caryophyllene, Patchoulane, Selenene, Aromadendrene	Walker and Crane (1987)
Sterols & steroid hydrocarbons: Cholestrilene, Cholinasterol, Stigmasterol, b-dihydrofucosterol, Lanosterol, Cholesterol	Walker and Crane (1987)
Minerals: Sr, Ba, Cd, Sn, Pb, Ti, Ag, Co, Mo, Al, Si, V, Ni, Mn, Cr, Na, Mg, Cu, Ca, Zn, Fe, K	Pasupuleti *et al.*, (2017),
Enzymes: Glucose-6-phosphatase, Acid phosphatase, Adenosine triphosphatase, Succinic dehydrogenase	Walker and Crane (1987)
Ketones: Acetophenone, p-acetophenolacetophenone, Dihydroxy acetope9i9inone, Methylacetophenone, Hept-5-en-2-one, 6-methylketone	Marcucci (1995)
Waxy acids: Archid acid, Behenic acid, Cerotic acid, Lauric acid, Linoleic acid, Lignoceric acid, Montanic acid	Marcucci (1995)
Aliphatic acids & aliphatic esters: Acetic acid, Angelic acid, Butyric acid, Crotonic acid, Fumaric acid, Isobutyric acid, Methylbutyric acid, Isobutyl acetate, Isopentyl acetate, Isopentinyl acetate	Marcucci (1995)
Alcohol: Benzene methanol, Cinnamyl alcohol, Glycerol, a-glycerophosphate, Phenethyl alcohol, Isobutenol, Hydroquinone, Prenyl alcohol	Marcucci (1995)
Aliphatic acids: Lactic acid, Hydroxyacetic acid, Malic acid, 5-Hydroxy-n-valeric acid, 2,3-Dihydroxypropanoic acid, Pentonic acid- 2-deoxy-3,5-dihydroxy-c-lactoneb, Pentonic acid- 2-deoxy-3,5- dihydroxy-c-lactone (isomer)b, Succinic acid, 2,3,4,5-Tetrahydroxypentanoic acid- 1,4-lactone, 2,3,4,5- Tetrahydroxypentanoic acid- 1,4-lactone(isomer)b, Nonanoic acid, Palmitic acid, Oleic acid, Decanoic acid, Dodecanoic acid, Tetradecanoic acid, Heptadecanoic acid, Octadecenoic acid, Tetracosanoic acid, Eicosanoic acid, Hexacosanoic acid, 2- Hydroxyhexacosanoicacid[b]	El Hady and Hegazi (2002)
Fatty acids (C7-C18 acids) and Other compounds: Phosphoric acid, 1,4-Dihydroxy benzene, 4 -Hydroxy-benzaldehyde, 4-Hydrory acetophenone,1,2,4-trihydroxy butane, 1,2,3-trihydroxy butanal, 1,2,3-trihydroxy butanal (isomer)b, Myristicin, 2,4-bis(dimethyl benzyl)-6-t- butyl phenol, 1,8-dihydroxy-3-methyl anthraquinone, Myristicin (isomer)	El Hady and Hegazi (2002)

Table.2 Different application of propolis

Application	Disease/agents/pathology	Reference
Anti-bacterial activity	*P. aeruginosa* and *S. aureus*	(Aryaei 2018)
	Lactobacillus acidophilus	(Airen *et al.*, 2018)
	S. typhimurium, and *L.monocytogenes*	(Bucio-Villalobos 2017)
	Streptococcus Mutans	(Becerra 2019)
	Escherichia coli and Staphylococcus aureus	(Gonsales 2006)
	Multi-drug Resistant Staphylococcus aureus,	(Al-Waili *et al.*, 2012)
	Bacillus subtilis	(Muli 2007)
Anti-fungal activity of propolis	*Penicilliumitalicum,*	Sforcin, 2016).
	C. pelliculosa, C. parapsilosis, and Pichia ohmeri, C. famata, C. glabrata	(Wagh, 2013)
	C. albicans	(Banskota *et al.*, 2001b).
	Helminthosponum carbon	(Özcan, 1999)
	Mycobacteria, Candida, Trichophyton, Fusarium	(Fokt *et al.*, 2010).
Anti-tumoural activity	cell-cycle arrest, inhibition of matrix metalloproteinases, anti-angiogenesis effect, inhibit disease transferring from one body part to another	Sforcin, 2016).
	stop DNA synthesis in tumor cells	(Salomão *et al.*, 2011; Wagh, 2013)
	Increase cytotoxic activity of natural killer cell (NK) against murine lymphoma increased	(Fokt et al., 2010; Sforcin, 2007)
	enhancing program cell	(Watanabe *et al.*, 2011)
Anti-protozoal activity of propolis	*Leishmaniadonovani, Trypanosoma cruzi, Giardia lamblia, Trichomonas vaginalis, Toxoplasma gondii* and *G. duodenalis*	Aminimoghadamfarouj and Nematollahi, 2017; Fokt *et al.*, 2010; Wagh, 2013).
	Chilomonas paramecium	(Marcucci, 1995).
	Trichomonas vaginalis	(Lotfy, 2006). Marcucci *et al.*, (2001)
	Toxoplasmosis	(De Castro, 2001; Salomão *et al.*, 2011; Torres *et al.*, 1990)
	Giardiasis	(Freitas *et al.*, 2006),
Anti-viral activity of propolis	Genital herpes infection (HSV-2)	(Kuropatnicki *et al.*, 2013)
	Herpes simplex virus (type1)	(Marcucci, 1995).
	Influenza virus A1 (H3N2)	(Lotfy, 2006).
	Avian influenza virus, rift valley fever virus, newcastle disease virus, herpes bursal disease virus and influenza virus	(El Hady and Hegazi, 2002).

Composition

Propolis is typically composed of 50% resin and vegetable balsam, 30% wax, 10% essential and aromatic oils, 5% pollen and 5% other substances (Cirasino *et al.*, 1987; Monti *et al.*, 1983). Chemically propolis is composed of more than 180 different types of chemicals (Kuropatnicki *et al.*, 2013). Propolis is collected both in temperate zone 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 (Chan *et al.,* 2013; El Sohaimy and Masry, 2014; Sforcin, 2016).

Application of Propolis

Propolis use has great effect on human and animal health and is used for various purposes. Nowadays, it is used as an antibacterial, antifungal, anti-inflammatory, antiviral, anesthetic, antioxidant (Omar *et al.,* 2017), antitumoural, antiprotozoal, anticancer (Abdulrhman *et al.,* 2012) antihypertensive, anticarcinogenic and anti-hepatotoxic in addition to possessing cytotoxic activity, etc. (Toreti *et al.,* 2013).

Production Status in Ethiopia

In Ethiopia, bee keeping practice had been an old age historical practice (Tessega 2009)). Ethiopia's tremendous variation of agro-climatic conditions and biodiversity favored the existence of diversified honeybee flora and huge number of honeybee colonies (Nuru 2007). The country has about 10 million bee colonies and over 800 identified honey-source plant (Kebede *et al.,* 2011). Ethiopia is fourth largest country next only to India, China and Turkey in the world by having 6,189,329 beehives. Presently, traditional forest and backyard, transitional and frame/modern hives practices are used in beekeeping. Out of total hives, there exist 95.73% traditional, 1.30 % transitional and 3.33% frame hives (CSA 2016/17). About one million households are involved in honeybee's business and more than 5.15 million hived honeybee populations are found in the country (Adgaba *et al.*, 2014).

Ethiopia stands ninth in the world and first in the Africa in honey production (Tesfaye *et al.,* 2017). Similarly, it stands first in Africa and third in the world in beeswax production (MoARD 2003). The country has the potential of producing up to 500,000 tons of honey and 50,000 tons of beeswax per annum (EIAR 2017). But currently production is limited to 47,706 tons of honey and 5542 tons of beeswax (FAO 2017). Honey is produced in almost all parts of Ethiopia. However, the most important honey regions are Oromia which accounts for over 51% of the bee colonies and 38% of the honey production, followed by Amhara which accounts for about 21% of the colonies and 26% of the honey production. The Southern Nations, Nationalities Peoples Regional State, on the other hand, accounts for about 18% of the bee colonies and 18% of the honey production. While Tigray and Benshangul-Gumuz accounts for 5% and 4% of the total bee colonies, and 8% and 7% of the total honey production, respectively (AAU 2015). In Ethiopia propolis is not collected and produced by commercial and farmers producers.

Propolis in Livestock Nutrition

In nutrition of laying hens, addition of propolis at a dose of 30 mg/l water or 5 g/kg feed increases the laying performance and egg shell thickness, which increases the weight of eggs (Chmieleski W 2005; Burdock GA 1998). Supplementation of broiler feed with propolis was found to result in greater weight gain and higher feed conversion efficiency (Ellman GL 1959; Shalmany K S and Shivazad M 2006).

Furthermore, the mortality rate was lower in a group of birds that received propolis supplementation. It is worth emphasising again that propolis is an alternative to antibiotics, since supplementation of feed while rearing broilers in the conditions of heat stress prevents occurrence of oxidative stress(Seven PT and Seven I 2008; Seven PT *et al.,* 2012). Propolis also increases immunity, as addition of 3 g of propolis/kg of feeding laying hens elevated the level of IgG and IgM in blood serum and increased the erythrocyte count in peripheral blood (Giurgea R *et al.,* 1984; Çetin E *et al.,* 2010). Addition of 20 mg of a propolis extract per 100 g of chicken feed everyday for 15 days resulted in an increase in total plasma protein, γglobulins, IgG and IgA (Mathivanan V *et al.,* 2013). Daily consumption of 20 mg of apropolis extract by chickens for 15 days was found to decrease thelevels of cholesterol and transaminases (ALT, AST) and to increase thelevel of proteins and amino acids in peripheral blood (Giurgea R, *et al.,* 1981).

Not only poultry responds positively to propolis supplementation innutrition. Addition of propolis to lamb diet increases weight gain, feed conversion and digestibility and the percent content of meat. Italso improves weight gain and feed conversion in pregnant cows [49]. Noteworthy, there is no toxic effect of substantial propolis doses on fishes. In order to demonstrate a toxic effect of propolis, the rainbow trout received it for 8 weeks at the doses of 0 g; 0, 5 g; 1, 5 g; 4, 5 g; and9 g/kg feed. The propolis doses neither exerted toxic effects nor caused significant changes in the parameters of fish growth (Bonomi A and Bonomi BM 2002).

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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