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Review of Anti proliferative, anti-oxidative and anti inflammatory biomedical applications of propolis in scavenging of human diseases

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Abstract
Propolis, byproduct of honey bees, has many anti microbial, antifungal and antitumor properties. Honey develop the Propolis to fasten the holes and fractures and also for restoration of the beehive which helps in lubrication, keeping the internal temperature (35ºC) and preventing the attack of predators. It also helps in saving the beehive from environmental erosion and weathering processes. Besides this utilization Propolis also has many benefits in curing various health problems like allergies, gynecological, oral and gastrointestinal disorders. However the accurate procedure in curing the illnesses have not been not completely evaluated and understood that's why more clearly scientific approach is needed to explore the procedure. This paper deals with review of different therapeutic and biological properties of propolis that are listed and analyzed in past years.

Keywords: propolis, honey bee, health effects

Introduction
Propolis is commonly called as the "bee glue", that is a generic name that suggests to the resin based substance collected by the bees from various kinds of plants. The word "propolis" is originated from Greek meaning defense city or community or it means beehive [1].

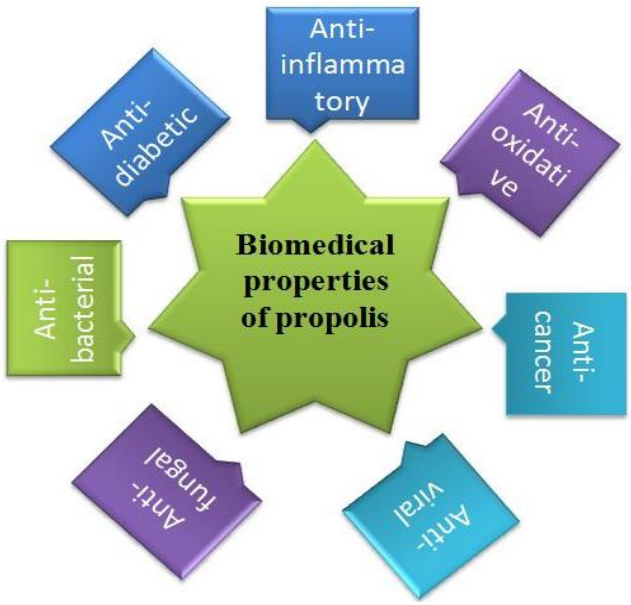

Fig 1: Biomedical properties ho honey bee propolis

Propolis function is lubricating and protecting the beehive from holes and cracks. It is also helps in making smooth internal beehive, keeping its internal temperature (35°C) so that no external damage for example weathering or predating can happen. Moreover, propolis strengthens the cell wall and helps in aseptic internal conditions. Propolis is soft and sticky with pleasant smell when it is heated. Propolis and its extracts are being applied in various treating many diseases because of its antiseptic, antibacterial, anti-inflammatory, antimycotic, antifungal, antioxidant, antiulcer, immunomodulatory and anticancer properties [2, 13].

Biochemical composition of propolis
Among bee products propolis is the third most important component. Its constituents are mostly of resin (50%), essential oils (10%), wax (30%), pollen (5%), and other organic compounds (5%) [7]. Among phenolic compounds propolis also have esters, terpenes, flavonoids, beta-steroids, alcohols and aromatic aldehydes, are the significant organic compounds present in [3]. Among twelve kinds of flavonoids chrysin, pinocembrin, rutin, acacetin, kaempferol, apigenin, luteolin, myricetin, naringenin, galangin, catechin and quercetin; two acids, cinnamic acid and caffeic acid; and one stilbene derivative also have been identified in extracts of propolis electrophoresis (capillary zone). Propolis also restrains significant vitamins, for example vitamins (B1, B2, B6, C, and E) including valuable minerals for example (magnesium (Mg), manganese (Mn), calcium (Ca), sodium (Na), copper (Cu), potassium (K), zinc (Zn), and iron (Fe). Some enzymes are also present in propolis ((succinic dehydrogenase, glucose-6-phosphatase, acid phosphatase and adenosine triphosphatase [5].

Table 1: Health Benefits of Propolis

Health benefits	Propolis extracts	Propolis activity	References
GIS activity	Ethanol extract	Anti-parasitic activity	[15]
	Alcoholic extract	Anti-ulcer genic effect	[16]
	Feed mixtures	Anti-microbial activity	[21]

	Ethanol extract	Protective effect in gastric ulcer	[22]
	Pollen and propolis dose	Simulation GIS activity	[24]
	Ethanol extract of propolis	Effect on digestive enzyme activity	[23]
	Hydrolcoholic extract	Anti-ulcer activity	[25]
Gynecological effect	Ethanol extract	Anti-fungal activity	[18]
		Anti-fungal activity	[17]
Oral activity	Propolis dose	Anti-bacterial activity	[19]
	50% propolis extract	Mouth wash	[26]
	propolis dentifrice with tooth paste	Anti-microbial activity against *Streptococcus mutans*	[27]
	Ethanol extract	Dental plaque removal	[28]
Anti-cancer treatment	Ethanol extract	Anti-breast cancer	[29]
	Ethanol extract	Anti-melanoma tumor	[30]
	Propolis extract	Anti-lung cancer	[31]
	extract	Anti-bladder cancer	[36]
	Aqueous extract	Anti-tumor	[20]
	Aqueous extract	Anti-cancer in lymphocytes culture	[35]
	Ethanol extract	Inhibition of carcinoma cells	[37]
	Propolis extract	Anti-carcinogenic and anti-biofilm	[38]
	Ethanol extract	Enhance apoptosis inducing potential in cancer cells	[39]
Dermatological effects	Ethanol extract	Anti-*acne vulgaris* treatment	[32]
	Ethanol extract	Healing of burn wounds	[33]
	Topical propolis	Healing of diabetic foot ulcer	[34]
	Pure Propolis 500mg/d	Treatment of cutaneous warts	[40]
	Ethanol extract	Treatment of onychomycosis	[41]
	Mixtures of propolis and aleovera	Treatment of psoriasis	[42]

Effects as anti-Gastrointestinal disorders

The contact with parasitically infected surfaces causes infection on contact. When gastro intestinal tract is disturbed by parasitic infection it causes nausea, diarrhea, bloating and abdominal pain. It also has been identified as useful therapeutic substance in antioxidant, anticancer and anti-inflammatory actions. However some researchers are also investigated use of propolis in viral infections. The in vitro effect on the growth and adherence was identified by using propolis ethanolic extract for *Giardia duodenalis trophozoites* [6]. Propolis inhibited the growth as well as adherence of the trophozoites by promoting detachment of this parasite. Its efficiency against giardiasis has also been analyzed by applying the propolis on giardiasis infected children and adults and their cure rate was among 52% and 60% more than the efficacy of synthetic drug (40% cure rate). Propolis also contains anti histaminergic, anti-inflammatory, anti-acid, and anti-*H. Pylori* properties which might be helpful in treating ulcer of gastro intestinal tract [8].

Care taker of Gynecological disorders

The causes of widely spread disease indicative vaginitis are vulvovaginal candidiasis (VVC) and bacterial vaginosis (BV). The lackining of *Lactobacillus* spp. in the vaginal tract is differentiated aspect of infections in vagina. The infection is happened with overly grown vaginal pathogens for example yeast-like fungi with increase in pH. *Candida albicans* causes more vaginal infections in diabetes patients. A research study was done on the efficacy of propolis 5% aqueous solution which showed vaginal improvement [11]. Because of propolis anesthetic properties it is useful in providing early relief in illness along with antiseptic effect. Therefore, propolis can be applied for Recurrent Vulvovaginal Candidiasis (RVVC) and very good option medicine for the patients who cannot take antibiotics because of concurrent pharmaceutical medicines. Propolis proved to be very effective when it is tested against conventionally available medicines. The solution of propolis extract depicts less toxicity which showed that it can be used as alternative to conventional medicines for vaginitis. Furthermore, PES is proficient against fungus so it is useful as anti-biofilm material to limit the growth of *C. albicans* for RVVC as well as to increase resistance in anti-fungal drugs [12].

Dentistry guard

Human oral cavity has space for many many microflora and growth of bacteria on extensive level may cause many oral diseases due o excessive pathogenic growth. Propolis might be helpful in rescuing he oral cavity from bacterial invasions to avoid plaque formation and periodonitis causing bacteria as it also have anti-bacterial characterization. Chlorhexidine used in oral treatment produce more cytotoxic actions than propolis solution in gum fibroblasts. It was also found that mouth wash containing propolis solution is curative in surgical wound healings. His idea proliferate the use of propolis solution to use as mouth wash and to disinfect the tooth brushes. Experimentally 3% extract of propolis in ethanol added to toothpaste gel was applied in group of patients resulted that propolis is effective in treating gingivitis caused by dental plague. Propolis extracts proved to be helpful in curing halitosis, where a person experience unpleasant breath because of bad oral health condition. Propolis based toothpastes and mouthwashes are applied because of they limit the growth of gingivitis and periodontitis causing bacterial plaque and other pathogenic microflora. This shows propolis is efficient therapeutic agent [27].

Anti-tumor effect

Propolis also found to be effective in treating the breast cancer as it has some antitumor traits that make it able to cure the disease by killing the breast cancer through induced apoptosis in human. Propolis is selectively toxic that means show no or very low toxicity toward normal cells and kills only cancer cells that can make it important agent in treating breast cancer [8]. Galangin which is very important flavonoid in Algerian propolis proved to be good killing agent of

melanoma tumor by inducing in vitro apoptosis and also inhibited the growth of tumor cells. Turkish propolis extracts are also applied to treat human lung cancer as it induces apoptosis and poses endoplasmic reticulum stress. It also induces caspase activity and reduces potential of mitochondrion cell membrane. These results showed that propolis might be helpful in lowering the cancer cell production [9].

Dermatological Care

Propolis is extensively applied in dermatological products (creams and ointments). Propolis is anti-allergic, anti-inflammatory and antimicrobial and has promptive action of formation of collagen which makes it suitable for skin care products. A comparative research study was done by comparing the efficacy of propolis and silver sulfadiazine, conventional drug. The results showed propolis lessened the formation of free radical activity in wound beds that helped in healing process. Acne vulgaris was also used to apply clinically to treat by propolis extracts. Propolis proliferate the production of collagen content in tissue. Propolis is helpful alternative therapeutic treatment in healing of wounds by promoting wound closure in case where patients are also suffering human diabetic foot ulcer [10].

Fibronectin (FN), a glycoprotein with many functions and has high molecular weight effects the various organs and tissues by influencing their functional properties and stability of structure [13]. The fibronectin matrix has several functions in cell proliferation, cell differentiation, cell migration, cell adhesion, cellular signaling and cell migration. It also functions in collagen biosynthesis, platelet activity, clot formation, angiogenesis and re-epithelialization. Fibronectins help in repairing in for circumstances like degradation of intensified glycoprotien that promotes in imperfect microenvironment a cellular level and cause structural granulation tissues affliction. In that situation wound is prevented from healing repairing process is inhibited completely. On the accumulation of fibronectin it releases repairing components for example tenascin, fibrillin, tenascin, type I and type III.

Propolis has showed some suitable effects in the healing process of wounds for example it has antifungal and antibacterial activities because of its components (flavonoids, terpenes, phenolic compounds and enzymes). Propolis reduces oxidative stress by lowering free radical activity. Propolis increases type I and type III collagens in tissues that effects in collagen metabolism. This process reducing of ROS and collagen accumulation helps in creating extracellular matrix balance and production granulation tissues. Propolis has great potential in treating many illnesses like it helps in modifying fibronectin metabolism. Its function is to inhibit disintegration fibronectin and produce fibrous network of extra cellular matrix. Quercetin and resveratrol inhibited biosynthesis of fibronectin and TGFβ-dependent production of fibronectin, respectively in C2C12 myoblasts, which are active constituents of propolis. These constituents help in regulating fibronectins expression. As the fibronectin content is reduced in extracellelar space, epithelial cells mobility and migration is affected. However, propolis effects fibronectin metabolism that changes the wound healing mechanism [14].

Conclusion and Future Prospects

The present review focused on the potential health benefits of propolis. This natural remedial material is higly rich in active compunds such as phenolic compounds, flavonoids, phenolic acid, phenolic compounds, terpenes, and enzymes, which biologically active in preventing some diseases and promoting good health. Propolis has distinct efficacies so these bee products can be developed into potent apitherapeutic agents. However, some precautions need to be taken in case of allergens associated with bee products and right intake dosage must be found out thrugh experimental designs. Hence, it is necessary to conduct further studies to determine the critical mechanisms related to the pharmacological activities of this bee product and the appropriate dosage that can be taken in order to obtain promising health benefits.

References

1. Shehu A, Ismail S, Rohin MAK, Harun A, Aziz AA, Haque M. *et al* Antifungal properties of Malaysian Tualang honey and stingless bee propolis against Candida albicans and Cryptococcus neoformans. Journal of Applied Pharmaceutical Science. 2016; 6(2):044-050
2. de Groot AC. Propolis a review of properties, applications, chemical composition, contact allergy, and other adverse effects. *Dermatitis*. 2013; 24(6):263-282.
3. Hirata AN, Bruschi ML. Development and characterization of semisolid systems to deliver propolis in the oral cavity. Journal Basic Applied Science. 2010; 31(1):33-39
4. Jung WK, Lee DY, Choi YH. Caffeic acid phenethyl ester attenuates allergic airway inflammation and hyperresponsiveness in murine model of ovalbumin-induced asthma. *Life Sciences*. 2008; 82(13-14):797-805.
5. Avanço GB, Braschi ML. Preparation and characterization of ethylcellulose microparticles containing propolis. Journal Basic and Applied Sciences. 2008; 29(2):129-134.
6. Saavedra N, Barrientos L, Herrera CL, Alvear M, Montenegro G, Salazar LA. *et al* Effect of Chilean propolis on cariogenic bacteria Lactobacillus fermentum. *Ciencia e Investigacion Agraria*. 2011; 38(1):117-125
7. Bankova V, Bertelli D, Borba R, Conti BJ, da Silva, Cunha IB. *et al*. Standard methods for Apis mellifera propolis research. Journal of Apicultural Research, 2016, 1-49.
8. Badria F, Fathy H, Fatehe A, Elimam D, Ghazy M. Evaluate the cytotoxic activity of honey, propolis, and bee venom from different localities in Egypt against liver, breast, and colorectal cancer. J Apither. 2017; 2(1):1-4.
9. Temizer İK, Guder A, Celemli OG. Botanical origin and antioxidant activities of propolis from the Irano-Turanian region. Istanbul Journal of Pharmacy. 2017; 47(3), 107-111.
10. de Francisco L, Pinto D, Rosseto H, Toledo L, Santos R, Tobaldini-Valerio F. *et al*. Evaluation of radical scavenging activity, intestinal cell viability and

antifungal activity of Brazilian propolis by-product. *Food Research International*. 2018; 105:537-547.
11. Imhof M, Lipovac M, Kurz C, Barta J, Verhoeven HC, Huber JC. *et al* Propolis solution for the treatment of chronic vaginitis. International Journal of Gynaecology and Obstetrics. 2005; 89(2):127-132
12. Sforcin JM. Biological properties and therapeutic applications of propolis. *Phytotherapy research*. 2016; 30(6):894-905.
13. Mouhoubi-Tafinine Z, Ouchemoukh S, Tamendjari A. Antioxidant activity of some algerian honey and propolis. *Industrial crops and products*. 2016; 88:85-90.
14. Pasupuleti VR, Sammugam L, Ramesh N, Gan SH. Honey, propolis, and royal jelly: a comprehensive review of their biological actions and health benefits. *Oxidative medicine and cellular longevity*, 2017.
15. Freitas SF, Shinohara L, Sforcin JM, Guimarães S. In vitro effects of propolis on Giardia duodenalis trophozoites. *Phytomedicine*. 2006; 13(3):170-175.
16. Paulino N, Coutinho LA, Coutinho JR, Vilela GC, da Silva, Leandro VP. *et al*. Antiulcerogenic effect of Brazilian propolis formulation in mice. *Pharmacology & Pharmacy*. 2015; 6(12):580.
17. Imhof M, Lipovac M, Kurz CH, Barta J, Verhoeven HC, Huber JC. *et al*. Propolis solution for the treatment of chronic vaginitis. International journal of gynecology & obstetrics. 2005; 89(2):127-132.
18. Capoci IRG, Bonfim-Mendonça PDS, Arita GS, Pereira RRDA, Consolaro MEL, Bruschi ML. *et al*. Propolis is an efficient fungicide and inhibitor of biofilm production by vaginal Candida albicans. *Evidence-Based Complementary and Alternative Medicine*, 2015.
19. Pereira EMR, da Silva, JLD C, Silva FF, De Luca MP, Lorentz TCM. *et al*. Clinical evidence of the efficacy of a mouthwash containing propolis for the control of plaque and gingivitis: a phase II study. *Evidence-based complementary and alternative medicine*, 2011.
20. Inoue Kohei, Masayoshi Saito, Takao Kanai, Tetsuya Kawata, Naoyuki Shigematsu, Takashi Uno. *et al*. Anti-tumor effects of water-soluble propolis on a mouse sarcoma cell line in vivo and in vitro." The American journal of Chinese medicine. 2008; 36(03):625-634.
21. Kačániová M, Rovná K, Arpášová H, Čuboň J, Hleba L, Pochop J. In vitro and in vivo antimicrobial activity of propolis on the microbiota from gastrointestinal tract of chickens. Journal of Environmental Science and Health, Part A. 2012; 47(11):1665-1671.
22. Kakino M, Izuta H, Tsuruma K, Araki Y, Shimazawa M, Ichihara K. *et al*. Laxative effects and mechanism of action of Brazilian green propolis. *BMC complementary and alternative medicine*. 2012; 12(1):192.
23. Eyng C, Murakami AE, Duarte CRA, Santos TC. Effect of dietary supplementation with an ethanolic extract of propolis on broiler intestinal morphology and digestive enzyme activity." Journal of animal physiology and animal nutrition. 2014; 98(2):393-401.
24. Yesiltas B, Capanoglu E, Firatligil-Durmus E, Sunay AE, Samanci T, Boyacioglu D. *et al*. Investigating the in-vitro bioaccessibility of propolis and pollen using a simulated gastrointestinal digestion System. Journal of Apicultural Research. 2014; 53(1):101-108.
25. de Barros MP, Sousa JPB, Bastos JK, de Andrade SF. Effect of Brazilian green propolis on experimental gastric ulcers in rats. Journal of Ethnopharmacology. 2007; 110(3):567-571.
26. Jain S, Rai R, Sharma V, Batra M. Propolis in oral health: a natural remedy. World J Pharm Sci. 2014; 2(1):90-4.
27. Bertolini PFR, Biondi Filho O, Pomilio A, Pinheiro SL, Carvalho MSD. Antimicrobial capacity of Aloe vera and propolis dentifrice against Streptococcus mutans strains in toothbrushes: an in vitro study. Journal of applied oral science. 2012; 20(1):32-37.
28. Skaba D, Morawiec T, Tanasiewicz M, Mertas A, Bobela E, Szliszka *et al*. Influence of the toothpaste with brazilian ethanol extract propolis on the oral cavity health. *Evidence-Based Complementary and Alternative Medicine*, 2013.
29. Xuan H, Li Z, Yan H, Sang Q, Wang K, He Q. *et al*. Antitumor activity of Chinese propolis in human breast cancer MCF-7 and MDA-MB-231 cells. *Evidence-Based Complementary and Alternative Medicine*, 2014.
30. Benguedouar L, Lahouel M, Gangloff S, Durlach A, Grange F, Bernard P. *et al*. Algerian ethanolic extract of propolis and galangin decreased melanoma tumour progression in C57BL6 mice. In *Annales de Dermatologie et de Vénéréologie* Elsevier Masson. 2015; 142(6-7):S294.
31. Demir S, Aliyazicioglu Y, Turan I, Misir S, Mentese A, Yaman SO. *et al*. Antiproliferative and proapoptotic activity of Turkish propolis on human lung cancer cell line. *Nutrition and cancer*. 2016; 68(1):165-172.
32. Ali BMM, Ghoname NF, Hodeib AA, Elbadawy MA. Significance of topical propolis in the treatment of facial acne vulgaris. Egyptian Journal of Dermatology and Venerology. 2015; 35(1):29.
33. Olczyk P, Komosinska-Vassev K, Wisowski G, Mencner L, Stojko J, Kozma EM. *et al.* Propolis modulates fibronectin expression in the matrix of thermal injury. *BioMed research international*, 2014.
34. Henshaw FR, Bolton T, Nube V, Hood A, Veldhoen D, Pfrunder L. *et al*. Topical application of the bee hive protectant propolis is well tolerated and improves human diabetic foot ulcer healing in a prospective feasibility study. Journal of Diabetes and its Complications. 2014; 28(6):850-857.
35. Ozkul Y, Silici S, Eroğlu E. The anticarcinogenic effect of propolis in human lymphocytes culture. *Phytomedicine*. 2005; 12(10):742-747.
36. Erhan Eroğlu H., Özkul Y, Tatlısen A, Silici S. Anticarcinogenic and antimitotic effects of Turkish propolis and mitomycin-C on tissue cultures of bladder cancer. *Natural product research*. 2008; 22(12):1060-1066.

37. Ishihara M, Naoi K, Hashita M, Itoh Y, Suzui M. Growth inhibitory activity of ethanol extracts of Chinese and Brazilian propolis in four human colon carcinoma cell lines. *Oncology reports*. 2009; 22(2):349-354.
38. Kouidhi B, Zmantar T, Bakhrouf A. Anti-cariogenic and anti-biofilms activity of Tunisian propolis extract and its potential protective effect against cancer cells proliferation. *Anaerobe*. 2010; 16(6):566-571.
39. Szliszka Ewelina, Zenon Czuba, Maciej Domino, Bogdan Mazur, Grzegorz Zydowicz, Wojciech Krol. Ethanolic extract of propolis (EEP) enhances the apoptosis-inducing potential of TRAIL in cancer cells." *Molecules*. 2009; 14(2):738-754.
40. Zedan H, Hofny ER, Ismail SA. Propolis as an alternative treatment for cutaneous warts. International journal of dermatology. 2009; 48(11):1246-1249.
41. Veiga Flavia F, Marina C, Gadelha Marielen RT, da Silva, Maiara I, Costa Brenda Kischkel, *et al.* Propolis extract for onychomycosis topical treatment: From bench to clinic." *Frontiers in microbiology*. 2018; 9:779.
42. El–Gammal E, Di Nardo V, Daaboul F, Tchernev G, Wollina U, Lotti J. *et al*. Apitherapy as a New Approach in Treatment of Palmoplantar Psoriasis. Open Access Maced J Med Sci, 2018.