

## Effect of Propolis on Fungal Infection for Denture Wearers and Dry Socket

Ibrahim Alfahdawi <sup>(1)</sup>

### Key words

Propolis, oral infection, denture stomatitis, dry socket, fungal infection

### Abstract

Propolis is consist of various amounts of resins and beeswaxes that produced by the honeybees from different natural plants, as leaf buds and flowers. It is a sticky and dark-brown color material that produced by honeybees from natural plants that the bees mixed it with wax and applied it in building, construction and adaptation of the nests specially in repair cracks and defects in the bees hive. They have been used in medical folk or medical traditional since times of ancient. It is now known to be natural medical treatment with, antifungal, antibacterial, antioxiditive, antitumor and mmunomodulatory properties. These medical properties of propolis are motivating isolation researches, identification of the possible relationship of these with its biological activity, and chemical compounds. It was used in dentistry for healing of surgical wound (or post-surgical mouth pain), tooth hypersensitivity, pulp capping and root canal treatment. Propolis has a promising goal in future medically. This research shows the application of propolis, clinically, as a natural dental medicine. Furthermore; systemic and clinical applications of these drugs may have some adverse effects like liver toxicity, drug interactions etc. Using propolis as antifungal by local application shown that it reduces the incidence of dry socket and denture stomatitis that associated with the Candida. In present study, the propolis has been used in the following manner. It is applied to the tissue surfaces of dentures, two times daily for two weeks. Propolis putty can also applied to dry socket cases after complete debridement and irrigation of it. The results showed after use propolis that the signs and symptoms including pain, redness and inflammation areas related stomatitis were gradually disappear, after 2 to 14 days the denture stomatitis is healing by using a propolis paste. Propolis putty has an effect on the fungal infection of dry socket that gradually reduced pain and inflammation until complete healing. Aim of the study, after the treatment of patients with denture stomatitis, they were subjected to examination and evaluation of the mucosa and socket, Candidal quantitative cultures and confirmation the diagnosis by three methods: Germ tube, Gram Stain, and ChromAgar media.

### Introduction:

Propolis or "bee glue" is consist of various amounts of resins and beeswaxes that produced by the honeybees from different natural plants, as leaf buds and flowers.

It would be considered in the process of gathering, shaping and remodeling the resins that are collected and added to saliva with other secretions of the bee in addition to wax <sup>(1,2)</sup>. The applications are important because they have a privilege of the propolis as antibacterial (it can inhibit

(1) Ass. Prof., Prosthodontic department, College of dentistry, university of Anbar.

bacterial RNA polymerase) and antifungal effects in keeping the bees colony against diseases<sup>(3-5)</sup>. As biocide to kill invasive bacteria and fungi, bee Propolis is considered to have a higher healing features in addition to its capability to increase the new cell growth<sup>(6,7)</sup>. The propolis word came from Greek language: "pro" mean, in front, "polis" mean, city. The meaning of "in front of the city" suits well, the propolis role in the protecting of the bees colony. The Greek word of propolis also known as glue and describe of the function of propolis to seals and cement the opening and cracks of the bee hives<sup>(8)</sup>. As well as antibacterial activity is high relevant than the antifungal activity of propolis, but many researches have reported the ability of clinically important yeasts belonging to *Candida*<sup>(9-11)</sup> like *Candida albicans*<sup>(12,13)</sup>, in addition to the sensitivity of some filamentous fungi mainly dermatitis<sup>(14,15)</sup>. Longhini and Co-workers,<sup>(16)</sup> stated that propolis had antifungal features for dermatitis even within small concentrations, having reduced toxicity also in turn it has topical application. Variety in antifungal activity of propolis extracts can again be due to the chemical structure differences, propolis elements concentration and composition. As well as antibiotics, observed a synergistic effect with conventional antimycotic drugs<sup>(17,18)</sup>. Propolis nature is lipophilic, rigid, fragile and when cold becomes brittle material, but it becomes soft, pasty, gummy and adhesive property and be sticky when temperature raise. It has a characteristic and pleasant aromatic smell and difference in color, depending on its source and age, from yellow, green, red and dark brown. Propolis differed from yellow to be more darker brown color according to the resins source<sup>(19,20)</sup>. Propolis is its pro inhibition effect on specific and particular prostaglandins that achieved by block the enzymes which form specific prostaglandins that more benefit to the throat and mouth. For example, a major reasons for dental problems are the gum and tissue erosion which line the tooth sockets. Infectious bleeding and Inflammation may lead to tooth loss as well as a weakening of the bone structure. Nevertheless, propolis, can

inhibits production of the prostaglandins that resulting in the bleeding, inflammation as well as decomposition eventually. Actually, in the same time, propolis promotes other specific enzymes that improved strength of walls of the blood vessels that distributed in gums leading to a two fold effect on the mouth also propolis as anti-inflammatory agents aid immune system by promote phagocytosis, stimulate cellular immunity and healing effect on epithelial tissue of mouth<sup>(21,22)</sup>. Propolis is a complex content that result from mixing of derived natural plants and bees released of compounds and elements. The amount of the different materials found in the propolis that related to its position and time of collection but, generally, raw propolis is estimated to have a composition about of 50% resins, waxes 30%, essential oils 10%, and 5% for each of pollen and various organic Compounds<sup>(23,12)</sup>. The structure and composition of propolis chemically, is complex. Flavonoid and cinnamic acid (hydroxyl) derivatives are found as the primary biological essential compositions in propolis extract<sup>(1)</sup>, other materials and elements like flavonoids, amino acids, vitamins B, and more important, antibiotic substances<sup>(24-26)</sup>. However, its compositions are highly variable, depending on its geographical origin. Above than 300 constituents are identify in different samples which includes phenolic acid, flavonoids, fatty acid, vitamins (A1, B1, B2, B3, and B7), ester, amino acids and trepans, new consists, during chemical characterization of new types of propolis, were still being recognized<sup>(18,27,28)</sup>. The most favorite solvents as ethanol (ethyl alcohol), ether, glycol and water can be applied to commercial extraction. Chemical analysis of different solvents can applied in order to the assorted fractions are extract. More of the components of bactericidal are soluble in alcohol or water<sup>(29)</sup>.

### Materials and method:

Propolis is collected from honeycombs, dry and subject to exhaustive maceration, a rotary evaporator was used filtered aqueous ethanol and concentrated.

Separated the residue, which were subjected to silica gel chromatography<sup>(30)</sup>. Propolis is a natural black-green putty derived from honeydew was produced by bees, used to close gaps occur in honeycomb and act as antifungal to prevent any contamination for it. The propolis either putty (Figure 1) used for dry socket or paste (putty dissolved in alcohol to produce creamy like mixture) (Figure 2) used for denture stomatitis. Fungal swabs were taken from palatal mucosa, tissue surfaces of the dentures and dry sockets from every patient for cultured before treatment (24 denture wearers patients with denture stomatitis and 21 patients with dry socket). The propolis paste has been used in the following manner: It was put in the tissue surface of denture, tow times daily for fourteen days. Patients with denture stomatitis were instructed to stop the treatment after five days for 48 hours before examination and swap was taken for culturing. After seven days repeat culture after stop treatment for 48 hours, and patients with dry sockets were examined and swap was taken after one week. Before cream was spread, the inner surfaces of the dental prostheses were cleaned carefully and thoroughly with toothbrush, soap and water to remove any depress from the preceding application. After complete removal of inflammatory tissues, dry socket was filled by propolis putty. Propolis putty has effect on the inflammation of the fungi in the dry socket that show gradually reduces of the pain and fungal inflammation. Putty dissolved inside socket and start action as antifungal after some hours. After the treatment, all patients were followed up by examination and evaluation of the dental socket as well as mucosa of the palate and Candidal quantitative culture from the mucosa of the palate and tissue surface of the denture and used the following three methods for diagnosis:

- 1-Germ Tube <sup>(31- 33)</sup>
- 2-Gram Stain <sup>(34, 35)</sup>
- 3-ChromAgar media <sup>(33)</sup>

## Results & Discussion:

In general, propolis is much more safe, non-toxic substance and non-irritant if used as supplements or topical applied on the skin. Furthermore, as other honeybees products, allergic or adverse reaction may be due to this substance as an occupational effect. Propolis is confirmed that caffeic acid substance to be one of the leading cause of propolis allergy. Denture stomatitis can be represents as a chronic illness in denture bearing area for denture wearers, specially under maxillary prostheses. Although, there are large numerate of antifungal agents treatment failure is noticed mostly, the results showed that all signs and symptoms of redness, bleeding, pain, tender area and inflammation related stomatitis were removed gradually within 2-14 days until no signs and symptoms were evident with the propolis treated. Since the reason of the denture stomatitis is varied, several treatment optional procedures are to be considered, as correction of ill-fitting dentures, control of plaque accumulation or used 'topical or systemic antifungal therapy'. Smoothened rough areas of tissue surfaces of the dentures are needed to be in dental labrotary. The result is in agreement with the following: Nystatin tablets 500,000 units were allowed to dissolved inside the mouth 3 times per day for two weeks. Bergendal and Isacson found the sam results during treating denture stomatitis with nystatin powder, applied on the tissue surface of the denture, 3 times per day for 2 weeks <sup>(36)</sup>. Nystatin drug was formulated for oral indication as suspension or pastille. A miconazole varnish or as gel was administrated topically in tissue surface of dentures related stomatitis. One time daily applied of the miconazole varnish or two times daily as gel for two weeks is effective <sup>(37)</sup>. Martins et al. (2002)<sup>(38)</sup>, find the propolis extract (in vitro) inhibited the growth of *C. albicans*. Santos et al. (2008)<sup>(39)</sup>, Parolia et al. (2010)<sup>(40)</sup> and Shahin Nejat etal (2015)<sup>(41)</sup>, evaluate the efficacy of a propolis gel formulation in patients diagnosed with denture stomatitis clinically. Propolis had been applied to

avoid the clinical application of systemic antifungal agents in nystatin resistant cases. Itching and complications like allergic contact dermatitis should be reported as side effects. However, propolis paste used by the patient easily without side effect as allergy or itching and easy removed from denture surface. Denture stomatitis is an inflammatory process that is appear in many dental patients people as result of candida related by the use of unhygienic denture or trauma. Though *Candida albicans* are components of ordinary oral micro flora, many local and systemic factors can alter them to be a pathogen. Management of Denture stomatitis related to accurate history taking, proper diagnosis identification and elimination of predisposing factors commonly by using antifungal agents. Topical application of nystatin, amphotericin, miconazole etc: are effective in many cases. Because formation of the biofilm in candidiasis is more resistant to antifungal agent, can be used the systemic ketoconazole, fluconazole, or itraconazole. Furthermore, there were some interactions of drugs to overcome the clinical application of systemic antifungal agents; propolis cream was tried in candida related denture stomatitis. Propolis in a paste form can be used twice times per a day on the fitting inner surface of the denture base for 14 days has been proved to be much more effective. Propolis putty was used as fungal inflammation treatment of, showed

gradual reduction of the clinical signs and symptoms of pain and inflammation. The putty dissolved inside socket and start action as antifungal after some hours.

### Conclusions:

1. Propolis "bee glue" is a natural product, sticky and dark-brown color material that produced by honeybees from natural plants that the bees mixed it with wax and applied it in building, construction and adaptation of the nests specially in repair cracks and defects in the bees hive.
2. Treated the oral diseases in terms of antimicrobial activity of propolis associate with flavonoids and hydroxyl cinnamic acid, and lower associated risks.
3. The dentistal application of propolis is probably the more well scientifically documented and now applied practically in many countries, commonly, the propolis is applied in the different dental specialties as periodontology, oral mucosa pathology, oral surgery, orthodontics and prosthodontics. Propolis putty was used as fungal inflammation treatment of, showed gradual reduction of the clinical signs and symptoms of pain and inflammation.
4. Propolis in a paste form can be used twice times per a day on the fitting inner surface of the denture base for 14 days has been proved to be much more effective.



Fig. (1): Propolis putty



Fig. (2): Propolis paste

## References:

- 1- Kosenco S.V. and Kosorich Tiu. The Treatment of periodontitis with research. *Stomatologia-MOSK*,1990;69:27-29.
- 2-Mathivanan V., et al, A review on Propolis – as Folk Medicine, *Indian J. of Scie.*2013; Vol. 2 No. 3 Jan.
- 3-CRANE, E. History of other products from bees The world history of beekeeping and honey hunting. Gerald Duckworth & Co Ltd:London; 1999; 545-553.
- 4- Vijay D. Wagh\*and Rameshwar D. Borkar. , indian propolis: a potential natural antimicrobial and antifungal agent. *International Journal of Pharmacy and Pharmaceutical Sciences*,2012; Vol 4, Issue 4.
- 5- Almas K. Propolis as a natural remedy: An update. *Saudi Dent J* 2001; 13(1):45-9.
- 6- Seidel V, Peyfoon E, Watson DG, Fearnley J. Comparative study of the antibacterial activity of propolis from different geographical and climatic zones. *Phytother. Res.*2008; 22(9):1256-1263. doi: 10.1002/ptr. 2480.
- 7-Velazquez C., Navarro M., Acosta A., Angulo A., Dominguez Z., Robles R.,Robles-Zepeda R., Lugo E., Goycoolea F.M., Velazquez E.F., Astiazaran H., Hernandez J. Antibacterial and free radical scavenging activities of Sonoran propolis. *J Appl. Microbiol.*2007; 103(5): 1747-1756.
- 8-Vijay D. Wagh and Rameshwar D. Borkar, indian propolis: a potential natural antimicrobial and antifungal agent, *International Journal of Pharmacy and Pharmaceutical Sciences* ISSN- 0975-1491 ,2012;Vol 4, Issue 4.
- 9-Kujumgiev A., Tsvetkova I., Serkedjieva Y., Bankova V., Christov R., Popov S. Antibacterial, antifungal and antiviral activity of propolis from different geographic origins. *Journal of Ethnopharmacology.*1999; 64(3):235–240.
- 10- Kartal M., Yıldız S., Kaya S., Kurucu S., Topcu G. Antimicrobial activity of propolis samples from two different regions of Anatolia. *Journal of Ethnopharmacology.*2003; 86(1): 69–73.
- 11- Stepanović S., Antić N., Dakić I., Švabić-Vlahović M. In vitro antimicrobial activity of propolis and synergism between propolis and antimicrobial drugs. *Microbiological Research.* 2003;158(4):353-357.
- 12- Hegazia A.G., Abd E.I. Hady F.K., Abd Allah F.A. Chemical Composition and Antimicrobial Activity of European Propolis. *Z. Naturforsch.*2000; 55(1-2): 70-75
- 13- Trusheva B., Popova M., Bankova V., Simova S., Marcucci M.C., Miorin P.L., da Rocha Pasin F., Tsvetkova I. Bioactive constituents of Brazilian red propolis. *Evidence-based Complementary and Alternative Medicine.* 2006; 3(2):249–254.
- 14- de Castro S.L. Propolis: biological and pharmacological activities. *Therapeutic uses of this bee-product. Annual Review Biomedical Sciences.* 2001;3:49–83.
- 15- Oadi N. Matny, Salim H. S. AL-Warshan and Amna M. Ali, Antifungal Evaluation of Iraqi Propolis against *Penicillium expansum* and Mycotoxin Production in Apple. *Int.J.Curr.Microbiol.App.Sci.* 2015; 4(11): 399-405.
- 16- Longhini R., Raksa S.M., Oliveira ACP., Svidzinski TIE., Franco SL. Obtencao. de extratos de propolis sob diferentes condicoese avaliacao de sua



- atividade antifúngica. *Brazilian Journal of Pharmacognosy*.2007;17(3); dx.doi.org/10.1590/S0102-695X2007000300015.
- 17- Oliveira ACP., Shinobu CS., Longhini R., Franco SL., Svidzinski TIE. Antifungal activity of propolis extract against yeasts isolated from onychomycosis lesions. *Memórias do Instituto Oswaldo Cruz*. 2006;101(5): 493-497.
- 18- Ana Beatriz Sotero SIQUEIRA, Larissa Rodrigues Nolasco de, Araújo RODRIGUEZ, Ruth Karine Barroso SANTOS, Ricardo Romulo Batista MARINHO, Sheila ABREU, Raniel Fernandes PEIXOTO, Bruno César de Vasconcelos, GURGEL, Antifungal activity of propolis against *Candida* species isolated from cases of chronic periodontitis. *Braz Oral Res* [online]. 2015; 29(1):1-6.
- 19- Bankova V., Castro SL. & Marcucci MC., Propolis: Recent advances in chemistry and plant origin, *Apidologie*, 2000;31:3-15.
- 20-Amal A. Al-Abbadil, Ihab H. Ghabeish, Mazen A. Ateyyat, Azmi D. Hawari and Salah-Eddin A. Araj, A Comparison between the Anti-microbial Activity of Native Propolis and the Anti-microbial Activity of Imported Ones against Different Health Microbes *Jordan Journal of Biological Sciences* Volume 8, Number 1, March, ISSN 1995-6673, 2015 Pages 65 – 70.
- 21- Koya-Miyata S., Arai N., Mizote A., Taniguchi Y., Ushio S., Iwaki K., Fukuda S. Propolis Prevents Diet-Induced hyperlipidemia and mitigates weight gain in Diet-Induced obesity in mice. *Biol. Pharm. Bull.*2009; 32(12):2022—2028.
- 22- Izuta H., Shimazawa M., Tsuruma K., Araki Y., Mishima S., Hara. Bee products prevent VEGF-induced angiogenesis in human umbilical vein endothelial cells. *BMC Complementary and Alternative Medicine*, 9:45. 1-10. doi:10.1186/2009, 1472-6882-9-45.
- 23-Burdock GA., Review of the biological properties and toxicity of bee propolis, *Food Chem Toxicol* 1998;36(4):347-363.
- 24- Park YK., Alencar SM. & Aguiar CL., Botanical origin and chemical composition of Brazilian propolis, *J Agric Food Chem* 2002;50(9):2502- 2506.
- 25- Almas K., Dahlan A., Mahmoud A. Propolis as a natural remedy: An update. *Saudi Dental J*. 2001; 13: 45-49.
- 26- Melyssa Negri, Tânia P. Salci, Cristiane S. Shinobu-Mesquita, Isis R. G. Capoci, Terezinha I. E. Svidzinski and Erika Seki Kioshima, Early State Research on Antifungal Natural Products. *Molecules*, 2014; 19, 2925-2956; doi:10.3390/molecules, 19032925.
- 27- Alencar SM., Oldoni TLC., Castro M.L, Cabral ISR., Costa-Neto CM., Cury JA., Rosalen PL. & Ikegakid M., Chemical composition and biological activity of a new type of Brazilian propolis: Red propolis, *J Ethnopharmacol* 2007;113(2):278-283.
- 28- Stefan Bogdanov, Propolis: Composition, Health, Medicine: A Review, *Bee Product Science*. 2012;15.
- 29- N. Kalavathy, Sridevi J., P. Roshan Kumar, Sharmila. M.R., Jayanthi N. Denture induced fibrous hyperplasia: A case report 258 *Streamdent*. 2010; 1(3).
- 30- Sabir A. The identification of flavonoid groups in trigona propolis collected from Bulukumba regency south Sulawesi used on direct pulp capping treatment. *Majalah Kedokteran Gigi (Dental Journal) (In Indonesia)*, 2003; 59-63.
- 31- Evans E. G. and Richardson, *Medical Mycology a practical approach*. IRL Press ,U.K. 1989;



- 32- Ron J. Doyle. Biofilms, *Methoda in Enzymology*, 1999;310: 644- 656.
- 33- James DB. Biofilms II: Process Analysis and Applications. New York, USA: Wiley-liss. 2000.
- 34- Philip D. Marsh and Michael V. Martin. *Oral Microbiology*.,Churchill livingstone Elsever., London, U. K. 2009;
- 35- Odds F.C. *Candida and Candidosis* .mLeicester University, U.K. 1979;
- 36- George. A. Zarb Charles L. Bolender; *Sequelae caused by wearing complete dentures*, 12th Edn :Elsevier, 2004; pp. 34-50.
- 37- Lucio Milillo, Lo. Muzio L, Carlino P., Serpico R., Coccia E., Scully CCandida related Denture Stomatitis A pilot study of the efficacy of an amorolfine antifungal varnish, *Int. J. Prosthodont* . . 2005; 18(1): 55-59.
- 38- Martins RS., Péreira ES. Jr., Lima SM., Senna MI., Mesquita RA., Santos VR. Effect of commercial ethanol propolis extract on the in vitro growth of *Candida albicans* collected from HIV-seropositive and HIV-seronegative Brazilian patients with oral candidiasis. *J. Oral Sci.* 2002; 44(1): 41-48.
- 39- Santos VR., Gomes RT., de Mesquita RA., de Moura MD., França EC., de Aguiar EG., Naves MD., Abreu JA., Abreu SR. Efficacy of Brazilian propolis gel for the management of denture stomatitis: a pilot study. *Phytother. Res.* 2008;22(11): 1544-1547. doi: 10.1002/ptr.2541.
- 40- Abhishek Parolia, Manuel S. Thomas, M. Kundabala and Mandakini Mohan. Propolis and its potential uses in oral health. *International Journal of Medicine and Medical Sciences* 2010;Vol. 2(7) pp. 210-215.
- 41- Shahin Nejat, Abdollah Ghasemi Pirbaluti, Masoud Yazdani and Maryam Foroughi, In Vivo Antifungal Activity of Some Medical Herbs and Propolis against Fungal pathogens Associated with Ringworm, *International Conference on Chemical, Environmental and Biological Sciences (CEBS-2015)* 2015;March 18-19, Dubai (UAE).