Moestopo International Review on Societies, Humanities, and Sciences (MIRSHuS)
http: mirshus.moestopo.ac.id/index.php/mirshus
ISSN: 2775-9601

PROPOLIS AS A HEALING AGENT FOR PULP INJURIES

Mirza Aryanto*
Department of Endodontics, Faculty of Dentistry
Universitas Prof. Dr. Moestopo (Beragama)

Siti Nur Khairunnisa Alala
Universitas Prof. Dr. Moestopo (Beragama)

*Correspondence: mirza.a@dsn.moestopo.ac.id

ARTICLE INFO

Article History:
received: 16/08/2021
revised: 26/09/2021
accepted: 31/10/2021

Keywords:
Propolis, Materials for pulp, Wound healing for pulp

DOI:
https://doi.org/10.32509/mirshus.v1i2.16

ABSTRACT

As one of the natural resin materials produced by bees, propolis has been used as a traditional medicine for various diseases because of its biological and pharmacological activities. The purpose of this study was to analyze the potential of propolis as a healing agent for pulp injuries. A total of 35 journals from PubMed, Ebsco, ResearchGate, Wiley Online Library, and other international journal databases were analyzed. Propolis is very rich in active components such as flavonoids that have biological functions such as anti-inflammatory, antibacterial, antifungal and antioxidant which can act as a potential healing agent.

INTRODUCTION

The data from results of RISKESDAS in 2018 states that the average prevalence of the Indonesian population experiencing dental erosion is 46,333 people with 95% of pulp involvement. Pulp and periapical diseases occupy the 7th position of all diseases in Indonesian hospitals.

Pulpal diseases can occur due to caries, trauma, or exposure of the cavity as a result of preparations that causes pulpal injury. The various types of vital pulp therapy are categorized into direct and indirect, pulp capping, partial and full pulpotomy (coronal or pulp chamber).

For more than 50 years, calcium hydroxide and chlorhexidine have been established as ideal standards for disinfecting agents in root canal treatment. In the past few decades, people's interest in using alternative or natural medicines has increased all over the world. One of the natural ingredients for such medicines is propolis. Propolis is used in dentistry and endodontic treatment, for example as a desensitizing agent to treat dentin hypersensitivity, intracanal irrigation, treatment during root canal treatment, and as a pulp capping material.

In recent years propolis has been the subject of several studies, with the aim of elucidating its biological and pharmacological properties. It is acknowledged that propolis has antimicrobial activity as well as anti-

inflammatory, antioxidant, antitumoral, and regenerative tissue properties. Propolis has been found to be very effective against Gram positive bacteria; especially against Staphylococcus aureus; and Gram-negative bacteria against Salmonella. The effect of propolis on the growth and glucosyltransferase activity of Streptococcus mutans (S. mutans) was observed and the results showed that the insoluble glycan synthesis and glucosyltransferase activity were inhibited by propolis. Koru et al. studied the antibacterial action against certain anaerobic oral pathogens and found to be very effective against Lactobacillus acidophilus, Actinomyces naeslundii, Prevotella oralis, Porphyromonas gingivalis, Fusobacterium nucleatum and Veillonella parvula. The results showed that the antibacterial property of propolis was due to the presence of flavanoids and aromatic compounds such as cafeic acid. Anti-inflammatory property of propolis was due to the presence of caffeic acid phenethyl ester (CAPE) in propolis.

Research on propolis as a healing agent for pulp injuries has been done, for instance, in a study conducted by Sardana et al. (2013) who reported that propolis had a greater inhibitory effect on *Enterococcus faecalis* compared to calcium hydroxide. A similar study conducted by Braakhuis (2019) also stated that propolis has shown antimicrobial activity. In contrast to previous studies, Kayaoglu et al. (2011) showed that the antibacterial activity of chlorhexidine was more effective in inhibiting the growth of *Enterococcus faecalis*.

Widjiastuti et al. (2020) proved the potential of propolis in healing wounds by observing the increase in odontoblast-like cells and type 1 collagen. This is also supported by Rahayu et al. (2020), whose study showed an increase in type 1 collagen in the group combination of $Ca(OH)_2$ with propolis extract.

The purpose of this paper is to analyze the potential of propolis as a healing agent for pulp injuries.

METHOD

A total of 35 journals from PubMed, Ebsco, ResearchGate, Wiley Online Library, and other international journal databases were analyzed using the keywords: propolis, materials for pulp injuries, and pulp injured in endodontic. These databases were searched for articles published between 2011 and 2021. The inclusion criteria were (I) access to full text of article, (II) articles in Bahasa or English and (III) adequate sample size and correct statistical analyses. The excluded articles were: (I) systematic reviews, case reports, letter to editors and congress abstracts.

Author reads full text of all articles that mentioned the use of propolis in their topics or abstracts and selected those that fulfilled inclusion criteria.

DISCUSSION

Propolis is a mixture of various beeswaxes and resins obtained from honeybees from various natural plants, especially from flowers and leaf buds. Propolis is a resinous substance derived from honey bees (*Apis mellifera*) and has long been used in medicine because of its beneficial properties.

Propolis is strong and brittle at lower temperatures, while flexible and sticky at higher temperatures. Its melting point is between 60 °C and 70 °C. The best solvent used for the preparation of propolis is ethanol.

The composition of propolis consists mainly of resins, waxes and fatty acids, essential oils, pollens, and other minerals and organic compounds. The main compound is a resin consisting of flavonoids and phenolic acids or their esters. These compounds usually make up up to 50% of all materials.

Several hundred compounds have been characterised in different propolis types; however, the main chemical constituents of propolis are flavonoids, various phenolic and aromatic compounds, amino acids, minerals and vitamins A, E and B complex. These constituents appear in various concentrations depending on geographical location and botanical origin. Howsoever the exact composition of propolis from different botanical origins may vary, the biological effects are similar. This may be because of similar active ingredients in different types of propolis.

Propolis has several biological activities, including: (1) antibacterial; (2) anti-inflammatory; (3)antifungal; (4) antioxidant.

1. **Antibacterial.** Veiga et al. (2017) showed that propolis has high antibacterial activity. The antibacterial activity of propolis is most often tested on *E. coli, S. aureus, Salmonella spp. and P. aeruginosa.* Torres et al, (2018) in his research also concluded that Propolis was a significant antimicrobial bee product. Propolis acts more effectively against Gram-positive bacteria than Gram-negative bacteria. Propolis extract is known to possess antimicrobial activity against *Streptococcus mutans* (*S. mutans*), a Gram positive cocci, facultative anaerobic bacterium commonly found in the human oral cavity and a significant contributor to tooth decay. The extract might be used as an alternative measure to prevent dental caries. Propolis has also been evaluated for antimicrobial activity as an intracanal medicament, and has shown promising results. Propolis has been found beneficial in the treatment of gingivitis and oral ulcers in several small case studies and pilot clinical studies.

2. Anti-inflammatory. As anti-inflammatory agent, propolis is shown to inhibit synthesis of prostaglandins, activate the tymus gland, aid the immune system by promoting phagocytic activity, stimulate cellular immunity, and augment healing effects on epithelial tissues. Additionally, propolis contains elements, such as iron and zinc that are important for the synthesis of collagen.

Braakhuis (2019) concluded that the anti-inflammatory activity of propolis is related to compounds: flavonoids, phenolic acids and their esters, as well as Caffeic Acid Phenethyl Ester (CAPE). Research conducted by Prasetyo et al. (2013) also proved that the CAPE contained in propolis has been shown to be effective in preventing inflammation with the effect that CAPE has on inhibiting the activation of Nuclear Factor kB (NF-kB).

3. Antifungal. Khurshid et al. (2017) have concluded that Propolis has been shown to exhibit excellent performance by in vitro studies of yeasts identified as onychomycosis agents. At low concentrations, propolis is not only found to be fungistatic but also fungicidal.

The major constituents of propolis are flavones, flavanones, and flavanols. It is used in homeopathic and herbal practice as an antiseptic, anti-inflammatory, antimycotic, and bacteriostatic agent. There are many clinical applications of propolis in dentistry. To exemplify, a few are: relief from denture ulcerations and stomatitis, halitosis, mouth freshener, periodontal pocket/abscess, mouthwash, cervical, dentinal, and root caries sensitivity. Treatment of lichen planus, candidal infections, angular cheilitis, xerostomia, orthodontic traumatic ulcers, erupting teeth, pulp capping, temporary restorations and dressings, covering tooth preparations, mummifying caries decidous teeth, socket "covering‟ after extraction, dry socket (similar to "bone wax‟ and Whitehead‟s varnish), Pre-anesthetic (topical), Periocoronitis, etc.

4. Antioxidant. Sardana et al. (2013) stated that propolis contains flavonoids which are organic compounds with antioxidant properties. Propolis functions as a strong antioxidant so that it can prevent the emergence of free radical compounds, especially useful in the management of sepsis. The flavonoids concentrated in propolis are powerful antioxidants. Antioxidants have been shown to be capable of scavenging free radicals and thereby protecting lipids and other amalgam such as Vitamin C from being oxidized or destroyed. It is probable that active free radicals, together with other factors are responsible for cellular aging and degradation in such conditions as cardiovascular diseases, arthritis, cancer, diabetes, Parkinson disease and Alzheimer disease. Oxidative damage may also result in poor liver function. Studies on rats in vitro show that propolis extracts protect against damage to liver cells.

A tooth is made up of 4 tissue structures: enamel, dentin, cementum, and pulp. The pulp contains a vascular supply and is rich in nerves. The pulp is formed by cells involved in the secretion and reorganization of the extracellular matrix (ECM) rich in collagen. The pulp has an important role in the formation of dentin and is a loose connective tissue located in the center of the tooth.

Injury to the pulp can occur due to caries, trauma due to exposure to the preparation, infection with microorganisms, mechanical causes such as fractures or cracks, chemical factors and thermal factors that will trigger various kinds of inflammatory responses. Injuries of weak or moderate intensity will often resolve with a brief inflammatory response followed by reactionary dentinogenesis. In more severe injuries, the odontoblasts will vanished and if the inflammation is not controlled, the differentiation of a new generation of odontoblast-like cells will form and lead to the formation of a dentinal bridge at the site of exposure. This process is called reparative dentinogenetic.

PROPOLIS AS A PULP CAPPING AGENT

Like other connective tissue, pulp tissue has the potential to heal. A medicament is placed directly over the exposed pulp (direct pulp capping), or a cavity liner or sealer is placed over residual tooth structure in an attempt to maintain pulp vitality. Key responses of the dentin-pulp to injury include the deposition of tertiary dentin, which increases the distance between the injury and the pulp, and a reduction in dentin permeability by the formation of sclerotic dentin.

Propolis has been used as a pulp-capping agent in permanent teeth and as a pulpotomy agent in primary teeth. It was found that teeth capped with propolis form a hard tissue barrier. The probable components of propolis responsible for the formation of the hard tissue barrier are the flavonoids, which have been shown to cause less inflammation and harder tissue formation than non-flavonoid components. Flavonoids have anti-inflammatory properties by virtue of their suppression of immune cell activation, macrophage-derived nitric oxide and cytokine production and neutrophil activation. Flavonoids may inhibit bacterial growth in the pulp chamber thereby reducing the host response to bacterial antigens.

The effectiveness of propolis was due to its resinous and adhesive properties, since it seals the dentinal tubules and has anti-inflammatory property that decreases pulpal inflammation. These effects have been shown to be the result of the presence of arginine, vitamin C, provitamin A, B complex, and trace minerals such as copper, iron, zinc as well as bioflavonoids. All these factors of propolis help in good wound healing. In addition to wound

healing ability, propolis is a good antimicrobial agent. It prevents bacterial cell division, breaks down bacterial cell wall and cytoplasm. The other possible explanation was that dentin formation following pulp capping is known to involve differentiation of odontoblast-like cells that form reparative dentin and biosynthetic activity by surrounding primary odontoblasts. Both phenomenons require interaction between extracellular matrix molecules and growth factors such as transforming growth factor (TGF)-β1 and bone morpho protein (BMP)-2 and BMP-4, growth factors known to be important for odontoblast-like cell differentiation. Indeed, propolis is also capable of stimulating the production of TGF-β.

PROPOLIS AS PULPOTOMY AND PULPAL REGENERATION

Propolis has been used as as a pulpotomy agent in primary teeth. Pulp tissue regeneration is a healing process of inflammatory responses, immune signaling, and cellular interactions accompanied by tissue restoration after exposure to infection. Cellular communication between cells in the pulp and immune cells is very important to get the right response. Along with cellular signaling, migrating Mesenchymal Stem Cells (MSCs), such as Dental Pulp Stem Cells (DPSCs) can proliferate and differentiate into pulp tissue-forming cells including neurovascular tissue regrowth, as part of the pulp tissue healing response.

Healing an injury is a complex process. It consists of 4 phases including bleeding, inflammation, proliferation, and remodeling. Dental pulp is similar to other connective tissues in that it has the ability to restore. Characteristics of pulp healing include restoration of damaged soft tissue, differentiation of subodontoblasts into odontoblast-like cells and construction of dentinal bridges in injured pulp tissue. To help the wound healing process, an agent is needed. A good wound healing agent is an effective agent for modulating inflammation, accelerating fibroplasia and promoting remodeling in the shortest amount of time and with the fewest side effects.

Medellin-Luna et al. (2019) said that years of overuse of antibiotics has led to bacteria that are eventually resistant to many drugs. In cases like this, other natural and promising alternatives are needed with antibacterial, antifungal, antioxidant, and anti-inflammatory properties. One such alternative is propolis. Propolis is known as a good tissue repair agent in natural wound healing.

This is also supported by Oryan et al. (2018) in his research stating that propolis has great potential in healing and tissue regeneration. Caffeic Acid Phenethyl Ester (CAPE) is an active component in propolis. CAPE can induce collagen formation in dental pulp and reduce inflammation and pulp degeneration. Hadagali and Chua (2014) said that certain varieties and sources of bee products such as propolis are very effective for curing various diseases and can be used as anti-inflammatory agents and effective for wound healing.

Healing of injury to the pulp undergoes an inflammatory phase. Neiva et al. (2014) proved that propolis is effective as an anti-inflammatory agent. Propolis can also be used as an intracanal medicament for root canal treatment. This is supported by Nani et al. (2019), stating that propolis has strong anti-inflammatory properties and works by reducing the activation of NF-κB and TNF-α releases in macrophages, will ultimately reduce the entry of neutrophils into the inflammatory area. Esmeraldo et al. (2013) proved that green propolis could induce an inflammatory reaction in the dental pulp of rats after pulpotomy. Prasetyo et al. (2013) also proved this by administering Ethanol Extract of Propolis (EEP) to sepsis model mice. Administration

of EEP at a dose of 200 mg/kgBW/day significantly reduced the degree of inflammation, especially CAPE contained in propolis has been shown to be effective in preventing inflammation with the effect of CAPE in inhibiting the activation of Nuclear Factor-kB (NF-kB).

The flavonoid content in propolis is reported to increase the permeability of bacterial membranes and inhibit bacterial genetic coding. Flavonoids can inhibit the synthesis of nucleic acids, thus indicating that propolis is an effective antibacterial agent. Many studies have shown that propolis can limit the development of bacteria, plaque and pathogens due to its antibacterial properties. Braakhuis (2019) reported that propolis has shown various antibacterial activities against various pathogens. Sardana et al. (2013) reported that propolis had a greater inhibitory effect on *Enterococcus faecalis* as an endodontic disinfection agent.

Propolis has shown beneficial effects in the wound healing process with its antifungal properties. Compounds like phenolics and flavonoids present in propolis are responsible for its antifungal activity. This is supported by the results of research on antifungal activity by Shehu et al. (2016) These results indicate that propolis has the potential to be used as an alternative therapeutic agent against fungi.

The flavonoids and phenolic acids in propolis are also components with strong antioxidant effects. According to Braakhuis (2019), propolis has been reported to reduce oxidative stress in wounds by inducing antioxidant-related genes (hemeoxygenase-1 (HO-1), glutamate-cysteine ligase-modifier GCLM and-catalytic GCLC subunits) as well as increasing collagen and cell viability in cells exposed to high oxidative stress.

Sabir et al. (2016) showed that Propolis Ethanol Extract (EEP), propolis containing flavonoids and calcium hydroxide, had a better effect than non-flavonoid propolis in stimulating type 1 collagen in inflamed pulp. Another study supporting propolis as a pulp capping material was by Widjiastuti et al. (2020) indicating that propolis can accelerate the formation of odontoblast-like cells. According to a review by Rojcyzk et al. (2020), analysis of the earliest observational literature on recent experiments using advanced molecular biology techniques has revealed that propolis can be a useful support for wound healing. It can accelerate wound healing process and improve healing physiology mainly due to its anti-inflammatory, antibacterial, antifungal and antioxidant properties. In addition, propolis has the potential to be used in many fields of medicine, including dentistry. This is also supported by Amir et al. (2018) in his review of the application of propolis in dentistry, stating that propolis is efficacious for healing wounds and can even be used as a root canal irrigation solution. Certain cases of action using propolis cause side effects such as hypersensitivity, especially in topical applications that may cause allergic reactions. Thus, despite the positive safety profile of propolis, it is advisable to seek medical advice before using propolis products.

There were basic research data of propolis effect on conservative dentistry and endodontic treatment, mostly come from Eastern Europe where propolis has been used as a natural medicine. Unfortunately, only a few reports were published about successful clinical use of propolis in that field, so there is a need further human trial of this natural remedy in treating oral diseases. That fact may be influenced by many factors such as standardization the composition of propolis due to its chemical diversity is still a problem because propolis was collected in different geographic region and allergy/sensitivity to propolis particularly if patients are taking propolis

systemically. However, it seems that the result of basic research of propolis was useful to support its clinical application in dentistry.

CONCLUSION

As a complementary and natural alternative with minimal side effects, propolis has the potential to heal wounds and injuries due to the presence of components in propolis such as flavonoids which have anti-inflammatory, antibacterial, antifungal and antioxidant biological activities. Propolis works better when combined with other conventional ingredients such as calcium hydroxide as a disinfecting agent and intracanal medication in root canal treatment.

As conclusion, propolis is a natural medication with a promising future but further studies should be conducted to investigate its merit and demerits in clinical dentistry

REFERENCES

Abbasi AJ, Mohammadi F, Bayat M, Gema SM, Ghadirian H, Seifi H et al. Applications of Propolis in Dentistry: a review. Ethiopian Journal of Health Sciences. 2018;28(4).

Alfahdawi I. Chemical Compotitions in Propolis. Propolis in Medicine & Dentistry. Baghdad: Lambert Academic Publishing. 2017:11-12.

Anonymous. Indonesian Ministry of Health. Indonesian Health Profile 2010. Jakarta: Ministry of Health of the Republic of Indonesia, 2011.

Anonymous. Agency for Health Research and Development. Basic Health Research. Jakarta: Ministry of Health of the Republic of Indonesia. 2018.

Bogdanov S. Propolis : Biological Properties and Medical Applications. The Propolis Book 2nd ed.Muehlethurnen: Bee Product Science, 2016:1

Braakhuis A. Evidence on the Health Benefits of Supplemental Propolis. Nutrients. 2019;11(11):2705.

Duncan H.F, Smith AJ, Cooper PR Maintaining Dental Pulp Vitality. In: BS Chung (Editor). Harty's Endodontics in Clinical Practice. 7th ed. London: Elsevier. 2017:70-71.

Esmeraldo MR, Carvalho MG, Carvalho RA, Lima RD, Costa EM Inflammatory Effect of Green Propolis on Dental Pulp in Rats. Brazilian Oral Research. 2013:27:417-22.

Goldberg M. Pulp Anatomy and Characterization of Pulp Cells. In: Goldberg M(Editor). The Dental Pulp: Biology, Pathology, and Regenerative Therapies. New York: Springer,2014:13.

Hadagali MD, Chua LS The Anti-inflammatory and Wound Healing Properties of Honey. European Food Research and Technology.

Holland R, Gomes JE, Cintra LT, Queiroz IO, Estrela C. Factors Affecting The Periapical Healing Process of Endodontically Treated Teeth. Journal of Applied Oral Science. 2017;25:465-76.. 2014;239(6):1003-14.

Inova Newsroom. Wound Healing Center at Inova Loudoun treats complex wound and ostomy casice. Available in: https://www.inovanewsroom.org/ilh/2017/05/wound-healing-center-at-inova-loudoun-treats-complex-wound-and-ostomy-cases/ [Accessed July 19, 2021].

Jain S, Rai R, Sharma V, Batra M. Propolis In Oral Health: A Natural Remedy. World J Pharm Sci 2014; 2(1): 90-94

Kayaoglu G, mürlü H, Akca G, Gürel M, Gençay , Sorkun K et al. Antibacterial Activity of Propolis versus Conventional Endodontic Disinfectants Against Enterococcus faecalis in Infected Dentinal Tubules. Journal of Endodontics. 2011;37(3):376-81.

Khurshid Z, Naseem M, Zafar MS, Najeeb S, Zohaib S. Propolis: A Natural Biomaterial for Dental and Oral Healthcare. Journal of Dental Research, Dental Clinics, Dental Prospects. 2017;11(4):265.

Likitpongpipat N, Sangmaneedet S, Klanrit P, Noisombut R, Krisanaprakornkit S, Chaireltvanitkul P. Promotion of

Dental Pulp Wound Healing in New Zealand White Rabbit's Teeth by Thai Propolis Product. Journal of Veterinary Dentistry. 2019;36(1):17-24.
Munir A, Zehnder M, Rechenberg DK Wound Lavage in Studies on Vital Pulp Therapy of Permanent Teeth with Carious Exposures: A Qualitative Systematic Review. Journal of Clinical Medicine. 2020;9(4):984.
Neiva KG, Catalfamo DL, Holliday S, Wallet SM, Pileggi R. Propolis Decreases Lipopolysacchafide-induced inflammatory mediators in pulp cells and osteoclasts. Dental Traumatology. 2014;30(5):362-7.
Oryan A, Mohammadalipor A, Moshiri A, Tabandeh MR Topical application of Aloe vera accelerated wound healing, modeling, and remodeling: an experimental study. Annals of plastic surgery. 2016;77(1):37-46.
Oryan A, Alemzadeh E, Moshiri A. Potential Role of Propolis in Wound Healing: Biological Properties and Therapeutic Activites. Biomedicine & Pharmacotherapy. 2018;98:469-83.
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.
Prasetyo DH, Suparyanti EL Ethanol Extract Propolis Isolate Reduces Inflammation and Malondialdehyde Levels in Sepsis Model Rat Serum. Bandung Medical Magazine. 2013;45(3):161-6.
Przybylek I, Karpinski TM Antibacterial Properties of Propolis. Molecules. 2019;24(11);2047.
Rahayu RP, Pribadi N, Widjiastuti I, Nugrahani NA Combinations of Propolis and Ca(OH)2 in Dental Pulp Capping Treatments for the Stimulation of Reparative Dentin Formation in a Rat Model. F1000Research. 2020;9.
Rojczyk E, Klama-Baryła A, abuś W, Wilemska-Kucharzewska K, Kucharzewski M. Historical and Modern Research on Propolis and its Application in Wound Healing and Other fields of Medicine and Contributions by Polish Studies. Journal of Ethnopharmacology. 2020:113-159.
Šabanović M, Saltovi S, Avdić-Mujkić A, Jašić M, Bahić Z. Impact of Propolis on the Oral Health. Balkan Journal of Dental Medicine. 2019;23(1):1-9.
Sabir A, Mooduto, L, Kaelan C, Horax S. Impact of the Use of Ethanolic Extract of Propolis, Flavonoid and Non-Flavonoid Propolis for Direct Pulp Capping in Collagen Type I Density. Brazilian Journal of Oral Sciences. 2016;15(4):264-8.
Sabir A. Prospect Of Using Propolis In Conservative Dentistry And Endodontic Treatment (Basic Research Vs Clinical Application). Dentika Dental Journal, Vol 18, No. 2, 2014: 185-189
Santoso ML, Sudirman A, Setyowati L. Minimum Inhibitory Concentration of Propolis Solution against Enterococcus faecalis Bacteria. PDGI Journal. 2012; 61(3):96-101
Sardana D, Indushekar KR, Manchanda S, Saraf BG, Sheoran N. Role of Propolis in Dentistry: a review of the literature. Focus on Alternative and Complementary Therapies. 2013;18(3):118-25.
Scheid RC, Weiss G. Woelfel's Dental Anatomy, Enhanced 9th ed. Massachusetts: Jones & Bartlett Publishers; 2020:12-13
Shah D, Lynd T, Ho D, Chen J, Vines J, Jung HD et al. Pulp-Dentin Tissue Healing Response: A Discussion of Current Biomedical Approaches. Journal of Clinical Medicine. 2020;9(2):434.
Shehu A, Ismail S, Rohin MA, Harun A, Aziz AA, Haque M. Antifungal Properties of Malaysian Tualang Honey and Stingless Bee Propolis Against Candida albicans and Cryptococcus neoformans. Journal of Applied Pharmaceutical Science. 2016;6(2):44-50.
Simon S, Smith AJ, Lumley PJ, Cooper PR, Berdal A. The Pulp Healing Process: From Generation to Regeneration. Endodontic Topics. 2012;26(1):41-56.
Sugiaman VK The Role of Stem Cells in Regenerating Dental Pulp Tissue.

SONDE (Sound of Dentistry). 2019;4(1):43- 51

Widjiastuti I, Subiyanto A, Ningtyas EK, Popyandra R, Kurniawan MG, Retnaningsih FD *et al*. Propolis Extract as Pulp Capping Material Enhances Odontoblast-like Cell Thickness and Type 1 Collagen Expression (in vivo). Dental Journal (Dentistry Magazine). 2020;53(1):1-5.