JFSP Vol.9, No.3, September-December 2023, Page: 261-269
pISSN: 2549-9068, eISSN: 2579-4558
Jurnal Farmasi Sains dan Praktis
(JFSP)
http://journal.unimma.ac.id/index.php/pharmacy

STUDY OF INDONESIAN STINGLESS BEE (*Trigona* sp.) PROPOLIS POTENTIAL AS ANTIOXIDANT: A REVIEW

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https://doi.org/10.31603/pharmacy.v9i3.7105

Article info:
Submitted : 03-05-2022
Revised : 19-08-2023
Accepted : 06-10-2023

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Publisher:
Universitas Muhammadiyah Magelang

ABSTRACT
Indonesia is known have rich biodiversity, one of that is propolis. Propolis was an abundance bee product, especially from stingless bee species. Propolis has been known to have various health benefits, such as antioxidant and can maintain the immune system. However, comprehensive information regarding this potential is not widely known. The purpose of this study was to determine the potential of propolis *Trigona* sp. as an antioxidant from Indonesia. This study uses a screening method in journals that have been found through the search systems of Google Scholar, PubMed, Scopus and Garuda. Classification of data was based on inclusion and exclusion by selecting research journals that do not meet the criteria. The results of the screening that have been carried out show that the flavonoid and phenolic compounds present in the propolis Trigona sp. has potential as an antioxidant. The flavonoid and phenolic compounds contained in the propolis Trigona sp. has an important role in absorbing free radicals and has the potential to be developed as a product.

Keywords: Propolis; Antioxidant; Stingless Bees; Phenolic

1. INTRODUCTION

Indonesia is rich in natural resources, such as bees with various species (Rasmussen & Gonzalez, 2017). *Trigona* sp. is a type of bee that exists in Southeast Asia and belongs to the stingless bee group. *Trigona* sp. itself has a variety of different regional names such as klenceng or lenceng (Java), kelulut (Kalimantan), teuwel (Sunda), and gala-gala (Sumatra). (Azlan et al., 2016). Stingless bees (Trigona sp.) can produce propolis or beeswax in higher quantities than Apis bees (Ibrahim et al., 2016).

Propolis is one of the products produced by bees that have collected resin substrates on plant parts (Kuropatnicki et al., 2013). Propolis has a fairly high price and has been used as an alternative medicine because propolis has components of bioactive compounds that can have a good effect on the body (Rosyidi et al., 2018). Propolis has several biological activities that are beneficial to the body such as antiviral, anti-inflammatory, antitumor, and antioxidant (Toreti et al., 2013). Propolis has the ability to inhibit free radicals because there are compounds that act as antioxidants in propolis, namely salicylic acid, bezoic acid, siamic esters, phenolics, flavonoids, triterpene alcohol, lipid components, vitamins C, E, β-carotene, and groups of enzymes (Zahra et al., 2021). Antioxidant activity on propolis produced by stingless bees from Pandeglan, Kendal, Banjarmasin, Makassar, and Pekanbaru showed different antioxidant values, obtained high antioxidant values in stingless bee propolis from Pandeglan compared tostingless bee propolis from 4 other regions. The antioxidant activity produced from bee propolis in the Pandeglang area is IC_{50} 68.935 µg/ml (Pujirahayu et al., 2019). Phenolic compounds and flavonoids act as antioxidants contained in stingless bee propolis (Rosli et al., 2016). The type of bee and the source of the material obtained by the bees will affect the content of propolis that will be produced by the bees (Nafi et al., 2019). There are several mechanisms of antioxidant activity from natural ingredients such as propolis. Each compound mechanism in natural products has certain specifications in absorbing free radicals.

In the body, cells will metabolize and produce free radicals. Free radicals are molecules that have unpaired electrons, have short half-lives and high reactivity. Free radicals that play a role in biological processes will involve reactive oxygen species (ROS) and reactive nitrogen species (RNS) (Stanković & Radovanović, 2012). When free radicals react with cells in the body, these reactions will cause an unwanted disease, such as diabetes mellitus, neurodegenerative disorders such as Alzheimer's and Parkinson's, can cause cardiovascular diseases such as atherosclerosis and hypertension (Kurnia & Taufikurohmah, 2017). The concentration of ROS can be controlled and balanced by the production of antioxidants, when endogenous antioxidants in the body are not balanced and insufficient in dealing with oxidative stress that occurs, exogenous antioxidants and natural antioxidants are needed. Antioxidant compounds can stop the chain reaction of free radicals, antioxidants will donate one or more electrons to molecules that do not have paired electrons so that free radicals can be quenched (Pratama et al., 2018).

Stingless bee propolis has great potential as an antioxidant. However, comprehensive information regarding the potency of Indonesian stingless bee propolis as an antioxidant is still limited. Based on this description, a literature review was conducted to determine the potential of propolis produced by stingless bees (Trigona spp.) from Indonesia as an antioxidant.

2. METHODS

In this study, the literature review method was used by searching for articles in the database using keywords propolis, *Trigona* spp., and antioxidant. The source of the data obtained was in the form of national and international research journals published in the last 10 years. The databases used include Google Scholar, ScienceDirect, Scopus, Taylor&Francis. The inclusion criteria used were journals both national and international with years of publication in the last 10 years (2011-2021), which are original journal types of research articles in full text format that discuss the potential of propolis compounds of the bee species Trigona spp. on antioxidant activity. The exclusion criteria in this study were journals published under the last 11 years (2010 and below), journals having themes that are not related to the research topic, and redundancy (repetition of words that have the same meaning). After that, screening and analysis is carried out on the suitability of the article title with the research objectives so that the relevant journal or article is obtained.

3. RESULTS AND DISCUSSION

After searching for journals and articles that have been published in the last 10 years in databases such as Google Scholar, Pubmed, and other databases. 225 journals related to keywords were obtained, from journals or articles in full text form, screening was carried out according to the inclusion criteria. and exclusion and obtained 24 journals that are appropriate to use and relevant (**Figure 1**).

3.1. Antioxidant Activity

Free radicals are compounds that have unpaired electrons. The electrons present in free radicals can change the structure and function of cells because electrons in free radicals are very easy to react with lipids, proteins, carbohydrates, and deoxyribonucleic acids (Saefudin et al., 2013). According to (Syahara & Vera, 2020), free radicals are atoms that have unpaired electrons outside their orbits, giving rise to highly reactive properties, to become stable free radicals will look for molecules around them to get electron pairs. Free radicals can occur continuously in the

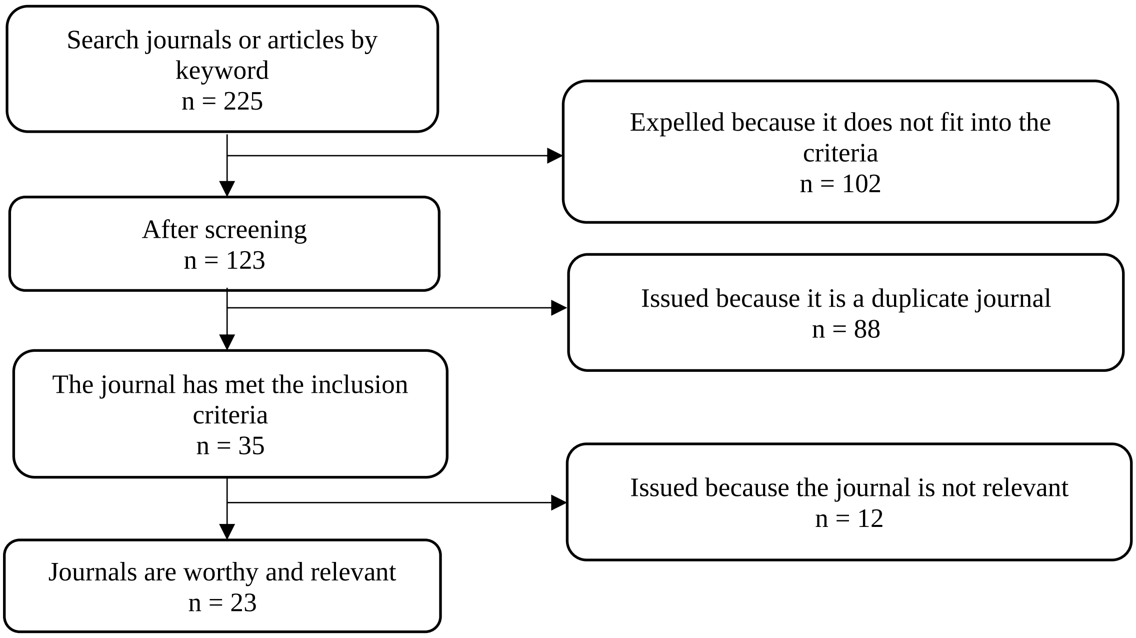

Figure 1. The results of the screening of journals or articles that have been carried out.

body to gain a partner on electrons and reach a stable state, it can cause various unwanted diseases (Huliselan et al., 2015). Through oxidative phosphorylation, cells will use oxygen as an energy source. In the process, the generation of ATP is combined with the addition of four electrons and four protons into O_2 to form two molecules, namely H_2O. when O2 only gains one electron which is used to form the superoxide anion, the reactive oxygen species (ROS) will gain three electrons and four electrons to form H_2O. The results of the reactive oxygen species production can produce other reactive oxygen (ROS) species such as hydrogen peroxide, hydroxyl radicals, and peroxynitrite. When the production of reactive oxygen species (ROS) in the body is not accompanied by a defense against antioxidant compounds, it can cause oxidative stress. Oxidative stress can cause various dangerous diseases such as cancer, atherosclerosis, hypertension, and cardiovascular-related diseases. This reactive oxygen (ROS) has an important role in the aging process in cells, and plays a role in the pathophysiology of various diseases such as preeclampsia, cancer, and myocardial ischemia. ROS is an inducer of various drug reactions that can harm the mind and body (Tolba et al., 2016).

Antioxidant compounds have been popular and are associated with various health benefits, antioxidant compounds are molecules that can protect macromolecules from oxidation reactions (Teixeira et al., 2013). Antioxidants obtained from natural ingredients and safe to use have been applied as nutraceutical as natural antioxidants (Do et al., 2014). Natural antioxidants can be obtained from compounds with the phenolic group such as flavonoids and phenolic acids, nitrogen compounds such as alkaloids and amino acids.

Free radicals that enter the body can cause various diseases and reduce the performance of the immune system (Kairupan et al., 2019). Propolis extract contains antioxidants that inactivate the development of the oxidation reaction so that it can prevent the formation of harmful radical compounds (Andre et al., 2021). Stingless bee propolis from Indonesia has potential as antioxidant (**Table 1**). Different species and locations also affect the chemical compounds and their antioxidant activity (Batistuta et al., 2021).

3.2. Antioxidant Activity Assay for Propolis

Antioxidant activity on propolis from stingless bees from Indonesia generally use the DPPH and FRAP methods, because both methods are easy to do, do not require more costs so that they are more efficient, and can produce antioxidant activity values quickly compared to other methods. The DPPH method has been used as one of the methods used to predict antioxidant free

Table 1. Antioxidant activity of stingless bee propolis from Indonesia

Bee Species	Location	Finding (IC_{50}, method)	Compound	References
Trigona sp.	Mataram, West Nusa Tenggara	0.983 mg/mL, DPPH	Ferulic acid, CAPE, Coumaric acid, Chysin	(Fachri, Rizkiana, et al., 2020)
Trigona sp.	North Lombok, West Nusa Tenggara.	493.3 ± 0.01 μg/mL, DPPH	Flavonoids Phenolic acid	(Zahra et al., 2021)
Trigona sp	Bandung, West Java	142 μg/mL, DPPH	Ferulic acid	(Sativa & Agustin, 2018)
Tetragonula biroi	Kalimantan	452 μg/mL, DPPH	Flavonoids phenolic	(Fikri et al., 2019)
Heterotrigona itama	Sulawesi	543 μg/mL, DPPH		
Tetragonula laeviceps	Banten	568 μg/mL, DPPH		
Trigona spp.	West Java West Nusa Tenggara South Sulawesi West Kalimantan	0.87 ± 0.14 μg/mL, DPPH 2.90 ± 0.55 μg/mL, DPPH 1.76 ± 0.35 μg/mL, DPPH 0.54 ± 0.06 μg/mL, DPPH	Flavonoids Phenolic	(Yuliana et al., 2013)
Trigona sp	Mataram, West Nusa Tenggara	24.7 μg/mL, DPPH	Galangin, Caffeic acid phenyl ester (CAPE)	(Fachri, Sari, et al., 2020)
Trigona spp.	Makassar Pekanbaru Kendal Pandeglang Banjarmasin	1125.56 μg/mL, DPPH 308 μg/mL, DPPH 114.06 μg/mL, DPPH 68.93 μg/mL, DPPH 4162.61 μg/mL, DPPH	Flavonoids	(Hasan et al., 2014)
Trigona itama	North Bintan, Riau	965.89 ± 8.14 μg/mL, DPPH	Flavonoids	(Nusa et al., 2015)
Trigona sp	Luwu, North Sulawesi	477.01 μg/mL, DPPH	Flavonoids	(K. Khairunnisa et al., 2020)
Trigona sp	Pandeglang	75.34 μg/mL, DPPH	Flavonoids (quercetin)	(Hasan et al., 2013)
Trigona sp	Batu Mojokerto	166.25 ± 0.42 μg/mL, DPPH 987.24 ± 4.03 μg/mL, DPPH	Flavonoids	(Rosyidi et al., 2018)
Tetragonula fuscibasis *Tetragonula fuscobalteata*	Samarinda, East Kalimantan	38.7 ± 0.02 mg/mL, DPPH 0.26 ± 0.00 mg/mL, ABTS 31.1 ± 0.01 mg/mL, DPPH 0.26 ± 0.00 mg/mL, ABTS	Kaempferol Glysperin A	(Arung et al., 2020)
Tetragonula sapiens	South Tenggara	2.213 ± 0.0389 μg/mL, ABTS EC_{50} = 32.10 g/mL, FRAP	Flavonoids	(Pratami et al., 2021)
Tetragonula indipennis	Samarinda, East Kalimantan	33.74 μg/mL, DPPH	Flavonoids Terpenoids Tannins	(B. Khairunnisa et al., 2020)
Trigona incisa	Samarinda, East Kalimantan	99.42 μg/mL, DPPH	Alkaloids	(Thamrin et al., 2016)

radical activity, free radicals in DPPH are stable free radicals (Kedare & Singh, 2011). The FRAP method is used to determine antioxidant activity, the FRAP method itself can be used for all concentrations and does not require the use of exclusive chemicals. In the ABTS method, the ABTS radicals obtained by the formation of ABTS oxidation with potassium persulfate. Antioxidant activity testing using the ABTS method requires a very long time compared to the DPPH method and the FRAP method because it takes about 12 hours to 16 hours to obtain ABTS radicals. ABTS radicals are soluble in water and organic solvents, the determination of antioxidant activity can be used for hydrophilic and lipophilic compounds (Shah & Modi, 2015). The antioxidant activity test can be indicated by the lC_{50} value, when the higher the lC_{50} value shown in the sample, the lower the antioxidant activity in the sample. However, when the sample produces a lower lC_{50} value, the antioxidant activity in the sample is higher (Nusa et al., 2015). In the DPPH method, the parameter used is lC_{50} (Inhibition Concentration 50) which means the value of the concentration of the extract that can inhibit free radicals in the DPPH method is 50%.

3.3. Antioxidant compound in stingless bee's propolis

Propolis produced by stingless bees from various regions of Indonesia shows different antioxidant activities in each region. The difference in antioxidant activity can be influenced by the geographical area where the bees are located and the time of harvesting the propolis. Geographical location can significantly affect the value of phenolic content and antioxidant activity in the sample (Agus et al., 2019); (Kustiawan et al., 2022). Antioxidant activity of honey and propolis produced by honey bees or *Trigona* sp. influenced by geographic location (Yuliana et al., 2013). Flavonoid and phenolic compounds are compounds that act as antioxidants in propolis produced by stingless bees, flavonoid and phenolic compounds are very dependent on geographic location and the type of bee that produces the propolis (Chan et al., 2013). The composition contained in propolis depends on the plants collected and used as resin materials, the geographic location of the beehive (Aziz et al., 2021). The quality of propolis can be seen from the location and color of the beehive.

The phenolic compound group is a group of compounds that have strong antioxidant activity because the phenolic compound group has a hydroxy group that has been substituted on the benzene ring with ortho and para positions on the –OH and –OR groups. The phenol group of compounds will ward off free radical molecules by donating protons to free radical molecules, this makes a change in the position of electrons in the aromatic ring and results in delocalization of the free electrons (Teixeira et al., 2013).

Caffeic acid phenyl ester (CAPE) is a compound that has been widely distributed in various natural materials such as plants, fruits and especially propolis (Tolba et al., 2013). CAPE is a derivative of simple cinnamic acid compounds which are included in sugar esters and glycosides, derivatives in complex forms such as rosmarinic acid and lithospermic acid compounds, besides that CAPE is a derivative related to flavonoid compounds. CAPE can protect cells from lipid peroxidation, necrosis, proliferation of stored cells and activation of p65 (Macías-Pérez et al., 2013). CAPE has a protective effect on cells from oxidative stress damage that occurs due to imbalance free radicals in the body (Yoncheva et al., 2019); (Song et al., 2012); (Şahin et al., 2013).

Flavonoid compounds are compounds derived from polyphenols and have antioxidant activity (Dewi et al., 2018). Flavonoid compounds have a hydroxyl B ring that can capture *reactive oxygen species* (ROS) and *reactive nitrogen species* (RNS) because flavonoids will donate hydrogen and electrons so that they can stabilize these radicals (Januarti et al., 2019). The number of benzene rings that are more than one in flavonoid compounds can scavenge free radicals (Omojate et al., 2014). According to (Kumar & Pandey, Abhay, 2013), flavonoid compounds have various mechanisms as antioxidants, such as inhibiting enzymes that play a role in the formation of reactive oxygen species (ROS), namely monooxygenase and NADH oxidase enzymes. Flavonoids will capture ROS and maintain antioxidants in the body. Flavonoid compounds in stingless bees will donate hydrogen and donate electrons to free radicals that have been produced by oxidative stress (Afroz et al., 2016).

The flavonoids contained in propolis produced by bees are strongly influenced by the plant used as a source by each bee. The chemical composition of propolis will depend on the plants in the stingless bee hive location (Jaya, 2017). When the plants around the beehive are few, it can affect the amount of flavonoid compounds in propolis because the range of each type of bee to fly in search of food sources is different (Rosyidi et al., 2018).

4. CONCLUSION

The antioxidant activity of propolis produced by stingless bees from Indonesia is generally tested using the DPPH and FRAP methods because these methods do not require a lot of time, are simple, and relatively inexpensive. The stingless bee propolis was showed different antioxidant values in each region. West Kalimantan region produced propolis with highest antioxidants activity with IC_{50} 0.54 ± 0.06 µg/mL, while stingless bees from Banjarmasin produced propolis with lowest antioxidants (4162.61 µg/mL). Differences in antioxidant activity in stingless bees in each region are influenced by various factors, such as the plants used by bees as a source used by bees, geographical location in which the bees live, and the compounds contained in the body. Flavonoid and Caffeic acid phenyl ester (CAPE) contained in stingless bees propolis have a role as antioxidants. This information is expected to be a reference in the development of propolis into derivative products and other activities.

5. ACKNOWLEDGMENT

We would like to express our gratitude to Universitas Muhammadiyah Kalimantan Timur, which always provides research fund and a platform for every activity.

6. CONFLICT OF INTEREST

All authors declare no conflict of interest.

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