Pharmacogn J. 2018; 10(1):120-122
A Multifaceted Journal in the field of Natural Products and Pharmacognosy
www.phcogj.com | www.journalonweb.com/pj | www.phcog.net

Original Article

Antiemetic Activity of *Trigona* spp. Propolis from Three Provinces of Indonesia with Two Methods of Extraction

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ABSTRACT

Introduction: Propolis is a resinous substance collected by bees to protect their hives. One of the least explored function of propolis is its antiemetic activity. The present study aimed to investigate the antiemetic activity of *Trigona* spp. propolis from three provinces of Indonesia. **Methods:** Ultrasound-assisted extraction using two kinds of solvent, water and ethanol was conducted to extract propolis from South Sulawesi, South Kalimantan and Banten. Antiemetic activity was observed on copper sulfate–induced emesis in young chicks. **Result:** All propolis indicated antiemetic activity, in which water extract had higher activity than ethanol extract. Regardless the type of solvents, propolis from South Sulawesi showed higher antiemetic activity than others. **Conclusion:** This study demonstrated that propolis has antiemetic activity, in which propolis from South Sulawesi showed the highest activity and water extraction is recommended.

Key words: Antiemetic, Propolis, Retching, Stingless bee, *Trigona* spp.

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History

- Submission Date: 02-10-17;
- Review completed: 27-10-17;
- Accepted Date: 20-11-17

DOI : 10.5530/pj.2018.1.21

Article Available online
http://www.phcogj.com/v10/i1

INTRODUCTION

Propolis is a resinous substance collected by bees from various plants for its adaptation and honeycomb construction.[1] It is the generic name of substance that protects the bees from unexpected environmental threats. Propolis acts as sealer and excluder for the honeycomb.[2,3] Propolis also ensures smooth, moist and pleasant hives.[4]

Propolis is a potential substance that could improve our health. It is considered by many researchers as a new drug.[5] Various functions of propolis have been widely investigated either by *in vitro* or *in vivo* assay. Some functions confirmed are; as antibacterial, antiviral, antifungal, anticancer, immunomodulatory, anti-inflammatory, and antioxidant agents.[6]

Beside of those functions, there is also a less explored biological activity of propolis, which is as antiemetic. Study by Eda and colleagues is the first article to confirm the antiemetic effect from Brazilian propolis. They found 50.9% of retching inhibition in young chick emesis model treated with Brazilian Propolis.[7] They also investigated several compounds (dehydrohautriwaic acid, propenoic acid, aromadandrane and dihydrocinamic acid) which are the basis of antiemetic activity of Brazilian propolis.

However, propolis properties tend to be inconsistent. It depends on its origins, seasons and plant sources.[8,9] The previous study confirmed the diversity of Indonesian propolis compounds.[10] The huge diversity of Indonesian propolis has made it generally considered as miscellaneous. In addition, solvent is also a crucial factor that influences propolis biological activity. However, there are conflicting result on types of solvent used to generate highest biological activity. Some studies found ethanol extract had higher antioxidant activity and total phenol compared to water extract. While, some other found water is a better solvent to generate high antioxidant activity and total phenol.[11,12,13] This study aimed to investigate the antiemetic activity of propolis from three provinces of Indonesia, using two types of solvent (ethanol and water). We applied ultrasound-assisted extraction to yield more efficient and effective extract.[14]

MATERIALS AND METHOD

Materials

Raw propolis were collected by bee-keeper in South Sulawesi, South Kalimantan and Banten. The species of bees were all stingless bees (*Trigona* spp.) namely *Tetragonula biroi*(South Kalimantan), *HeteroTrigona itama* (South Kalimantan) and *Tetragonula laevicep* (Banten). We used copper sulfate ($CuSO_4$) as emetogenic substance and metoclopramide as positive control. Dimethyl sulfoxide (DMSO) and Tween 80 were used as solvent for injected propolis.

Animals

The young chicks (aged 4 days) and weighing from 50-80 g were purchased from Cibadak Indah Sari Farm, Jakarta, Indonesia. All animal experiments were carried out in accordance with the acts of The

Cite this article: Fikri AM, Sulaeman A, Marliyati SA, Fahrudin M. Antiemetic Activity of *Trigona* spp. Propolis from Three Provinces of Indonesia with Two Methods of Extraction. Pharmacog J. 2018;10(1):120-2.

Ethical Committee of Institute of Research and Community Services of Bogor Agricultural University (No. 64-2017IPB).

Preparation of extract

The extracts were prepared using ethanol and water extraction. It was carried out in a sonicator bath (Branson 2000). The wave increases cell permeability thus result in optimum solubility of the active component.[15] The procedures refered to Trusheva method with slight modification.[16] Raw propolis was added to solvents (1:10) then treated with ultrasound for 4h. Subsequently, propolis was filtered by what man No.41 and evaporated using vacuum evaporator.

Antiemetic activity assay

The young chicks were divided into 8 groups of treatments, 4 chicks in each group. They were set aside for 10 min for stabilization before any treatment was given. The groups of treatments were; water extract of propolis from South Sulawesi (WS), South Kalimantan (WK), Banten (WB), ethanol extract of propolis from South Sulawesi (ES), South Kalimantan (EK) and Banten (EB), negative control (0.9% saline) and positive control (metoclopramide). The extracted propolis sample were dissolved in 0.9% saline (containing 5% DMSO and 1% Tween 80) to create injection solution. Subsequently, 300 mg/kg of propolis was injected abdominally. 10 minutes post injection, $CuSO_4$ was then administered orally (50 mg/kg). The number of retching was calculated for 10 min.[7,17] The results were compared to control group. The percent of inhibition was calculated by the following formula:

$$\text{Inhibition (\%)} = [(A-B)/A] \times 100$$

A: Frequency of retching in negative control group

B: Frequency of retching in tested group

Statistical analysis

Number of retching was expressed as mean ± SEM. The difference was determined by univariate analysis of variance and considered to be significant when $p< 0.05$.

RESULT

Our present study showed that all propolis possess antiemetic activity. Propolis ES, WS, WB and WK were not significantly different in the number of retching to control (+). The inhibition ranged from 44.96 up to 98.51 % (Table 1). For ethanol extract, propolis from South Sulawesi had the highest retching inhibition. While for water extract, all kinds of propolis were not significantly different to control (+).

According to univariate analysis of variance, both the solvents and origins of propolis had significant effect on antiemetic activity (p=0.001, respectively). Regardless the type of solvents, propolis from South Sulawesi had the highest inhibition power compared to the others and water extract had higher inhibition power than ethanol extract for all propolis origins.

Table 1: Antiemetic activity of *Trigona* spp propolis.

Origin of Propolis	Solvent	Code	No. Retching	Inhibition (%)
Banten	Ethanol	EB	102.50±3.45[b]	49.17
Banten	Water	WB	6.00±0.44[a]	97.02
South Sulawesi	Ethanol	ES	8.75±0.72[a]	95.66
South Sulawesi	Water	WS	3.00±0.37[a]	98.51
South Kalimantan	Ethanol	EK	111.00±3.37[b]	44.96
South Kalimantan	Water	WK	16.50±2.38[a]	91.82
Control (+)			2.75±0.40[a]	98.64
Control (-)			201.67±2.69[c]	-

*Values in the same column followed by the same uppercased letter are not significantly significant (p<0.05)

EB : Ethanol extract of propolis from Banten
WB : Water extract of propolis from Banten
ES : Ethanol extract of propolis from South Sulawesi
WS : Water extract of propolis from South Sulawesi
EK : Ethanol extract of propolis from South Kalimantan
WK : Water extract of propolis from South Kalimantan

DISCUSSION

Emesis, nausea and/or vomiting, is an unpleasant state which is a manifestation of several conditions including pregnancy, toxicants ingestion, and side effect of medication, surgery and cancer chemotheraphy.[18] Emesis could lead to loss of appetite, fluid and electrolyte disturbance, and decreased nutritional status.[19,20]

Propolis works as antiemetic through several mechanisms. Hydroxycinamic acids of propolis act as δ (enkephalinergic)-receptor antagonist and inhibit dopamine receptor. Propolis also contains tritepens which are 5-HT_3, 5-HT_4 and/or NK_1 receptors antagonist. These receptors are involved in emesis stimulation.[21] Our research supports the previous study about the antiemetic activity of Brazilian propolis.[7] The study also found water extract of Brazilian propolis demonstrated higher antiemetic activity than hydro alcohol extract. The reason is still unclear. However, it is suspected that there are other water soluble compounds, such as glucoside, polysaccharides, saponins that work as inhibitor of some emesis receptors.[22]

Some experimental animals have been widely developed as an emetic model such as: ferret, mink, monkey, pig, rat, frog, dog and chick.[23] Chick as emesis animal model has been used by many researchers.[7,17,24,25,26] These model is better than frog emesis model because it has some advantages such as, easy to handle and able to visually observed and required shorter time.[26]

$CuSO_4$-induced chicks emesis model are suitable for screening for the potency of product as antiemesis.[17] $CuSO_4$ induces emesis through direct stimulation of the stomach wall (gastric irritation) and/or through 5-HT4 stimulation.[22] Those are the part of mechanisms that participate in nausea and vomiting action. In addition, this model is also suitable for evaluating brain participation in emerging emesis.[23]

CONCLUSION

Our results demonstrated that Indonesian propolis has antiemetic activity, in which propolis from South Sulawesi has indicated the highest activity. Water extracts have shown higher activity compared to the ethanol extract thus we recommend water extraction for generating higher antiemetic activity.

ACKNOWLEDGEMENT

We wish to thank the Ministry of Research Technology and Higher Education of the Republic of Indonesia that funded this research.

CONFLICT OF INTEREST

We have no conflict of intereset to disclose.

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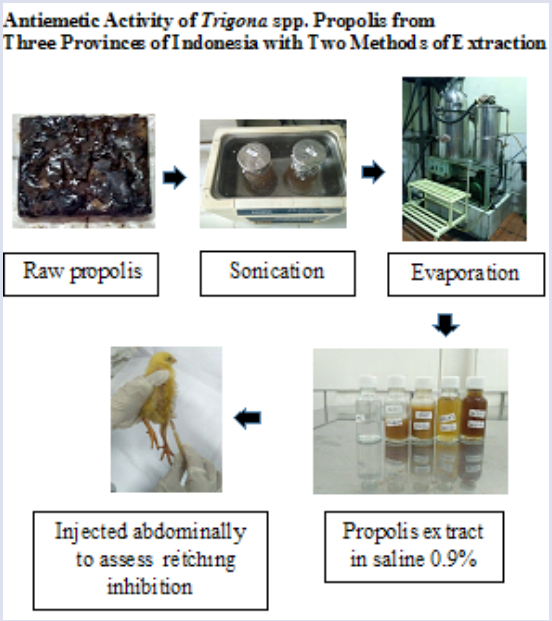
GRAPHICAL ABSTRACT



SUMMARY

- Indonesian propolis shows antiemetic activity, in which propolis from South Sulawesi indicates the highest activity.
- Water extracts have shown higher activity compared to the ethanol extract .

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