PLANT SCIENCE TODAY
ISSN 2348-1900 (online)
Vol x(x): xx–xx
https://doi.org/10.14719/pst.1602

HORIZON
e-Publishing Group
HePG

REVIEW ARTICLE

Ethnopharmacology of *Hyptis capitata*

Nelsiani To'bungan[1,4], Sitarina Widyarini[2], Laurentius Hartanto Nugroho[3] & Rarastoeti Pratiwi[3*]

[1]Doctoral Program in Tropical Biology, Faculty of Biology, Universitas Gadjah Mada, Teknika Selatan Street, Sekip Utara, Sleman 55281, Yogyakarta, Indonesia
[2]Department of Pathology, Faculty of Veterinary Medicine, Universitas Gadjah Mada. Fauna Street Number 2, Karangmalang, Sleman 55281, Yogyakarta, Indonesia
[3]Faculty of Biology, Universitas Gadjah Mada, Teknika Selatan Street, Sekip Utara, Sleman 55281, Yogyakarta, Indonesia
[4]Faculty of Biotechnology, Universitas Atma Jaya Yogyakarta, Babarsari Street, Sleman 55281, Yogyakarta, Indonesia

*Email: rarastp@ugm.ac.id

OPEN ACCESS

ARTICLE HISTORY

Received: 23 November 2021
Accepted: 05 March 2022

Available online
Version 1.0: 02 May 2022

Check for updates

Additional information

Peer review: Publisher thanks Sectional Editor and the other anonymous reviewers for their contribution to the peer review of this work.

Reprints & permissions information is available at https://horizonepublishing.com/journals/index.php/PST/open_access_policy

Publisher's Note: Horizon e-Publishing Group remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Indexing: Plant Science Today, published by Horizon e-Publishing Group, is covered by Scopus, Web of Science, BIOSIS Previews, Clarivate Analytics, etc. See https://horizonepublishing.com/journals/index.php/PST/indexing_abstracting

CITE THIS ARTICLE

To'bungan N, Widyarini S, Nugroho L H, Pratiwi R. Ethnopharmacology of *Hyptis capitata*. Plant Science Today (Early Access). https://doi.org/10.14719/pst.1602

Abstract

Hyptis capitata is one of the important traditional medicinal plants, in which different parts of the plant are used in various countries in treating several diseases. This review was conducted to present a comprehensive overview of distribution, taxonomic characters, ethnobotany and the various pharmacological properties of *H. capitata.* This review presents scientific information about pharmacological potentials of *H. capitata* as a medicinal ingredient and its opportunities to be developed and utilized more broadly. The literature review was carried out on both abstracts and full articles, further analyzed and included in this review. *H. capitata* is used to treat various diseases such as fever, digestive disorders and open wounds. The pharmacological study of *H. capitata* showed that this plant has the potential to be developed as an antioxidant, antibacterial, antiviral and anticancer. Due to being widely used by the community, further studies regarding the pharmacological potential and the safety parameters of *H. capitata* are needed.

Keywords

Hyptis capitata, ethnobotany, antioxidant, antibacterial, anticancer

Introduction

Hyptis genus is one of the largest plant genera (1). Plants of this genus are characterized by glandular trichomes that produce essential oils and has a strong aroma (2, 3). There are about 290 species, which are adapted in tropical areas (4, 5). Some spesies used as traditional medicine, to treat various diseases (6). Some species that have an ethnobotanical history are *Hyptis mutabilis* (3), *Hyptis obtusiflora* (6), *Hyptis brevipes* (7), *Hyptis suaveolens* (8), *Hyptis martiusii* (9), *Hyptis pectinata* (10), *Hyptis artroruben* (11), *Hyptis crenata* (12), *Hyptis alata* (13), *Hyptis verticillata* (14), *Hyptis passerine* (15), *Hytpis actinocepala* (16), *Hyptis spicigera* (17), *Hyptis marruboides* (18), *Hyptis lanceolata* (19) and *Hyptis capitata* (20).

H. capitata (Fig. 1) is also broadly applicable as medicinal ingredient. It is frequently used as a traditional medicine to treat coughs, treatment of open and internal wounds. This plant comprises cytotoxic and anti-HIV activity (20, 21). In addition, it owns the potential of a bioinsecticide (22). Bioactive components leaves of *H. capitata* have been studied since 1952 in Japan (23).

It is a tropical American plant, able to grow in tropical, subtropical and residential areas and generally known as a weed and belongs to invasive sp. (25, 26). *H. capitata* has a different name for each tribe and na-

Fig. 1. *Hyptis capitata.* **A**. Aerial part, **B**. Flower, **C**. Leaf, **D**. *Hyptis capitata* (24).

tion. In Indonesia, the Toraja tribe calls it *narang-narang* or *sualang*, and the Banggai tribe calls it pago-pago grass (27, 28). In English, it is known as *knob weed*, *button weed* or *false ironwort*; Japanese call it *iganigakusa*; Chinese people go for *mu-go-xiao*; in Suriname it is popular as *foegoe foegoementi, mintie, voekoe voekoe menti voe boesi*;

in Vietnam it goes by the name *of e hoa dau*; Spain people call it as *biojo, cartagena amarilla, chirrite, cordon de fraile*; In Bangladesh it is called as *pukain tong pang*; and in the Philippines it is *botonesan* (29).

H. capitata has some synonyms such as *H. decurrens* (Blanco) Epling, *Clinopodium capitatum* (Jacq.) Sw., *Mesosphaerum capitatum* (Jacq.) Kuntze, *Pycnanthemum decurrens* Blanco, *H. mariannarum* Briq, *H. macrochila* Mart. ex Steud., *H. pittieri* Briq., dan *H. rhomboidea* M. Martens & Galeotti (25, 30). Over the past few years, we have found no comprehensive review about *H. capitata*. Hence, the present study was undertaken to perform a systematic review on the traditional uses and pharmacological properties of *H. capitata*.

Taxonomical characters

H. capitata is a herbaceous plant and that grow up to 2 m and branching from the base, with quandrangular stem. Leaves with strong aroma when crushed opposite, oval, pointed and jagged (20, 25, 31); veins are clearly visible on the underside of the leaves; leaf blade measures about 6-14 × 1.5-6 cm with many pale glands on the underside; upper surface of the leaf blade is covered with branched stirdy glandular trichromes; the trichrome on the underside of the leaf blade is much slenderer than those on the upper surface (26). The flowers are united in a dense sphere which is a tube-shaped petals (sepals), that are united. The flower petals unite to form a head-like circle supported by the flower stalk. The flower crown is white with a size of 5-6 mm and the petals are about 3-4 mm. The anthers are purple, pink, to red-brown. The collection of petals will increase in size after the flowers wither and turn brown. Inside the flower petals are small 4-lobed fruits (Schizocarp) that produce small seeds (25, 32). The seeds are elliptical, brown in size of 1.5 mm (27). They are small and light, making it easier for this plant to spread and grows to fill an area.

Distribution and Habitat

H. capitata is native to Florida, Mexico, Central America and South America. However, this plant has been naturalized in Southeast Asia and some tropical islands. This plant is highly popularly used in rural areas of Latin America (21). In Indonesia, this plant has also been naturalized since 1880 in Java, including Madura. *H. capitata* is known as weeds in Tana Toraja (33) and oil palm plantations's weeds in South Sulawesi. This plant also easily found there as well as in cashew plantations of Cihea Cianjur, West Java (25). In Purwodadi Botanical Garden, the plant is in undergrowth condition (25, 32).

Tropical Asian regions such as Vietnam, Thailand, Singapore and Malaysia have also naturalized this plant. This plant can also be found on islands in the Pacific such as Hawaii, Solomon Islands, French Polynesia, Palau and Guam. Unlike in Asia, *H. capitata* has not been naturalized much in Australia. It is mostly distributed in northern coastal areas, like Queensland, Central Queensland, Northern territory and on Christmas Island (34).

The height of place for the plant to grow is around 750 m above sea level (25). *H. capitata* can grow easily in the idle land close to water sourses and wet lowlands. It can easily be discovered on barren agricultural lands, as well as on roadsides (26).

Traditional medicinal uses

The use of *H. capitata* as a traditional medicine is different from one country to another. Table 1 shows information on the use of *H. capitata* to treat various diseases in 16 countries. The part of the plant that is most widely used is leaf, while it's most common processing method is the decoction. This plant appears to be frequently reported in the treatment of stomatchache or gastrointestinal disorder, wound, sore eyes and fever.

The popular use of *H. capitata* as a medicine for gastrointestinal disorders is influenced by its tannin and flavonoid content (33). When the tannin interacts with the intestinal mucosal layer, it causes the astringency and impermeability. This provides a protective effect on the mucosal lining of the digestive tract so that it becomes more difficult for pathogenic microorganisms to penetrate (47). Meanwhile, flavonoids which act as antioxidants, anti-inflammatory and analgesic properties, they are involved in reducing pain and inflammation in gastrointestinal disorders, and even other diseases (48, 49). The properties of *H. capitata* in curing various diseases are affected by its phytochemical content.

Antioxidant activity

Antioxidant activity extracts, fractions and essential oil of *H. capitata* have applied the DPPH method ((2,2-diphenyl-1-picrylhydrazil) and superoxide radical scavenging. Based on Table 2 it can be seen that the IC_{50} values of extracts, fractions and essential oils of *H. capitata* are below 100 µg/ml. This value indicates high antioxidant activity (50). Antioxidants are important for maintaining the physiological function of various organ systems. It is also important for the prevention of cardiovascular disease and cancer (51). Plant secondary metabolites that are closely related to antioxidant activity are mainly due the polyphenolic compounds. Oxidation rate of organic matter can be reduced by phenolic compounds (52). The essential oil of the plant contains methyl eugenol, plays a role in its antioxidant activity. Furthermore, based on the qualitative phytochemical test, the extract and leaf fraction contains flavonoids. Methyl eugenol and flavonoids are a group of phenolic compounds (53-55).

The genus Hyptis itself, is also reported to have promising antioxidant content. The methanol extract of the leaves of *H. suaveolens* tested by the DPPH method had an IC_{50} of 40.91 µg/ml, with the maximum inhibition of 69.46% at 100 µg/ml (56).

Anticancer activity

The potentiality of *H. capitata* as an anticancer has not been widely explored. Leaf infusion of *H. capitata* showed moderate cytotoxic activity on MCF-7 cells (Table 3) (57). Hyptatic acid-A and 2α-Hydroxyursolic acid from aerial parts of the plant indicated cytotoxicity activity. The IC_{50} of these compounds presented a very high cytotoxic activity

Table 1. The use of *H. capitata* as traditional medicine in various countries

Sl. No.	Country	Ethnomedical use	Plant Part (s)	Preparation	References
1	America latin	Respiratory and gastrointestinal disorder	Leaf	Infusion	6
		Open wound, cough, sore eyes	No remark	No remark	21
2	Bangladesh	Malaria	Whole plant	Turned in to Juice	35
		Open wound	Root and leaf	Pasted	
3	Central America	Toothache, gastrointestinal disorder, oedema, intermitten fever, bronchial complaints, spasmodic	Whole plant	Decoction	34
		Wound, cough, sore eyes	No remark	No remark	21
4	Colombia	Snakebite	Leaf, branch, stem	No remark	36
5	Costa Rica	Toothache, gastrointestinal distress	Whole plant	Decoction	28
6	Ecuador	Fungal disease	Aerial part	No remark	37
7	El Savador	Tonic	Whole plant	No remark	28
8	French Guianas	Heart palpitation	Leaf	Infusion	38
		Sedative	Leaf	No remark	
9	India	Gastointestinal disorder, hemorrhoids	Leaf and flower	No remark	39
		Antibacterial, anticancer		Essential oil	
10	Indonesia	Joint and bone pain	Leaf	Boiled, as spice when bathing	40
		Diabetes	Whole plant	No remark	26
		High cholesterol, gastritis, ear problem	Leaf and stem	No remark	41
		Kidney problem	Leaf	No remark	42
		Sore eyes	Fruit	Roasted	43
		Internal wound	Leaf	Crushed	44
		Fever	Young leaf	Decoction, as herb when bathing	33
		Stomachache	Shoot, young leaf and stem	Brewed, decoction, eaten directly	33,45
		Diarrhae	Shoot, young leaf and stem	Brewed, decoction, eaten	33, 44
		Open wound	Young leaf	Decoction. Pounded, smear on the wound	33
		Headache	Leaf and stem	Decoction, as herb when bathing	23
11	Jamaica	Influenza	Whole plant	Decoction	28
		Cold, ulcer, asthma, constipation	No remark	No remark	46
12	Malaysia	Stomachache	Young leaf	Pounded	28
13	Martiniqie	Tonic, excitant	No remark	No remark	28
14	Northwest Amazonia	Black diarrhea	Leaf	Infusion	39
15	Philippine	Wound,	Leaf	Decoction	34
		Amenorrhoea	Root	Decoction	
16	Taiwan	Cold, fever, asthma	Aerial part	No remark	37

Table 2. Antioxidant activity of *H. capitata*

Sl. No.	Tested material	IC50 Value	Method	Reference
1	Leaf fraction	40.321(ppm)	DPPH	53
2	Leaf methanolic extract	13.6 (µg/mL)	DPPH	54
		65.11 (µg/mL)	Superoxide radical scavenging	
3	Aerial part essential oil	2.591 (µg/mL)	DPPH	55

against HCT-8 cells (58). Another species that has also been reported to have anticancer activity is *H. suaveolens*. The essential oil of *H. suaveolens* showed a cytotoxicity activity against MCF-7 cells, with an IC_{50} of 90.6 µg/ml. The content of terpenoids in essential oils is related to their anticancer activity (59). Research on cytotoxicity that has

Table 3. Anticancer activity of *H. capitata* in various cell model

Sl. No.	Samples	Cell model	IC_{50} (µg/mL) Value	Reference
1	Leaves Infusion	MCF-7	248.6	57
		HCT-8	4.2	
		A549	5.9	
	Hyptatic acid-A (isolated from methanol extract aerial part)	P388	6.7	
		KB	>4.0	
		L1210	>10	
2		HCT-8	2.7	58
		A549	4.9	
	2α-Hydroxyursolic acid (isolated from methanol extract aerial part)	P388	6.1	
		KB	>4.0	
		L1210	>10	

been carried out in previous studies, only investigated the cytotoxicity in cancer cells. In addition to cytotoxicity tests on cancer cells, another thing that is no less important is cytotoxicity tests on non-cancerous cells. This is intended to further evaluate its selectivity and the opportunity to be developed as an anticancer candidate. It is also important to test the mechanism of anticancer to determine the characteristics of cancer cells that are suppressed by phytochemical compounds contained in *H. capitata.*

Antimicrobial and antivirus activity

Studies on the antibacterial and antiviral activity of *H. capitata* are very limited. In Table 4, the Anti-human immunodeficiency virus type 1 (HIV-1) and antimicrobial potential of *H. capitata* is presented. The whole plant extract of *H. capitata* showed maximum anti-HIV activity with an EC_{50} of 1.4 µg/ml. Meanwhile, the leaf extract indicated the ability to inhibit the growth of *Streptococcus sobrinus, Staphylococcus aureus* and *Propionibacterium acnes* bacteria at a concentration of 500 µg/ml. The essential oil also exhibits promising antibacterial potential compared to other extracts of the plant. The compound methyl eugenol present in the essential oil contributes for to its significant antibacterial activity (42).

Toxicity

The toxicity profile of *H. capitata* is provided in Table 5. It could found that the acute toxicity study on *Artemia salina* L. can be an initial screening of a material's anticancer potential. The level toxicity of leaves ethanolic and steam extract, also essential oil of aerial part based on IC_{50} value is categorized as toxic (<1000 µg/ml) (60, 61). Several active compounds were evaluated for their toxicity by the Brine Shrimp Lethality Test (BSLT) method showing correlation with specific anticancer tests (41, 60, 62). The toxicity of the ethanolic extract of the leaves of *H. capitata* against *Rattus norvegicus* at 300 µg/Kg BW dose indicated the pathological changes in liver, indicated its toxic effect (63).

Phytochemistry

The secondary metabolite components of *H. capitata* have been investigated in several countries. The content of secondary metabolites in leaves, stem and flower of the plant are presented in Supplementary Table 1. The most dominant group of compounds contained are sesqiterpenes (23.53%) and monoterpenoids (11.76%). The other group of compounds are also reported such as alkaloids (2.21%), diterpenoids (2.21%), triterpenoids (6.62%), lignin (2.21%),

Table 4. Antimicrobial and antiviral activity of *H. capitata*

Sl. No.	Samples	Tested microorganism/Virus	EC_{50} µg/mL	MIC (µg/mL)	Reference
1	Leaves extract	*S. sobrinus*	-	500	54
		S. aureus		500	
		P. acnes		500	
		Escherichia coli		NI	
		Candida albicans		NI	
2	Whole plant extract	HIV-1	1.4	-	20
3	Aerial part essential oil	*S. aureus*	-	12.5	55
		Bacillus subtilis		12.5	
		E. coli		6.25	
		Pseudomonas aeruginosa		6.25	
		Fusarium graminearum		25	
		Botrytis cinerea		12.5	
		Exerohilum turcicum		25	
		Lecannosticta acicula		25	

Table 5. Toxicity of *H. capitata*

Sl. No.	Sample	Toxicity	Value	Reference
1	Methanolic leaves extract	Toxic effect on *Artemia salina* L.	>1000 µg/mL	54
2	Ethanolic leaves extract	Toxic effect on *Artemia salina* L.	183.91µg/mL	24
3	Aerial part essential oil	Toxic effect on *Artemia salina* L.	65.9 µg/mL	55
4	Ethanolic stem extract	Toxic effect on *Artemia salina* L.	880.579 µg/mL	64
5	Methanolic leaves extract	Larva of Culex *quinquefasciatus*	25 mg/mL	65
6	Ethanolic leaves extract	*Rattus norvegicus*	Treatment of 300 µg/KgBW is not significantly different from negative control	63

steroids (2.94%), phenolic (10.30%), fatty alcohol (7.35%), fatty esters (1.47%), fatty acids (0.73%), aromatic compounds (6.61%) and others (20.59%). The dominant terpenoid contents were also reported in *H. suaveolens*, predominantlysesqiterpenes, diterpenes, triterpenes and β-sitosterol (66).

Conclusion

H. capitata as a traditional medicine, has the potential to be developed as a source of antioxidants, antibacterial, antiviral and anticancer plant. In addition, research on the safety of using *H. capitata* also needs to be carried out, to assess the level of toxicity in both long-term and short-term use.

Acknowledgements

We would like to thank Universitas Gadjah Mada for supporting this research through RTA grants 2021.

Authors contributions

NT collected the references and wrote the content of review. RP participated in the design of the study and gave advice on important points that need to be discussed in the review. SW was involved in compiling data. LHN conceived of the study and coordination. All authors read and approved the final manuscript.

Compliance with ethical standards

Conflict of interest: Authors do not have any conflict of interests to declare.

Ethical issues: None

Supplementary data

Supplementary Table 1. Phytochemical Components of *H. capitata.*

References

1. Harley RM. Revision of generic limits in *Hyptis* Jacq. (Labiatae) and its allies. Botanical Journal of the Linnean Society. 1988;98 (2):87-95. https://doi.org/10.1111/j.1095-8339.1988.tb016972.
2. de SáS, Fiuza TS, Borges LL, Ferreira HD, Tresvenol LMF, Ferri FH, Rezende MH, Paula JR. Chemical composition and seasonal variability of the essential oils of leaves and morphological analysis of *Hyptis carpinifolia*. Revista Brasilleira de Farmacognosi. 2016;26:688-93. https://doi.org/10.1016/j.bjp.2016.05.011
3. McNeil M, Facey P, Porter R. Essential oils from the *Hyptis* genus-a review (1909-2009). Natural Product Communications. 2011;6 (11):1775-96. https://doi.org 10.1177/1934578X1100601149.
4. Kubitzki K, Kadereit JW. Flowering Plants Dicotyledons. In The Families and Genera of Vascular Plants. Springer: Germany. 2004. https://doi.org/10.1007/978-3-662-07257-8
5. Harley RM, Pastore JFB. A generic revision and new combinations in the Hyptidinae (Lamiaceae), based on molecular and morphological evidence. Phytotaxa. 2012;58:1-55. https://doi.org/10.11646/phytotaxa.58.1.1
6. Luzuriaga-Quichimbo CX, Blanco-Salas J, Cerón-Martínez CE, Stanković MS, Ruiz-Téllez T. On the possible chemical justification of the ethnobotanical use of *Hyptis obtusiflora* in Amazonian Ecuador. Plants. 2018;7(4):1-8. https://doi.org/10.3390/plants7040104.
7. Bhuiyan MNI, Begum J, Nandi NC. Chemical component studies on the leaf and inflorescence essential oil of *Hyptis brevipes* (Poit.). Journal Medical Plants Researches. 2010;4:2128–31.
8. Pachkore GL, Dhale DA, Dharasurkar N. Antimicrobial and phytochemical screening of *Hyptis suaveolens* (L. Poit) Lamiaceae. International Multidisciplinary Research Journal. 2012;1(4):01-03.
9. Caldas GFR, Oliveira ARdS, Arau´jo AV, Quixabeira DCA, Silva-Neto JdC et al. Gastroprotective and ulcer healing effects of essential oil of *Hyptis martiusii* Benth. (Lamiaceae). PLoS ONE. 2014;9(1):e84400. http://dx.doi.org/10.1371/journal.pone.0084400
10. Arifin Z, Suzery M, Cahyono B. Kandungan minyak atsiri daun *Hyptis pectinata* Poit dari Jawa Barat. Seminar Nasional II USM. 2017;1:541–46.
11. Abedini A. Evaluation biologique et phytochimique des substances naturelles *d'Hyptis atrorubens* Poit. (Lamiaceae), Sélectionnée par un Criblage d'extraits de 42 plantes [Thesis]. Français:Université du Droit et de la Santé - Lille II. 2013.
12. Coelho-De-souza AN et al. The essential oil of *Hyptis crenata* Pohl ex Benth. presents an antiedematogenic effect in mice. Brazilian Journal Medical and Biological Research. 2021;54:1–9. http://dx.doi.org/10.1590/1414-431X20209422.
13. Anonymous. *Hyptis alata*. Plant Database [Internet]. [cited 3 March 2022]. Available from: https://www.wildflower.org/plants/result.php?id_plant=hyal
14. Picking D, Delgoda R, Boulogne I, Mitchell S. *Hyptis verticillata* Jacq: a review of its traditional uses, phytochemistry, pharmacology and toxicology. Journal of Ethnopharmacology. 2013; 147(1):16-41. https://doi.org/10.1016/j.jep.2013.01.039.
15. Zellner BD et al. Screening of the odour-activity and bioactivity of the essential oils of leaves and flowers of *Hyptis passerina* Mart. from the Brazilian Cerrado. Journal of Brazilian Chemical Society. 2009;20:322–32. https://doi.org/10.1590/S0103-50532009000200018
16. Jiménez-Romero E M et al. Ethnobotanical study and commer-

cialization of Medicinal Plants in the Murocomba Protected Forest and its Influence Area in the valencia canton, Ecuador. Ciencia Tecnologia Agropecuaria. 2019;20:491–506. https://doi.org/10.21930/rcta.vol20num3art:1597.

17. Ladan Z, Amupitan JO, Okonkwo EM, Aimola IA, Habila N. Antimicrobial potency of *Hyptis spicigera* leaf extracts against some pathogenic microorganisms. Journal of Medicinal Plant Researches. 2009;3:902–05.

18. da Silva AC, de Souza PE, Amaral DC, Zeviani WM, Pinto JEBP. Óleos essenciais de *Hyptis marrubioides*, *Aloysia gratissima* e *Cordia verbenacea* reduz o progresso da *Ferrugem asiática* da soja. Acta Scientiarum Agronomy. 2014;36:159–66. https://doi.org/10.4025/actasciagron.v36i2.17441.

19. Anonymous$_b$. *Hyptis lanceolata* Poir. [family Labiatae]. Global Plants [Internet]. [cited 2022 March 2]. Available from: htpps://[lants.jstor.org/stable/10.5555/al.ap.upwta.320.

20. Kashiwada Y, Wang HK, Nagao T, Kitanaka S, Yasuda I, Fujioka T et al. Anti-AIDS agents, 30. Anti-HIV activity of oleanolic acid, pomolic acid and structurally related triterpenoids. Journal of Natural Products. 1988;61(9):1090–95. https://doi.org/10.1021/np9800710.

21. Sumitha V, Murugan K, Mini I. Physico-chemical and phytochemical evaluation of a medicinal herb *Hyptis capitata* Jacq. (Lamiaceae). Trends in Bioscince. 2018; 11(7):1188-93.

22. Facey PC, Porter RB, Williams LA. The chemical composition and insecticidal activity of the essential oils from Jamaican *Hyptis capitata* Jacq. In Biologically Active Natural Products for 21st Century. India: Research Signpost; 2006. p.13-19.

23. Kobayasi K. 1952. Studies on the components of the leaves of *Hyptis capitata* Jacq. Pharmaceutical Society Japan.1952;72 (1):1-3. https://doi.org/10.1248/yakushi1947.72.1_1

24. To'bungan N, Jati WN, Zahida F. Acute toxicity of knop weed leaves etanolic extract of *Hyptis capitata* Jacq. using brine shrimp lethality test (BSLT) method. Sciscitatio. 2020;1(2):64–69. https://doi.org/10.21460/sciscitatio.2020.12.30.

25. Setyawati T, Narulita S, Bahri IP, Raharjo GT. A guide book to invasive alien plant spesies in indonesia. Indonesia: Development and Innovation Agency Ministry of Environment and Forestry Republic of Indonesia. 2014.

26. Datar MN, Lakshminarasimhan P, Rao PSN. *Hyptis capitata* Jacq. (Lamiaceae)-a new record for northern Western Ghats. Indian J Forest. 2007;30(3):355–56.

27. Khairiyah N, Anam S, Khumaidi A. Studi etnofarmasi tumbuhan berkhasiat obat pada suku Banggai di kabupaten Banggai Laut, provinsi Sulawesi Tengah. Galenika Journal of Pharmacy. 2016;*2*(1):1-7. https://doi.org/10.22487/j24428744.2016.v2.i1.5224

28. Pasorong YS, Tambaru E, Umar MR, Masniawati A. Identifikasi tumbuhan berkhasiat obat dan potensi pemanfaatannya pada beberapa desa di sekitar gunung Sesean kabupaten Toraja Utara [Thesis]. Makassar: Fakultas Matematika dan Ilmu Pengetahuan Alam Universitas Hasanuddin. 2015.

29. Anonymous$_c$. Philippine Medical Plants [Internet]. [cited 2021 September 18]. Available from: http://www.stuartxchange.org/Botonesan.

30. Wiart C. Antiparasitic asian medicinal plants in the clade Lamiids. In: Medicinal plants in Asia and Pacific for Parasitic infections. USA: Academic press. 2021;p.365-460. https://doi.org/10.1016/B978-0-12-816811-0.00010-X

31. Arif MM. Essential oil composition of *Pogostemon paniculatus* and *Hyptis* [Thesis]. India:University of Calicut. 2007.

32. Anonymous$_d$. Weed Plants Australia [Internet]. [cited 2021 September 8]. Available from: https://keyserver.lucidcentral.org/*Hyptis capitata*.

33. To'bungan N. Utilization and phytochemical screening of knobweed (*Hyptis capitata* Jacq.) leaves infusion. Biota : Jurnal Ilmiah Ilmu-Ilmu Hayati. 2020;*5*(3):149–54. https://doi.org/10.24002/biota.v5i3.3520

34. Anonymous$_e$. *Hyptis capitata* (PROSEA) [Internet]. 2016 [cited 2021 September 12]. Available from: https://uses.plantnet-project.org/e/index.php?title=Hyptis_capitata_(PROSEA)&oldid=218094.

35. Biswas A, Bari MA, Roy M, Bhadra SK. Inherited folk pharmaceutical knowledge of tribal people in the Chittagong hill tracts, Bangladesh. Indian Journal of Traditional Knowledge. 2010;*9* (1):77–89.

36. Otero R, Fonnegra R, Jiménez SL, Núñez V, Evans N, Alzate SP et al. Snakebites and ethnobotany in the northwest region of Colombia. Part I: Traditional use of plants. Journal of Ethnopharmacology. 2000;71(3):493–504. https://doi.org/10.1016/S0378-8741(00)00243-9

37. Almtorp GT, Hazell AC, Torssell KBG. A lignan and pyrone and other constituents from *Hyptis capitata*. Phytochemistry. 1991;30(8):2753–56. https://doi.org/10.1016/0031-9422(91)85137-O.

38. DeFilipps RA, Maina SL, Crepin J. Medicinal plants of the Guianas (Guyana, Surinam, French Guiana) [Internet]. [cited 2021 September 20]. Available from: https://naturalhistory.si.edu/.

39. Thoppil JE, Jose J. Chemical composition of essential oil in two ethnomedicinal species of *Hyptis*. Acta Pharmaceutica. 1955;45 (4):551–53.

40. Rizki R, Nursyahra N, Fernando O. Study of weeds as traditional medicinal plants used by indigenous people of west pasaman, Indonesia. Journal of Tropical Horticulture. 2019;*2*(2):81–85. https://doi.org/10.33089/jthort.v2i2.21

41. Mustofa FI, Rahmawati N, Aminullah. Medicinal plants and practices of rongkong traditional healers in South Sulawesi, Indonesia. Biodiversitas. 2020;21(2):642–51. https://doi.org/10.13057/biodiv/d210229

42. Anggraeni HRE. Jenis-jenis tumbuhan berpotensi obat di desa Bambapuang kabupaten Enrekang [Thesis]. Indonesia: Universitas Hasanuddin. 2017.

43. Indrayanto G. Produksi metabolit sekunder dengan teknik kultur jaringan. dalam buku risalah seminar nasional metabolit sekunder. 1987. (Ed.) Suwijiyo Pramono, D. Gunawan dan C.J. Soegiarto. Yogyakarta: PAU Bioteknologi UGM. 1987;p.32 – 44.

44. Rupa D, Sulistyaningsih CY, Dorly,Ratnadewi. Identification of secretory structure, histochemistry and phytochemical compound of medical plant *Hyptis capitata* Jacq. Biotropia. 2017;24 (2):94–103. https://doi.org/10.11598/btb.201

45. Aththorick TA, Berutu L. Ethnobotanical study and phytochemical screening of medicinal plants on Karonese people from North Sumatra, Indonesia. Journal of Physics: Conference Series. 2018;1116(5):1-11. https://doi.org/10.1088/1742-6596/1116/5/052008

46. Mitchell SA, Ahmad MH. A review of medicinal plant research at the university of the West Indies, Jamaica, 1948-2001. West Indian Medical Journal. 2006;55(4):243-69. https://doi.org/10.1590/S0043-31442006000400008

47. Russo M, Coppola V, Giannetti E, Buonavolontà R, Piscitelli A, Staiano A. Oral administration of tannins and flavonoids in children with acute diarrhea: A pilot, randomized, control-case study. Italian Journal of Pediatrics. 2018;44(1):4-9. https://doi.org/10.1186/s13052-018-0497-6

48. Panche AN, Diwan AD, Chandra SR. Flavonoids: An overview. Journal of Nutritional Science. 2016;*5*(e47):1–15. https://doi.org/10.1017/jns.2016.41

49. Ferraz CR, Carvalho TT, Manchope MF, Artero NA, Rasquel-

Oliveira, FS, Fattori V, Casagrande R, Verri WA. Therapeutic potential of flavonoids in pain and inflammation: Mechanisms of action, pre-clinical and clinical data and pharmaceutical development. Molecules. 2020;25(3):1-35. https://doi.org/10.3390/molecules25030762

50. Jun M, Fu HY, Hong J, Wan X, Yang CS, Ho CT. Comparison of antioxidant activities of isoflavones from kudzu root (*Pueraria lobata* Ohwi). Journal of Food Science. 2003;68(6):2117–22. http://doi.org/ 10.1111/j.1365-2621.2003.tb07029.x

51. Wilson DW, Nash P, Singh H, Griffiths K, Singh R, De Meester F et al. The role of food antioxidants, benefits of functional foods and influence of feeding habits on the health of the older person: An overview. Antioxidants. 2017;*6*(4):1–20. https://doi.org/10.3390/antiox6040081.

52. Foti MC. Antioxidant properties of phenols. Journal of Pharmacy and Pharmacology. 2007;59(12): 1673-85. https://doi.org/10.1211/jpp.59.12.0010

53. Zuliani NE, Erwin, Kusuma IW. Test of antioxidant activity (DPPH Method) of methanol extract and its fractions from leaves of Knobweed (*Hyptis capitata* Jacq.). Jurnal Atomik. 2019;4(1):36-40.

54. Kusuma IW, Rahmini, Arung ET, Pramono AY, Erwin, Supomo. Biological activities and phytochemicals of *Hyptis capitata* grown in east kalimantan, Indonesia. Journal of Applied Biology and Biotechnology. 2020;8(2);58–64. https://doi.org/10.7324/JABB.2020.80210

55. Xu DH, Huang YS, Jiang DQ, Yuan K. The essential oils chemical compositions and antimicrobial, antioxidant activities and toxicity of three *Hyptis* species. Pharmaceutical Biology. 2013;51(9):1125-30. https://doi.org/10.3109/13880209.2013.781195

56. Agarwal K,Varma R. Antioxidant activity and Phytochemical analysis of *Hyptis suaveolens* (L.) Poit. Journal of Advanced Pharmacy Education and Research. 2013;3(4);541–49.

57. Haryanti S, Widiastuti Y. Aktivitas Sitotoksik pada Sel MCF-7 dari Tumbuhan Indonesia untuk Pengobatan Tradisional Kanker Payudara. Media Litbangkes. 2017;27(4):247–54. https://doi.org/10.22435/mpk.v27i4.5010.247-254

58. Yamagishi T, Zhang DC, Chang JJ, McPhail DR, McPhail AT, Lee KH. The cytotoxic principles of *Hyptis capitata* and the structures of the new triterpenes hyptatic acid-A and -B. Phytochemistry. 1988;27(10):3213–16. https://doi.org/10.1016/0031-9422(88)80028-1

59. Poonkodi K, Karthika J, Tamilselvi V, Anitha R, Vasanthamani S. Chemical composition of essential oils of *Hyptis suaveolens* (L.) Poit and its *In vitro* anticancer activity. Journal of Pharmacy Research. 2017;1(5):410-13.

60. Meyer BN, Ferrigni NR, Putnam JE. Brine shrimp: A convenient general bioassay for active plant constituents. Planta Medica. 1982;45(1):31–34. https://doi.org/10.1055/s-2007-971236

61. Harmita, Radji M. Buku Ajar Analisis Hayati. Jakarta: Erlangga. 2008; p.76-77.

62. Ogbole OO, Segun PA, Adeniji AJ. *In vitro* cytotoxic activity of medicinal plants from Nigeria ethnomedicine on Rhabdomyosarcoma cancer cell line and HPLC analysis of active extracts. BMC Complementary and Alternative Medicine. 2017;17(1):1–10. https://doi.org/10.1186/s12906-017-2005-8.

63. Yahya SAS, Harso W, Jannah M. Profil toksikologis ekstrak daun tumbuhan Baka-Baka (*Hyptis capitata* Jacq.) pada hati tikus putih (*Rattus norvegicus*). Biocelebes. 2020;14(1):10–21. https://doi.org/10.22487/bioceb.v14i1.15082.

64. To'bungan N, Jati WN, Zahida F. Acute toxicity of ethanolic extract of *Hyptis capitata* Jacq. stem using brine shrimp lethality test (BSLT) method. Biota: Jurnal Ilmiah Ilmu-Ilmu Hayati. 2021;6(1),52. https://doi.org/10.24002/biota.v6i1.3577

65. Sumitha V, Mini I, Nair LS. Larvicidal efficacy of *Hyptis capitata* Jacq. against *Culex quinquefasciatus* mosquito (Culicidae). International Journal of Mosquito Research. 2021;8(4):42–46.

66. Li R, Tang G, Liu X, Li J, Wang D, Ji S. An ethnopharmacological review of *Hyptis suaveolens* (L.) Poit. Tropical Journal of Pharmaceutical Research. 2020;19(7):1541–50. https://doi.org/10.4314/tjpr.v19i7.29.

§§§