



REVIEW ARTICLE

Ethnopharmacology of *Hyptis capitata*

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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 species 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), *Hyptis actinocephala* (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 quadrangular 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 trichomes; 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 sources 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 stomachache 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 IC₅₀ 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 IC₅₀ 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 2 α -Hydroxyursolic acid from aerial parts of the plant indicated cytotoxicity activity. The IC₅₀ 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	
		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
10	Indonesia	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	Martinique	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 IC₅₀ 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		
2	2α-Hydroxyursolic acid (isolated from methanol extract aerial part)	L1210	>10	58	
		HCT-8	2.7		
		A549	4.9		
		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 antiviral 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 EC₅₀ 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 its significant antibacterial activity (42).

Toxicity

The toxicity profile of *H. capitata* is provided in Table 5. It could be 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 IC₅₀ 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 sesquiterpenes (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	<i>S. sobrinus</i>		500	54
		<i>S. aureus</i>		500	
		<i>P. acnes</i>	-	500	
		<i>Escherichia coli</i>		NI	
		<i>Candida albicans</i>		NI	
2	Whole plant extract	HIV-1	1.4	-	20
		<i>S. aureus</i>		12.5	
		<i>Bacillus subtilis</i>		12.5	
		<i>E. coli</i>		6.25	
		<i>Pseudomonas aeruginosa</i>		6.25	
3	Aerial part essential oil	<i>Fusarium graminearum</i>		25	55
		<i>Botrytis cinerea</i>		12.5	
		<i>Exerohilum turcicum</i>		25	
		<i>Lecanosticta acicula</i>		25	

Table 5. Toxicity of *H. capitata*

Sl. No.	Sample	Toxicity	Value	Reference
1	Methanolic leaves extract	Toxic effect on <i>Artemia salina</i> L.	>1000 µg/mL	54
2	Ethanolic leaves extract	Toxic effect on <i>Artemia salina</i> L.	183.91µg/mL	24
3	Aerial part essential oil	Toxic effect on <i>Artemia salina</i> L.	65.9 µg/mL	55
4	Ethanolic stem extract	Toxic effect on <i>Artemia salina</i> L.	880.579 µg/mL	64
5	Methanolic leaves extract	Larva of <i>Culex quinquefasciatus</i>	25 mg/mL	65
6	Ethanolic leaves extract	<i>Rattus norvegicus</i>	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*, predominantly sesquiterpenes, 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.

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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*.

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