**Review** article

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# Medicinal plant genetic resources of Bangladesh exhibiting anti-dengue activity: A review

#### A.K.M. Golam Sarwar\*, Mahmudul Hasan, Farhan-Ul-Islam, Tajneem Ibne Hossain, M. Ashrafuzzaman

Laboratory of Plant Systematics, Department of Crop Botany, Bangladesh Agricultural University, Mymensingh 2202, Bangladesh. \*Email: drsarwar@bau.edu.bd

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#### ABSTRACTS

Dengue fever, caused by the arthropod-borne dengue virus, has experienced a global increase, with the number of cases rising from 500,000 to 5.2 million and over 5000 deaths within the last two decades. Although dengue incidence in Bangladesh fluctuated from 1964 to 1999, peaking in 2000, it has since spread, impacting thousands of lives and causing diseases. There is currently no (or limited availability of) effective dengue vaccination and antiviral medication. A comprehensive review was conducted to identify the local medicinal plants with anti-dengue activity. A total of 73 species belonging to 42 families possess anti-dengue properties; some also have insecticidal properties, especially against Aedes species. Medicinal plants possess different types of secondary metabolites, for example, phenolic derivatives, alkaloids, flavonoids, terpenoids, and polysaccharides with compound-specific dengue preventing mechanisms. The conversion of these medicinal plants into prescription drugs to treat dengue infections requires more clinical investigation.

Key words: Alkaloids, dengue, flavonoids, polysaccharides, terpenoids, total phenolics

#### **INTRODUCTION**

Dengue fever is the most emerging viral human disease caused by the arthropodborne dengue virus (DENV), which belongs to the genus Flavivirus in the family Flaviviridae (Goel et al., 2004). Dengue incidence has surged globally, with the World Health Organization (WHO) reporting a tenfold increase from 500,000 to 5.2 million cases between 2000 and 2019; the year 2019 experienced an all-time high, with cases reported in 129 countries (https://www.who.int/emergencies/diseaseoutbreak-news/item/2023-DON498). Since the start of 2023, more than 5000 denguerelated deaths and nearly a historic five million cases have been reported in more than 80 countries and territories due to transmission continuous and an unanticipated increase in dengue infections (https://www.who.int/emergencies/diseaseoutbreak-news/item/2023-DON498). With 40% of the world's population living in areas at risk for transmission, dengue virus infection is a leading cause of illness in the and subtropics tropics (https://www.cdc.gov/dengue/training/cme/c cm/page52245.html). About 8 million people worldwide may be afflicted by dengue and malaria in 2080 (Hillary et al., 2024). The dengue virus is spread through two species of Aedes, A. aegypti and A. albopictus, mosquitoes (Hossain et al., 2023). When an infected mosquito bites a human, it transmits the disease. There are four serotypes of DENV: DENV-1, DENV-2, DENV-3, and DENV-4. Among these, DENV-2 is more lethal than any other serotype (Saleh and Kamisah, 2021). Infection of one serotype confers permanent immunity to that serotype and only temporary immunity to the other serotypes; subsequent infections with a different serotype raise the risk of developing severe

dengue (Reich *et al.*, 2013). Symptoms of dengue fever include fever, headache, joint, and muscle pain (Gubler, 2006). Chronic symptoms include dengue fever to severe hemorrhagic, characterized by low platelet levels and blood plasma leakage, also known as dengue shock syndrome (Pigili and Runja, 2014). First infections with DENV-1 or DENV-3 often led to more severe illness than main infections with DENV-2 or DENV-4 (Tang *et al.*, 2012).

Dengue incidence in Bangladesh was intermittently reported from 1964 to 1999. The first significant dengue outbreak happened in 2000, and since then, it has spread throughout the country, affecting thousands of people's quality of life and creating diseases (Hossain et al., 2023). According to the most recent official statistics (November 22, 2024), at least 438 individuals died from connected issues in 2024, while 84,826 patients were admitted hospitals across the country to (https://dashboard.dghs.gov.bd/pages/heoc\_ dengue\_v1.php). The climatic conditions of Bangladesh are favourable for dengue infection. Although dengue is endemic in Bangladesh, the current dengue surge is unusual in terms of seasonality and the early sharp increase compared to previous years, where the surge typically starts around late June (Hossain et al. 2023). The case fatality rate (CFR) so far this year is relatively high compared to previous years for the full-year pre-monsoon Aedes survey period. The shows that the density of mosquitoes and the number of potential hotspots are at the highest level in the past five years (WHO, 2023). Hossain et al. (2023) recently conducted a thorough analysis of the entire dengue situation, including illness burden, clinical spectrum, seroprevalence, circulating serotypes/genotypes, and spatial distribution since the first outbreak was documented in Bangladesh.

Dengue fever does not currently have a specific treatment. Therefore, with the rapid expansion of dengue disease, it is imperative to create efficient preventative and control strategies, such as antiviral medications and dengue vaccinations. However, there is currently no effective dengue vaccination or antiviral medication (Zandi et al., 2011; Tang et al., 2012) or limited availability (a Sanofi Pasteur-developed dengue vaccine has been approved in 24 nations and included in public vaccination programs in Brazil and the Philippines) (Hossain et al., 2023). Typically, dengue patients get supportive care until they fully recover without particular therapeutic interventions. Traditional herbal remedies have been thoroughly studied as an alternative treatment due to the adverse (or disastrous) side effects of synthetic medications and the increasing resistance of bacteria to conventional antimicrobial therapy. About 80% of the population in developing countries, especially in Asia and Africa, use natural products from plants for their primary healthcare (WHO, 2020). Plants and chemicals produced by them continue to be valuable sources for developing novel antiviral medications due to their high accessibility in nature and anticipated low side effects. Several medicinal plants have been shown to have significant antiviral properties at various stages of viral development, and many have been used to treat viral infections in both humans and animals, including DENV infection (Ganjhu et al., 2015; Sarwar et al., 2022; Firuj et al., 2023). Bangladesh is rich in medicinal plant genetic resources (Sarwar, 2020); therefore, this study aims to identify the medicinal plants of Bangladesh, plant parts used, and active constituents that could be used for dengue disease treatments.

## METHODOLOGY

A narrative literature review was conducted on the possibility of using medicinal plants in Bangladesh to treat dengue. Different electronic sources of databank - PubMed, SpringerLink, MDPI link, ResearchGate, Google and Google Scholar, ScienceDirect, etc.—were searched for the article. Bangladeshi articles were searched in the BanglaJol database (an exclusive database of Bangladeshi Journals) with a combination keywords "dengue", "antiviral", of "medicinal plants", "Bangladesh", etc. Articles published in other languages except English and editorials and comments not subjected to peer review were excluded. Internationally recognised websites such as Plants of the World Online (https://powo.science.kew.org/), the International Plant Names Index (https://www.ipni.org/), and World Flora Online (https://www.worldfloraonline.org/) have been checked for current nomenclature and family delimitation.

# **RESULTS AND DISCUSSION**

Medicinal plants of 73 species belonging to 42 families could be used to treat dengue fever (Table 1). With seven species (9.59% of total), the family Lamiaceae emerged as the largest source of anti-dengue plants, followed by Fabaceae (8.22%; six species), Asteraceae and Zingiberaceae (5.48%; four species each) (Figure 1). Twenty-seven families were represented by a single species each (Table 1). In other publications, Lamiaceae is also identified as one of the most useful families for treating dengue and other viral diseases. For example, according to Saleh and Kamisah (2021), 54 species from 31 families exhibited anti-dengue activity; the most prominent representatives were the Lamiaceae (10.5%), Asteraceae (9.9%), Aristolochiaceae, and Loganiaceae (each 7.2%).

In terms of plant parts used, more than one plant part was used for 18 plant species (24.66% of the total), followed by the whole plant (13.70%; 10 species) (Table 1; Figure 2). Individually, leaves were the most common (36.99%; 27 species) plant part used, followed by fruits (5.48%; 4 species) (Table 1; Figure 2).

Medicinal plants possess different types of secondary metabolites, for example, phenolic derivatives (4-hydroxy panduratin,  $\alpha$ -mangostin, methyl geraniin, gallate), (castanospermine, alkaloids hirsutine. flavonoids palmatine). (chartaceones, pectolinarinandacactein-7-O-rotinosides,

catechin, 5-hydroxy-7-methoxy-6-methyl flavanone), terpenoids (betulinic acid  $3\beta$ caffeate, lupeol acetate, celastrol, andrographolide), and polysaccharides (fucoidan, carrageenan, galactomanns) *IJMFM&AP, Vol. 11, No. 1*  (Table 1; Altamish et al., 2022; Dhiman et al., 2022); although the mechanism of preventing dengue infections is different (Figure 3) and compound-specific. Saleh Kamisah (2021) enumerated and 51 bioactive substances in total with different degrees of anti-dengue activity, including seven polysaccharides, 14 flavonoids, 17 phenolics and flavonoid glycosides and derivatives, two alkaloids, a saponin, six and four phenolic terpenoids, acids. Quercetin, one of several compounds, showed significant anti-DENV-2 inhibitory al., 2011). effects (Zandi et More importantly, both DENV and SARS-CoV viral infections are inhibited by quercetin (Saleh and Kamisah, 2021). The plant compounds demonstrate bioactive an antiviral response either directly or via inducing immunomodulatory response cascades against DENV at various stages of infection, such as inhibition of viral entry and/or viral cell adhesion, viral adsorption, intracellular replication, proliferation, and cellular metabolism (Figure 3; Loaiza-Cano et al., 2021; Dhiman et al., 2022). Certain medicinal plants, such as Houttuynia cordata and Boesenbergia rotunda and their bioactive compounds effectively inhibit both DENV and SARS-CoV infections, despite their distinct viral families, structures, entry mechanisms, replication, and pathogenicity (Saleh and Kamisah, 2021). Flavonoids also facilitate the entry of infectious virus particles into phagocytes, immune cells that generate several proinflammatory cytokines involved in the pathophysiology of severe dengue (Loaiza-Cano et al., 2021). Additionally, plant metabolites aid in lowering the antigen burden and regulating several host immunological components 2022). Plant-mediated (Dhiman *et al.*, immunomodulation results in increased platelet counts, phagocytic pathway activation. and controlled cytokine production.

The insecticidal qualities of medicinal plants, such as *A. paniculata*, *A. calamus*, *A. indica*, *C. citratus*, etc., are another important feature that makes them a viable and environmentally benign alternative to

controlling Aedes mosquitoes and dengue infection (Table 1; Senthil-Nathan, 2020; Saleh and Kamisah, 2021; Dhiman et al., Medicinal plant extracts have 2022). pupicidal, larvicidal, ovicidal, and adulticidal properties, and act as repellents, toxins, feeding deterrents, growth retardants, and bite protectors. These extracts target cellular mechanisms, potentially disrupting vector mosquitoes' functions by disturbing proteins, ion channels, nucleic acids, and other cellular components; reducing enzyme levels, affecting metamorphosis and body tissues like epithelium layer, muscles, midgut, and nervous systems (Hillary et al., Medicinal plant 2024). extracts. as bioinsecticides, are effective alternatives to chemical insecticides in integrated mosquito management programs due to their multiple modes of action and synergic compounds, which lower the possibility of development of resistance to it (Demirak and Canpolat, 2022). These products of plant origin offer the combined benefits of being affordable, safe for non-target creatures, biodegradable, and environmentally benign. Moreover, some medicinal plants are still utilised in traditional ways for their anti-dengue qualities and have not yet been studied for scientific validation (Table 1; Dhiman et al., 2022).

# CHALLENGES AND FUTURE DIRECTIONS

The absence of an effective and widely accessible dengue vaccine and antiviral medications, along with difficulties in outbreak prediction and management in Bangladesh, coupled with fluctuating incidence, necessitates localized strategies and the utilization of medicinal plants with anti-dengue properties. Constraints for the integration of traditional medicine into the modern healthcare system could be divided into organizational, legal, policy, and sociocultural. The efficacy, safety, uniformity, and quality of conventional medicine are sometimes a matter of debate. Traditional approaches to prescribing medicinal plants with anti-dengue properties are yet to be scientifically validated. Extensive research is, therefore, required to assess immunologic

potentials, phytochemical richness, and clinical probing of these plants for effective development. medicine Moreover. comparison among medicinal plants (and/or phytochemicals) could be an interesting biopesticides topic for commercial development. Collaboration between traditional medicine practitioners and modern pharmaceutical researchers should be fostered to integrate traditional knowledge with contemporary science effectively.

## CONCLUSION

This review shows the enormous potential of Bangladeshi medicinal plants, available in other parts of the world as well, for the treatment of dengue. Several interesting medicinal plants have been identified that could be developed into prescription medications to treat dengue infections. To create a successful medication, further clinical research is needed to evaluate the immunologic potential of plants and their phytochemical diversity as well.

### CONFLICT OF INTEREST STATEMENT

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Figure 1. Family-wise distribution of medicinal plants in Pie graph.



Figure 2. Plant parts use of medicinal plants in Pie graph.



**Figure 3.** Illustration of dengue virus inhibition mechanisms by medicinal plants (adopted from Altamish *et al.*, 2022).

Sl. No.	Bangla/Common Name	Scientific name	Family	Part used	Active constituents	Reference
1.	Kalmegh	Andrographis paniculata (Burm.f.) Wall. ex Nees*	Acanthaceae	Whole plant	Diterpneoid, Andrographolides	Divyaa <i>et al.</i> , 2020
2.	Sabah Snake Grass	Clinacanthus nutans (Burm.f.) Lindau	Acanthaceae	Leaves, Whole plant	-	Julsrigival <i>et al.</i> , 2021
3.	Bashak	Justicia adhatoda L.	Acanthaceae	Arial parts	-	Wilson et al., 2021
4.	Botch	Acorus calamus L.*	Acoraceae	Leaves, Roots	β-asarone. Acoric acid, Calamusin D	Rosmalena et al., 2019
5.	Elder	Sambucus nigra L.	Adoxaceae	Flower, Leaves	Alkaloids, Flavonoids, Coumarins	Julsrigival et al., 2021
6.	Malancha	Alternanthera philoxeroides (Mart.) Griseb.	Amaranthaceae	Whole plant	Flavonoids, Saponins	Altamish et al., 2022
7.	Shalinche/Carpet Weed	Alternanthera sessilis (L.) DC.	Amaranthaceae	Leaves	-	Saleh and Kamisah, 2021
8.	Garlic	Allium sativum L.	Amaryllidaceae	Bulb	Diallyl disulfide (DADS)	Altamish et al., 2022
9.	Cheshunt	Anacardium occidentale L.	Anacardiaceae	Nutshell	Cardol Triene	Loaiza-Cano et al., 2021
10.	Atta/Custard apple	Annona reticulata L.	Annonaceae	Bark, Fruit	-	Saleh and Kamisah, 2021
11.	Soursop	Annona muricata L.	Annonaceae	Fruit	-	Saleh and Kamisah, 2021
12.	Chatim	Alstonia scholaris (L.) R.Br.	Apocynaceae	Leaves	Alstotides	Julsrigival et al., 2021
13.	Nayantara	Catharanthus roseus(L.) G.Don	Apocynaceae	Whole plant, Leaves	-	Islam et al., 2014
14.	Assamlata	Mikania cordata (Burm.f.) B.L.Rob.	Asteraceae	Leaves	-	Rahmatullah et al., 2009
15.	Bikashlata/Bittervine	Mikania micrantha Kunth	Asteraceae	Leaves	-	Bradacs et al., 2011
16.	Tridhara	Tridax procumbers L.	Asteraceae	Stem	Flavonoids	Bhuiyan et al., 2020
17.	Cucushim	Vernonia cinereal (L.) H.Rob	Asteraceae	Leaves	Phenolics (gallic acid)	Bhuiyan et al., 2020
18.	Field Mustard	Brassica campestris L.	Brassicaceae	Oil	-	Saleh and Kamisah, 2021
19.	Papaya	Carica papaya L.	Caricaceae	Leaves, Fruits	Quercetin	Sarker et al., 2021
20.	Mangosteen	Garcinia mangostana L.	Clusiaceae	Fruit pericarp	α-mangostin	Altamish et al., 2022
21.	Sweet potato	Ipomoea batatas (L.) Lam.	Convolvulaceae	Leaves		Saleh and Kamisah, 2021
22.	Bitter gourd	Momordica charantia L.	Cucurbitaceae	Roots, Fruits	Potent protein	Desai et al., 2020
23.	Seaberry	Hippophae rhamnoides L.	Elaeagnaceae	Leaves	-	Divyaa <i>et al.</i> , 2020
24.	Bishkatali	Cladogynos orientalis Zipp. ex Span.	Euphorbiaceae	Whole plant	-	Klawikkan et al., 2011
25.	Dudhia/Asthma-plant	Euphorbia hirta L.	Euphorbiaceae	Leaves, stems. roots	-	Fiscal, 2017
26.	Multigreen	Breynia androgyna (L.) Chakrab. & N.P.Balakr.	Euphorbiaceae	Leaves	β-sitosterol	Joshi et al., 2023
27.	Black Bean	Castanospermum australe A.Cunn. ex Mudie	Fabaceae	Seeds	Castanospermine	Altamish et al., 2022
28.	Licorice	Glycyrrhiza glabra L.	Fabaceae	Root	Glycyrrhizin	Babbar et al., 2023
29.	Ipil Ipil	Leucaena leucocephala (Lam.) de Wit	Fabaceae	Seeds	Galactomannan	Altamish et al., 2022
30.	Khair	Senegalia catechu (L.f.) P.J.H.Hurter & Mabb.	Fabaceae		Pep-RTYM, Catechin, Quercetin	Altamish et al., 2022
31.	Sonalata	Senna alexandrina Mill.	Fabaceae	Leaves	Phenolic glycosides	Dhiman <i>et al.</i> , 2022
32.	Methi/Fenugreek	Trigonella foenam-graecum L.	Fabaceae	Leaves	-	Deep et al., 2018
33.	Bon Chad	Flagellaria indica L.	Flagellariaceae	Whole plant	-	Klawikkan et al., 2011
34.	Musk Basil	Basilicum polystachyon (L.) Moench	Lamiaceae	Whole plant	-	Altamish et al., 2022
35.	Bhat/Glory bower	Clerodendrum viscosum L.	Lamiaceae	Leaves	-	Rahmatullah et al., 2011
36.	Patabahar/Coleus	Coleus scutellarioides (L.) Benth.	Lamiaceae	Leaves	-	Gascon, 2011
37.	Wild Pudina/Wild mint	Mentha arvensis L.*	Lamiaceae	Leaves	-	Gascon, 2011
38.	Tulsi/Holy Basil	Ocimum tenuiflorum L.	Lamiaceae	Leaves	-	Chand et al., 2018
39.	Java Tea	Orthosiphon aristatus (Blume) Miq. var. aristatus	Lamiaceae	Leaves		Saleh and Kamisah, 2021
40.	Nishinda	Vitex negundo L.	Lamiaceae	Leaves	-	Gascon, 2011

	Table	1:	List	of	the	medicinal	p	lants	used	against	dengue.
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41.	Avocado	Persea americana Mill.	Lauraceae	Fruits	(2 <i>R</i> ,4 <i>R</i> )-1,2,4-trihydroxyheptadec-16- yne (THHY)	Altamish et al., 2022
42.	Dalim/Pomegranate	Punica granatum L.	Lythraceae	Fruits	Punicalagin	Loaiza-Cano et al., 2021
43.	Magnolia	Magnolia officinalis Rehder & Wilson	Magnoliaceae	Bark, Seed cones	Honokiol (Lignan Biphenol)	Fang et al., 2015
44.	Neem	Azadirachta indica A.Juss.*	Meliaceae	Leaves	Azadirachtin	Parida et al., 2002
45.	Velvet leaf	Cissampelos pareira L.	Menispermaceae	Aerial parts	Cissampelo flavone	Babbar et al., 2023
46.	Gulancha/Heart-leaved	Tinospora cordifolia (Willd.) Hook.f. & Thomson	Menispermaceae	Leaves. Stems	Alkaloids, Glycosides, Steroids,	Deep et al., 2018
	moonseed	1 5 ( )	1	,	Flavonoids	1
47.	Hauili	Ficus septica Burm.f.	Moraceae	Leaves, Stem, Fruit, Heartwood	Alkaloids, Lignans, Triterpenes, Flavonoids, And Steroids	Altamish et al., 2022
48.	Banana	Musa $\times$ paradisiaca L.	Musaceae	Latex of stems	-	Saleh and Kamisah, 2021
49.	Nutmeg	Myristica fatua Houtt.	Myristicaceae	Seeds	Artesunic acid. Homoegonol. Myristicin	Rosmalena <i>et al.</i> , 2019
50.	Nutmeg	Myristica fragrans Houtt.	Myristicaceae	Leaves	-	Saleh and Kamisah. 2021
51.	Guava	Psidium guajava L.*	Myrtaceae	Leaves, Bark,	-	Deep et al., 2018; Batoro
		0.7	5	Young fruits		& Siswanto, 2017
52.	Jamrul	Syzygium samarangense (Blume) Merr. & L.M.Perry	Myrtaceae	Leaves	5-hydroxy- 7- methoxy- 6-methylfla vanone (FN5Y)	Altamish et al., 2022
53.	Punarnava Red	Boerhavia diffusa L.	Nyctaginaceae	Leaves, Stem	tannins, phenols, Flavonoids, Others	Babbar et al., 2023
54.	Sheuli, Shefali	Nyctanthes arbor-tristis L.	Oleaceae	Leaves	β-Sitosterol, Calceolarioside A	Morshed et al., 2022
55.	Kamranga/Carambola	Averrhoa carambola L.	Oxalidaceae	Leaves, Barks, Fruit	2-dodecyl-6-methoxycyclohexa -2,5- diene-1,4-dione	Wei et al., 2018
56.	Bhui amla	Phyllanthus amarus Schumach. & Thonn.	Phyllanthaceae	Whole plant	, _	Altamish et al., 2022
57.	Southern pokeweed	Phytolacca bogotensis Kunth.	Phytolaccaceae	Fresh leaves	-	Bussmann & Sharon, 2006
58.	Chuijhal	Piper retrofractum Vahl.*	Piperaceae	Whole plant	-	Klawikkan et al., 2011
59.	Lemon grass	Cymbopogon citratus (DC.) Stapf.*	Poaceae	Oil	Geranial, Geranyl acetate	Rosmalena et al., 2019
60.	Banar-mul	Vetiveria zizaniodes L.*	Poaceae	Roots	Khushimol, $\alpha$ -vetiverone, $\beta$ -vetiverone, ethyl 4-(4- methylphenyl)-4- pentenoate	Firuj et al. 2023
61.	Garjan	Rhizophora apiculata Blume	Rhizophoraceae	Whole plant	-	Klawikkan et al., 2011
62.	Cinchona	Cinchona spp.	Rubiaceae	Bark	-	Sarah et al., 2020
63.	Bishphal	Pavetta tomentosa Roxb. ex Sm.	Rubiaceae	Leaves	Saponins, Flavonoids and Alkaloids,	Pratheeba et al., 2019
64.	Thankuni	Tarenna asiatica (L.) Kuntze ex K.Schum.	Rubiaceae	Leaves	Saponins, Favonoids and Alkaloids,	Pratheeba et al., 2019
65.	Lemon	Citrus limon (L.) Osbeck*	Rutaceae	Pulps	-	Hajdu & Hohmann, 2011
66.	Euodia	Euodia species	Rutaceae	Leaves	-	Kandowangko et al., 2011
67.	Miracle fruit	Synespalum dulcificum (Schumach. & Thonn.) Daniell.	Sapotaceae	Leaves	-	Gascon, 2011
68.	Aishta nagini	Houttuynia cordata Thumb.	Saururaceae	Whole plant	Chlorogenic acid	Klawikkan et al., 2011
69.	Bon tepari	Physalis angulata L.	Solanaceae	Leaves	-	Bradacs et al., 2011
70.	Chinese Ada/Fingerroot	Boesenbergia rotunda (L.) Mansf.	Zingiberaceae	Rhizomes	Cardamonin	Kiat et al., 2006
71.	Holud/Curcuma	Curcuma longa L.*	Zingiberaceae	Rhizomes, Leaves	Curcumin	Ichsyani et al., 2017
72.	Ada/Ginger	Zingiber officinale L.*	Zingiberaceae	Rhizomes, Leaves	-	Sharma et al., 2015
73.	Bon Ada/Ginger	Zingiber purpureum Rosc.	Zingiberaceae	Rhizomes, Leaves	-	Kandowangko et al., 2011

\* Plants with insecticidal properties