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Botany, uses, phytochemistry and bioactivities of mangrove associates I: *Hibiscus tiliaceus*

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Background

The genus *Hibiscus* (family Malvaceae) consists of some 275 species in the tropics and sub-tropics with some 43 species occurring in the Malesian region (Dasuki, 2001). China has 12 species that are endemic and four are introduced (Tang *et al*., 2007). Generally, leaves of *Hibiscus* are simple, lobed, alternately or spirally arranged and have paired stipules (Chan *et al*., 2016; Wong *et al*., 2016). Flowers are radially symmetrical with cup-shaped calyx, five petals joined at the base, style bearing many stamens, and stigma with five hairy lobes.

Flowers of most *Hibiscus* species have a remarkable colour pattern with the inner base of petals forming a deep-coloured heart (Lowry, 1976). Another feature of *Hibiscus* is flower color change which can be spectacular in some species. *Hibiscus* species are widely cultivated as ornamental, food and medicinal plants (Dasuki 2001). The genus has been reported to possess a wide range of pharmacological properties such as antioxidant, antibacterial, antihypertensive, anti-inflammatory, antipyretic, anti-cancer, anti-tumour, hepatoprotective, hypoglycemic, antidiabetic, anticonvulsant, antihelminthic, anti-spermatogenic and antimutagenic activities (Maganha *et al*., 2010; Chan *et al*., 2016; Wong *et al*., 2016).

Botany and Uses

Hibiscus tiliaceus L. (sea hibiscus or cotton tree) is a coastal plant associated with mangroves of the tropics and sub-tropics. Although *Talipariti tiliaceum* (L.) Fryxell is now the accepted name (Fryxell, 2001), the old name is still widely used. Trees of *H. tiliaceus* are fast-growing, reaching 10 m tall and producing low-spreading branches (Lim, 2014; Chan *et al*., 2016). Leaves are heart-shaped and spirally arranged. Flowers are bell-shaped with maroon-colored heart and stigma. They are yellow in the morning, turning orange-red in the evening, and mauve the next morning (Figure 1). The change in flower color from yellow to red may be due to an increase in flavonols (e.g., gossypetin 3-*O*-glucoside) and anthocyanins (e.g., cyanidin 3-*O*-sambubioside) (Shimokawa *et al*., 2015).

Figure 1 A freshly open flower of *Hibiscus tiliaceus* is yellow in the morning (left) and mauve the next morning (right).

Fibers from the bark of *H. tiliaceus* make excellent cordage and paper (Elevitch & Thomson, 2006; Lim, 2014). Leaves are fed to cattle as fodder. The light wood can be used for making canoe parts, wood carvings and household utensils. The species has cultural significance throughout the Pacific. The leaves, bark and flowers of the plant have traditionally been used to treat fever, cough, phlegm and dysentery, and consumed as a laxative (Cheng *et al*., 2013).

Phytochemistry

Many types of terpenoids, steroids, flavonoids, benzaldehydes and benzaldehydes have been isolated from different parts of *H. tiliaceus*. In this article, only compounds that are new to science and new to the species are listed (Table 1). They include sesquiterpenoids (16), triterpenoids (6), pentacyclic terpenoids (4), benzaldehydes (4), coumarin (1), amide (1) and steroid (1). Of the various types of new compounds, sesquiterpenoids are dominant and most recently isolated.

Table 1 New compounds isolated from different parts of *Hibiscus tiliaceus*.

Compound type	Compound name	Plant part	Reference
Sesquiterpenoids	Hibisceusones A–C •	Infected stem	(Chen *et al*., 2022a)
	Hibisceusin A–H •		(Chen *et al*., 2022b)
	Hibiscusterpenes I–V •	Stem & twig	(Matsumoto *et al*., 2020)
Triterpenoids	(20*E*)-22-Hydroxynigrum-20-en-3-one •		(Feng *et al*., 2008)
	21α-Hydroxynigrum-22(29)-en-3-one •		
	21β-Hydroxynigrum-22(29)-en-3-one •		
	27-Oic-3-oxo-28-friedelanoic acid •	Bark	(Li *et al*., 2006)
	Tiliacols A & B •	Leaf & twig	(Cheng *et al*., 2013)
Pentacyclic terpenoids	Ergosta-4,6,8(14),22-tetraen-3-one ◦	Stem & bark	(Wang *et al*., 2011)
	Germanicol ◦		
	Glutinol ◦		
	Lupeol ◦		
Benzaldehydes	2-(2′,3-Epoxy-1′-heptenyl)-6-hydroxy-5-(3″-methyl-2″-butenyl)benzaldehyde •	Endophytic fungus	(Li *et al*., 2008)
	1,8-Dihydroxy-4-methyl-7-(3-methyl-2-butenyl)-1,2,3,3α,4,9β-hexahydrocyclopenta[*c*]chromene-9-carbaldehyde •		
	2-(1′,5′-Heptadienyl)-3,6-dihydroxy-5-(3″-methyl-2″-butenyl) benzaldehyde •		
	(*E*)-6-Hydroxy-7-(3-methyl-2-butenyl)-2-(3-oxobut-1-enyl)chroman-5-carbaldehyde •		
Coumarin	Hibiscusin •	Stem wood	(Chen *et al*., 2006)
Amide	Hibiscusamide •		
Steroid	Tiliaceic acid A •	Leaf	(Vinh *et al*., 2019)

• New to science, ◦ New to *H. tiliaceus*

Bioactivities

Antioxidant: Out of leaves and flowers of six Hibiscus species screened for total phenolic content (TPC) and free radical scavenging (FRS), extracts of *H. tiliaceus* ranked first with outstanding values (Wong *et al*., 2009; 2010a). Out of leaves of nine coastal plant species screened for antioxidant properties, TPC and FRS values of H. tiliaceus were the highest with young leaves having slightly higher values than mature leaves (Nivas *et al*., 2010). A similar trend was also observed for total flavonoid content and ferric reducing power. A comparison between the antioxidant properties of coastal and inland populations of *H. tiliaceus* did not show any distinct variation for both leaves and flowers (Wong *et al*., 2010b).

Antibacterial: The antibacterial activity of the methanol leaf extract of *H. tiliaceus* has been reported with minimum inhibitory doses of 1.0, 0.5 and 0.25 mg/disc against Gram-positive bacteria of *Bacillus cereus*, *Micrococcus luteus* and *Staphylococcus aureus*, respectively (Wong *et al*., 2010a). No inhibition was observed with Gram-negative bacteria.

Anti-inflammatory and analgesic: Successive methanol, petroleum ether, and chloroform leaf extracts of *H. tiliaceus* were tested for anti-inflammatory and analgesic effects in mice at oral doses of 250 and 500 mg/kg (Narender *et al*., 2009). Results showed significant anti-inflammatory activity against carrageenan-induced paw oedema after 2 and 3 h, and significantly inhibited acetic acid-induced abdominal writhing after 1 h. The leaf and bark extract of *H. tiliaceus* had analgesic effects by producing 40% and 52% writhing inhibition in mice (Abdul-Awal *et al*., 2016).

Anti-tyrosinase: Leaf extracts of *H. tiliaceus* showed strong anti-tyrosinase activity. Out of 39 seashore plant species, and 36 edible and medicinal plant species found in Okinawa, Japan, leaves of *H. tiliaceus* had the highest tyrosinase inhibition (Masuda *et al*., 2005). Of four species of *Hibiscus* tested, leaves of *H. tiliaceus* had the strongest anti-tyrosinase activity (42%), comparable to leaves of guava (41%) used as positive control (Wong *et al*., 2010a). Recently, a study on leaves of six coastal tree species showed that the dichloromethane extract of *H. tiliaceus* displayed the strongest anti-tyrosinase activity with IC_{50} value of 0.13 mg/ml (Lim *et al*., 2021).

Anti-cancer: Hibiscusamide isolated from the stem wood of *H. tiliaceus* had cytotoxic activity against P388 murine leukemia and HT-29 colon cancer cells with IC_{50} values of 1.7 and 3.8 g/ml, respectively (Chen *et al*., 2006). Of the three tetracyclic triterpenoids isolated from the leaf and branch extracts of *H. tiliaceus*, the analog of tiliacol A showed potent cytotoxicity against P388 murine leukemia and HeLa cervical cancer cells with IC_{50} values of 11.2 and 11.5 mmol/L, respectively (Cheng *et al*., 2013). Against MCF-7 breast cancer cells, leaves of *H. tiliaceus* displayed moderate cytotoxicity with an IC_{50} value of 10 µg/ml (Andriani *et al*., 2020).

Out of three sesquiterpenoids (hibisceusones A−C) isolated from the infected stem of *H. tiliaceus*, the cytotoxicity of hibisceusone B was the strongest against MDA-MB-231 breast and HepG2 liver cancer cells with IC_{50} values of 3.12 and 3.45 µM, respectively (Chen *et al*., 2022a). The anti-cancer effect involved the induction of apoptosis of by inhibiting the PI3Kα pathway. From the infected stem of *H. tiliaceus*, eight sesquiterpenoids (hibisceusins A−H) isolated exhibited cytotoxicity against HepG2 liver cancer cells with IC_{50} values of 3.5−6.8 µM (Chen *et al*., 2022b).

Anti-diabetic and hypolipidemic: The methanol flower extract of *H. tiliaceus* was evaluated for anti-diabetic and hypolipidemic effects using streptozotocin-induced diabetic rats, orally administered with the extract at doses for 250 and 500 mg/kg for 21 days (Kumar *et al*., 2010). The extract showed significant anti-diabetic activity with improvement in body weight, reduction in serum cholesterol and triglycerides, and improvement in high density lipoprotein (HDL)-cholesterol level.

Cytoprotective: Flower extracts of *H. tiliaceus* have antioxidant effect protecting several strains of yeast cells against cytotoxicity of hydrogen peroxide (H_2O_2) and tert-butyl-hydroperoxide (TBHP), (Rosa *et al*., 2006), and showed antigenotoxic and antimutagenic effects against oxidative DNA damage induced by H_2O_2 and TBHP in V79 cells (Rosa *et al*., 2007).

Anti-depressant-like: The same group of researchers also reported that the flower methanol extract of *H. tiliaceus* had anti-depressant-like influence on male Swiss albino mice without sedative side effect (Vanzella *et al*., 2012).

α-Glucosidase inhibitory: Trans-tiliroside a flavonoid glycoside isolated from the leaves of *H. tiliaceus* showed strong α-glucosidase inhibitory activity with an IC_{50} of 78 µM compared with the positive control acarbose at 106 µM (Vinh *et al*., 2019).

Anthelmintic: The anthelmintic activity of leaf and wood extracts of *H. tiliaceus* has been reported (Vijay & Rajendra, 2014). Tested against *Pheretima posthuma* based on time of paralysis and time of death using 10−40 mg/ml of extracts, good activity was shown by the ethyl acetate leaf extract (28−46 min and 45−74 min) and petroleum ether wood extract (29−45 min and 47−78 min), respectively.

Thrombolytic: Using the clot lysis assay, the thrombolytic activity of the methanol leaf extract of *H. tiliaceus* (14%) was found to be 14%, compared to that of streptokinase (62%) (Surana *et al*., 2022).

Conclusion

Distinguishing features of *H. tiliaceus* are the yellow bell-shaped flowers with maroon-colored heart and stigma that exhibit spectacular flower color change from yellow to mauve red. The new compounds from *H. tiliaceus* include sesquiterpenoids, triterpenoids, pentacyclic terpenoids, benzaldehydes, coumarin, amide and steroid. Sesquiterpenoids dominate and are the most recently isolated. Pharmacological properties of *H. tiliaceus* include antioxidant, antibacterial, anti-inflammatory, analgesic, anti-tyrosinase, anti-cancer, anti-diabetic, hypolipidemic, cytoprotective, anti-depressant-like, α-glucosidase, anthelmintic and thrombolytic activities. Anti-cancer is the most often reported activity.

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