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Review Article

A Review on the Phytochemistry and Pharmacology of Two Lesser-known *Hibiscus* species: *H. taiwanensis* and *H. schizopetalus*

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ABSTRACT
In this short review, the current knowledge on the chemical constituents and pharmacology of two lesser-known *Hibiscus* species of *H. taiwanensis* and *H. schizopetalus* is updated with some description of their botany and uses. With phenolic acids, flavonoids, phenylpropanoids, and sterols as chemical constituents, *H. taiwanensis* has pharmacological properties of antioxidant, cytotoxic, HIV replication inhibition, hypoglycaemic, anti-inflammatory and analgesic activities. Chemical constituents of *H. schizopetalus* include anthocyanins and triterpene esters with pharmacological properties of antioxidant, antipyretic, anti-inflammatory, analgesic, hypoglycaemic and hypolipidemic activities. Possessing diverse chemical constituents and pharmacological properties, both *H. taiwanensis* and *H. schizopetalus* have anti-inflammatory, analgesic and hypoglycaemic activities in common. Other *Hibiscus* species possessing such properties include *H. tiliaceus*, *H. mutabilis*, *H. cannabinus*, *H. rosa-sinensis* and *H. sabdariffa*.

Keywords: *H. taiwanensis*, cream hibiscus, *H. schizopetalus*, coral hibiscus, anti-inflammatory, analgesic, hypoglycaemic.

INTRODUCTION

The genus *Hibiscus* (Malvaceae) comprises herbaceous plants, woody shrubs and small trees. There are some 275 species in the tropics and sub-tropics of which 43 species are found in the Malesian region[1]. Two species occur in the temperate zone. Leaves of *Hibiscus* are alternately or spirally arranged with lobed or toothed margin and paired stipules[2,3]. Flowers are large showy and often bell-shaped. They are radially symmetrical with cup-shaped calyx and five petals joined at the base. Stamens are united into a tubular structure surrounding the style and stigma have five hairy lobes. Flowers of most *Hibiscus* species are remarkably colourful with the inner base of petals forming a deep-coloured heart[4]. Some species display spectacular flower colour change. *Hibiscus* is widely cultivated as ornamental, food and medicinal plants[1]. With large colourful flowers, *Hibiscus* species are commonly planted in parks and gardens. Leaves of some species are consumed as vegetable, and stem fibres are also used for pulp and paper. The mucilage is used as emollient and demulcent for abscesses, ulcers, cutaneous infections, swellings, boils, and mumps. The mucilage is believed to have a cooling effect enabling burns and scalds to heal. The mucilage is also used as medication for treating cough, bronchitis, dysuria and menorrhagia, and midwives use it to facilitate child birth. *Hibiscus* species have been reported to possess a wide range of pharmacological properties such as antioxidant, antibacterial, anti-hypertensive, anti-inflammatory, antipyretic, anti-cancer, anti-tumour, hepatoprotective, hypoglycaemic, antidiabetic, anticonvulsant, antihelminthic, anti-spermatogenic and antimutagenic activities[5,6]. In this short review, the chemical constituents and pharmacological properties of two lesser-known *Hibiscus* species of *H. taiwanensis* and *H. schizopetalus* are reviewed with some description of their botany and uses. Both species are accepted names in the Plant List 2013[7]. They have been documented in a book chapter on edible medicinal and non-medicinal plants[8]. A review on the pharmacological activities and secondary metabolites of eight *Hibiscus* species has included *H. taiwanensis* as one of the species[9]. To-date, there are no reviews on *H. schizopetalus*. We have a concurrent review in IJPPR on the phytochemistry and pharmacology of *H. tiliaceus* and *H. mutabilis*, two *Hibiscus* species with spectacular flower colour change.

HIBISCUS TAIWANENSIS

Botany and uses

Hibiscus taiwanensis S.Y. Hu (cream hibiscus) is a shrub 3−8 m tall that is native to Taiwan[2,8]. Leaves are sub-orbicular, papery with 3−5 lobes and serrate or dentate margins (Figure 1). Flowers are broadly funnel-shaped, solitary, white or creamy yellow with a prominent deep brown or purple heart. In traditional Chinese medicine, stems and roots of *H. taiwanensis* have been used as anti-inflammatory, antifungal, antipyretic, and antihelminthic

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Figure 1: Flower and leaves of *Hibiscus taiwanensis.* (photo taken by the Taiwan Forest Research Institute)

agents[10]. Based on an ethnobotanical survey conducted on the Rukai tribe in Wutai district, southern Taiwan, uses of *H. taiwanensis* included leaves for treating roundworm infection, wood for fuel, tools and fishing gear, flowers for garlands, and foliage as fodder for pigs[11]. Flowers are edible as salad or cooked[8].

Phytochemistry

From the stem of *H. taiwanensis*, three new phenylpropanoid esters identified as (7*S*,8*S*)-demethylcarolignan E, hibiscuwanin A and hibiscuwanin B together with eight known phenylpropanoids (threocarolignan E, erythrocarolignan E, cleomiscosin A, cleomiscosin C, 9,9'-*O*-feruloyl-(β)-secoisolariciresinol, dihydrodehydrodiconiferyl alcohol, boehmenan and (β)-syringaresinol) have been isolated[12]. Further analysis led to the isolation of five new compounds, identified as hibisculide A, hibisculide B, hibisculide C, hibiscutaiwanin and hibiscusin, together with 51 known compounds from the stem of *H. taiwanensis*[10]. A list of compounds isolated from the stem of *H. taiwanensis*[10,12] is shown in Table 1.

Pharmacology

Cytotoxic and antiviral activities

Of three new and eight known phenylpropanoids isolated from the stem of *H. taiwanensis*, 9,9'-*O*-feruloyl-(β)-secoisolariciresinol showed strong cytotoxic activity against A549 human lung carcinoma and MCF-7 breast carcinoma cell lines with EC_{50} values of 1.8 and 3.9 μg/ml, respectively[12]. None of the phenylpropanoids inhibited HIV replication in H9 lymphocyte cells. Among the five new and 51 known compounds isolated from the stem of *H. taiwanensis*, myriceric acid C and uncarinic acid A showed cytotoxic activity against A549 human lung carcinoma and MCF-7 breast carcinoma cell lines[10]. IC_{50} values of myriceric acid C were 3.9 and 4.1 μg/ml and 4.6 and 7.7 μg/ml for uncarinic acid A. Uncarinic acid A also inhibited HIV replication in H9 lymphocyte cells with EC_{50} value of 1.5 μg/ml.

Anti-inflammatory and analgesic effects

The anti-inflammatory effects of the aqueous stem extract of *H. taiwanensis* were tested in lipopolysaccharide (LPS)-stimulated mouse macrophage cells and carrageenan-induced mouse paw oedema[13]. When the LPS-stimulated macrophages were treated with the stem extract, a concentration-dependent inhibition of nitric oxide, tumor necrosis factor and prostaglandin E2 production was detected. Protein expression of inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2), and elevated heme oxygenase-1 (HO-1) were inhibited. In the animal test, the extract decreased the paw oedema after 4−5 h, and increased the activities of antioxidant enzymes in the paw tissue. The extract decreased iNOS and COX-2, and increased HO-1 expressions after 5 h in the oedema paw. The study concluded that the *H. taiwanensis* extract possessed anti-inflammatory effects and the mechanism may be related to iNOS, COX-2, HO-1, which is associated with the increase in the activities of antioxidant enzymes. In the analgesic tests, the extract at 0.25, 0.5 and 1.0 g/kg significantly inhibited the number of acetic acid-induced writhing and formalin-induced licking time.

Anti-hyperglycemic activity

The hypoglycemic activity of aqueous acetone stem extract of *H. taiwanensis* was investigated in streptozotocin (STZ)-induced diabetic rats[14,15]. The extract exhibited an increase of glucose uptake activity. Bolus intravenous injection of syringaldehyde, a biological active compound isolated from the stem extract, was found to show anti-hyperglycemic activity at an effective dose of 7.2 mg/kg. Besides increased in glucose uptake activity, syringaldehyde enhanced insulin sensitivity in the STZ-diabetic rats. These results suggest that the stem extract of *H. taiwanensis* and syringaldehyde can lower plasma glucose in STZ-diabetic rats through an increase of glucose utilization. Concurrently, the effects on diabetic hyperglycemia in STZ-diabetic rats were also assessed using aqueous acetone leaf, stem and fruit extracts of *H. taiwanensis*[16]. The extracts showed a significant plasma glucose lowering effect in STZ-diabetic rats with the stem extract being the most effective. Oral administration of the extracts (500 mg/kg) three times daily for 3 days into STZ-diabetic rats showed an increase in insulin sensitivity, marked reduction of phosphoenolpyruvate carboxykinase (PEPCK) expression in the liver and an increased expression of glucose transporter subtype 4 (GLUT 4) in the skeletal muscle. Overall, the results showed that the extracts have the ability to lower plasma glucose through an increase in glucose utilization *via* elevation of skeletal GLUT 4 and decrease of hepatic PEPCK in STZ-diabetic rats. In another related study, syringaldehyde isolated from stems of *H. taiwanensis*, has the ability to lower hyperglycemia[17]. The compound significantly decreased post-prandial plasma glucose in rats, while plasma insulin was not modified. Administration of syringaldehyde for three days in STZ-diabetic rats resulted in a marked reduction of PEPCK expression in the liver and an increased expression of GLUT 4 in the skeletal muscle, suggesting that

Table 1: Chemical constituents of stems of *Hibiscus taiwanensis*[10,12]

Terpenes	**Steroids**
Cleomiscosin A, C	*β*-Sitosterol
Mansonone E, H	*β*-Sitosteryl-*β*-D-glucoside
Hibiscone C	Stigmasterol
Phenolics	
Benzoic acid	Isohemigossypol-1-methyl ether
Boehmenan	Lignocerylferulate
Caffeic acid	Methyl caffeate
erythro-Carolignan E	Methyl *p*-coumarate
threo-Carolignan E	Methyl *cis*-ferulate
p-Coumaric acid	Methyl *trans*-ferulate
(7*S*,8*S*)-Demethylcarolignan E	Methyl *p*-formyl benzoate
Dihydrodehydrodiconifenyl alcohol	Methyl vanillate
Ferulic acid	Myriceric acids A−C
9,9'-*O*-Feruloyl-(−)-secoisolariciresinol	Myricerol
N-cis-Feruloyltyramine	3-*oxo*-Olean-12-en-28-oic acid
N-trans-Feruloyltyramine	Scoparone
Ficusol	Scopoletin
p-Formylbenzoic acid	Sinapinaldehyde
Gossyvertin	Syringaldehyde
Hexacosanyl caffeate	(−)-Syringaresinol
Hibicusin	Syringic acid
Hibicuslides A−C	*threo*-1-C-Syringylglycerol
Hibicutaiwanin	Uncarinic acids A, B
Hibiscuwanin A, B	Vanillic acid
4-Hydroxybenzoic acid	Vanillin

syringaldehyde can increase glucose utilization and lower hyperglycemia in diabetic rats. A major derivative of sinapic acid, syringaldehyde is a phenolic aldehyde with similar molecular structure and applications as vanillin[18,19]. Besides *H. taiwanensis*, SA has also been reported in *Hibiscus cannabinus* or kenaf[20]. The compound has been found in spruce, pine, eucalypt, jute, flax, corn, sugar cane, rice, wheat, oil palm and coconut[18]. The molecular strucutures of sinapic acid, syringaldehyde and vanillin are shown in Figure 2. Among the pharmacological properties[18,19,21], syringaldehyde has anti-hyperglycemic activity in STZ-diabetic rats[14], neuroprotective effect on cerebral ischemia in rats[22], anti-plasmodial activity against *Plasmodium falciparum*[23], anti-inflammatory effect on ear oedema in rats[24], COX-2 enzyme inhibition in mouse macrophages[25], DNA strand scission activity[26], and antimicrobial activity against bacteria of *Staphylococcus aureus*, *Klebsiella pneumonia* and *Pseudomonas aeruginosa*[27], and fungal pathogen of *Candida guilliermondii*[28].

HIBISCUS SCHIZOPETALUS

Botany and uses

Hibiscus schizopetalus (Dyer ex Mast.) Hook. (coral hibiscus) is a fast-growing shrub that can reach up to 3 m in height[2]. Leaves and flowers of *H. schizopetalus* resemble those of *Hibiscus rosa-sinensis* (Figure 3). Flowers are solitary, pendulous with a long extended style, and petals are bright red, finely dissected and strongly reflexed. Morphological similarities suggest that *H. schizopetalus* could be a cultivar of *H. rosa-sinensis*[1]. A study the identification and genetic variation among *Hibiscus* species using RAPD markers reported 72% similarly between *H. schizopetalus* and *H. rosa-sinensis*[29]. Leaves of *H. schizopetalus* are consumed to cure spermatorrhoea[30]. Fruits are consumed to treat urinary problem arising from endocrinological disorder or diabetes, and young fruits are chewed raw[31]. Fruit infusion is drank to facilitate childbirth[32]. In Chittagong, Bangladesh, a paste prepared from crushed flowers of *H. schizopetalus* is applied to the hair as tonic before bath[33].

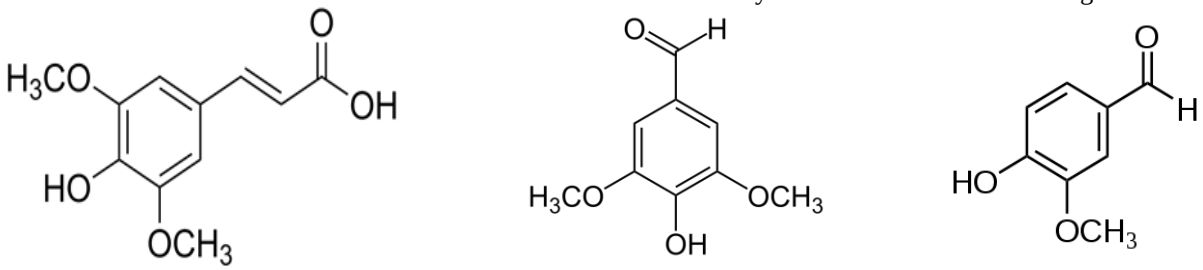
Phytochemistry

Among some *Hibiscus* species in the Malesian region, cyanidin 3-sophoroside has been reported to be the major anthocyanin in flowers of *H. schizopetalus* and the closely-related *H. rosa-sinensis*[34]. Two new triterpene esters, namely, 22-hydroxytaraxeryl acetate and 22-hydroxytaraxeryl-cis-*p*-coumarate, have been isolated from leaves[35]. Phytochemical screening of leaves and flowers showed the presence of alkaloids, steroids and triterpenoids[36].

Pharmacology

Antioxidant properties

Out of six *Hibiscus* species screened, antioxidant properties based on total phenolic content (TPC) and free radical scavenging (FRS) activity of flowers and leaves of *H. schizopetalus* ranked fourth and fifth[37,38]. Values were higher in flowers (516 mg GAE/100 g and 520 mg AA/100 g) than in leaves (336 mg GAE/100g and 94 mg AA/100g), respectively. However, in terms of ferrous ion chelating ability and lipid peroxidation inhibition, leaves and flowers of *H. schizopetalus* displayed the highest values. The high anthocyanin content in the bright red flowers may have contributed to the strong ferrous ion



Sinapic acid Syringaldehye Vanillin

Figure 2: Molecular strucutures of sinapic acid, syringaldehyde and vanillin.


Figure 3: Flowers of *Hibiscus schizopetalus.*

chelating ability and lipid peroxidation inhibition. TPC and FRS values were higher in flowers than in leaves. Screening of antioxidant activities (DPPH radical and NO scavenging), and urease inhibitory activities of different concentrations of flower and leaf methanol extracts of *H. schizopetalus* similarly showed stronger activities in flowers than leaves, although their values were significantly lower than ascorbic acid and thiourea used as the controls[39].

Analgesic and antipyretic effects

The analgesic and antipyretic effects of methanol flower and leaf extracts of *H. schizopetalus* were investigated in rats at doses 50, 100 and 200 mg/kg, using the tail-flick, tail-immersion and yeast-induced pyrexia tests[40]. The extracts were found to be non-toxic up to doses of 5 g/kg and did not cause any mortality of the tested animals. In the tail-flick and tail-immersion tests, oral administration of the extracts showed significant prolongation of reaction time and dose-dependent analgesic effects at all tested doses. In the yeast-induced pyrexia test, the extracts significantly reversed hyperthermia. The results of all pharmacological tests performed suggested that the flower and leaf extracts of *H. schizopetalus* possess potent analgesic and antipyretic effects.

Anti-inflammatory activity

The anti-inflammatory activity of petroleum ether, chloroform, and methanol leaf extracts of *H. schizopetalus* was evaluated against carrageenan-induced paw oedema in rats[41]. Results showed that the methanol extract (86% inhibition) was found to be the most effective followed by the chloroform extract (81% inhibition) and petroleum ether extract (77% inhibition), 4 h after treatment with 200 mg/kg.

Hypoglycemic and hypolipidemic effects

The hypoglycemic and hypolipidemic effects of methanol flower and leaf extracts of *H. schizopetalus* were investigated in alloxan-induced diabetic rats[42]. At doses of 100 mg/kg, both extracts resulted in a significant reduction of blood glucose level in normal fasting rats. In diabetic rats, blood glucose reduced by 60% and 45%, respectively. Cholesterol and triglycerides levels were significantly decreased in rats administered with the flower extract. The results demonstrated the potential hypoglycemic activity of flowers and leaves of *H. schizopetalus*.

CONCLUSION

Although *Hibiscus* species are endowed with chemical compounds that have different pharmacological properties, both *H. taiwanensis* and *H. schizopetalus* exhibit hypoglycemic, anti-inflammatory and analgesic activities in common. Other *Hibiscus* species possessing such properties include *H. tiliaceus*, *H. mutabilis*, *H. cannabinus*, *H. rosa-sinensis* and *H. sabdariffa*. Being native to Taiwan, much of the information on the phytochemistry and pharmacology of *H. taiwanensis* has been generated by scientists of the Department of Chemistry, National Cheng Kung University in Tainan and other national universities. There was a dearth of information on *H. schizopetalus* until a research group from the Department of Pharmacognosy, University of Karachi in Pakistan started their research on the pharmacological properties of its leaves and flowers. The phytochemistry of *H. schizopetalus* remains poorly studied.

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