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Biologically Active Compounds from the Genus *Hibiscus*

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Abstract

Since ancient times, *Hibiscus* species (Malvaceae) have been used as a folk remedy for the treatment of skin diseases, as an antifertility agent, antiseptic, and carminative. Some compounds isolated from the species, such as flavonoids, phenolic acids, and polysaccharides, are considered responsible for these activities. This review aims to summarize the worldwide reported biological activities and phytoconstituents associated with this genus for the past 40 years.

Keywords: Biologically active substances, flavonoids, polysaccharides.

Introduction

Hibiscus (Malvaceae) is a genus of herbs, shrubs, and trees; its 250 species are widely distributed in tropical and subtropical regions of the world. About 40 species occur in India. Many *Hibiscus* species are valued as ornamental plants and are cultivated in gardens. Some species, such as *Hibiscus cannabinus* L. and *Hibiscus sabdariffa* L., are important sources of commercial fiber, whereas some species are useful as food, and yet others are medicinal (Anonymous, 1959). Many species belonging to this genus have been used since ancient times as folk remedies for various disorders. In Ayurveda, *Hibiscus esculentus* L. fruits are considered tonic, astringent, and aphrodisiac. In Unani medicine, the fruits are considered emollient and useful for treating urinary disorders (Parrotta, 2001). The leaves and roots of *Hibiscus manihot* L. are used as a poultice for boils, sprains, and sores, and the flowers are used to treat chronic bronchitis and toothache. The mucilage of the bark is considered to be an emmenagogue (Chopra et al., 1950). The seeds of *Hibiscus abelmoschus* L. are valued for their diuretic, demulcent, and stomachic properties and are considered stimulant, antiseptic, cooling, tonic, carminative, and aphrodisiac. The bark, flowers, and fruits of *Hibiscus bauiferus* J.G. Froster are used externally for the treatment of skin diseases such as eczema, scabies, psoriasis, and ringworm. In Ayurvedic medicine, the bark is the official source of the drug "parisha," a reputed remedy for skin diseases (Parrota, 2001).

According to the literature, many *Hibiscus* species have been investigated and found to contain many classes of secondary metabolites, including flavonoids, anthocyanins, terpenoids, steroids, polysaccharides, alkaloids, amino acids, lipids, sesquiterpene, quinones, and naphthalene groups. Some of these compounds have been shown to have antibacterial, anti-inflammatory, antihypertensive, antifertility, hypoglycemic, antifungal, and antioxidative activities (Kholkute et al., 1977a; Parmar & Ghosh, 1978; Gangrade et al., 1979; Jain et al., 1997; Faraji & Tarkhani, 1999; Lin et al., 2003; Sachdewa & Khemani, 2003).

This review describes the currently available chemical and biological data on the genus *Hibiscus* and suggests that the flavonoids and phenolic acids are the main classes of substances of interest to a phytochemist and pharmacologist. A number of reports have been published to establish the biological potential of this genus (Table 1).

Anti-inflammatory

Gossypin (**1**) (Fig. 1), isolated from *Hibiscus vitifolius* L. flowers, showed significant anti-inflammatory activity at a dose of 200 mg/kg body weight against carrageenan-induced rat paw edema and increased vascular permeability induced by various phlogistic agents. It also inhibited significantly the accumulation of the pouch fluid and granulation tissue formation in carrageenan-induced granuloma pouch in rats, which could be attributed to decreased

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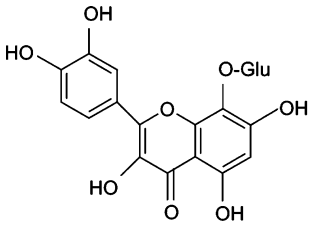
Table 1. Bioactive compounds, parts, or fractions, and activities derived from *Hibiscus* species.

Plant sources	Bioactive compounds, parts, or fractions, and activities	References
H. ablemoschus	Aqueous extract of root (larvicidal)	Dua et al., 2006
H. cannabinus	Trinorcandalene phytolexins	Bell et al., 1998
	Volatile oil from leaves (antifungal)	Kobaisy et al., 2001
H. elatus	Flavonoid (antioxidant)	Perez-Trueba et al., 2003
H. macaranthus	Ethanol extract of aerial parts and root (antifungal and antimicrobial)	Jain et al., 1997
	Aqueous extract of leaves (female antifertility) and virilizing effect)	Telefo et al., 1998
	Aqueous extract of leaves (anabolizing	Moundipa et al., 1999
H. rosa-sinensis	Benzene and alcohol extract of flowers (antifertility)	Murthy et al., 1997; Kholkute et al., 1976, 1977; Kholkute & Udupa, 1976a,b
	Aqueous extract of leaf (antifertility)	Nivsarkar et al., 2005
	Benzene, chloroform, and ethanol extract of flowers (antispermatogenic)	Reddy et al., 1997
	Glycoside from leaves (hypotensive, antispasmodic)	Agarwal & Shinde, 1967
	Aqueous extract and ethanol extract of leaves	Sachdewa et al., 2001a,b
	Ethanol extract of flowers (hypoglycemic)	
	Ethanol extract of flowers (anticonvulsant)	Kasture et al., 2000
H. sabdariffa	Oil and unsaponifiable matter (antifungal and antibacterial)	Gangrade et al., 1979
	Protocatechuic acid and aqueous extract of flowers (antibacterial)	Liu et al., 2005
	Polysaccharides from flower buds (antitumor)	Miiller et al., 1992
	Phenolic acid from flower bud (antitumor)	Tseng et al., 2000
	Anthocyanin (antitumor)	Hou et al., 2005
	Aqueous extract of petals (antihypertensive)	Obiefuna et al., 1994; Owolabi et al., 1995; Adegunloye et al., 1996
	Chloroform and ethanol fraction, phenolic acid from flowers (antioxidant)	Tseng et al., 1996
	Aqueous extract of flowers (antioxidant)	Ali et al., 2003
	Anthocyanins from flowers (antioxidant)	Wang et al., 2000; Chang et al., 2006
	Methanol extract (smooth muscle relaxant)	Salah et al., 2002
	Aqueous extract of petals (antispasmodic)	Ali et al., 1991
H. syriacus	Seed oil (antimicrobial and antifungal)	Shah et al., 1988
	Fatty acids from the bark (antifungal)	Masami et al., 1978
	Napthalenes from root bark (antitumor, antioxidant)	Yoo et al., 1998
	Pentacyclic triterpene esters (antioxidant)	Yun et al., 1999
	Lignans from root bark (antioxidant)	Lee et al., 1999
H. taiwanensis	9,9′-*O*-Ferulolyl-(–)-secisolaricinresinol, uncarinic acid (inhibits HIV replication)	Wu et al., 2005
	Myriceric acid (cytotoxic)	
H. vitifolius	Flavonoid from flowers (anti-inflammatory)	Parmar & Ghosh, 1978
	Flavonol (hypoglycemic)	Raghunathan & Sulochana, 1994

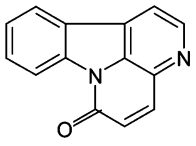
formation of collagen tissue. Leukocyte migration and formation of pleural exudates were also reduced by gossypin (**1**) in carrageenan- and turpentine-induced pleurisy in rats; the efficiency was lower than phenylbutazone, but it possesses a greater margin of safety (Parmar & Ghosh, 1978).

Antimicrobial

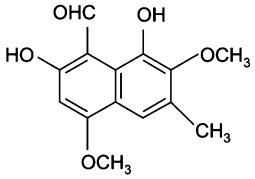
Canthin-6-one (**2**) and a fatty acid fraction that contained lauric, myristic, and palmitic acids isolated from stem bark of *Hibiscus syriacus* L. showed antifungal activity against *Trichophyton interdigitale* (Yokata et al., 1978). The seed oil of *Hibiscus syriacus* has shown antimicrobial activity against Gram-negative and Gram-positive microorganisms. The oil was resistant against *Salmonella typhi* but showed activity against *Escherichia coli, Salmonella newport, Staphylococcus aureus, Staphylocoecus albus, Bacillus subtilis*, and *Bacillus anthracis*. The oil has shown significant fungicidal activity against tested plant pathogens, viz., *Alternaria solani, Aspergillus niger, Colletotri-chum dematium*, and *Fusarium oxysporum* (Shah et al., 1988). The oil and the unsaponifiable matter from *Hibiscus sabdariffa*



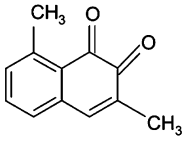
(1) Gossypin



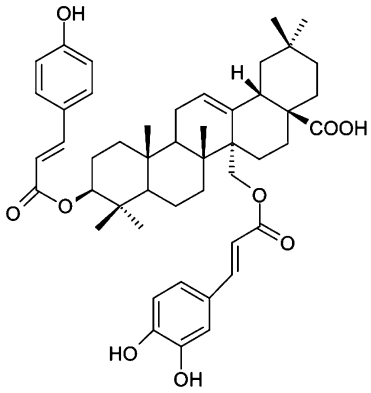
(2) Canthin-6-one



(3) Hibiscanal

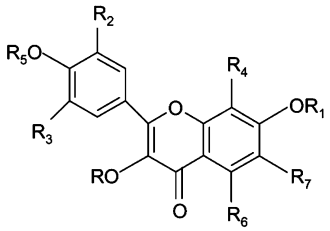


(4) *O*-Hibiscanone



(5) Myreceric acid (3, 27 di-*O*-caffeolyl)

(6) Uncarinic acid (3-*O*-27-*O*-*trans*-feruloyl)

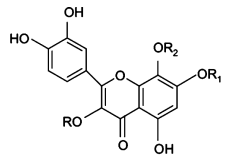


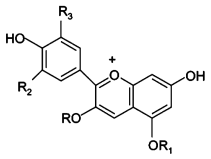
(8) Hibiscatin: R = R_3 = R_4 = R_7 = H; R_1 = Me; R_2 = OMe; R_6 = OH; R_5 = Glu.

(9) Hibiscitrin; R = Glu; R_1 = R_5 = R_7 = H; R_2 = R_3 = R_4 = R_6 = OH.

(10) Quercitin; R = R_1 = R_2 = R_4 = R_5 = R_7 = H; R_3 = R_6 = OH.

Figure 1. Structures of compounds.





(11) Gossytrin; R = Glu; R_1 = R_2 = H. **(7)** Delphenidin; R = Glu(2→1)xly; R_2 = R_3 = OH; R_1 = H

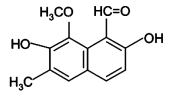
(12) Gossypitrin; R_1 = Glu; R = R_2 = H. **(14)** Cyanin; R = R_1 = Glu; R_2 = OH; R_3 = H.

(13) Gossypetin; R = R_1 = R_2 = H. **(15)** Cyanidin-3-glucoside; R = Glu; R_1 = R_3 = H; R_2 = OH

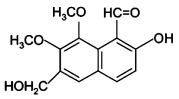
(16) Cannabinin; R = Glu; R_1 = R_3 = H; R_2 = OH.

(17) Cyanidin-3-sambuboside; R = Glu(2→1)xly;

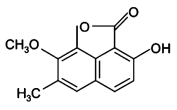
R_1 = R_3 = H; R_2 = OH.



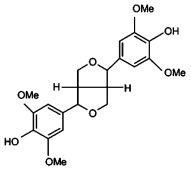
(18) Syriacusin A



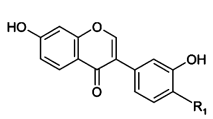
(19) Syriacusin B

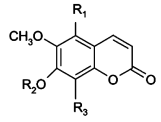


(20) Syriacusin C



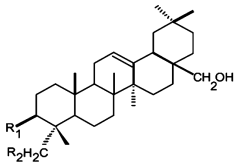
(26) Syringaresinol





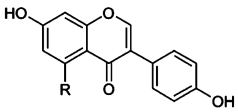
(23) Daidzein; R = R_1 = H. **(27)** Coumarino-lignan; R_1 = OCH_3; R_2 = CH_3; R_3 = OH.

(24) Genistein; R = OH; R_1 = H **(28)** Scopoletin; R_1 = R_2 = H.



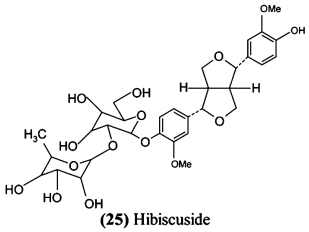
(21) 3-β-23, 28 Trihydroxy-12-oleanene 3-β-caffeate; R_1 = OH; R_2 =

(22) 3-β-23, 28 Trihydroxy-12-oleanene 3-β-caffeate; R_2=OH; R_1 =



(23) Daidzein; R = H.

(24) Genistein; R = OH.



(25) Hibiscuside

Figure 1. (continued)

were found to exert antibacterial activity against *Escherichia coli, Staphylococcus typhimurium, Bacillus anthracis, Bacillus subtilis, Staphylococus aureus, Staphylococcus albus* and *Klebsiella pneumoniae.* These compounds also exhibited antifungal activity against *Aspergillus flavus, Trichophyton equingea, Helminthosporum rostatum, Crypto-coccus neoformans, Tricnoderm viridi, Colletotrichum falca-tum,* and *Alternaria solanacea* (Gangrade et al., 1979). The aqueous extract of the calyx of *Hibiscus sabdariffa* and protocatechuic acid derived from roselle calyx inhibited effectively the growth of bacterial

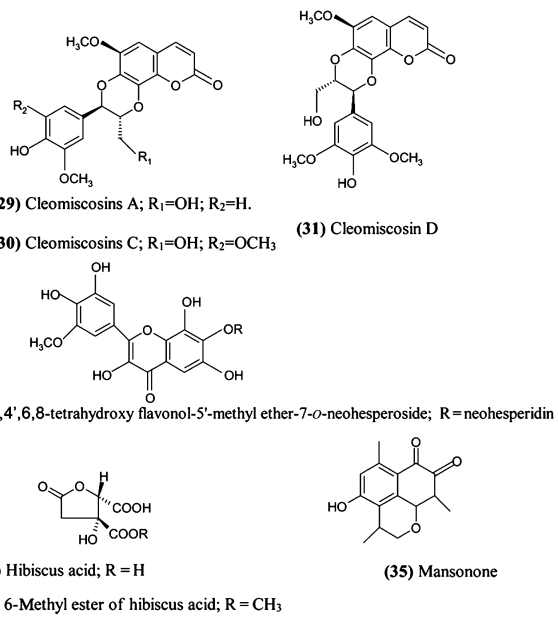


Figure 1. (continued).

pathigens, viz., methicillin-resistant *Staphylococcus aureus, Klebsiella pneumoniae, Pseudomonas aeruginosa,* and *Acinetobacter baumannii.* The antibacterial activity of protocatechuic acid was greater than the extract (Lin et al., 2005). The ethanol extract of aerial parts and roots of *Hibiscus micranthus* L. showed antibacterial activity against *Staphylococcus aureus* and antifungal activity against *Fusarium moniliforme, Aspergillus flavus, Aspergillus niger,* and *Rihzoctonia bataticola* (Jain et al., 1997).

The trinorcandalene phytoalexins, hibiscanal (**3**) and *o*-hibiscanone (**4**) isolated from stem stele of *Hibiscus cannabinus* inoculated with fungal pathogen *Verticillium dahliae* killed all propagules of *Verticillium dahliae* in the concentration range of 1–18 μg/mL (Bell et al., 1998). The volatile oil from the leaves *of Hibiscus cannabinus,* composed of 58 components of which the major components were (*E*)-phytol, (Z)-phytol, *n*-nonanol, benzene acetaldehyde, (*E*)-2-hexenal, and 5-methylfur-fural, showed antifungal activity against *Colletotrichum fragariae, Colletotrichum gloeosporioides,* and *Colletrotri-chum accutatum* at 400 and 100 μg. Among the major components of the oil, only 5-methyl furfural, *n*-nonanol, and benzene actaldehyde have shown antifungal activity (Kobaisy et al., 2001).

Fertility

The use of *Hibiscus* species as an antifertility agent has been a long-time rural folk practice in India (Chopra et al., 1950; Anonymous, 1959). Bhavamishra also mentioned this during the 18th century in Yonirogadhikar, in the 70th chapter of *Bhavaprakash.* He stated that a woman could never get pregnant if she consumes during her menses a preparation made from the flowers of *Hibiscus rosa-sinensis* L. and fermented rice broth, along with the old jaggery. An extensive study to screen the antifertility effect of *Hibiscus rosa-sinenesis* has been done. The benzene extract of the flower of *Hibiscus rosa-sinensis* at the dose of 73 mg/kg body weight, disturbed the estrous cycle in rats and reduced ovarian, uterine, and pituitary weight (Kholkute et al., 1976). The maximum antifertility activity of the total benzene extract of *Hibiscus rosa-sinensis* was mediated via inhibition of implantation (Kholkute & Udupa, 1976a). The total ethanol extract of the flowers of *Hibiscus rosa-sinensis* also showed similar activity but was less potent than the benzene extract (Kholkute & Udupa, 1976b). The antifertility activity of flowers of *Hibiscus rosa-sinensis* was affected by seasonal variations. The benzene extract of the flowers collected in winter showed maximum potency, followed by those collected in the spring, rainy season, and summer, in decreasing order (Kholkute et al., 1977). The ether-soluble portion of the water-insoluble fraction of the benzene extract of *Hibiscus rosa-sinensis* flowers have shown significant anti-implantation and abortifacient effects in female albino rats (Singh et al., 1982). The benzene extract of *Hibiscus rosa-sinensis* flowers, when administered intraperitoneally at dose levels of 125-250 mg/kg body weight to adult mice, resulted in an irregular estrus cycle with prolonged estrus and metestrus. An increase in the atretic follicles and absence of corpora lutea indicated the antiovulatory effect of the extract. Estrogenic activity of the benzene extract in immature mice was also evident by early opening of the vagina, premature cornification of the vaginal epithelium, and an increase in uterine weight (Murthy et al., 1997). The aqueous extract of the leaves of *Hibiscus rosa-sinensis* at a dose of 100 mg/kg body weight has shown anti-implantation activity. The extract showed a sharp increase in superoxide anion radical and a sharp fall in superoxide dismutase activity. It also showed antiestrogenic activity (Nivsarkar et al., 2005).

An aqueous extract from the leaves of *Hibiscus macaranthus* Hochst ex A.Rich, when given daily to 22-day-old female rats for 5, 10, 15, 20, and 25 days, have shown a decrease in the growth rate of animals. The ovarian and uterine weights were high during the pubertal period (36–41 days). During the same period, the ovarian and uterine protein, ovarian cholesterol, and serum cholesterol levels showed significant differences in treated rats when compared with controls. The ovarian and uterine protein levels as well as the serum cholesterol level were high in animals treated with 49 mg/kg per day of plant extract. A decrease in ovarian cholesterol level was observed in the same group thereby suggesting the presence of an estrogenic compound in plant extract (Telefo et al., 1998).

The oral administration of benzene extract of *Hibiscus rosa-sinensis* was found to affect spermatogenesis as well as the endocrine function of the testis as evidenced by reduction in weight of the testis, accessory sex organs,

and pituitary glands. The alkaline phosphatase in ventral prostrate, citric acid content in seminal vesicles, and dorsolateral prostate fructose concentrations were also reduced (Kholkute, 1977). The benzene, chloroform, and ethanol extracts of the flowers of *Hibiscus rosa-sinensis* at a dose level of 250 mg/kg body weight have shown antispermatogenic activity as indicated by significant reduction in number of spermatogenic elements like spermatogonia, spermatocytes, spermatids, and cauda epididymal sperms (Reddy et al., 1997). The aqueous extract of the fresh leaves of *Hibiscus macaranthus,* at a dose equivalent to 0.720 g of plant, has anabolizing and virilizing effect as indicated by increased serum level of testosterone in male albino rats. The histologic analysis of testis of rats showed abundant spermatozoa in the lumen of seminiferous tubules. Testis of treated rats showed high testosterone production *in vitro.* Activity of prostatic acid phosphatase increased in prostate, testis, and serum of treated rats (Moundipa et al., 1999). The subchronic effect of *Hibiscus sabdariffa* calyx aqueous extract on rats has been investigated to evaluate the pharmacological basis for the use of *Hibiscus sabdariffa* as an aphrodisiac. The extract significantly decreased the epididymal sperm counts in the 4.6 g/kg dose group. The 1.15 g/kg dose group showed disruption of normal epithelial organization, and the 2.3 g/kg dose group showed hyperplasia of testis with thickening of basement membrane. The 4.6g/kg dose group showed disintegration of sperm cells. *Hibiscus sabdariffa* calyx extract has been shown to induce testicular toxicity in rats (Orisakwe et al., 2004).

Antitumor

The water-soluble polysaccharide fraction of *Hibiscus sabdariffa* flower buds have shown antitumor activity in sensitive allogenic transplanted tumor sarcoma 180/CD-l mice at a concentration of 5 mg/kg. Tumor growth was inhibited to 50%, 20 days after tumor inoculation (Miiller & Franz, 1992). A phenolic compound, protocatechuic acid, isolated from the dried flower buds of *Hibiscus sabdariffa*, at the concentration of 0.2 to 2mM, exhibited an antiproliferative effect on HL-60 cells by inducing apoptosis, which was associated with the phosphorylation and degradation of RB and suppression of Bcl-2 protein (Tseng et al., 2000). Myriceric acid (**5**) and uncarinic acid A (**6**), isolated from the stems of *Hibiscus taiwanensis* Hu., have shown cytotoxic activity against human lung carcinoma and breast carcinoma (Wu et al., 2005). Delpenidin 3-sambubioside (7), an anthocyanin isolated from the dried calyx of *Hibiscus sabdariffa*, was shown to induce dose-dependent apoptosis in human leukemia cells (HL-60) through a reactive oxygen species (ROS)-mediated mitochondrial dysfunction pathway (Hou et al., 2005).

Antihypertensive

The glycosidic material obtained from air-dried powdered leaves of *Hibiscus rosa-sinensis* when given intravenously in doses of 40-80 mg/kg exhibited hypotensive action in intact and spinal dogs, which persisted for 1–2 h (Agarwal & Shinde, 1967). An Indian anti-atherosclerotic drug "Anna Pavala Sindhooram," a herbomineral preparation, also includes flowers of *Hibiscus rosa-sinensis* (Shanmugasundaram et al., 1983). The crude hydroalcohol extract of *Hibiscus sabdariffa* has shown *in vitro* an appreciable enzyme inhibiting activity toward the angiotensin I converting enzyme (ACE) attributable to flavones (**1**, **8**–**13**), but weak inhibitory activities toward elastase, trypsin, and α-chymotrypsin (Jonadet et al., 1990). The aqueous extract of the petals of *Hibiscus sabdariffa* caused vasorelaxation of the rat isolated aorta via both endothelium-dependent and independent mechanisms (Obiefuna et al., 1994). The vasorelaxant effect of aqueous extract of petals was mediated through inhibition of Ca^{2+} influx from extracellular medium as well as inhibition of Ca^{2+} release from intracellular stores (Owolabi et al., 1995). Some clinical trials have been carried out to see the effect of sour tea of *Hibiscus sabdariffa* on essential hypertension, which yielded positive results (Faraji & Tarkhani, 1999). Other studies have shown that the antihypertensive effect of aqueous extract of calyx of *Hibiscus sabdariffa* is not mediated through inhibition of the sympathetic nervous system but could be mediated through acetylcholine-like and histamine-like mechanisms as well as via a direct vasorelaxant effect (Adegunloye et al., 1996). Infusion of *Hibiscus sabdariffa* calyx lowered both systolic and diastolic pressure in spontaneously hypertensive Wistar-Kyoto rats in doses of 500-1000 mg/kg body weight. It increased urinary output and decreased serum creatinine, cholesterol, and glucose (Onyenekwe et al., 1999). The infusion prepared from the calyx of *Hibiscus sabdariffa* has been shown to decrease both systolic and diastolic blood pressure in patients from 30 to 80 years of age with diagnosed hypertenion. The *Hibiscus sabdariffa* extract, standardized on 9.6 mg of total anthocyanins, and captopril 50 mg/day, showed comparable hypotensive results. The rates of therapeutic effectiveness were 0.7895 and 0.8438 with *Hibiscus sabdariffa* and captopril, respectively, while the tolerability was 100% for both treatments (Herrera et al., 2004).

Hypocholesterolemic

When New Zealand white rabbits were fed with normal diet, high cholesterol, lard oil diet, along with *Hibiscus sabdariffa* extract, the level of triglyceride, cholesterol, and low-density lipoprotein cholesterol (LDL-C) were lower in the serum of these rabbits compared with the control rabbits. Histopathologic examinations have shown that *Hibiscus sabdariffa* extract reduced foam cell formation and inhibited smooth cell migration and calcification of the blood vessels of rabbits. Thus, *Hibiscus sabdariffa* extract inhibited serum lipids and showed anti-atherosclerotic activity (Chen et al., 2003). The dried calyx extract of *Hibiscus sabdariffa* at doses of 500 and 1000mg/kg together with continuous cholesterol feeding to hypercholesterolemic rats

for 6 weeks have been shown to decrease serum cholesterol levels by 225% and 26%, respectively, and serum triglyceride levels by 33% and 28%, respectively (Hirunpanich et al., 2006). The ethanol extract of the dried calyx of *Hibiscus sabdariffa,* when administered to Sprague-Dawley rats on rich cholesterol, cholic acid, and lard oil diet in concentrations of 5%, 10%, and 15%, has shown a significant decrease in triglycerol, cholesterol, and LDL levels. The decrease in level of total lipids was caused by 10% and 15% concentration of the extract. This effect could be attributed to the racemization of hibiscus acid, (+)-HCA to (−)-HCA, mediated by intestinal flora enzymes (Carvajal-Zarrabal et al., 2005).

Antioxidant

The chloroform-soluble fraction and ethyl acetate-soluble fraction of the crude ethanol extract of *Hibiscus sabdariffa* flowers have shown efficient protective action against *t*-butyl hydroxy peroxidase (*t*-BHP)-induced hepatic cytotoxicity and genotoxicity, possibly by different mechanisms associated with different antioxidants existing in the crude extracts. Chloroform-soluble fraction displayed inhibition of XO (a flavoprotein, which catalyzes the oxidation of hypoxanthine to xanthine) activity ($EC_{50} = 0.742$ mg/mL). Ethyl acetate-soluble fraction had capacity for scavenging l,l-diphenyl-2-picrylhydrazyl (DPPH) free radicals ($EC_{50} = 0.017$ mg/mL) (Tseng et al., 1997). Protocatechuic acid, isolated from *Hibiscus sabdariffa,* has also shown antioxidant properties.

It possesses free radical scavenging capacity that protects oxidative damage induced by *t*-BHP in rat primary hepatocytes (Tseng et al., 1996). Protocatechuic acid also inhibited *t*-BHP-induced tyrosine phosphorylation, an implication of the activation of a stress signal pathway in the liver. Its antioxidant and anti-inflammatory characteristics were accompanied by blocking of stress signal transduction (Liu et al., 2002). The protocatechuic acid obtained from dried flowers of *Hibiscus sabdariffa* presented an inhibitory potential in nitric oxide synthase and hepatic damage induced by lipopolysaccharide, an endotoxin (Lin et al., 2003). The aqueous extract of dried flowers of *Hibiscus sabdariffa* and *Hibiscus* anthocyanins (**14**–**17**) can potentially be used in mitigating paracetamol-induced hepatotoxicity (Ali et al., 2003). The anthocyanins (**14**–**17**) isolated from the dried flowers of *Hibiscus sabdariffa* can quench the free radicals of DPPH. *Hibiscus* pigments reduced the incidence of liver lesions, including inflammation, infiltration, and necrosis induced by *t*-BPH in rats (Wang et al., 2000). The aqueous extract from the dried calyx of *Hibiscus sabdariffa* has shown antioxidant activity in Cu^{2+}-mediated oxidation of low-density lipoprotein (LDL) *in vitro.* The inhibitory effect of the extract on LDL oxidation was dose-dependent at a concentration ranging from 0.1 to 0.5 mg/mL. At 0.5 mg/mL, the extract inhibited thiobar-bituric acid reactive substances (TBARS) formation with greater potency than 100 μg of vitamin E (Hirnupanich et al., 2005). *Hibiscus* anthocyanins isolated from the flowers of *Hibiscus sabdariffa* could be used to inhibit LDL oxidation and oxLDL-mediated macrophage apoptosis and thus can act as a chemopreventive agent (Chang et al., 2006).

The antioxidative activities of napthalenes, viz., syriacusins A, B, and C (**18**–**20**) (Yoo et al., 1998) and pentacyclic triterpene esters (**21**, **22**) (Yun et al., 1999), isolated from the root bark of *Hibiscus syriacus,* have shown inhibitory activity against lipid peroxidation in rat liver microsomes. The phenolic compounds, structurally related to daidzein (**23**) and genistein (**24**) isolated from the root bark of *Hibiscus syriacus,* significantly inhibited lipid peroxidation in rat liver microsomes. Hibscuside (**25**) and syringaresinol (**26**), isolated from *Hibiscus syriacus,* exhibited moderate antioxidant activity (Lee et al., 1999). A coumarino-lignan (**27**), scopolotin (**28**), and clemiscosins A, C, and D (**29**–**31**), isolated from *Hibiscus syriacus,* have shown lipid peroxidation inhibitory activity comparable with vitamin E (Yun et al., 2001). The heat-treated stem and root of *Hibiscus syriacus* were effective antioxidants compared with nontreated *Hibiscus syriacus* as it more effectively reduced the stable free radical DPPH (Kwon et al., 2003). Treatment of rats with gossypitrin (**9**), a flavonoid extracted from *Hibiscus elatus* S.W., 2 h before and 2 h after $CC1_4$ injection, protected hepatocytes against $CC1_4$ induced cell injury in rats. The protective effect of gossypitrin (**9**) may be related to its direct radical scavenging ability (Perez-Trueba et al., 2003).

Hypoglycemic

A flavonol bioside 3′,4′,6,8-tetrahydroxy flavonol-5′-methylether 7-*O*-neohesperidoside (**32**), isolated from the flowers of *Hibiscus vitifolius,* showed significant hypoglycemic activity, comparable with glibenclamide (Ragnunathan & Sulochana, 1994). The aqueous and alcohol extract of *Hibiscus rosa-sinensis* leaves at a dose of 250 mg/kg body weight showed significant hypoglycemic activity in streptozotocin-induced hyperglycemia in rats when compared with tolbutamide (100 mg/kg) (Sachdewa et al., 2001a). The extract improves glucose tolerance by 47% compared with tolbutamide. The ability of animals to utilize an external glucose load under the influence of plant extract suggested that *Hibiscus rosa-sinensis* may have a mechanism similar to that of sulfonylurea rather than that of biguanides (Sachdewa et al., 2001b). The hypoglycemic activity of ethanol extract of *Hibiscus rosa-sinensis* flowers in streptozotocin-induced diabetes in rats was comparable with glibenclamide, but was not mediated through insulin release (Sachdewa & Khemani, 2003).

Miscellaneous

A glycosidic material obtained from the leaves of *Hibiscus rosa-sinensis* possesses a spasmogenic action on the

intestinal muscle, lungs, tracheal muscle, and uterus, all of which were blocked by atropine. On the skeletal muscle, *d*-tubocurarine showed a partial antagonism to contractions induced by glycoside, indicating that the glycoside possesses a cholinergic type of action (Agarwal & Shinde, 1967). The aqueous extract of *Hibiscus sabdariffa* calyx inhibited the tone of various muscle preparations, viz., rabbit aortic strip, rhythmically contracting rat uterus, guinea pig tracheal chain, and rat diaphragm, but the extract stimulates quiescent rat uterus and frog rectus abdominis (Ali et al., 1991).

The lyophilized aqueous extract (800 mg/kg) of *Hibiscus sabdariffa* caused a pronounced increase in the number of wet feces without any significant increase in propulsive intestinal movement (Haruna, 1997). The methanol extract of *Hibiscus sabdariffa* showed a significant dose-dependent relaxant effect on rat ileal strip, comparable with the effect shown by nifedipine and papaverine. The extract, when administered intraperito-neally, reduced intestinal transit in rats. The extract also potentiated the diarrhea-inducing effects of castor oil. These effects were possibly generated by constituents such as quercetin (**10**) and eugenol via a Ca^{+2} channel modulated mode of action (Salah et al., 2002).

Gossypin (**1**), a bioflavonoid isolated from *Hibiscus vitifolius* flowers, has shown a protective effect on X-ray induced increase in capillary permeability of rat intestine (Parmar & Ghosh, 1977).

The ethanol extract of the flowers of *Hibiscus rosa-sinensis* protected animals from maximum electroshock, electrical kindling, and pentylenetetrazole-induced convulsions in mice. It also inhibited convulsions induced by lithium-pilocarpine and antagonized the behavioral effects of amphetamine and potentiated phenobaritone-induced sleep (Kasture et al., 2000). Fresh fruits of *Hibiscus esculentus* L. have shown a significant anti-ulcerogenic effect (Gurbuz et al., 2003).

The aqueous methanol extract of the calyx of *Hibiscus sabdariffa,* when administered to Wistar albino rats orally, increased the level of serum asparate aminotrans-ferase and alanine aminotransferase. Long term usage of the aqueous methanol extract caused liver injury. The extract should be taken with caution bearing in mind that the higher dose could affect the liver (Akindahunsi & Olaleye, 2003).

Low dose (16 g/day) of the juice of *Hibiscus sabdariffa* (roselle) caused a greater decrease in salt output than a high dose (24 g/day). After consumption of roselle juice, urine has shown a decrease of creatinine, uric acid, citrate, tartarate, calcium, sodium, potassium, and phosphate, but not oxalate (Kirdpon et al., 1994). Hibiscus acid (**33**), a lactone form of (+)-allo-hydroxy citric acid and its 6-methylester (**34**), found in the calyces of *Hibiscus sabdariffa,* possesses inhibitory activity against procine pancreatic α-amylase (Hansawasdi et al., 2000). Raw polysaccharides and three acidic subfractions isolated from the flowers of *Hibiscus sabdariffa* were shown to cause a strong induction of proliferation of human keratinocytes (Ha CaT), up to 40% (Brunold et al., 2004). Mansonone H (**35**) and uncarinic acid (**6**), isolated from the stems of *Hibiscus taiwanensis,* were shown to inhibit HIV replication in H9 lymphocytic cells (Wu et al., 2005).

The aqueous extract of the roots of *Hibiscus ablemoschus* showed larvicidal activity against the larvae of *Anopheles culicifacies, Anophlese stephensi,* and *Culex quinquefasciatus.* The mean lethal concentration values of the extract against these mosquitoes were 52.3, 52.6, and 43.8 ppm, respectively (Dua et al., 2006).

Discussion

The plant kingdom holds many species of plants containing substances of medicinal value that have yet to be discovered. A large number of plants is constantly being screened for their possible pharmacological value. The *Hibiscus* genus may prove to be a richer source of compounds with possible pharmacological value, but more investigations are necessary in this direction.

The reported biological studies of *Hibiscus* were carried out mostly on various extracts, but more attention is required to screen the phytoconstituents responsible for these activities.

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