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Review Article

Taxonomy, Phytochemistry, and Therapeutic Potentials of the Genus *Ceiba* (Bombacaceae): A Review

Mohamed E. Abouelela[1], Reda A. Abdelhamid[1], Mohamed A. A. Orabi[1,2*] & Faten M. M. Darwish[3]

[1]Department of Pharmacognosy, Faculty of Pharmacy, Al-Azhar University, Assiut Branch, P.O. Box 71524, Assiut, Egypt
[2]College of Pharmacy, Najran University, P.O. Box 55461, Najran, Kingdom of Saudi Arabia
[3]Department of Pharmacognosy, Faculty of Pharmacy, Assiut University, P.O. Box 71526, Assiut, Egypt

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***Corresponding author:** Mohamed A. A Orabi

Abstract

Plants of the genus *Ceiba* (Bombacaceae) are widely implemented in folklore treatment of diabetes, bronchitis, chronic fever, diarrhea, dysentery, gastritis, peptic ulcers and parasitic infections in many countries. Over the years, at least eighty-three compounds have been isolated from different parts of plant species of *Ceiba*. These compounds belong to the plant steroids, triterpenes, sesquiterpenes, sesquiterpene lactones, coumarins, flavonoids, anthocyanins, oxidized naphthalenes, phenolic acids, alcohols, fatty acids and esters. Extracts and isolated compounds of *Ceiba* plants have been extensively examined for their possible analgesic, antipyretic, anti-inflammatory, anti-microbial, cytotoxicity, antitumor, antidiabetic, hypolipidemic, antioxidant, and hepatoprotective, activities. In this review, we compile, for the first time, the different isolated phytochemicals of *Ceiba* plants as well as we comprehensively discuss the various biological studies carried out on extracts and isolated compounds of the genus *Ceiba*. We aim to provide the necessary knowledge for the researchers in the field of natural therapeutics to explore further alternative medicine from *Ceiba* plants.

Keywords: Review, Bombacaceae, *Ceiba*, Phytochemistry, Biological activity.

Abbreviation list

B16F10	B16 melanoma F10 subline.
DPPH	2,2-diphenyl-1-picrylhydrazyl.
EAC	Ehrlich-Lettre ascites carcinoma.
FRAP	Ferric reducing ability of plasma.
HCT116	Human colorectal carcinoma.
HeLa	Henrietta Lacks cervical cancer.
HEp-2	Human epithelial type 2.
HepG2	Hepatoma G2 cell.
JAK3	Janus kinase 3.
MCF-7	Michigan Cancer Foundation-7.
MRC-5	Medical Research Council cell strain 5.
ORAC	Oxygen radical absorbance capacity.
TNF-α	Tumor necrosis factor alpha.
U251	Human glioma cell line.

INTRODUCTION

Bombacaceae (Bombax, Baobab or Kapok family) is a small family of flowering plants named to the genus *Bombax*. It includes around 25 genera and 250 species of tropical trees [1, 2]. Plant species of the genera *Adansonia* L., *Ceiba* Mill., *Ochroma* Sw., and *Durio* Adans have horticultural and economic importance [3]. Many species of Bombacaceae are naturally growing throughout the tropical and subtropical regions of the world especially in tropical America [4, 5], but those of the genera *Adansonia* L., *Bombax* L., *Camptostemon* Mast., and *Lagunaria* (DC.) Rchb., are restricted to the old-world tropics [6].

The brilliant showy flowers of *Ceiba* trees have promoted their global cultivation for ornamental purposes. The fruit's silky white fibers are economically important in mattresses, pillows and soft toys manufacture, and as oil sorbent for oil spill cleanup [7-10].

Ceiba plants have been widely used in folk medicine in different regions of the world against gastrointestinal disorders, emesis, diarrhea, spasm, dysentery, gastritis, peptic ulcers and parasitic infections [11-14]. They have been also recommended for kidney maladies, headache, diabetes, bronchitis, skin diseases, wounds, eye diseases, insect bite, chronic fever, arthritis and rheumatism [12, 15, 16]. Plants of *Ceiba* have thus attracted the interest of many researchers to explore their phytochemicals, and consequently several molecular structures of the steroids, triterpenes, sesquiterpenes, sesquiterpene lactones, coumarins, flavonoids, anthocyanins, oxidized naphthalenes, phenolic acids, alcohols, fatty acids and esters have been determined. Extracts and isolated compounds of *Ceiba* plants were extensively examined for the discovery of their possible therapeutic potentials. In this article, we put focus on the botanical and taxonomical profiles, and comprehensively review the reported phytochemicals and pharmacological effects of the genus *Ceiba*.

MATERIAL AND METHOD

The available literatures in scientific search data bases, ScienceDirect, PubMed, Ebscohost, Medline, Scielo, Scialert, Web of Science, ProQuest, Springer Link, Google Scholar and Google, were used for reviewing data on the genus *Ceiba*.

Taxonomy of the genus *Ceiba*

The Angiosperm Phylogeny Group I, 1998 and II, 2003 and Kubitzki system, 2003, were early placed family Bombacaceae as subfamily (Bombacoideae) with family Malvaceae in the order Malvales due to the close affinities with Malvaceae in several floral and anatomical characters [17-19]. Currently, the majority of the taxonomic works, and classification systems have treated Bombacaceae as an independent family of the order Malvales on the basis of molecular data, pollen morphology and habit [2, 20, 21]. Also, The genus *Chorisia* Kunth has been revised into *Ceiba* Mill, where *Chorisia* Kunth was considered a synonym for *Ceiba* after Kubitzki, 2003 and P.E.Gibbs & Semir 2003 [19, 22]. The genus *Ceiba* comprises around 21 species including *Ceiba acuminate* (S.Watson) Rose, *Ceiba aesculifolia* (Kunth) Britten & Baker f., *Ceiba allenii* Woodson., *Ceiba boliviana* Britten & Baker f., *Ceiba chodatii* (Hassl.) Ravenna., *Ceiba crispiflora* (Kunth) Ravenna. *Ceiba erianthos* (Cav.) K. Schum., *Ceiba glaziovii* (Kuntze) K. Schum., *Ceiba insignis* (H.B.K.) P.E.Gibbs & Semir., *Ceiba jasminodora* (A.St.Hil.) K. Schum., *Ceiba lupuna* P.E.Gibbs & Semir., *Ceiba pentandra* (L.) Gaertn., *Ceiba pubiflora* (A.St.-Hil.) K. Schum., *Ceiba rubriflora* Carv.-Sobr. & L.P.Queiroz., *Ceiba salmonea* (Ulbr.) Bakh., *Ceiba samauma* (Mart. & Zucc.) K. Schum., *Ceiba schottii* Britten & Baker f., *Ceiba soluta* (Donn.Sm.) Ravenna., *Ceiba speciosa* (A.St.-Hil.) Ravenna., *Ceiba trischistandra* (A.Gray) Bakh., *Ceiba ventricosa* (Nees & Mart.) Ravenna [22, 23].

Botanical features of the genus *Ceiba*

The genus *Ceiba* is commonly 5–50 m height trees which sometime show well developed buttresses at the base e.g. *C. pentandra* (30–50 m, Fig. 1C). Many *Ceiba* species show spines on the trunk and branches (Fig. 1H). Some species, *C. chodatii*, *C. pubiflora*, *C. speciosa* and *C. insignis*, show markedly ventricose trunk (Figs 1F and 1G). The leaves are palmately compound, commonly 5–9 leaflets. The leaflets usually have long, slender and diminutive petioles (Figs 1E and 1H). The leaflets are more or less lanceolate, chartaceous to coriaceous, with entire to dentate margin. The flowers are radially symmetrical, varies in size from small and inconspicuous (*C. pentandra*) to large and showy (Fig. 1B). They are usually leathery white, pinkish-white or red. The fruit is rotund to ellipsoidal, 5-valvate capsule, with a mostly smooth exterior (Fig 1D). The endocarp develops into a white cotton-fibered mass, which surrounds many seeds (Fig 1D). When the capsule valves fall away, this cottony kapok aids in the wind dispersal of the seeds. Seeds are many, round to pyriform or reniform, usually large (5–10 mm), with dark brown to black testa, and matt to smooth surface. They always embedded into cottony fibers [11, 22].

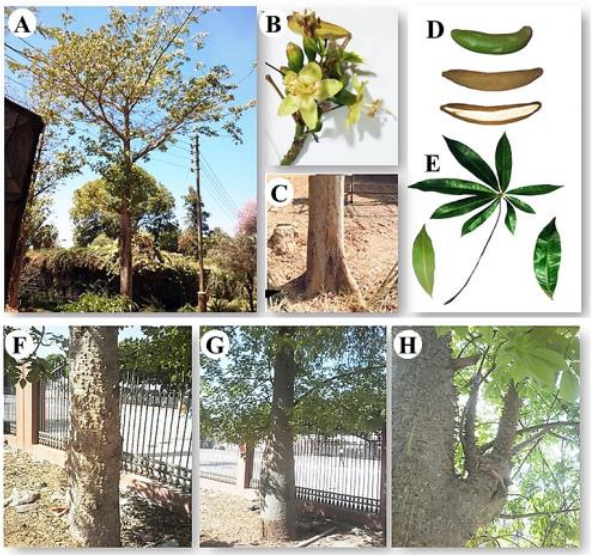


Fig-1: A; The whole *C. pentandra* tree during new foliage, B; The flower of *C. pentandra*. C; *C. pentandra* tree base showing buttresses at the tree base, D; fruits of *C. pentandra* E; leaves of *C. pentandra*, F; The ventricose trunk *C. crispiflora* tree, G; *C. speciosa* tree. H; spiny branches and leaves of *C. speciosa*

Phytochemistry of the genus *Ceiba*

Reviewing literatures on phytochemical investigations revealed that plant sterols, triterpenes, sesquiterpenes, sesquiterpene lactones, coumarins, flavonoids, anthocyanins, oxidized naphthalenes, phenolic acids, esters, alcohols, fatty acids and their esters are the common metabolites produced by plant species of the genus *Ceiba* (Table-1, Figs 3-6).

Table-1: List of isolated compounds from plant species of genus *Ceiba*

	Compound	Species	Organ	Ref.
Sterols				
1	Cholesterol	*C. insignis* H.B.K.	Seeds	[24]
		C. speciosa A.St.Hil.	Seeds	[24]
2	Campesterol	C. *insignis* H.B.K.	Seeds	[24]
		C. speciosa A.St.Hil.	Seeds	[24]
3	Brassicasterol	*C. insignis* H.B.K.	Seeds	[24]
		C. speciosa A.St.Hil.	Seeds	[24]
4	Stigmasterol	*C. insignis* H.B.K.	Seeds	[24]
		C. speciosa A.St.Hil.	Seeds	[24]
5	*β*-Sitosterol	*C. pentandra* L.	Stem barks	[25]
		C. pentandra L.	Aerial parts	[26]
		C. crispiflora Kunth.	Leaves	[24]
		C. insignis H.B.K.	Seeds	[24]
		C. speciosa A.St.Hil.	Seeds	[24]
		C. chodatti Hassl.	Flowers	[27]
		C. speciosa A.St.Hil	Leaves	[12]
6	Daucosterol	*C. pentandra* L.	Stem barks	[25]
		C. pentandra L.	Aerial parts	[26]
		C. crispiflora Kunth.	Leaves	[24]
		C. chodatti Hassl.	Flowers	[28]
		C. speciosa A.St.Hil	Leaves	[12]
7	24-Ethylcholesta-1,3,5-triene	*C. insignis* H.B.K.	Seeds	[24]
		C. speciosa A.St.Hil.	Seeds	[24]
8	Stigmast-3,5-dien-7-one	*C. insignis* H.B.K.	Seeds	[24]
		C. speciosa A.St.Hil.	Seeds	[24]
9	Stigmast-4-ene-3-one	*C. insignis* H.B.K.	Seeds	[24]
		C. speciosa A.St.Hil.	Seeds	[24]
10	Stigmast-4,6-dien-3-one	*C. insignis* H.B.K.	Seeds	[24]
		C. speciosa A.St.Hil.	Seeds	[24]
11	Stigmast-4-ene-3,6- dione	*C. insignis* H.B.K.	Seeds	[24]
		C. speciosa A.St.Hil.	Seeds	[24]
Triterpene				
12	3*β*-Taraxerol	*C. pentandra* L.	Aerial parts	[26]
13	3*β*-Taraxerol acetate	*C. pentandra* L.	Aerial parts	[26]
14	*β*-Amyrin	*C. speciosa* A.St.Hil.	Leaves	[12]
		C. pentandra L.	Aerial parts	[26]
15	*β*-Amyrone	*C. crispiflora* Kunth.	Leaves	[24]
16	Epifriendelanol	*C. crispiflora* Kunth.	Leaves	[24]
17	Friedelin	*C. crispiflora* Kunth.	Leaves	[24]
18	Trans-squalene	*C. pentandra* L.	Aerial parts	[26]
Sesquiterpenes and sesquiterpene lactones				
19	7-Hydroxycadalene	*C. pentandra* L.	Root barks	[29]
20	Hemigossylic acid lactone-7-methyl ether	*C. pentandra* L.	Root barks	[29]
21	Isohemigossylic acid lactone-2-methyl ether	*C. pentandra* L.	Root barks	[29]
22	5-Isopropyl-3-methyl-2,7-dimethoxy-8,1-naphthalene carbolactone	*C. pentandra* L.	Root barks	[29]
Coumarins				
23	Aesculetin	*C. chodatti* Hassl.	Flowers	[28]
24	Scopoletin	*C. chodatti* Hassl.	Flowers	[28]
Flavonoids				
25	(+)-Catechin	*C. pentandra* L.	Stem barks	[30]
26	Apigenin	*C. crispiflora* Kunth.	Flowers	[24]
27	Isorhoifolin	*C. insignis* H.B.K.	Leaves	[31]
28	Rhoifolin	*C. crispiflora* Kunth.	Leaves, Flowers	[24, 32]
		C. insignis H.B.K.	Leaves	[32]
		C. pubiflora A.St.Hil.	Leaves	[32]
		C. speciosa A.St.Hil	Leaves, Flowers	[12, 32, 33]
		C. chodatti Hassl.	Flowers, leaves	[7, 28]
29	Luteolin	*C. crispiflora* Kunth.	Flowers	[24]
		C. crispiflora Kunth.	Flowers	[24]
30	Cynaroside	*C. chodatti* Hassl.	Flowers	[28]
		C. speciosa A.St.Hil	Leaves	[12]
31	Luteolin-7-*O*-neohesperidoside	*C. crispiflora* Kunth.	Leaves, Flowers	[24]
32	Luteolin-7-*O*-*β*-D-rutinoside	C. insignis H.B.K.	Leaves	[31]
33	Tricin	*C. crispiflora* Kunth.	Flowers	[24]
34	Linarin	*C. pentandra* L.	Leaves	[34]

35	Kaempferol	*C. pentandra* L.	—	[27]
36	Astragalin	*C. chodatti* Hassl.	Flowers	[28]
		C. speciosa A.St.Hil	Leaves	[12]
37	6"-*O*-Acetylastragalin	*C. chodatti* Hassl.	Flowers	[28]
		C. crispiflora Kunth.	Flowers	[24]
38	Tiliroside	*C. speciosa* A.St.Hil	Flowers, Leaves	[12, 33]
		C. chodatti Hassl.	Flowers	[28]
39	Quercetin	*C. pentandra* L.	—	[27]
		C. speciosa A.St.Hil	Flowers	[33]
40	Rutin	*C. insignis* H.B.K.	Leaves	[31]
Isoflavonoids				
41	Vavain	*C. pentandra* L.	Stem barks	[25, 30, 35, 36]
42	Vavain-3'-*O*-*β*-D-glucopyranoside	*C. pentandra* L.	Stem barks	[25, 30, 35]
43	5-Hydroxy-7,4',5'-trimethoxyisoflavone 3'-*O*-α-L-Arabinofuranosyl(1→6)-*β*-D-glucopyranoside.	*C. pentandra* L.	Stem barks	[35]
Anthocyanidins				
44	Cyanidin-3-glucoside	*C. acuminata* S.Watson	Flowers	[27]
		C. speciosa A.St.Hil	Flowers	[27]
45	Cyanidin-3,5-diglucoside	*C. speciosa* A.St.Hil	Flowers	[27]
Quinones				
46	Isohemigossypolone	*C. pentandra* L.	Heart wood	[37]
47	Bombaxquinone B	*C. pentandra* L.	Root barks	[29, 37]
Megastigmanes				
48	(6S,7E,9R)-6,9-Dihydroxy-4,7 megastigmadien-3-one 9-*O*-[*α*-L-arabinopyranosyl(1→ 6)-*β*-D-glucopyranoside]	*C. chodatti* Hassl.	Leaves	[7]
49	(3S,5R,6R,7E,9S)-Megastigma-7-ene-3,5,6,9-tetrol 3-*O*-*β*-D-glucopyranoside	*C. chodatti* Hassl.	Leaves	[7]
50	Cucumegastigmane II	*C. chodatti* Hassl.	Leaves	[7]
51	Chodatiionoside A	*C. chodatti* Hassl.	Leaves	[7]
52	Chodatiionoside B	*C. chodatti* Hassl.	Leaves	[7]
Phenolic acids and esters				
53	4-Hydroxybenzoic acid	*C. chodatti* Hassl.	Flowers	[28]
		C. speciosa A.St.Hil	Leaves	[12]
54	Vanillic acid	*C. chodatti* Hassl.	Flowers	[28]
55	Ethyl vanillate	*C. chodatti* Hassl.	Flowers	[28]
56	Protocatechuic acid	*C. pentandra* L.	Leaves	[34]
57	Protocatechuic acid ethyl ester	*C. chodatti* Hassl.	Flowers	[28]
58	Caffeic acid	*C. pentandra* L.	—	[27]
Fatty Alcohols and acids				
59	1-Hexacosanol	*C. pentandra* L.	Aerial parts	[26]
60	1-Triacontanol	*C. crispiflora* Kunth.	Leaves	[24]
61	Myristic acid (Tetradecanoic acid)	*C. insignis* H.B.K.	Seeds	[24]
		C. pentandra L.	—	[27]
62	Palmitic acid (hexadecanoic acid)	*C. insignis* H.B.K.	Seeds	[24]
		C. speciosa A.St.Hil	Seeds	[38]
63	Palmitoleic acid	*C. speciosa* A.St.Hil	Seeds	[38]
64	Margaric acid	*C. speciosa* A.St.Hil	Seeds	[38]
65	Heptadecenoic acid	*C. speciosa* A.St.Hil	Seeds	[38]
66	Stearic acid	*C. insignis* H.B.K.	Seeds	[24]
		C. speciosa A.St.Hil	Seeds	[38]
		C. pentandra L.	Aerial parts	[3, 26]
67	Oleic acid	*C. insignis* H.B.K.	Seeds	[24]
		C. speciosa A.St.Hil.	Seeds	[38]
		C. pentandra L.	Seeds	[27]
68	Linoleic acid	*C. insignis* H.B.K.	Seeds	[24]
		C. speciosa A.St.Hil	Seeds	[38]
69	Arachidic acid	*C. insignis* H.B.K.	Seeds	[24]
		C. speciosa A.St.Hil	Seeds	[38]
70	Trans-11-eicosenoic acid	*C. speciosa* A.St.Hil	Seeds	[38]
71	Behenic acid	*C. insignis* H.B.K.	Seeds	[24]
72	Vernolic acid	*C. speciosa* A.St.Hil.	Seeds	[38]
73	Malvalic acid	*C. acuminata* S.Watson	Seeds	[27]
		C. pentandra L.	Seeds	[27]
		C. insignis H.B.K.	Seeds	[24]
		C. speciosa A.St.Hil.	Seeds	[24, 27]
74	Dihydromalvalic acid	*C. pentandra* L.	Seeds	[39]

		C. acuminata S.Watson	Seeds	[27]
		C. pentandra L.	—	[27]
75	Sterculic acid	*C. insignis* H.B.K.	Seeds	[24]
		C. speciosa A.St.Hil	Seeds	[24, 40]
Miscellaneous				
76	Verbascoside	*C. speciosa* A.St.Hil	Leaves	[12]
77	*n-trans*-Caffeoyl-L -DOPA-methyl ester	*C. pentandra* L.	Leaves	[34]
78	Argentilactone	*C. crispiflora* Kunth.	—	[41]
79	Mono-*n*-octyl phthalate	*C. chodatti* Hassl.	Flowers	[28]
80	Di-*n*-octyl phthalate	*C. pentandra* L.	Leaves	[42]
81	5-Hydroxymethyl furfural	*C. chodatti* Hassl.	Flowers	[28]
82	(3*R*, 4*R*, 5*S*)-3, 4-Dihydroxy- 5-methyl-dihydrofuran-2-one	*C. chodatti* Hassl.	Flowers	[28]
83	Succinic acid	*C. chodatti* Hassl.	Flowers	[28]
		C. speciosa A.St.Hil	Leaves	[12]

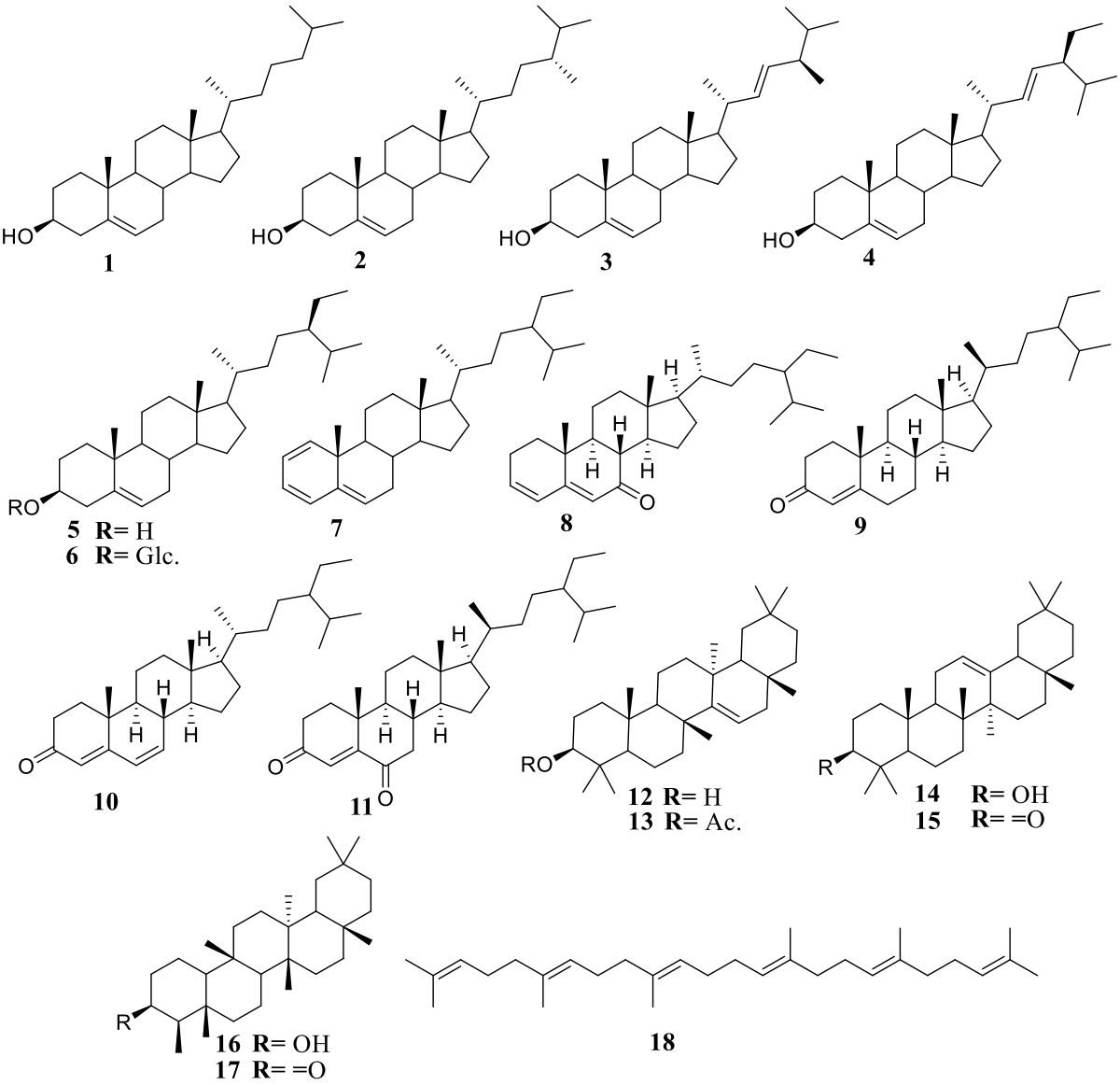
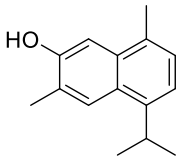


Fig-2: Structures of the isolated compounds (1-18) from plant species of the genus *Ceiba*



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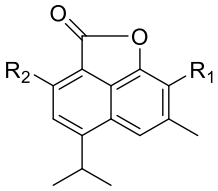
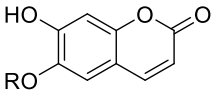
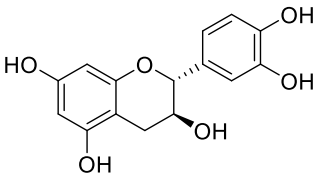


	R_1	R_2
20	OH	OCH_3
21	OCH_3	OH
22	OCH_3	OCH_3



23 R= H

24 R=CH_3



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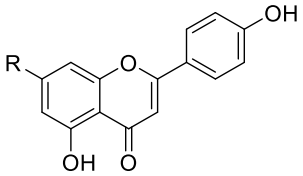
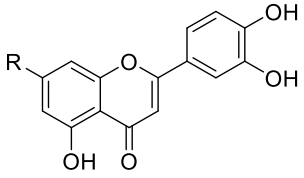


26 **R**= OH

27 **R**= *β-O*-Glc.(6→1)Rha.

28 **R**= *β-O*-Glc.(2→1)Rha.

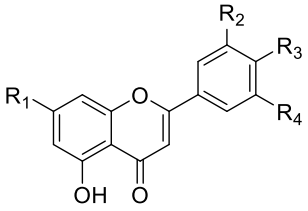


29 **R**= OH

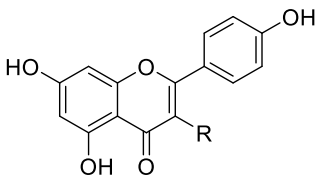
30 **R**= *β-O*-Glc.

31 **R**=*β-O*-Glc.(2→1)Rha.

32 **R**= *β-O*-Glc.(6→1)Rha.



	R_1	R_2	R_3	R_4
33	OH	OCH_3	OH	CH_3
34	*β-O*-Glc.(6→1)Rha.	H	OCH_3	H

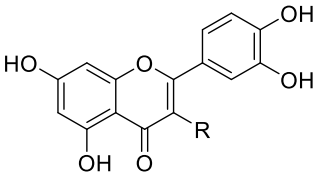


35 **R**= OH

36 **R**= *β-O*-Glc.

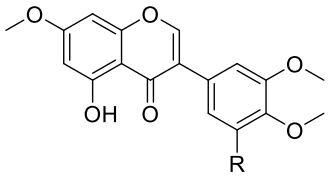
37 **R**= *β-O*-(6″– OAc.) Glc.

38 **R**= *β-O*-(6″– *p*-coumaroyl.) Glc.



39 **R**= OH

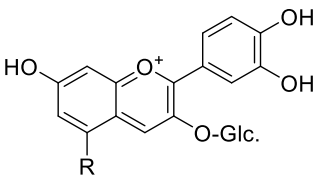
40 **R**= *β-O*-Glc.(6→1)Rha.



41 **R**= OH

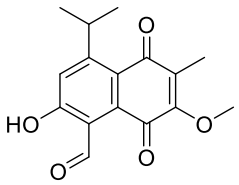
42 **R**= *β-O*-Glc.

43 **R**= *β-O*-D-Glc.(6→1)-L-Ara.



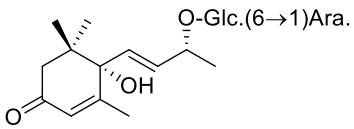
44 **R**= OH

45 **R**= *β-O*-Glc.



46 **R**= OH

47 **R**=OCH_3



48

Fig-3: Structures of the isolated compounds (19-48) from plant species of the genus *Ceiba*

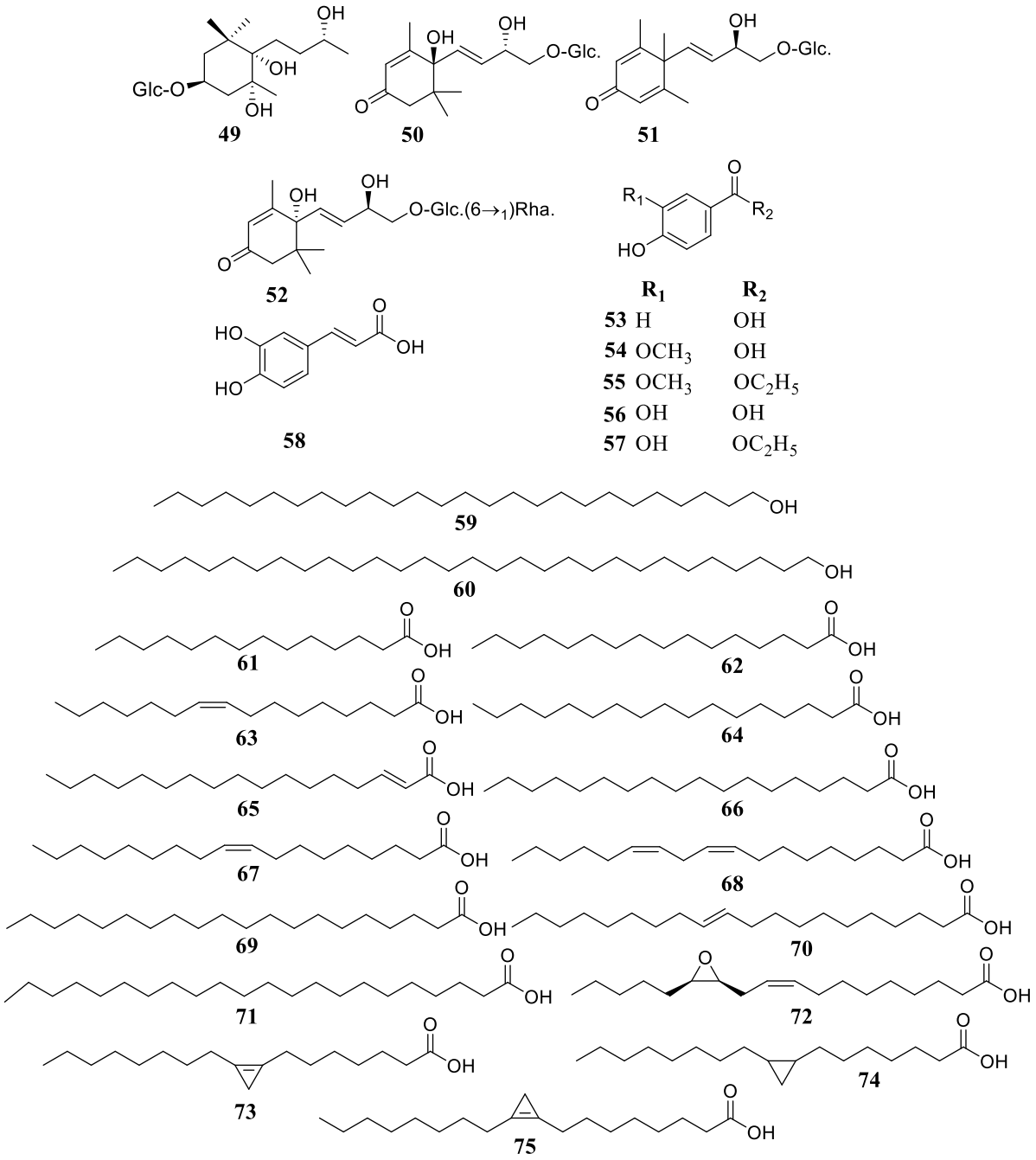


Fig-4: Structures of the isolated compounds (49-75) from plant species of the genus *Ceiba*

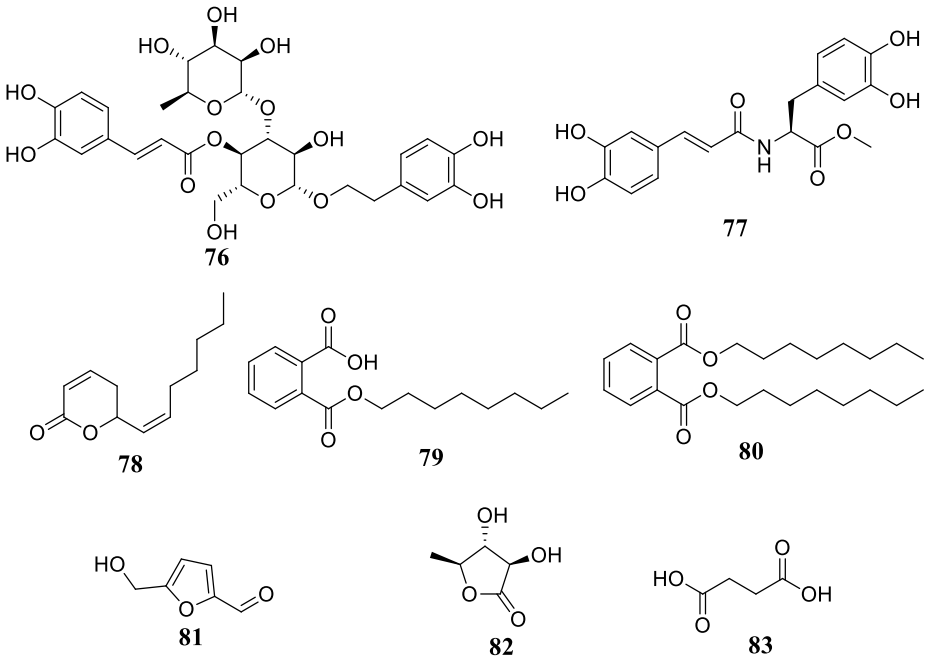


Fig-5: Structures of the isolated compounds (76-83) from plant species of the genus *Ceiba*

Biological activities of the genus *Ceiba*

Extracts and isolated compounds from different morphological parts of *Ceiba* plants were examined pharmacologically as follows:

Analgesic, antipyretic and anti-inflammatory activities

Oral administration of a total 70% ethanolic extract and its successive fractions of *C. insignis* leaves showed significant anti-inflammatory activity against carrageenan-induced paw edema in mice [31]. Consistently, extracts of *C. pentandra* seeds and stem bark showed significant dose dependent anti-inflammatory activity in xylene-induced ear oedema and egg albumin-induced paw oedema, besides reduction of acetic acid-induced vascular permeability in rats [43-45]. The same extracts exhibited dose dependent potent analgesic activity in acetic acid-induced writhing test, heat-induced pain and the tail flick latency test in comparison with Aspirin, Indomethacin and Diclofenac [44-46]. The leaves extract of *C. pentandra* has a moderate antipyretic activity against the thermogenic effect induced by 20% yeast suspension [47]. Methanol and chloroform extracts of *C. speciosa* showed effective anti-inflammatory activity in Carrageenan-induced rat hind paw oedema [48]. The chloroformic extract has also demonstrated dose dependent antipyretic activity in Brewer's yeast induction method [48].

The analgesic and anti-inflammatory activities of *Ceiba* extracts were attributed to the presence of flavonoids as main active constituent [30]. The flavonoids vavain (41), vavain-3'-O-*β*-D-glucoside (42) and (+)-catechin (25) isolated from *C. pentandra* inhibited cyclooxygenase-I-catalyzed prostaglandin biosynthesis in *in vitro* assay [30]. Rhoifolin flavonoid (28) from *Ceiba* species reduced the carrageenan-induced paw oedema and inhibited prostaglandin E2 and TNF-α release in the inflammatory exudates [49].

Antioxidant Activity

Extracts of different morphological parts of *C. speciosa* showed elevated antioxidant activity as determined by DPPH˙ scavenging, nitric oxide reducing power, metal chelating activity and phospho-molybdenum antioxidant methods of assay [12, 50-54]. In the same way, 70% ethanolic extracts along with their successive fractions of various parts of *C. chodatii* showed free radical scavenging powers in correspond with their polyphenol content [53]. Additionally, the ethyl vanillate (55), protocatechuic acid ethyl ester (57) and aesculetin (23) isolated from *C. chodatii* flowers also afforded a significant DPPH˙ scavenging properties [28]. *C. insignis* leaves 70% ethanol extract and its sub-fractions displayed *in vitro* DPPH˙ free radical scavenging activity as well as significant *in vivo* antioxidant activities as determined by estimation of the blood glutathione levels in alloxan-induced diabetic rats [31, 52].

Studies on antioxidant activities of different extracts and fractions from *C. pentandra* evaluated by DPPH˙, FRAP and ORAC showed prominent effects [51, 55-62]. The *n-trans*-caffeoyl-DOPA-methyl ester (77), linarin (34), protocatechuic acid (56) isolated from *C. pentandra* showed high antioxidant properties. The bark of *C. aesculifolia* subsp. *Parvifolia* methanol extract also showed potential free radical scavenging activity [16].

Cytotoxic and antitumor activities

C. pentandra was the most studied species for its cytotoxic and antitumor effects. The methylene chloride fraction of a 80% methanolic extract of *C. pentandra* aerial parts showed prominent cytotoxic activity against HepG2 and MCF-7 cancer cell lines [26]. The 50% ethanolic extract of *C. pentandra* roots showed a very low toxicity on human fibroblast primary culture in *in vitro* cytotoxicity evaluation using resazurin reduction test [59]. The petroleum ether, acetone and ethanolic stem bark extracts were assessed for *in vitro* cytotoxicity on EAC, MCF-7 and B16F10 cells lines. Acetone and ethanol extracts showed highest cytotoxicity in B16F10 cell line, while only acetone extract showed a potent long-term cytotoxic effect on EAC. On the other side, petroleum ether and ethanol extracts showed a reduced cytotoxic potential on MCF-7 and B16F10 short term cytotoxic effect [63]. In addition, *in vivo* assessment of bark extracts on EAC (Liquid tumor) model and Dalton's lymphoma ascites (DLA or solid tumor) model revealed increase in mean survival time of tumor bearing mice in both models with more prominent effect in the solid tumor model compared to the liquid tumor model. These results indicate a potential anticancer activity of the bark extract as potent inhibitor of tumor progression and development [63]. Furthermore, the leaves extracts showed *in vitro* significant inhibition on the tube-like formation induced by human umbilical venous endothelial cells in the angiogenesis assay [64].

C. speciosa aqueous stem bark extract significantly reduced the viability of MCF-7 cells in H_2O_2-induced MCF-7 toxicity in addition to its potential inhibitory effect on JAK3 and p38α kinases [54]. The total 70% ethanol extract and its successive fractions of *C. insignis* leaves were tested for their *in vitro* cytotoxicity and showed significant activity against a number of tumor cell lines as the larynx (HEp-2), breast (MCF-7), liver (HepG-2), brain (U251), colon (HCT-116) and cervix (HeLa) cell lines [65].

The ethyl acetate extract [24, 66, 67], rhoifolin (28) [68, 69], argentilactone (78) [41] isolated from *C. crispiflora* leaves showed significant cytotoxic effects against wide range of carcinoma cell lines MCF-7, HeLa, HCT-116, MRC-5 and EAC.

The cumulative production of oxidative free radicals is well recognized to induce oxidative stress and is common cause for many types of cancer cells due to resulted cellular redox imbalance. Antioxidant activity reported for *Ceiba* extracts could be helpful in prevention of tumors by maintaining the normal cellular redox balance [70].

Hepatoprotective Activity

Pretreatment of rats with 70% aqueous ethanolic extract, aqueous extract, and ethyl acetate fraction of *C. insignis* leaves produced hepatoprotective effects against CCI_4 liver damage of the rats as indicated from significant decrease in AST, ALT and ALP levels [31]. In the same way, Rhoifolin (28) isolated from *C. crispiflora* leaves showed a great protection against CCI_4-induced hepatotoxicity in mice [24]. The ethyl acetate fraction of the methanolic extract of *C. pentandra* stem bark produced significant reduction in serum ALT, AST, ALP and total bilirubin levels, demonstrating promising hepatoprotective effect against paracetamol induced liver damage in rats [71].

Anti-Obesity Activity

C. pentandra leaves ethanolic extract exhibited a therapeutic potential in management of obesity in animals through partial inhibition of intestinal lipid absorption and thermogenesis. The extract decrease fat absorption by preventing breakdown of dietary fats in the gastrointestinal tract with no effect on fat liver metabolism [72].

Antidiabetic and Hypolipidemic Effects

The ethanolic extract of aerial parts, and stem bark of *C. pentandra* extract showed significant antihyperglycemic and antihyperlipidemic activities with no effect on blood glucose levels of healthy individuals. It has the ability to increase glucose uptake and to reduce glucose release in target organs. Moreover, it decreased the elevated levels of LDL, VLDL, TC, TG and increased the HDL level, liver and tissue glycogen contents and decreased the reduction of body weight in diabetic rats [56, 73-75]. The methanolic extract of *C. pentandra* fresh stem bark significantly reduced the blood glucose level in diabetic and normoglycemic rats in dose dependent manner in comparison with glibenclamide in alloxan-induced diabetic rats [76]. Further, ethanol, methanol and ethyl acetate extracts of *C. pentandra* leaves exhibited a remarkable reduction in blood glucose level. The body weight and high-density lipoprotein level of the extract treated groups increased significantly as compared with normoglycemic group. A concomitant reduction in the concentrations of low-density lipoprotein, triacylglycerol, and cholesterol of the same group was obtained. the study has also demonstrated high reduction in the biochemical abnormalities in lipid metabolism and hematological complications associated with diabetes mellitus [15, 77-81]. Evaluation of the antidiabetic properties of *n*-hexane and chloroform fractions of an ethanol extract of *C. pentandra* leaves showed potent hypoglycemic and hypolipidemic effects in alloxan induced diabetic rats. The activity of both fractions is dose dependent and capable of reversing hyperglycemia and the abnormalities associated with the pathophysiology of diabetes mellitus. The results showed significant decrease in low density lipoprotein, total cholesterol, triglyceride, alkaline phosphatase, alanine aminotransferase, alkaline aminotransferase, potassium, urea and chloride levels [78]. By the same

way, the different extracts of *C. pentandra* root bark exhibited antidiabetic activity in normal, alloxan and streptozotocin-induced type-II diabetic rats. The extracts significantly reduced both food and water intake and lowered blood glucose levels, serum cholesterol, triglyceride, creatinine and urea in comparison with diabetic controls [15, 82, 83].

Further, the root bark of *C. pentandra* decreased the blood glucose level in normal and streptozotocin induced diabetic rats in time-dependent manner [84]. In another study, a possible mechanism of the hypoglycemic action exerted by this plant was determined when 50% aqueous methanol extract of *C. pentandra* roots lead to significant and dose-dependent α-glucosidase inhibitory activity without prevention of the ingested carbohydrates absorption coupled with a reduction in the postprandial glucose and insulin peaks [59].

The *Ceiba insignis* leaves 70% ethanol and aqueous extracts along with the ethyl acetate fraction showed substantial anti-hyperglycemic activities in alloxan-induced diabetic male albino rats [31].

Anti-Diarrheal Activity

The aqueous and methanolic extract of *C. pentandra* stem bark showed significant protection against castor oil-induced diarrhea in mice with reduced signs and increased onset of appearance of diarrheal symptoms. In addition, aqueous extract inhibits the fecal excretion but no considerable delay in intestinal transit time was observed for methanol extract. This antidiarrheal effect could explained by the antagonist of acetylcholine or agonist of α-adrenergic or morphinic receptors [85, 86].

Anti-Ulcerogenic Activity

Evaluation of *C. pentandra* stem bark extracts showed anti-ulcerogenic effects against both indomethacin and ethanol-induced gastric ulcers in albino rats [79, 87, 88], while root methanolic extract revealed a significant dose-dependent antiulcer effects of *C. pentandra* against ethanol and pylorus ligated-induced ulcers [89].

Anti-Microbial Activities

The different extracts of *C. pentandra* stem bark exerted inhibitory effects on *Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli, Klebsiella pneumoniae* and *Shigella dysentriae* [90-92]. Furthermore, *C. pentandra* and *C. speciosa* stem bark aqueous extracts showed antibacterial activity against *E.coli, P. aeruginosa* and *Bacillus subtilis* [93].

The roots and stem bark of *C. pentandra* hot Soxhlet successive extraction with *n*-hexane, ethyl acetate, acetone, methanol and water were tested against different clinical isolates of *E. coli, S. aureus, Aspergillus Niger* and *Candida albicans*. Methanol and water extracts exhibited significant antibacterial activities on the *S. aureus* and *E. coli*, with low anti-fungal activities [94]. The dichloromethane extract of *C. pentandra* flowers show potent antimicrobial activity of on *A. fumigatus, C. albicans, T. rubrum, Corynebacterium diphtheriae, S. mutans* while the aqueous and methanolic extracts were more potent on *S. pneumonia* [95].

Furthermore, the aqueous and ethanol extracts of *C. pentandra* inhibited the growth of *Epidermophyton flocosum, Microsporum canis, Trichopyton rubrum C. albicans* and *A. flavus* in disc diffusion and agar dilution assays [92, 96]. The aqueous, methanol, ethanol and acetone seeds extracts of *C. pentandra* were tested for their antibacterial activity against *E. coli, S. aureus, K. pneumonia, E. aerogenes, P. aeruginosa, Salmonella typhi, S. epidermidis* and *Proteus vulgaris*. The acetone extract showed wide range of antibacterial activity than the ethanol, methanol extract and aqueous extract [97].

Antimycobacterial activity of methanolic and dichloromethane extracts of the stem bark and leaves of *C. pentandra* was performed against *Mycobacterium fortuitum, M. smegmatis, M. abscessus* and *M. phlei*. Only the methanolic extract inhibited the growth of all tested organisms, while the dichloromethane extract demonstrated little or no activity [98]. The leaves and bark ethyl acetate extracts of *C. pentandra* revealed potential antimicrobial activity in agar dilution assay method against *E. coli, Salmonella typhi, B. subtilis, K. pneumonia* and *S. aureus* [99, 100]. In addition, hexane and dichloromethane extracts of stem bark *C. pentandra* and *C. aesculifolia* exhibited quorum sensing systems activity with the ability to attenuate virulence factors in *P. aeruginosa* [101].

The Gram-positive and Gram-negative bacteria (*Vibrio cholera, E. coli, Enterobacter agglomerans, Salmonella typhi, S. aureus, Enterobacter aerogenes, Staphylococcus epidermidis, B. subtilis and Sarcina lutea, Yersinia enterocolitica*) were sensitive to methanolic extract of *C. aesculifolia* subsp. *parvifolia* bark extract with a bactericidal effect on *S. epidermidis* and *V. cholera* [16]. The antimicrobial activity of the total 70% ethanol and petroleum ether extracts and fractions of the 70% ethanol extract of *C. insignis* leaves was investigated against *B. subtilis, B. cereus, S. aureus, Streptococcus pyogenes,* and *E. coli*. The ether, chloroform and ethyl acetate fractions showed reasonable activity in comparison with ampicillin. The extracts have also showed reasonable antifungal activity against *A. niger, Fusarium oxysporum, Botrytis allii, Trichoderma viride* and *Saccharomyces cervisiae* in a study carried out in comparison with clotrimazole [102].

C. crispiflora leaves different extracts exhibited antifungal activities against three plant pathogenic fungi, *Alternaria solani*, *Botrytis* and *Fusarium oxysporum* [24].

Antibacterial and antifungal activities of different *C. speciosa* leaves extracts were evaluated by disk diffusion method against six bacterial strains (*B. cereus*, *P. aeruginosa*, *K. pneumonia*, *E. coli*, *S. aureus*, and *S. enterica*). The antibacterial activity was most prominent for methanolic and chloroform extracts against *B. cereus*. Moderate activity was shown against *P. aeruginosa*, *K. pneumonia* and *S. aureus*, whereas no activity was detected against *E. coli* and *S. enterica*. The methanolic, chloroform and *n*-hexane extracts showed moderate antifungal activity against *C. albicans* [48]. The *C. speciosa* flowers ethyl acetate extract revealed significant antibacterial activity against *S. aureus, Sarcino lutea, B. subtilts, E.coli and P. aeruginosa*.

The methanolic extract of *C. aesculifolia* subsp. *Parvifolia* fiber showed potent antibacterial activity against *Enterococcus faecalis*, *S. aureus* and *V. cholera* in comparison with chloramphenicol. The tested *V. cholerae* were the most sensitive strains. Moreover, The methanolic extract had potential activity against *Trichophyton mentagrophytes* and *Rhizoctonia lilacina* fungal strains [103].

In addition, the isolated acylated flavonoid tiliroside (38) exhibited substantial antibacterial effects against *B. subtilis* [33]. Isohemigossylic acid lactone-2-methyl ether (21) isolated from genus *Ceiba* displayed inhibitory effects on the growth of *Verticillium dahliae conidia* (strain V76) [29, 104].

Anti-Parasitic Activity

The anti-parasitic activity of the 90% ethanol extract of *C. pentandra* showed potential anthelmintic actions in a larvicidal test against *Haemonchus contortus*. These results confirmed the traditional use of different organs of *C. pentandra* as anthelmintic drug [15, 105].

Table-2: Summary of biological activities of *Ceiba* plants

Plant species	Biological activity
C. aesculifolia	Antibacterial Activity [16, 101] Antifungal Activity [103] Antioxidant Activity [16]
C. crispiflora	Antifungal Activity [24]
C. speciosa	Antioxidant Activity [12, 48, 50-54] Anti-Inflammatory Activity [48] Antibacterial Activity [48] Antifungal Activity [48] Antipyretic Activity [48] Cytotoxic Activity [54] Antifungal Activity[48]
C. chodatii	Antioxidant Activity [28]
C. insignis	Anti-Inflammatory Activity [31] Antibacterial Activity [102] Antifungal Activity [102] Antioxidant Activity [31, 52] Antidiabetic and Hypolipidemic Activity [31] Cytotoxic Activity [65] Hepatoprotective Activity [31]
C. pentandra	Anti-Inflammatory Activity [31, 43-45] Antibacterial Activity [90-93, 95, 97, 99-101] Antifungal Activity [92, 94-96] Anti-parasitic Activity [15, 105] Antidiabetic and Hypolipidemic Activity [15, 56, 73, 75-83, 106, 107] Anti-Diarrheal Activity [82, 86] Anti-ulcerogenic Activity [79, 87-89] Anti-obesity Activity [72] Antioxidant Activity [51, 55-62] Antipyretic Activity [47] Cytotoxic[26, 59, 63, 64] Antitumor Activity [63] Hepatoprotective Activity [71]

Table-3: Summary of biological activities of compounds isolated from the genus *Ceiba*

Isolated compounds	Biological activity
(+)-Catechin (**25**)	Anti-Inflammatory Activity [30]
Aesculetin (**23**)	Antioxidant Activity [28]
Argentilactone (**78**)	Cytotoxic Activity [41]
Ethyl vanillate (**55**)	Antioxidant Activity [28]
Isohemigossylic acid lactone-2-methyl ether (**21**)	Antibacterial Activity [29, 104]
Linarin (**34**)	Antioxidant Activity [34]
n-trans-caffeoyl-L-dopa-methyl ester (**77**)	Antioxidant Activity [34]
Protocatechuic acid (**56**)	Antioxidant Activity [34]
Protocatechuic acid ethyl ester (**57**)	Antioxidant Activity [28]
Rhoifolin (**28**)	Anti-Inflammatory Activity [49] Cytotoxic activity [68, 69] Hepatoprotective Activity [24]
Tiliroside (**38**)	Antibacterial Activity [33]
Vavain (**41**)	Anti-Inflammatory Activity [30]
Vavain-3'-*O*-*β*-D-glucoside (**42**)	Anti-Inflammatory Activity [30]

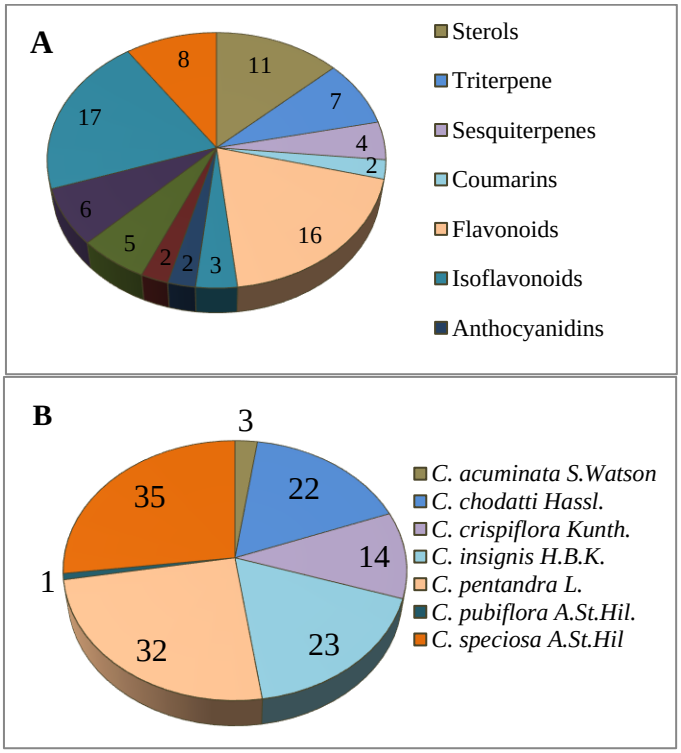


Fig-6: (A) Number of the isolated compounds/phytochemical class, and (B) total number of the isolated compounds/plant species of the genus *Ceiba.*

CONCLUSION

Plant species of the genus *Ceiba* are common ornamental plants in many countries due to their shiny flower and shading ability. In the modern classification systems, the genus *Chorisia* has been revised into *Ceiba* and they are now synonyms [19, 22]. The *Ceiba* plants are important sources of biologically promising compounds (Table-1 and Figs. 2-5) which are certainly the responsible for the various biological effects summarized in Table 2. The pure phenolics from *Ceiba* plants almost exert the same biological effects shown by extracts of the plants, suggesting their large contribution to the health benefits of these plants (Tables 2 and 3). Certain plant species of *Ceiba* such as *C. speciosa* and *C. pentandra* have been extensively studied, although, about 13 species have not investigated by any phytochemical or biological experiments yet (Figs. 6A and 6B). The compounds *β*-sitosterol, daucosterol, rhoifolin, cynaroside, tiliroside, oleic acid, linoleic acid, malvalic acid, sterculic acid were commonly isolated from more than three species of the investigated plants (Table-1). The ongoing phytochemical and pharmacological studies should focus on the uninvestigated *Ceiba* species (*C. allenii*, *C. boliviana*, *C. erianthos*, *C. glaziovii*, *C. jasminodora*, *C.lupuna*, *C. rubriflora*, *C. salmonea*, *C. samauma*, *C.*

schottii, *C. soluta*, *C. trischistandra*, *C. ventricosa*) which could be source of further phytomolecules possessing promising therapeutic potentials.

Conflict of Interest

The authors declare that they have no conflict of interest.

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