

Some members of genus *Cassia* (*Senna*): Their Ethnobotany, Potency and Prospects of Drug discovery

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ABSTRACT

Plants from *Cassia* species have been used traditionally all over the world in the treatment of various diseases. Various compounds with diverse bioactivities have been isolated from the *Cassia* species. However, this has not been done exhaustively in all the species. Moreover, only a few drugs are associated with cassia species as their origin despite the knowledge that plants are a good source of drugs. Further investigations are required to isolate more compounds from these species, verify their bioactivities, conduct clinical and toxicological studies and eventually come up with lead drugs. This review relates the ethnobotanical uses of various *Cassia* species with the isolated bioactive compounds. It pinpoints the limited compounds that have been isolated compared to their traditional benefits justifying the potential and potency of the species as a drug source.

Key words: *Cassia*, *Senna*, ethnopharmacology, phytochemicals, bioactivity

Medicinal plants are critical to developing novel medications [1-3]. 70-90% of the population in Asia, Africa, Latin America and the Middle East rely on traditional medicine for primary healthcare [3]. The global acceptability of popular and efficient species from Europe, North America, Africa and Asia is expanding due to increased demand for medicinal plants in many countries [4]. The percentage of individuals using herbal plants has increased: to 40–50% in Germany, 42% in the USA, 48% in Australia, and 49% in France [3,5]. There is also an ever increase in microbial resistance to antibiotics. The trend is causing concern when it involves the continuous evolution of new strains that use resistance strategies against antimicrobial drugs. It could be possible that plant extracts may offer a solution to the puzzle. Such disease management methods rely on ethnobotany and ethnopharmacology methods used in identifying the plants of interest for pharmacological and phytochemical studies [6]. Ethnobotany has played and will continue to play a significant role in drug discovery [7].

In addition, traditional medical practices involving plant or plant parts are embedded in virtually all community cultures [8]. During the literature review of *Chamaecrista nigricans* syn. *Cassia nigricans*, it became clear that there was significant documentation; however, there was still room to add more knowledge to this already exciting genus *Senna* (*Cassia*). *Cassia* genus belongs to the family Fabaceae and comprises about 600 species of herbs, shrubs, and trees distributed in

tropical and subtropical countries, mainly Africa, Asia, and South America [9,10].

The species have been used, anciently *in vogue*, to treat various ailments that include: skin diseases (such as scabies, eczema, and ringworm), helminthiasis, impetigo, ulcers, pesticide, laxatives, rheumatic diseases, headache, and fever [2]. Most of these species are used as anti-inflammatory, antimicrobial, antivirals, antimutagenic antioxidants, antiplasmodial anticancer, laxative hypoglycaemic, and hyperglycaemic [11-13]. Several secondary metabolites have been isolated and identified from the *Cassia* species. They include peridine alkaloids, anthraquinones, anthracenes, tannins, phenylpropanoids, pentacyclic triterpenoids, essential oils, polyphenols, flavonoids, fatty acids, γ -naphthopyrones, sterols and polysaccharides [13-16]. Such compounds have been proven to be bioactive and found in different parts of plants, such as flowers, seeds, fruits, leaves, roots, and bark [11].

This article has attempted to give an overview of the ethnopharmacology and bioactivity of the phytochemical compounds isolated from various species of the genus *Cassia* and their potency and potential as new drug sources. It summarises advances in bioactive isolates from this genus and the discovery of new therapeutic agents. It is expected to emphasize the importance and traditional utilization of the genus for novel drug discovery. This effort will incentivize more research to isolate bioactive constituents and develop

drugs from the already bioactive compounds from the genus. Virtually all the members of this genus are of economic importance as fodder for foraging bees and nitrogen fixers, thus increasing soil fertility in essential nutrients [14]. The relevant information on the botanical description, ethnopharmacological uses, phytochemicals, and the bioactivities of the isolated compounds were collected from various search engines, including Google Scholar, Google, Springer, Elsevier, PubMed, Science Direct, and ResearchGate. *Cassia* or *Senna* and its associated plant names were employed as keywords to find the pertinent information. The chemical structures of the compounds were drawn using ChemDraw Ultra 8.0 software. PubChem and ChemSpider databases were used to verify the IUPAC names of the isolated phytochemicals. The data includes species name, habitat distribution, extracted phytochemical compounds, and the bioactivities performed on the phytochemical compounds.

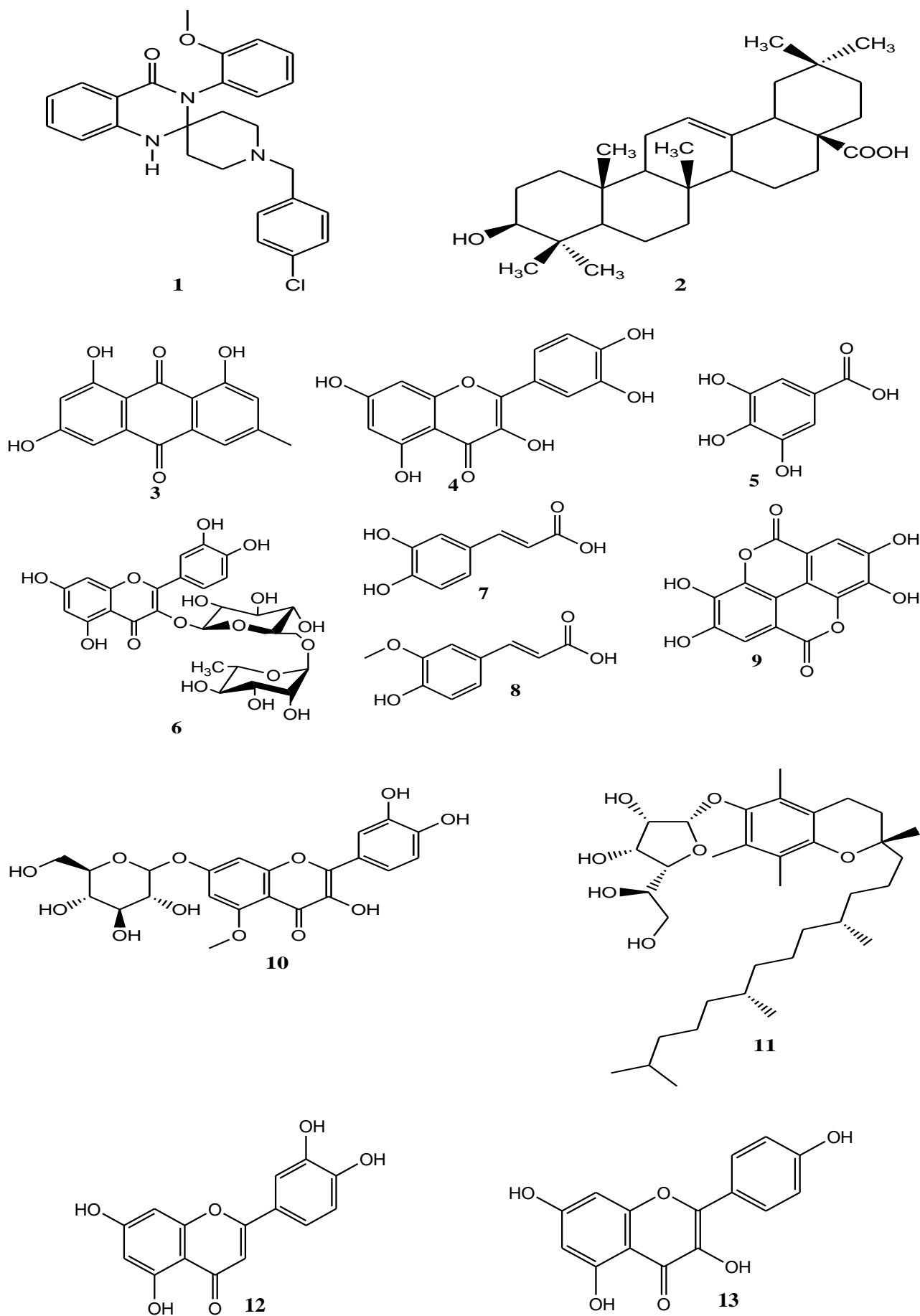
Cassia auriculata Linn synonyms are *Senna auriculata* and *C. densistipulata* (L.) Roxb. It is a fast-growing shrub to a small tree used in green manuring, ornamental, soil reclamation, and tannin. The plant possesses some cardiac glycosides [15]. It is commonly found in Asia [16]. The whole plant treats liver ailments [17]. The leaves have been used for ulcers, skin diseases, anthelmintics, and leprosy [18]. The bark is an astringent [19], while the roots have been used to treat skin conditions such as leprosy, tumours, urethroea, and asthma [20]. The roots are also used in managing ailments in the urinogenital system, fever, constipation, and diabetes [21,22]. The flowers cure nocturnal emissions, urinary discharges, throat irritation, and diabetes [23]. Flowers are also used as a body coolant, treating yellow fever and in blood and liver purification [24]. The seeds are used in chylous urine, diabetes, ophthalmic, and aphrodisiac complaints [25]. The leaves have also been used as hair cleaner and to cure common cold, whereas roots also cure diarrhea, abdominal pains, and vomiting [26]. The plant is also used generally for intestinal problems, female infertility, worms, leprosy, conjunctivitis, rheumatism, and diarrhea [27].

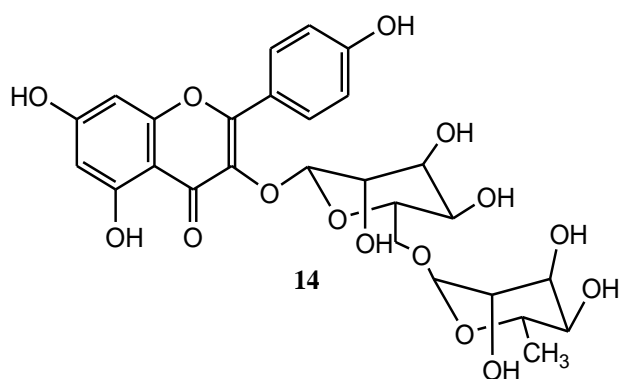
Some compounds that have been isolated from the species include 4-(4-chlorobenzyl)-2,3,4,5,6,7-hexahydro-7-(2-ethoxyphenyl)benzo[h][1,4,7]triazecin-8(1H)-one (**1**), an anticancer compound, isolated from ethanolic leaves extracts of the plant. This compound has been confirmed to inhibit the growth of human colon cancer cells [28]. Oleanolic acid (**2**) isolated from methanolic leaf extracts has antimicrobial activity against *Klebsiella pneumonia*, *Proteus mirabilis*, *Escherichia coli*, and *Salmonella typhi* [29]. Methanol and chloroform crude extracts showed potent inhibitory activity against the above microbes [30]. Ayurvedic hydro-alcoholic seed extracts of *C. auriculata* have been reported to possess antidiabetic activity [31]. Antidiabetic compounds: 1,3,8-trihydroxyanthraquinone (emodin) (**3**) and quercetin (**4**) have been isolated from n-butanol seeds extracts, while gallic acid (**5**), quercetin-3-O-rutinoside (**6**), caffeic acid (**7**), ferulic acid (**8**), and ellagic acid (**9**) were isolated from methanol: water (1:1) seeds extract [32].

5-O-methylquercetin-7-O-glucoside (**10**) has been isolated from the plant's 50% acetone flower extracts and has anti-inflammatory activity [33]. Furthermore, α -Tocopherol- β -D-mannoside (**11**) is also an anti-inflammatory compound isolated from the plant's methanolic leaf extracts [34]. Refluxed dried powdered leaves concentrates in 1N NaOH solution contain Luteolin (**12**), Quercetin (**4**), Kaempferol (**13**), and Kaempferol-3-O- β -D-rutinoside (**14**). These compounds inhibit the aluminium corrosion activity without harming living organisms, unlike chemical inhibitors, which are quite toxic and expensive, harmful to bio-organisms and non-biodegradable [35,36].

Cassia glauca (Lam) synonym is *Senna sulfurea* (Collad.) H.S.Irwin & Barneby A shrub usually with yellow flowers and is used as an ornamental. It is found in Tropical Asia, India, Australia, South America, Malaysia, Pakistan, and China [37,38]. The leaves have been used to manage blennorrhagia [39,40]. The seeds treat skin diseases and leucoderma, whereas the bark and leaves treat gonorrhoea and diabetes [37]. The plant has been used for common cold, as an antimalarial, central depressant, purgative, and diuretic [41]. A compound of biological interest that has been isolated is: Kaempferol 3-O- β -D-rutinoside (**14**) from the methanolic leaves extracts and has been reported to harbour *in vitro* cytotoxic effects against human liver carcinoma (HepG-2) and human breast adenocarcinoma (MCF-7) cell lines [42]. Moreover, it can be combined with other chemotherapeutic drugs to boost their cytotoxic activity and guard against their side effects, suggesting that Kaempferol 3-O- β -D-rutinoside can be a potent anticancer agent [38].

Cassia angustifolia Vahl synonyms are *Senna alexandrina* Mill, *C. acutifolia* Delile, *C. lanceolata* Forssk, *C. senna* L., *Senna acutifolia* (Delile) Batka and *S. angustifolia* (Saheed S.A & Illoh H.C). The plant is also referred to as Indian *Senna*. It is found in India, Saudi Arabia, Pakistan, Egypt, Somalia, Arabia, and Yemen [43,44]. The leaves have been used to manage hepatomegaly, anemia, constipation, malaria, loss of appetite, indigestion, jaundice, ringworm, splenomegaly, and to increase peristaltic movement of the colon [9,43]. The leaves and pods are used for splenic enlargements, cholera, antipyretic in typhoid, anthelmintic, and laxative [44]. Dry tubers have been used as an aphrodisiac, general debility tonic, and rheumatism [45]. Various isolates from parts of the plant, including Quercimeritrin (**15**), scutellarein (**16**), and rutin (**17**), have been isolated from methanol, ethyl acetate, and ethanol seed powdered extracts. All these extracts possess anticancer and antioxidant activities. In addition, the mentioned three compounds have antimicrobial activity; they inhibit the microbial growth of *E. cloacae*, *P. aeruginosa*, *S. mercensens*, and *S. typhi* [44]. The leaves and the pods of this species have been reported to contain dianthone glucosides, sennosides A (**18**) and B (**19**), commonly used as laxatives [46-49].





Other compounds also isolated from methanolic leaves extracts of *C.angustifolia* and known to display various activities, including antimicrobial compounds such as 2, 5-dimethyl-4-hydroxy-3(2h)- furanone (**20**), 4a-acetoxy-5,5,8a,-trimethyloctahydrobenzo[b] pyran (**21**) and 1-ethynyl-4-fluorobenzene (**22**); anti-inflammatory compounds such as caryophyllene(**23**), estragole(**24**) and 1-(1,5-dimethyl-4-hexenyl)-4-methylbenzene (**25**); antihyperglycemic compound such as anethole (**26**); antioxidant compounds such as 2-methylene-(3 β ,5 α)-5-cholestan-3-ol (**27**), 2-Methoxy-4-vinylphenol (**28**); anticancer compounds such as 5-Hydroxymethylfurfural (**29**), β -curcumene (**30**) as well as antiviral compound such as 2-[6-(2,6,6-trimethylcyclohex-1-enyl)-4-methylhexa-1,3,5-trienyl]cyclohexanal (**31**) [46]. *Cassia fistula* L synonyms are: *Bactrylobium fistula* (L.) Willd; *C.bonplandiana* DC; *C. excels* Kunth; *C.fistuloides* Collad; *C.Rhombifolia* Roxb; *Cathartocarpus excelsus* G. Don; *Cathartocarpus fistula* (L.) Pers; *Cathartocarpus fistuloides* (Collad) G. Don; and *Cathartocarpus hombifolius* (Roxb) G. Don. The medicinal use of the species date from ancient times and has been the main factor in its spread. It is called "Aragvadha," a word that can be translated as "elimination of diseases" in Sanskrit. The plant must have originated from the Indian Subcontinent. It is widespread in East Africa and several of the Indian Ocean Islands [48]. The roots, bark, leaves, flowers, and seeds are all used for therapeutic purposes. The leaves have been used as a purgative against ringworms [49]. The whole plant treats anorexia, skin diseases, rheumatism, jaundice, and inflammatory diseases [50]. The roots also cure heart diseases, dysentery, joint pain, retained excretions, chest pain, fever, and migraine [51].

Ayurvedic medicines recognize the use of the plant for skin diseases, tubercular glands, adenopathy, burning sensations, syphilis, and leprosy [52]. The fruit, seeds, flowers, and pulps are all used for skin diseases; the pulp is also used to treat gout and rheumatism, while the leaves have been used as a laxative [53]. In addition, flowers, leaves, bark, root, and pulp have been used in wound healing, liver protection, and as an antimycotic [54]. The whole plant also treats ulcers, purgative, impetigo, and helminthiasis, although the leaves and the seeds act as a liver tonic, cardiogenic, laxative, antihelminthic, ophthalmic, antiperiodic expectorant as well as in treating constipation and

bronchitis [55]. The species' seeds have been used in treating swollen throats, oral sores, jaundice, and biliousness [56]. The plant is also used as a hair cleanser and in the treatment of venereal diseases, diarrhea, toothache, muscle pain, cold, inflammation, reducing body heat, vomiting as well as diabetes [26,48].

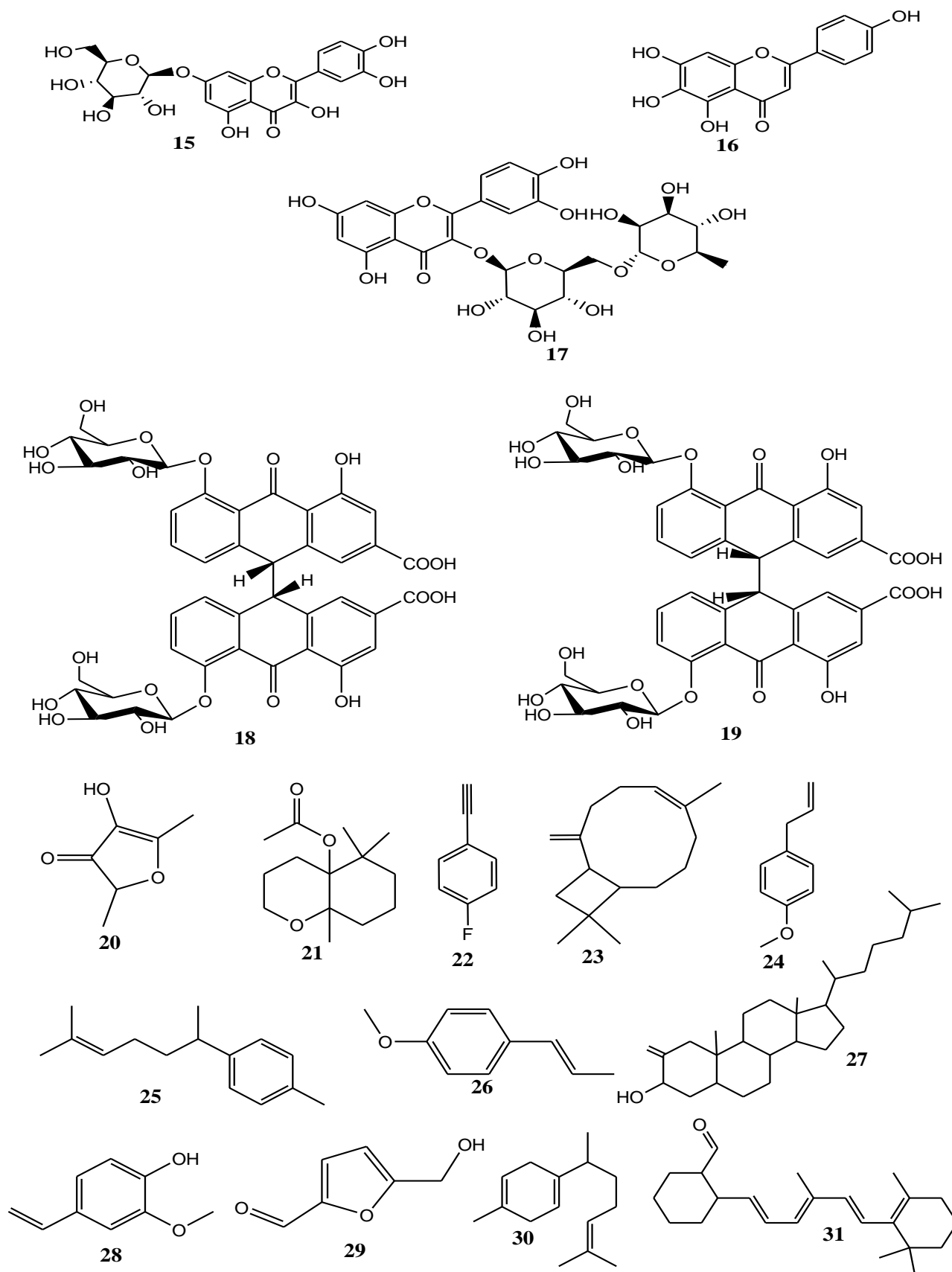
Phytochemical elucidation of *Cassia fistula* has led to isolating compounds with therapeutic values.:4-hydroxy benzoic acid hydrate (**32**) (from the ethyl acetate extracts of the flower) was confirmed to possess antifungal activity against *Trichophyton mentagrophytes* and *Epidermophyton floccosum* [57]. Rhein (1,8-dihydroxyanthraquinone-3-carboxylic acid) (**33**) has also been isolated from ethyl acetate extract of *C. fistula* flower and showed inhibition against fungi such as *Trichophyton mentagrophytes*, *Trichophyton simii*, *Trichophyton rubrum*, and *Epidermophyton floccosum* [58]. Benzyl 2-hydroxy-3,6-dimethoxybenzoate (**34**) and dibenzyl-2,2'-dihydroxy-3,6,3',6''-tetramethoxy-biphenyl-1,1'-dicarboxylate (**35**) isolated from methanol extracts of seed showed antifungal activity against *Cladosporium cladosporioides* and *Cladosporium sphaerospermum* [59].

Phytol (**36**), lutein (**37**), and di-lineolylgalactopyranosyl-glycerol (DLGG) (**38**) are antiplasmodial compounds that have been isolated from chloroform leaf extract of the plant. Di-lineolylgalactopyranosyl-glycerol portrayed weak toxicity against cytotoxicity test carried out using the Chinese Hamster Ovarian (CHO) cell line, while phytol and lutein were nontoxic [60]. Rhein (**33**), 2(3H)-furanone (**39**), thymol (**40**), and oleic acid (**41**) have been isolated from ethyl acetate extract of seeds and pulp of *C. fistula* [61]. Butanol extracts of the seed yielded inositol (**42**) and palmitic acid (**43**), whereas the butanol extract of the pulp yielded inositol (**42**) and 2-pyrrolidone (**44**). All these compounds were reported to inhibit breast cancer (MCF-7) and human cervical cancer (SiHa) cell growth, and they also induced cell death [61]. *Cassia alata* L synonyms are *Senna alata* L and *Herpetica alata*. It is distributed in Africa, South and North America, and India [62,63]. The plant leaves treat ulcers, scabies, ringworm, and skin diseases such as eczema, itching, and pruritis [62]. The leaves and stem bark are used to treat burns, diarrhea, jaundice, gastroenteritis, and hepatitis, whereas the immature leaves are effective against food poisoning and constipation [64]. This plant is good against insect bites, worms, goiter, fever, blemishes, sexually transmitted diseases, and fungal skin infections [65-67]. The leaves also cure asthma and bronchitis [67]. The roots are used for uterus disorder [68,69].

Some compounds of interest have been isolated from this species. Cannabinoid alkaloids, 4-butylamine-10-methyl-6-hydroxy cannabinoid dronabinol (**45**), have been isolated from the ethanolic seed extracts of the plant and is known to possess bioactivities against microbes such as *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *Escherichia coli*,

Staphylococcus aureus, *Candida albicans* and *Aspergillus niger* [70]. Luteolin (**12**), kaempferol (**13**), and aloe-emodin (**46**) have been isolated from methanolic leaf extracts, and they all showed antibacterial activity against *Vibrio cholerae* and *Shigella flexneri*., with aloe-emodin showing the highest

activity [71]. Kaempferol (**13**) and ω -hydroxyemodin (**47**) have been isolated from the acetone leaves extracts ω -hydroxyemodin showed antibacterial activity against methicillin-resistant *Staphylococcus aureus* (MRSA) and kaempferol posses antioxidant activity [72].

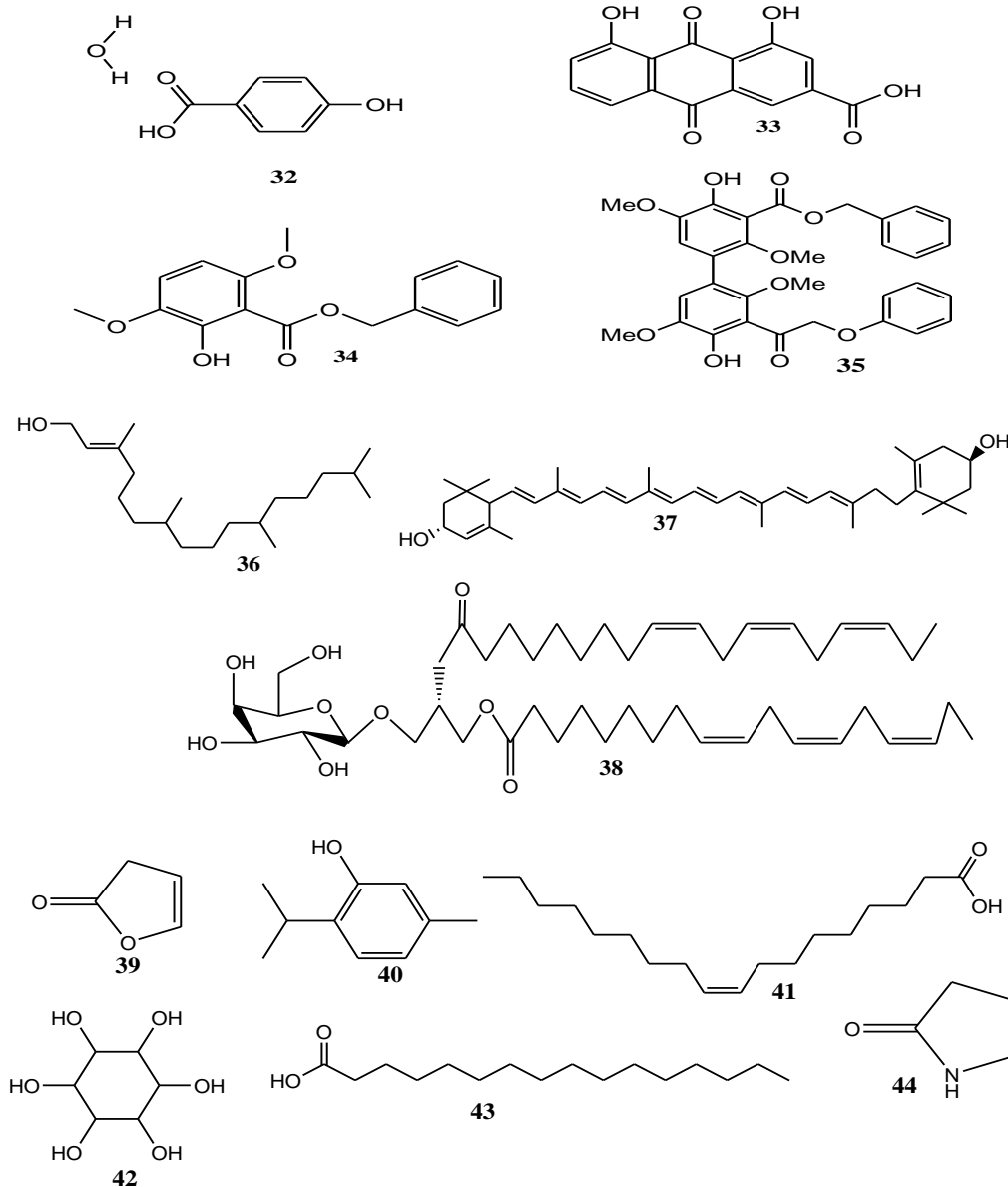


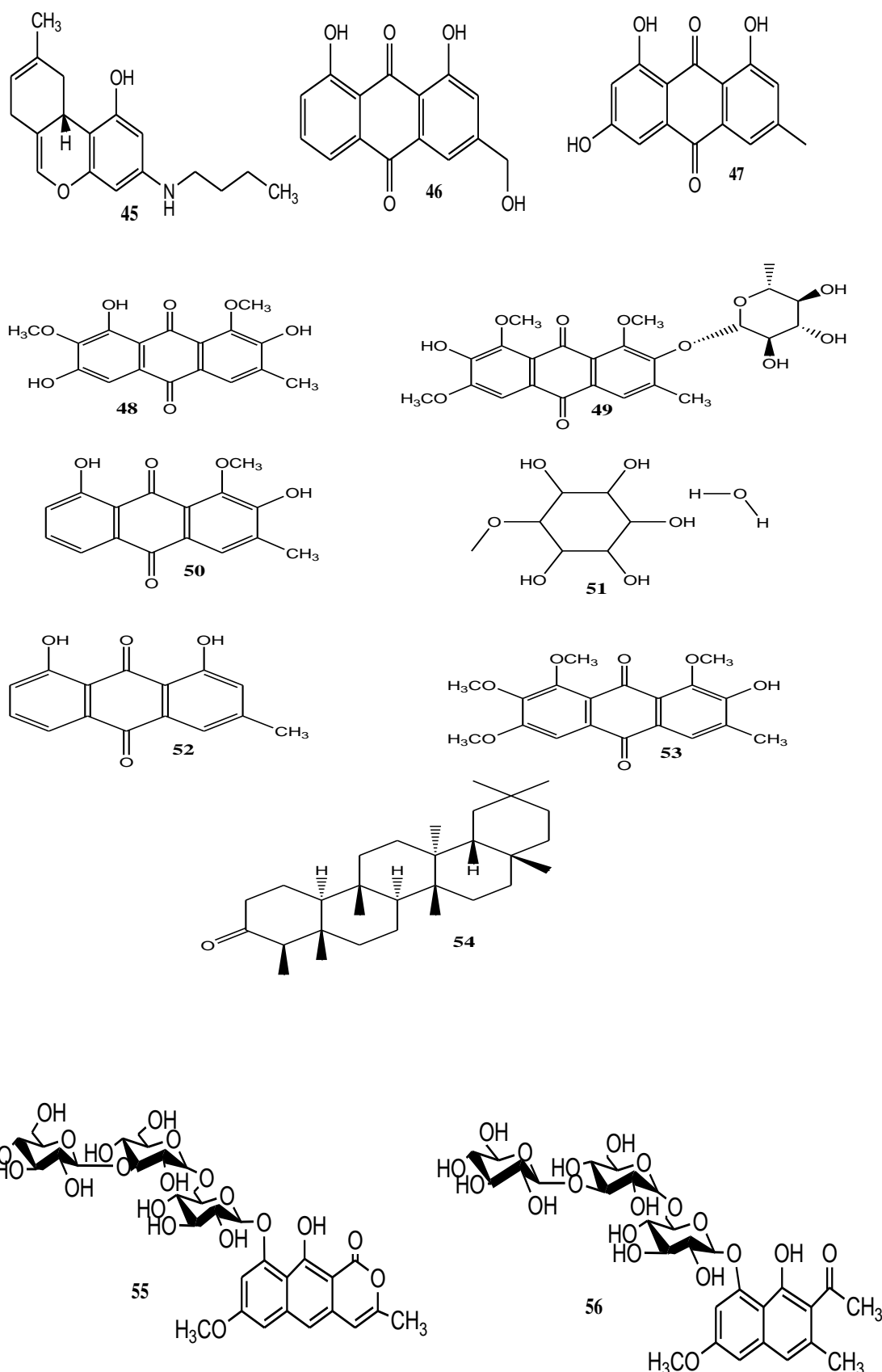
Cassia tora L synonyms are *Senna obtusifolia* (L.) H.S.Irwin & Barneby, *Cassia numilis* Collad, *C. obtusifolia* (L.), *C. toroides* Raf., *Diallobus uniflorus* Raf and *Senna toroides* Roxb. It is found in Africa, Fiji, Southeast Asia, Northern Australia, and Latin America [73,74]. The species has been used in Folklore medicine in that the leaves of the plant are used for the treatment of jaundice, eczema, ringworm, intestinal impetigo, and helminthiasis; the decoction of leaves and flowers are used against asthma and bronchitis; and the seeds are used to treat leprosy, psoriasis, earache, itching, eye diseases, liver problems while pods are used against dysentery and in eye diseases [75]. Its fermented leaves have purgative properties [72]. Traditionally, the plant has been widely employed in managing hemorrhoids, vitiated tridosha, hepatitis, skin diseases, dandruff, cough constipation, and fever [74]. The leaves and seeds possess cardiotoxic, ophthalmic, antimicrobial, and liver tonic properties [76].

Emodin(3), aurantio-obtusin (48), chryso-obtusin-2-O- β -D-glucoside (49), and obtusifolin (50) have been isolated from ethyl acetate soluble extracts of the seeds of *C. tora*. They are

known to inhibit diabetic complications (advanced glycation end products (AGEs) and cataract formation (rat lens aldose reductase (RLAR)) [77]. Ononitol monohydrate (6-methoxycyclohexane-1,2,3,4,5-pentaol hydrate) (51) occurred in the leaves of ethyl acetate extracts and was found to exhibit *in vivo* hepatoprotective activity [78] Aurantio-obtusin (48), chrysophanol (52), and chryso-obtusin (53) have been isolated from dichloromethane fraction of methanolic seed extracts, and the compounds showed significant antimutagenic activity [79].

Additionally, friedelin (54), a triterpene, is a compound that was isolated from ethanolic leaves extract of the plant and found to possess anticancer activity against human cancer cell lines; HeLa (cervical carcinoma) and HSC-1 (squamous carcinoma) [73]. Two phenolic triglycosides: toralactone 9-O- $[\beta$ -D-glucopyranosyl-(1 \rightarrow 3)-O- β -D-glucopyranosyl-(1 \rightarrow 6)-O- β -D-glucopyranoside] (55) and torachryson 8-O- $[\beta$ -D-glucopyranosyl(1 \rightarrow 3)-O- β -D-glucopyranosyl(1 \rightarrow 6)-O- β -D-glucopyranoside] (56) occurred in 70% ethanol extracts of the seeds and was found to possess estrogenic activity [80].





Advanced chemical studies and elucidation of ethyl acetate soluble seed extract yielded Emodin (**3**), rhein (**33**), aloemodin (**46**), torachryson (**57**) and toralactone (**58**), which possess significant antibacterial activity against methicillin-resistant *staphylococcus aureus* [81].

Cassia abbreviata Oliv synonyms are *Cassia afrofitula* Brenan, *Cassia beareana* Holmes and *Cassia kassneri* Bak. It is a medium-sized tree widely distributed in the tropics of Asia and other tropical Worlds [82] and used as medicine. The roots treat malaria, fever, impotence, abdominal pain, wounds,

dysentery, syphilis, snake bite, body weakness, and hernia [83-84]85]. The plant is used to treat cancer [86]. Its root bark manages vaginal candidiasis [87]. The leaves, roots, and bark have been used to treat cough, epilepsy, diarrhea, fever, convulsion, vomiting, abortion, infertility, earache bilharzia, syphilis, hemorrhoids, gonorrhea, jaundice hernia, and stomach ache [88]. The bark and the roots cure dysentery, bloody vomiting, and menstrual cycle problems [89]. Fruits are used against eye infections and malaria [82]. The bark is also used in treating toothache and sexually transmitted diseases [90]. The roots are also used as an aphrodisiac [91].

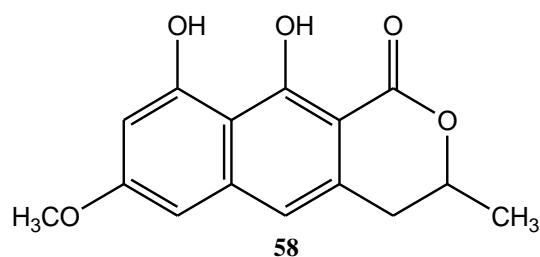
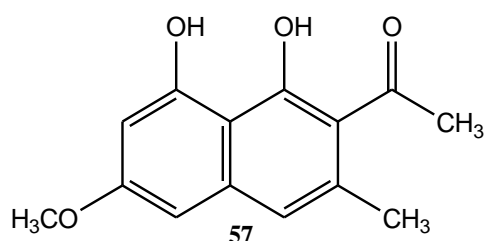
Further, advanced studies in chemistry identified compounds that could enhance drug discovery. Such compounds are Trimericproanthocyanidins; 3,7,4'-trihydroxyflavan-(4 β →8)-3,5,7,4'-tetrahydroxyflavan-(3'→6)-3,5,7,2',4'-pentahydroxyflavan (cassinidin A) (**59**) and 3,7,2',4'-tetrahydroxyflavan-(4 α →8)-3,5,7,4'-tetra-hydroxyflavan-(4 α →6)-3,5,7,2',4'-pentahydroxy- flavan (cassinidin B) (**60**) which were isolated from methanol root bark extracts and they exhibited antibacterial activities on *Escherichia coli*, *Bacillus subtilis*, *Staphylococcus aureus* and *Candida mycoderma* [92]. 2,3-dihydro-5-hydroxy-8-methoxy-2-(4-methoxyphenyl)chromen-4-one (**61**) and 3,4-dihydro-2-(4-hydroxy-phenyl)-4-methoxy-2H-chromen-7-ol (**62**) have been isolated from methanol root extracts and found to have antiplasmodial activities on both chloroquine-resistant and chloroquine-sensitive strains of *Plasmodium falciparum* [93].

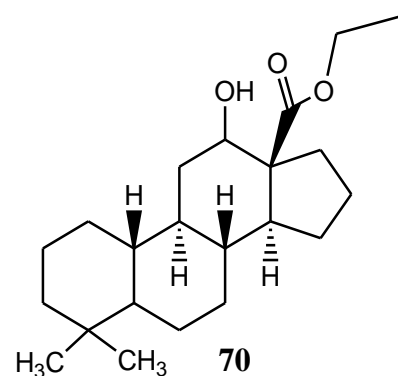
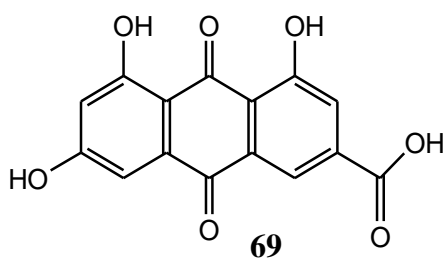
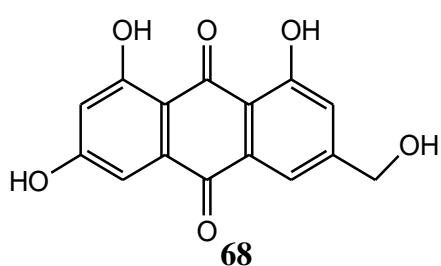
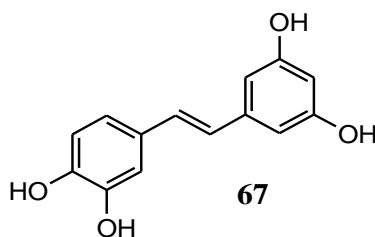
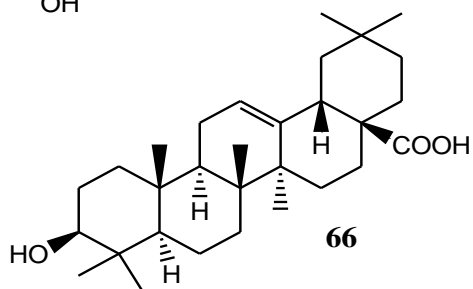
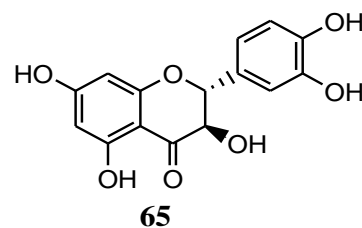
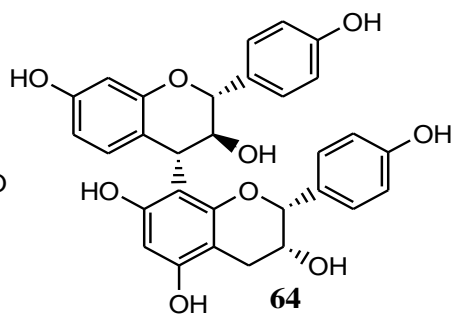
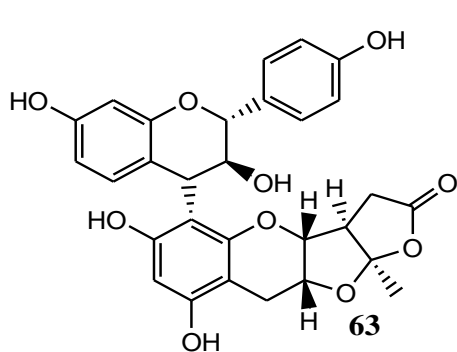
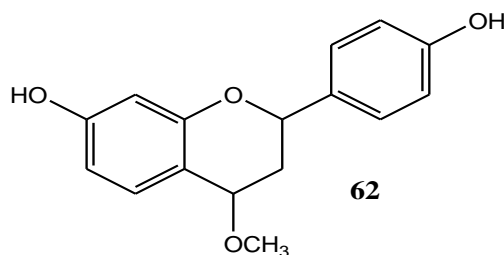
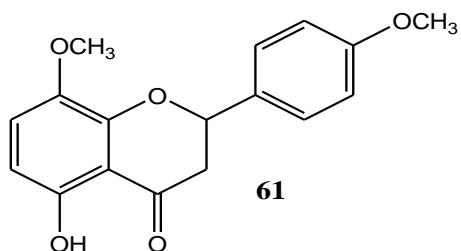
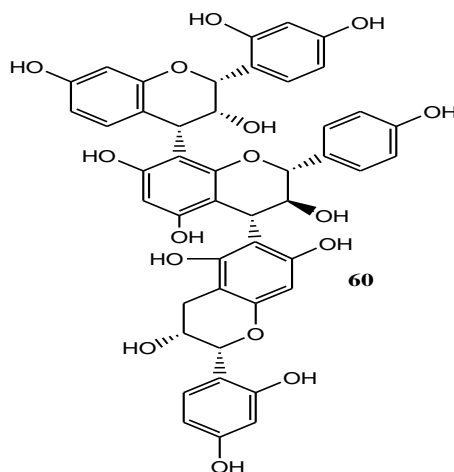
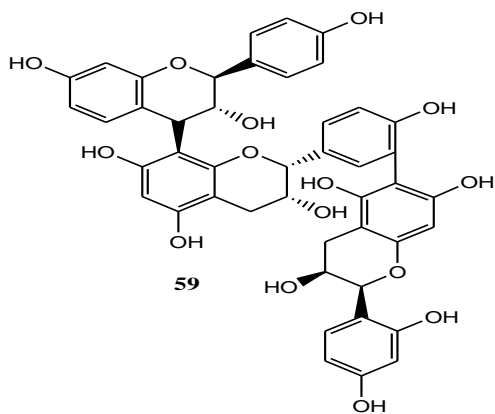
Cassiabrevone (**63**), guibourtinidol-(4 α →8)-epiafzelechin (**64**), taxifolin(**65**), oleanolic acid (**66**), piceatannol(**67**), and palmitic acid (**43**) were isolated from ethanolic bark and root extracts and posses anti-HIV-1 activity [94,95]. *Cassia nigricans* Vahl synonym is *Chamaecrista nigricans* Vahl The roots and leaves are vermifuge and antiperiodic [80]. The leaves also treat fever, sore throat, rheumatoid pains, gastrointestinal disorders, and family planning [12, 96,97]. The plant treats skin diseases, ulcers, diarrhea, and gastrointestinal disorders [98,99]. Various compounds have been isolated from this species, justifying its continued use in folklore medicine. It was reported that 1,3,8-trihydroxy-6-methyl-9,10-anthracenedione (Emodin) (**3**) isolated from methanol extract of the whole plant showed *in vitro* antiplasmodial activities against *Plasmodium falciparum*[100]. Emodin has also been isolated from the ethyl

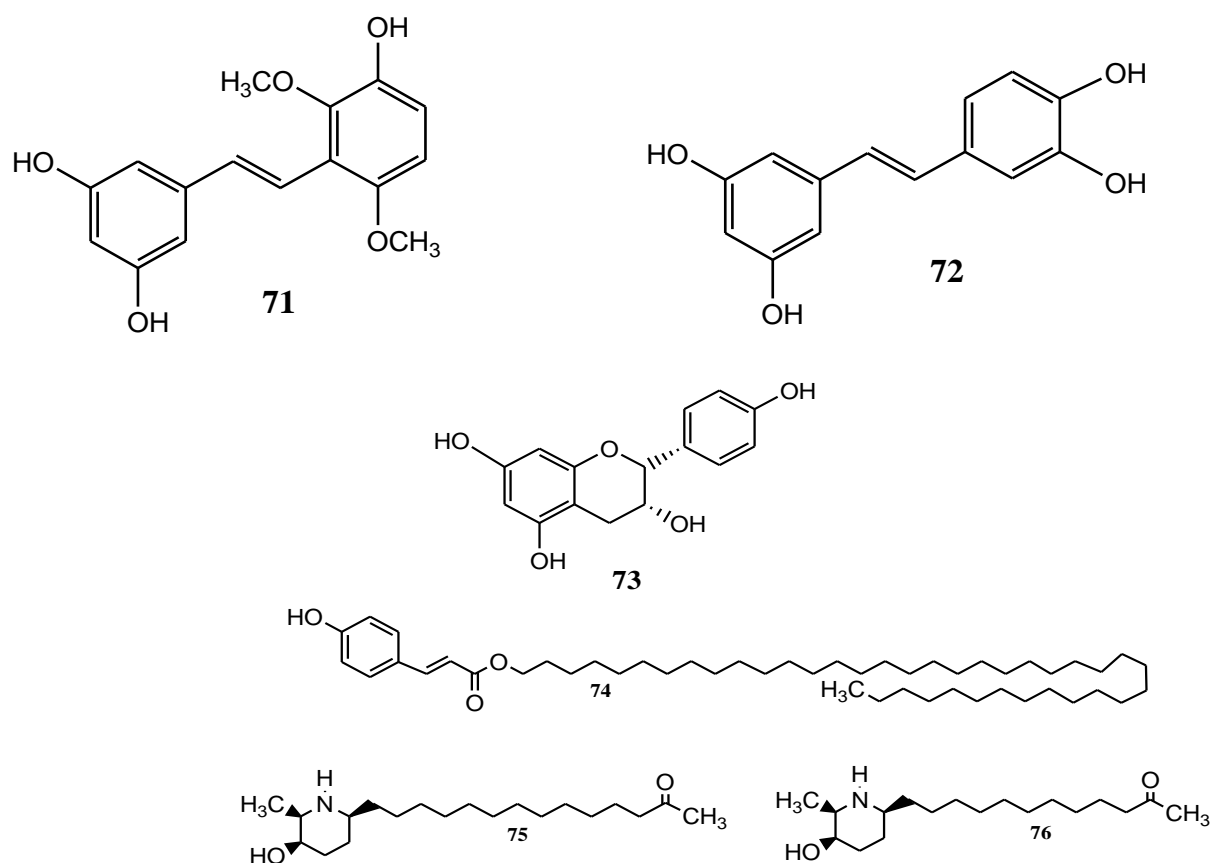
acetate leaf extract and found to be highly cytotoxic despite having antimicrobial activity [101]. Emodin (**3**), luteolin(**12**), citreorosein (**68**), and emodic acid (**69**) have been isolated from n-hexane, ethyl acetate, and methanol combined extracts. Emodin, citreorosein, and emodic acid showed larvicidal activity on *Anopheles gambiae* larvae [102]. Steroidal ester and hydroxyestrane acid ethyl ester (**70**) have been isolated from methanol leaves extracts and showed antimicrobial activities on *Staphylococcus aureus*, *Streptococcus pyogenes*, *Corynebacterium pyogenes*, *Bacillus subtilis*, *Salmonella typhi*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Candida albicans*, *Neisseria gonorrhoea* and *Klebsiella pneumoniae* [103].

Cassia sieberiana D.C. This species is a medium-sized tree widely distributed in Sub-Saharan Africa, from Senegal to East Africa [104]. The root bark and rootlets treat toothache, abdominal pains, skin diseases, hemorrhoids, helminths, and leprosy [105]. The roots also treat hemorrhoids and skin irritation and manage indigestion, stomach pains, and gastric ulcer [106,107]. The seeds have been used in weight reduction, clearing of acne, detoxification, and driving out internal heat [108]. The folklore uses of *C. sieberiana* have led to the isolation of such compounds as quercetin (**4**), cassiberianol A (**71**), and piceatannol (**72**) from methanol extracts of the roots. They all had inhibitory activity on 15-lipoxygenase, while piceatannol and quercetin also showed acetylcholinesterase inhibitory activity [109].

Flavanoids, epiafzelechin (**73**), have been isolated from ethanol extracts of the plant's stem bark and possess antioxidant activity [110]. Moreover, cassiphenol (**74**), spectraline (**75**), and iso-6-cassine (**76**) are also compounds that have been isolated from ethanol extracts of the stem bark. Cassiphenol has weak antibacterial activity against *Pseudomonas aeruginosa*, *Providencia stuartii*, *Enterobacter aerogenes*, and *Klebsiella pneumoniae*. Spectraline and iso-6-cassine were the only compounds that portrayed antioxidant activity [111,112]. *Cassia absus* L. Synonym is *Chamaecrista absus* H.S.Irwin & Barneby It is a small hairy herb, a native of Africa; however, a common monsoon weed in South East Asia [113]. In folklore medicine, the seeds have been used to treat syphilitic ulcers, skin infections, leukoderma, ophthalmia and as a cathartic [114]. The leaves are used for nasal diseases, cough, and as an astringent to the bowel [115]. The leaves are used in curing tumours, while the roots are used against constipation [116].







From this Ethnobotanical information, guided chemical profiling has been done, and the following noble compounds like Aloe-emodin (**46**), chrysophanol (**52**), and chaksine (**77**) have been isolated from the ethanol root extracts [117, 118]. The ethnomedicinal use of the roots is associated with the presence of chrysophanol and aloe-emodin and has also been verified by the bioactivity of these compounds from this genus. It has been reported that chaksine has antidepressant activity, anesthetic activity, and antibacterial activity against *Streptococcus hemolyticus* [113]. 5,7,4'-trihydroxy-8,3'-dimethoxyflavone-5-O- α -L-rhamnopyranosyl-7-O- β -D-xylopyranosyl-(1 \rightarrow 4)-O- β -D-galacto-pyranoside (**78**) is a compound that has been isolated from methanolic seeds of the plant. Reports indicate that the isolates possess antimicrobial activity on *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Penicillium digitatum*, and *Fusarium oxysporum* [119]. *Senna septemtrionalis* H.S.Irwin & Barneby synonyms are *Cassia aurata* Roxb., *C. elegans* Kunth, *C. Floribunda* Kunth *C. laevigata* Willd., *C. quadrangularis*, *C. septemtrionalis* Viv and *C. vernicosa* Clos. A shrub to a

sub-shrub native to America now spreads in the tropic and subtropics up to India and South Africa [120]. The roots treat malaria, gonorrhoea, syphilis, intestinal worms, and blood cleansing [120,90]. The leaves are used as a vermifuge [121,122]. It is also used in treating stomach aches, wounds, fever, gastroenteritis, snakebites, burns, epilepsy, hemorrhoids, anxiety, and as a laxative, fungicide agent, antidiuretic as well as expectorant [123]. This plant has also been used as a medication for rabies, cold, alopecia, earache, bile diseases,

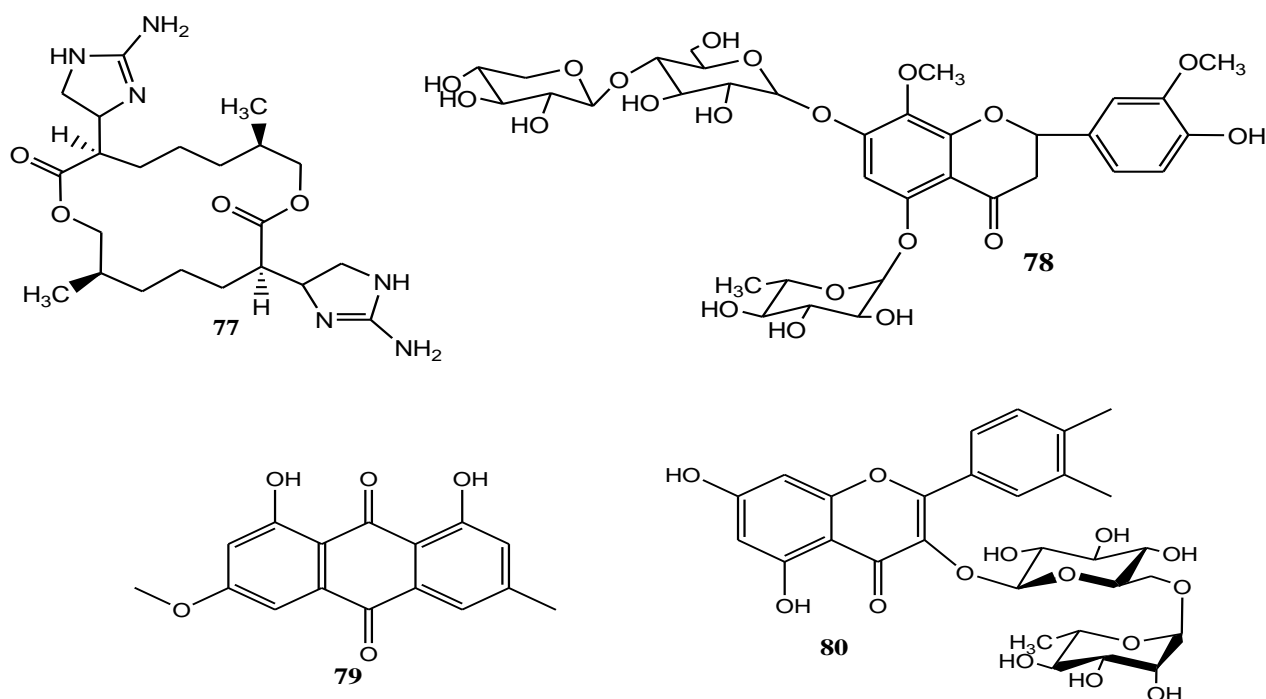
pain, inflammation, and cholera [124,125]. Its chemical elucidation yielded two compounds. Physcion (**79**) has been isolated from this plant and possesses bioactivities against *Chlorella fusa* and *Bacillus megaterium* [126]. Rutin (**80**) and Kaempferol 3-O-rutinoside (**14**) hexoside are also compounds isolated from this plant, posing both anti-inflammatory and antinociceptive activities [125]. *Senna petersiana* (Bolle) Lock synonym is *Cassia petersiana* (Bolle) Lock This small tree is generally found in Tropical and sub-Tropical Africa and can grow to 12 m [127]. The root extracts treat infertility, malaria and are also used as inhalers and for deworming [128-130]. The leaves cure skin diseases, backaches, stomach aches, and febrifuge [127,130]. The plant is used to treat arthritis and management of diabetes [131]. The roots also treat a loss of appetite [132]. The plant also cures cholera, cold, and fever [133]. The plant's roots, leaves, and stems have been used for convulsion and relieving pain in the bones [134].

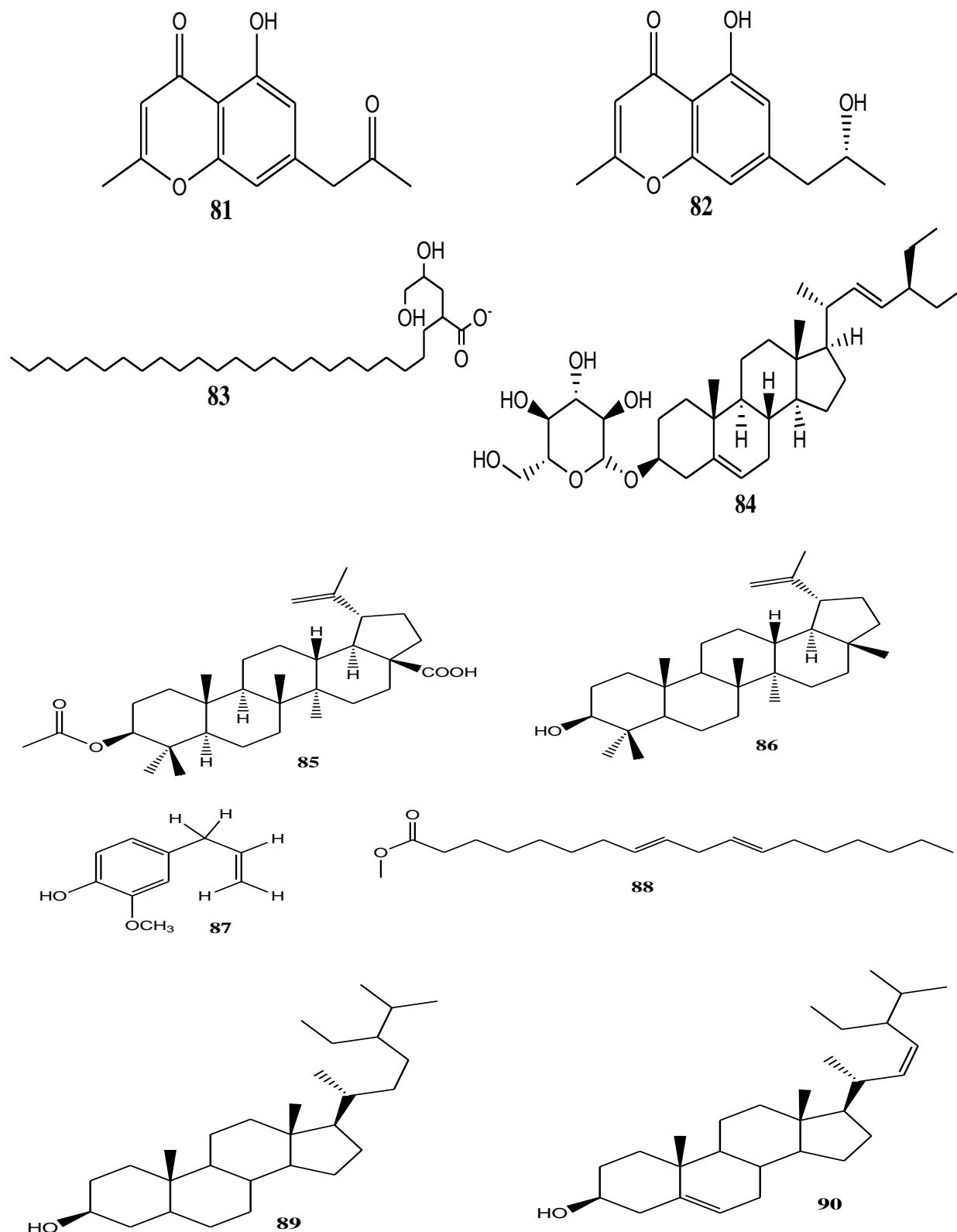
As a result of its use in traditional medicine, several natural compounds have been isolated from its various parts. Luteolin (**12**) isolated from ethanol extracts of the seed possesses bioactivities against *Bacillus cereus*, *Bacillus pumilus*, *Serratia marcescens*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus* [135]. Four compounds: 7-acetyl-5-hydroxy-2-methylchromone (petersinone A) (**81**), 5-hydroxy-2-methyl-7-(propan-2-yl)-chromone (petersinone B) (**82**), glyceryl-1-hexacosanoate (**83**) and stigmastosterol-3-O- β -D-glucoside (**84**) were isolated from CH₂Cl₂-MeOH (1:1) leaves extract of this plant. Stigmastosterol-3-O- β -D-glucoside showed the highest anti-inflammatory antitumor, antioxidant, macrophage

proliferation, and immune proliferative activities [127]. *Senna singueana* Del Lock synonyms are *S. goratensis* Fresen, *Cassia zanzibarensis* Vatke, *C. singueana* Delile, and *C. tettensis* Bolle. The species is a medium-sized tree used as ornamental and, like most family members, can fix gaseous nitrogen into the soil, thus enriching it with an essential nutrient. It is widely distributed in East and West Africa [136]. Various parts of the plant have been used in traditional medicine in different parts of the world [137]. The leaves and bark have been used to treat skin cancer [138]. The stem, bark, leaves, and roots treat a sprain, stomach pain, and tooth infection [139]. The leaves cure hepatitis, vomiting, and loss of appetite, and the stem bark prevents stillbirth [140]. The roots treat epilepsy and agitation [141]. The flowers are used as an anti-inflammatory, anti-ulcer, antispasmodic agent and in treating respiratory tract infections, malaria, and typhoid [142]. The root bark is also used for abdominal pain, bilharziosis, mental disorder, women's infertility, constipation, convulsion, painful uterus, swollen breast, fever, menstruation, gonorrhoea, anti-emetic, hernia, and in managing snakebites [143,144]. Some beneficial compounds that have been isolated from the plant through phytochemistry include 3 β -O-acetyl betulinic acid (**85**) isolated from the ethyl acetate bark of this plant. It inhibited α -glucosidase and α -amylase activity, thus delaying carbohydrates digestion and glucose assimilation, eventually restraining postprandial hyperglycemia, thus treating type 2 diabetes (T2D) [145]. Lupeol (Lup-20(29)-en- triterpene) (**86**), Eugenol (4-allyl-2-methoxyphenol) (**87**) and 8-11-Octadecadienoic acid methyl ester (Methyl-8, 11-octadecadienoate) (**88**) are compounds which have been isolated from its methanolic root extracts. Eugenol showed antioxidant activity and a broad spectrum of antimicrobial activity against *Candida albicans*, *Staphylococcus aureus*, *Escherichia coli*, *Streptococcus pneumoniae*, and *Pseudomonas aeruginosa*. Lupeol and

Methyl- 8,11-octadecadienoate also possessed certain antioxidant activity and antimicrobial activity levels against *S. aureus* [146].

Senna didymobotrya (Fresen.) H.S.Irwin and Barneby synonyms are *Cassia didymobotrya* Fresen, *C. nairobiensis* H. Bailey, *C.verdickii* De Wild and *Chamaesenna didymobotrya* Sunarno. It is an invasive shrub that forms a dense growth that hinders the development of other plant species in a given area [147]. It is distributed in North, West, East, Southern Africa, and Madagascar [148]. This plant's leaves, stem, and roots have been used in treating sickle cell anaemia, backache, fibroids, inflammation of fallopian tubes, and hemorrhoids [149]. The bark is an antihemorrhagic [150]. The plant has been used in treating skin disease, jaundice, purgative, malaria, sexually transmitted diseases, intestinal worms, and as an appetizer and antibiotic [148,151,152]. The leaves are used in curing dysentery, diarrhoea, and as an emetic and diuretic, while the root is used to treat ringworm, malaria, intestinal worm, fever, and jaundice [151]. Through natural product chemistry, some compounds have been isolated from this species; they include: Chrysophanol (**52**), physcion (**76**), 3 β -sitosterol {17-(4-Ethyl-1,5-dimethyl-hexyl)-10,13,dimethyl-2,3,4,7,8,9,-10,11,12,13,14,15,16,17-tetradecahydro-1H cyclopenta[a]phenanthren-3-ol} (**89**) and stigmasterol {(3S,9S,10R,13R,14S,17R)-17-[E,2R,5S)-5-ethyl-6-methylhept-3-en-2-yl]-10,13-dimethyl-2,3,4,7,8,9,11,12,14,-15,17-dodecahydro-1-H-cyclopentanal[a]-3-ol (**90**) were compounds isolated from the hexane and DCM root bark extracts of this plant. The specific activity of the individual compounds was not reported; however, the crude extracts showed antimicrobial activities on *Staphylococcus aureus*, *Escherichia coli*, *Bacillus subtilis* and *Candida albicans*[153].





Senna bicapsularis (L) Roxb synonyms are *Cassia bicapsularis* L., *C. emarginata* L., *C. berterii* Colla, *Adipera bicapsularis* (L.), *Adipera spiciflora* Pittier, *Cathartocarpus bicapsularis* (L.) Ham Isandrina *emarginata* (L.) Britt. & Rose ex Britt. & Wilson, *Chamaefistula inflata* G. Don and *Isandrina arborescens* Raf. It is distributed in South America and tropical countries [154]. The species is cultivated in many parts of the

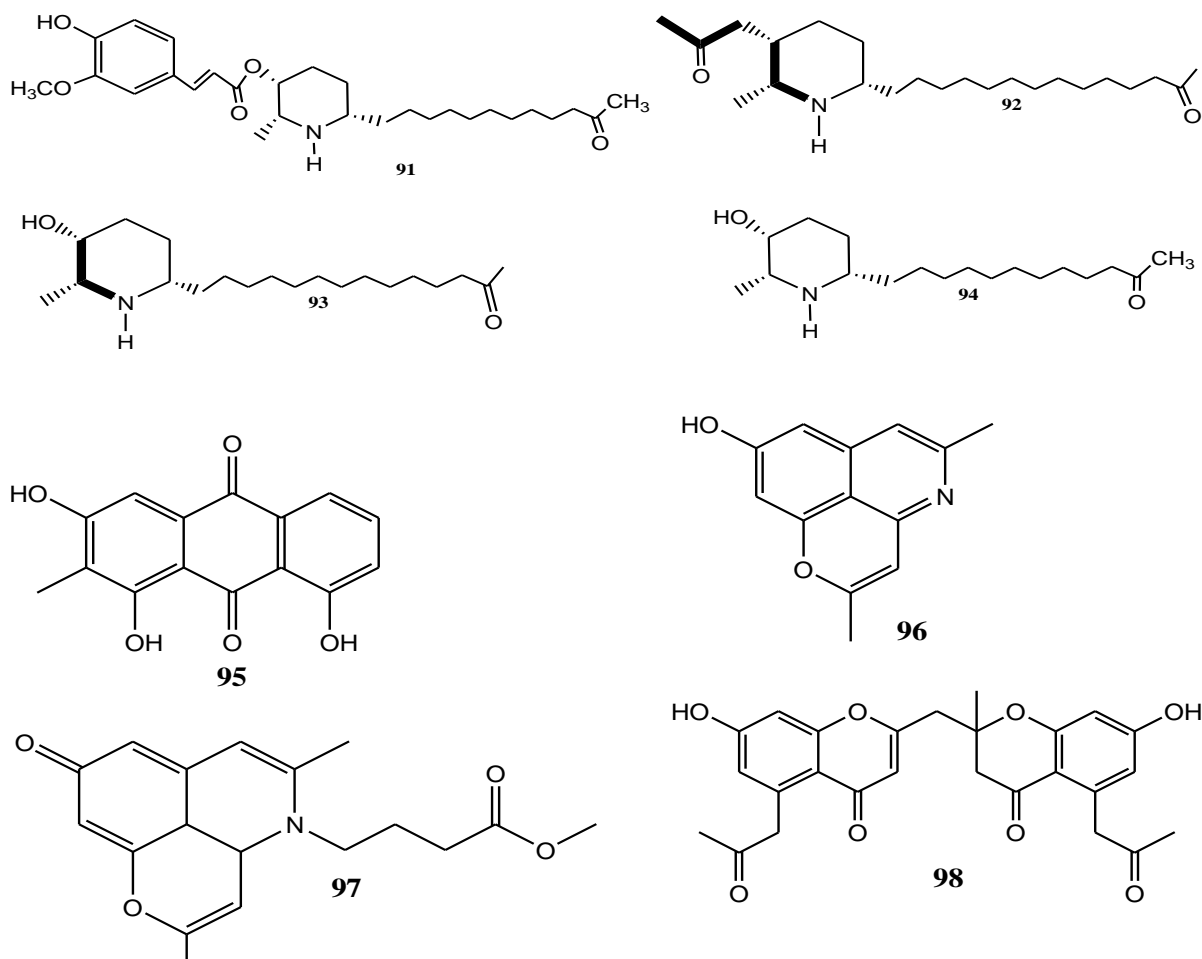
world; however, it has escaped being naturalized and has an unpleasant odor [155]. Roots and leaves are used for stomach aches [156]. The leaves have been used in treating skin ailments [157]. The flowers have been used as an abortifacient and contraception agent for both males and females [158]. The plant has been used to treat pain as well as a muscle relaxant and purgative [159]. Due to its aromatic nature, several compounds

like Emodin (**3**), rhein (**33**), chrysophanol (**52**), physcion (**76**), and stigmasterol (**90**) have been isolated from it with biological activities including sedative effect, anti-inflammatory, analgesic effect and muscle relaxing effect [159].

Cassia spectabilis (D.C.) H.S. Irwin & Barneby Synonyms: *Cathartocarpus humboldtianus* Loudon; *Cathartocarpus speciosus* (D.C.) G.Don; *Cathartocarpus trinitatis* (D.C.) G.Don; *Cassia trinitatis* Rchb.ex D.C. *Cassia carnaval* Speg, *Pseudocassia spectabilis* (DC.) Britton & Rose, *Senna speciosa* Roxb, *Senna surattensis* (Burm. f.) Irwin & Barneby. *Cassia amazonica* Ducke and *Senna spectabilis* (D.C.) Irwin & Barneby. The species is a native of South America, Brazil, and coastal Ecuador and has migrated throughout Central America, the West Indies, the tropics, and sub-tropic parts of the world [160-162]. The leaves are used in throat inflammation and diarrhoea [162]. The plant is used to cure headaches, malaria, and dysentery, while the leaves treat anxiety, epilepsy, insomnia, constipation, and anxiety [163]. The species has also been used in treating ringworm, skin disease, flu, cold, whooping cough, menstrual cramps, and diabetes [160,164,165]. Natural products that have been isolated from this plant are: (-)-spectaline (**72**), (+)-2-Methyl-3-feruloyl-6-(dodecyl-11'-one) piperidine ((+)-3-O-feruloylcassine) (**91**) and (-)-3-O-acetylspectaline (**92**), isolated from methanol extract of green fruits of this plant and they showed moderate antioxidant activities [162]. Iso-6-spectaline (14-[(2R, 3R, 6R)-

3-hydroxy-2-methylpiperidine]-tetradecan-13-one) (**93**) was isolated from ethanol leaf extracts and showed central nervous system (CNS) depressant and anticonvulsant activities [166]. Piperidine alkaloids; (-)-3-O-acetylspectaline (**92**) and iso-6-spectaline (**93**), have also been isolated from the flowers and fruits of the plant, and they possessed DNA damaging activities in *Saccharomyces cerevisiae* [162,167]. (-)-Cassine (**94**) has been isolated from the leaves, flowers, and fruits of this plant and possesses anti-inflammatory and antinociceptive activities [160].

Additionally, alkaloids; (-)-spectaline (**75**) and (-)-cassine (**94**) were isolated from ethanol extracts of the flower of *Senna spectabilis*, and they showed antiproliferative activity on HepG2 cells and antitumor activity against hepatocellular carcinoma cells [168]. (-)-spectaline (**75**) and (-)-cassine ((+)-3-O-feruloylcassine) (**91**) have also been reported to possess schistosomicidal activity against adult worms and cercaricidal activity [169]. Several anthraquinones have been isolated from this plant, including physcion (**76**) and 1,3,8-trihydroxy-2-methylanthraquinone (**95**), which were isolated from methanol leaf extracts of *Senna spectabilis* and showed antimicrobial activity against *Mycobacterium tuberculosis*, *Bacillus subtilis*, *Sarcina lutea*, *Staphylococcus albus*, and *Staphylococcus aureus*. Chrysophanol (**52**) and physcion (**76**) isolated from the plant possessed hepatoprotective, antimicrobial, and anticancer activities [161].



Cassia siamea Lam synonyms are *Senna siamea* Lam.; *Senna sumatrana* Roxb, *Cassia florida* Vahl, *Cassia arayatensis* Naves, *Cassia sumatrana* Roxb, *Cassia arborea* Macfad, *Cassia gigantea* DC., and *Sciaccassia siamea* Lam. It is widely spread in South Africa, East Africa, Brazil, Mexico, China, West Indies, and Asia [170]. The fruits prevent convulsion and expel intestinal worms [171,172]. The plant treats asthma and microbial infections [170]. Leaves treat stomach pains, malaria, constipation, sleeplessness, liver disorder, hypertension, cough, and toothache; the roots are used for diabetes mellitus, malaria, and snake bite; flowers and seeds are used to cure convulsion, typhoid fever, snake and scorpion bites while the stem is used against herpes, scabies, rhinitis, urogenital diseases, diabetes and as a laxative [173,174]. The plant is also used to reduce blood sugar levels and to treat abdominal pain, fever, typhoid, menstrual pain, and jaundice [175]. Compounds isolated from this plant include: cassiarin A (**96**) and cassiarin B (**97**), isolated from the methanol leaf extracts, and these compounds showed moderate *in vitro* antiplasmodial activity against *Plasmodium falciparum* [176]. Chrobisiamone A (**98**) has also been isolated from methanolic leaf extracts and possesses antiplasmodial activity [177].

Cassiarin A (**96**) and barakol (**99**) also showed vasorelaxant activity [178,179]. Barakol (**99**), isolated from this plant's ethanol flower extracts, also showed antioxidant activity [180,181]. Chrysophanol (**52**), physcion (**76**), betulinic acid (**85**), lupeol (**86**), and lupenone (**100**) are some of the compounds that have been elucidated from the methanol stem bark and showed anti-polio virus activity with lupeol possessing the most significant activity [182]. *Cassia mimosoides* L synonyms are *Chamaecrista mimosoides* L., *Chamaecrista nictitans* (L.) Moench, *Cassia aescynomene* D.C., *Cassia aspera* Muhl. ex Ell., *Cassia multipinnata* Pollard, *Cassia procumbens* Stickman, and *Cassia nictitans* Sickmann. It is native to China but has spread to different countries [183]. The leaves cure swelling of the legs during pregnancy; [184], facilitate urination, and act as an anti-inflammatory agent [183]. Roots treat colic pain, stomach spasms, and diarrhoea [185]. The plant also cures chronic hepatitis and other liver diseases, including liver cirrhosis and fibrosis [186]. Phytochemicals such as Emodin (**3**), Luteolin (**12**), Oleanolic Acid (**66**), β -Sitosterol (**101**), α -L-Rhamnase (**102**), and Carotene (**103**) have been isolated from this species, and showed anti-HMG-CoA reductase activity, with Emodin and luteolin showing the highest activity; an indication that the plant has potential in treating liver diseases.

Chrysophanol(**52**), an essential bioactive component of the plant, possesses blood lipid regulation, antidiabetic, anti-inflammatory, and anticancer activities, as well as alleviating metabolic disorders and obesity properties [187]. *Cassia occidentalis* L synonyms are *Senna occidentalis* (L.) Roxb, *Cassia caroliniana* Walter, *Cassia obliquifolia* Schrank, *Cassia ciliata* Raf, *Cassia planisiliqua* L, *Cassia falcate* L, *Cassia*

macradenia, *Cassia torosa* Cav, and *Ditrimexa occidentalis* (L.) Britt & Rose. It is distributed in Asia, South America, Australia, and Africa [188]. The plant treats diarrhoea and dysentery [189]. The leaves are used for throat infections, itching, and bone fractures. It also manages fever, anaemia, leprosy, tuberculosis, menstrual, and liver problems [190]. Moreover, the leaves and seeds are used for skin disorders such as eczemas and mycoses [191]. Additionally, the plant is used to treat cancer, eye inflammation, and venereal diseases [192]. The roots cure diabetes, elephantiasis, epilepsy, and convulsion [193,194].

The *C. occidentalis* isolates include 1, 3,8-trihydroxy-6-methyl-anthraquinone (Emodin) (**3**) and 4, 5-dihydroxy-9, 10-dioxo-4a, 9, 9a, 10- tetrahydro-anthracene-2-carboxylic acid (rhein) (**33**); isolated from alcoholic extracts (R-spirit) and found to possess antimicrobial activity on β -Lactum resistant strains of *Aspergillus niger*, *Pseudomonas aeruginosa*, *Aspergillus clavatus*, *Candida albicans*, *Escherichia coli*, *Streptococcus pyogenus*, and *Staphylococcus aureus* [195]. Chrysophanol (**52**) was isolated from the leaf extracts and showed wound healing activities [192]. *Cassia italica* Mill synonyms are *Senna italica* Mill, *Cassia obovata* Collad, and *Cassia aschrek* Fors., Its origin is in the equatorial region and surrounding areas [196]. The plant treats venereal diseases [197]. The roots are used for dysmenorrhoea, nausea, and liver problems, whereas the pods and the leaves are used for burns, skin diseases, and ulcers [198]. Leaves are used as hair conditioners, while roots are used to cure diarrhoea [199]. The whole plant is used as a urinary tract purifier and laxative, while its leaves, seeds, and pods are used as a purgative and also to treat elephantiasis and eye diseases [200]. Compounds isolated from the species is 2-methoxy-emodin-6-O- β -D-glucoopyranoside (**104**), which was isolated from DCM/MeOH (1:1) extract of aerial parts of the plant and possessed mild anticancer activity against hepatocellular carcinoma (HePG-2) and mammary gland breast cancer (MCF-7) [201].

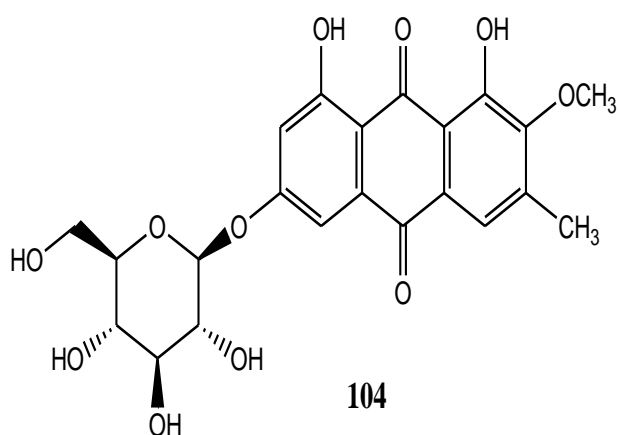
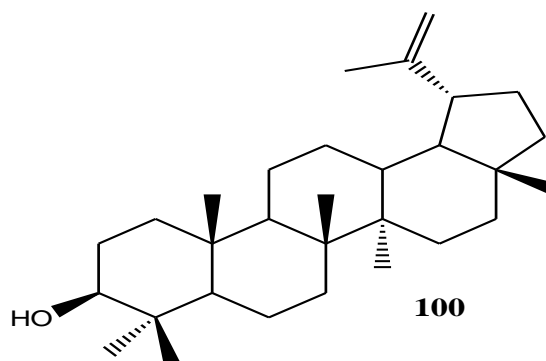
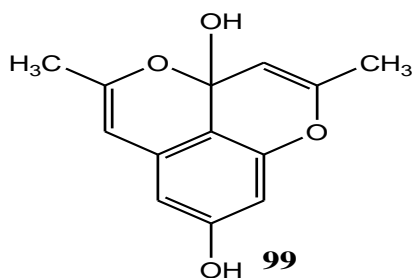
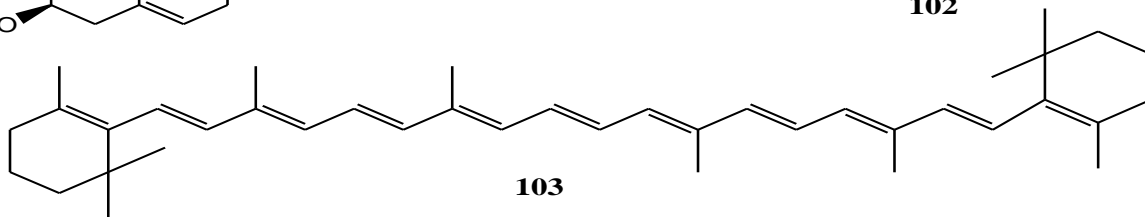
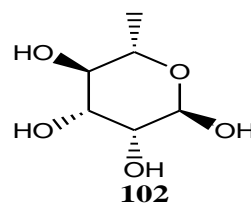
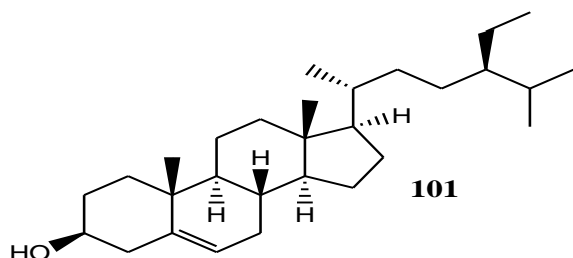
Cassia afrodistula Brenan synonyms are *Cassia beareana* Holmes and *Cassia kassneri* Bak. F. It is distributed in Madagascar, Mozambique, Tanzania, and Kenya [202]. The roots treat hernia and body weaknesses, while the stem is used for kidney diseases and liver pains [83]. The bark is used as an aphrodisiac and laxative. The bark also cures pneumonia, fever, stomach aches, backache, and blood pressure [203]. It is also used to manage uterine complaints, fever, malaria, syphilis, gonorrhoea, pneumonia, and snakebites [203]. No bioactive compounds have been reported from this species. *Cassia falcinella* Oliv synonym is *Chamaecrista afalcinella* Oliv. It is found in Kenya, Tanzania, Uganda, Rwanda, Namibia, Zambia, Zimbabwe, Mozambique, Botswana, and DR Congo [202]. The roots are used as an aphrodisiac and in treating gonorrhoea [204]. Its leaves are used to cure broken bones and rheumatism, while the roots are also used to treat diarrhoea [202]. Bioactive compounds have not *Cassia kirkii* Oliv synonym is *Chamaecrista kirkii* Oliv. It is widely spread in tropical and

subtropical Africa [205]. Leaves are used for upsetting pains [206]. The plant is used for skin diseases and fertility [207]. Bioactive compounds have not been isolated from this species.

Cassia leptocarpa Benth. Synonyms are *Senna hirsuta*

L, *Cassia caracasana* Jacq, *Cassia hirsuta* L, *Cassia tomentosa* L, *Cassia. longisiliqua* Blanco, *Cassia. venenifer* Rodsch. ex

G.Mey, *Cassia neglect* Vogel var. *acuminata* Benth, *Cassia pubescens* Jacq, and *Cassia gooddingii* A. Nelson. It is distributed in North, Central, South America, and tropical regions [208,209]. It is used to treat liver diseases, malaria, high blood pressure, diarrhoea, typhoid fever, and skin rashes and to reduce cholesterol levels [9,210]. Various compounds have been isolated from this plant; however, there is no literature report on their bioactivities.



CONCLUSION

The genus *Cassia* has been widely used in Chinese, Ayurveda, African, and South American folklore medicines to manage various ailments. Various studies have been done on their crude extracts, and isolated phytochemicals from different plant parts of individual species of this genus have been accomplished. It

has been established that several species have a wide range of bioactivities: antimalarial, larvicidal, antimicrobial, wound healing, laxative, antiasthmatic, hepatoprotective, antidiabetic, antiparasitic, antioxidant, analgesic, anti-inflammatory and anticancer. This makes the genus a hive under pharmacological research. Despite the genus portraying a lot of bioactivities, most of the compounds responsible for these bioactivities have not been entirely isolated and their activities verified. Additionally, studies on synergistic effects, toxicology, in vivo activities, and clinical trials on isolated compounds with biological potency have not been done effectively. Unfortunately, this has been a setback in discovering new drugs that could have solved drug resistance issues and side effects.

Regardless of all these challenges, some countries use dosage forms of *Cassia*, including *Senna*, under different brand names [12]. Some compounds isolated from *Cassia* species, such as sennosides, are currently being used as allopathic laxative medicine with a prescribed dosage, while others, such as ononitol monohydrate and chrysophanol, are still under clinical assessment as hepatoprotective agents. This indicates

the potential of the isolated compounds as leads for new drug discovery as most conventional drugs are currently unaffordable; hence, the genus *Cassia* species continues to serve communities as a cheap drug source. They are assumed to be safe even though many side effects have been reported from herbs, including interactions with allopathic medicines and herbs, preparations, contaminations, allergic reactions, transformed food consumption, distorted body and organ weights [211,212]. Hence, further toxicological studies, dosage determination, and regimes are imperative to avoid side effects and complicated conditions in these herbal preparations. It is expected that this review will stimulate more research for the elucidation and isolation of bioactive compounds from the genus leading to more new drug discoveries for the sake of humanity.

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