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# Bioactive compounds from ten species of the genus *Combretum*: Review

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**Abstract**
Medicinal plants contain bioactive compounds. These compounds are used to cure different diseases of humans and animals and they are also the starting points for modern drug development. Combretum is the largest and most widespread genus of Combretaceae. The genus comprises approximately 370 species distributed throughout tropical and subtropical Africa. With increasing chemical and pharmacological investigations, combretum has shown its potential as a source of various secondary metabolites like alkaloids, flavonoids, phenols, saponins, steroids and tannins in varying proportions. Combretum extracts or isolates of bioactive compounds have shown in vitro bioactivities such as antibacterial, antifungal, antihyperglycemic, cytotoxicity, anti-inflammatory, anti-snake, antimalarial, anticancer and antioxidant properties. The present review highlights about the chemistry of bioactive compounds isolated and identified from ten selected species of combretum.

**Keywords:** combretaceae, combretum, bioactive compounds, medicinal plants

## Introduction

The association of humans and animals with plants obviously originated with the beginning of life on earth. Plants supplied much of the shelter, oxygen, food and medicine needed by higher life forms. Overtime and with the beginning of societies, human learned to recognize and categorize plant materials suited for use in meeting the necessities of life. Of these necessities, the use of herbs and herbal extracts for their healing powers can be traced to earliest of myths, traditions and writings used to codify those plants that can ease pain and treat diseases [1].

According to WHO, about 70% of the world's population rely on plants for their primary health care and some 35,000-70,000 species has been used as medicines, a figure corresponding to 14-28% of the 250,000 plants species estimated to occur around the world [2-4] and equivalent to 35-70% of all species used worldwide [4]. From about 250,000 species of higher plants around the world, only 17% have been scholarly investigated for medical potential [5]. The chemical and biological diversity of plants represent a potentially limitless renewable source for the use in the development of new pharmaceuticals. Medicinal plants have been used since ancient times in virtually all cultures as a source of medicines [6], and are of great importance to the health of individuals and communities [7].

Some plants having the medicinal value in form of chemical substances that produce a definite physiological action on the human body are called phytochemicals. Since the ancient time these phytochemicals are used to cure the disease in herbal and homeopathic medicines. These arenon-nutritive substances, have protective or disease preventive property. There arises a need and therefore to screen medicinal plants for bioactive compounds as a basis for further biomedical studies. With advances in phytochemical techniques, several active principles of many medicinal plants have been isolated and introduced as valuable drug in modern systems of medicine. The most important of these bioactive compounds are alkaloids, flavonoids, tannins and phenolic compounds [8]. These are the important raw materials for drug production [9].

Most plants contain several compounds with antimicrobial properties for protection against aggressor agents, especially microorganisms [10]. At present 32% of drugs are introduced in to international markers which are plant origin [11]. The Ethiopian ecosystem is gifted by a wide range of ecological, edaphic, and climatic conditions that resulted in to wide diversity of its biological resources, both in form of flora and fauna wealth. Medicinal plants contain many essential secondary metabolites including bioactive compounds. In Ethiopia there are 600 species of medicinal plants which may contain disease-curing secondary metabolites which are distributed all over the country especially, in the south and south-western part of the country. The woodlands of Ethiopia are the source of most of the medicinal plants, followed by the montage grassland or dry montage forest complex of the plateau. Other important vegetation types for medicinal plants are the evergreen bush land and rocky areas. Most of them are confined and have been used as a source of traditional medicine to treat different human and livestock ailments [12-13].

The medicinal plants and products, minerals have been primary and important source of healthcare in fight against various health problems of the 85% of rural people including the poor in urban area [14-16]. The importance and role of these traditional healthcare systems will not diminish in the future because they are both culturally acceptable, safer to health and expected to remain affordable while the modern healthcare service is both limited and expensive [17-19].

The medicinal use of plants of the family *Combretaceae* is widely described in the scientific literature [20-22]. This family is distributed in approximately 20 genera with 600 species. The largest genera are *Combretum* and *Terminalia*, with about 370 and 200 species, respectively [23]. Members of the *Combretaceae* occur mainly in tropical and subtropical areas, for example, in Africa and Brazil [24].

Considerable attention has been given to screening of plant extracts for possible antimicrobial activity. Such endeavors

have been undertaken with the aim of isolating bioactive compounds as an alternative source to chemical synthesis [25]. In Brazil, around 80,000 species of higher plants were described which offer enormous prospects for discovery of new compounds with therapeutic properties [26].

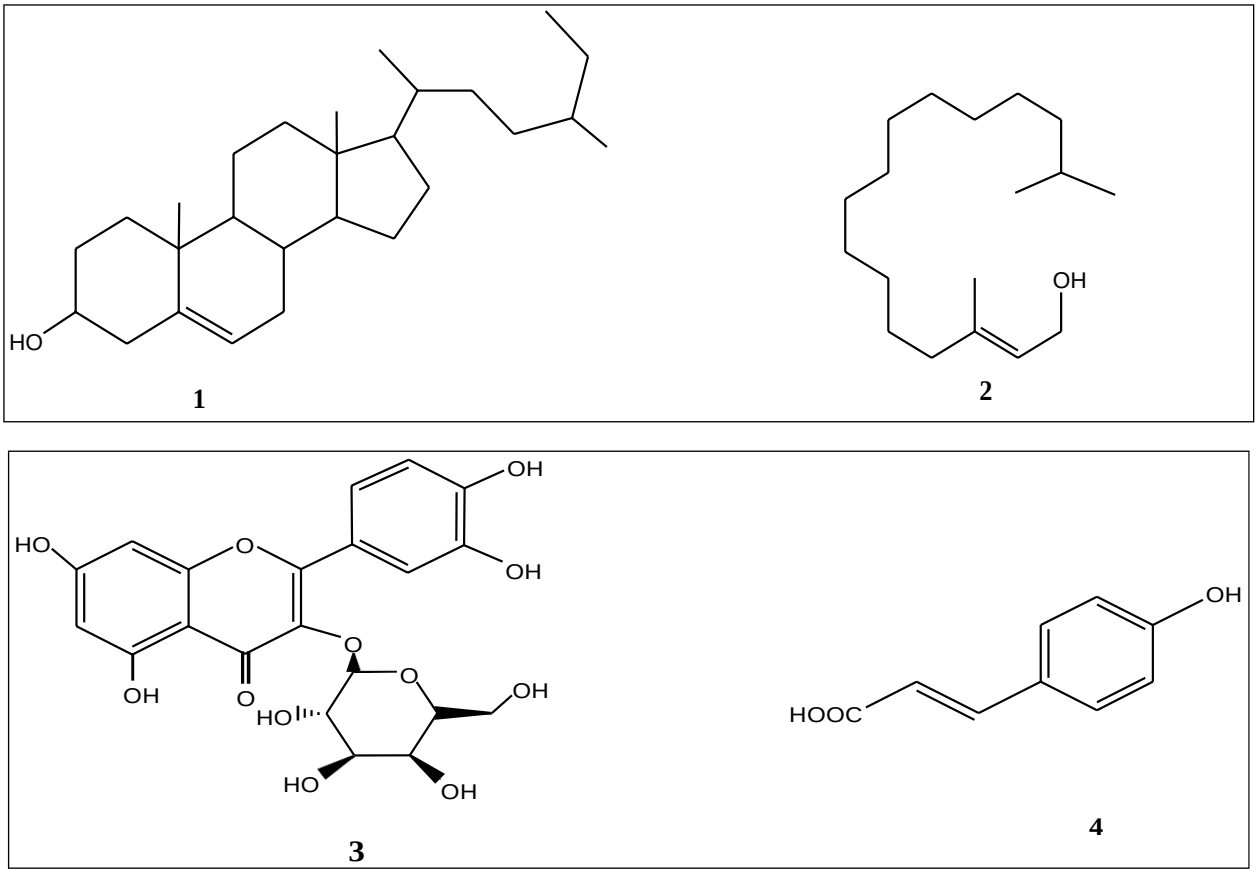
**The Genus of *Combretum***

The genus *Combretum* is the largest among genera of *Combretaceae*. The genus *Combretum* includes almost 370 species found all across Africa, many of which are widely used in African traditional medicine [27]. Several species of the genus have been reported for their biological activities. *Combretum* species are used in many cultures in folk medicine for treatment of microbial infections and several inflammatory conditions such as abdominal pains, headache and toothache [28-29]. Antimicrobial activity of many *Combretum* species has been confirmed [30-33]. Phytochemical studies carried out in the genus *Combretum* have demonstrated the occurrence of many classes of constituents, including triterpenes, flavonoids, alkaloids, saponins, stilbenoids, phenanthrenes, lignans and non-protein amino acids, among others [34].

**Results and Discussion**

***Combretum paniculatum***

*Combretum paniculatum* is a several-stemmed liana and can climb up and over adjacent vegetation to a height of 15 m or more and is widespread in tropical Africa. The foliage is dense, dark green and rather shiny and is not shed during winter. It is brilliant scarlet flowering resembles that of *Combretum microphyllum*. It is very showy shrub which grows over tall trees. It is seen growing in the warm, moist areas of Kaffa, Jimma, Wollega and Shewa Ethiopia, and flowers in January and February. The local name of this plant is “baggo” (Kafi Noono), “baggii” (Afaan Oromo) and “baye” (Amharic). According to the WHO, a variety of drugs are obtained from different medicinal plants and about 80% of the world’s developing population depends on traditional medicine for their primary health care needs. *Combretum paniculatum* has been used widely in ethnomedicine in the treatment of leprosy, chronic diarrhea, dysentery, flatulence, vomiting, colic, enlarges spleen and liver [35]. Isolation of active compounds from a 70% acetone extract of 40 grams of *C. paniculatum* leaf material was carried out using bioassay guided fractionation. The bioassay used to select the active fractions for further fractionation was an antibacterial assay since it is easier and more rapid to detect antibacterial activity than antiviral activity. Various techniques including column chromatography and HPLC were used to fractionate the extract to result in pure compounds. The isolated compounds were structurally elucidated by NMR and MS analysis. Nine compounds were identified from the leaves of *combretum paniculatum* as cholest-5-en-3-ol (1), 2-phyten-1-ol (2), quercitrin-3-glucopyranoside (3), p-coumaric acid (4), 2, 3, 8-tri-O-methylellagic acid (5), beta-sitosterol (6), gallocatechin (7), apigenin (8) and apigenin-7-glucoside (9) [36]. From *Combretum paniculatum* flowers, two diglucosylated derivatives from cyanidin and pelargonidin were identified (cyanidin 3, 5-O-*β*-D-diglu-copyranoside (10) and pelargonidin 3, 5-O-*β*-D-diglucopyranoside (11) (Figure 1) [37].



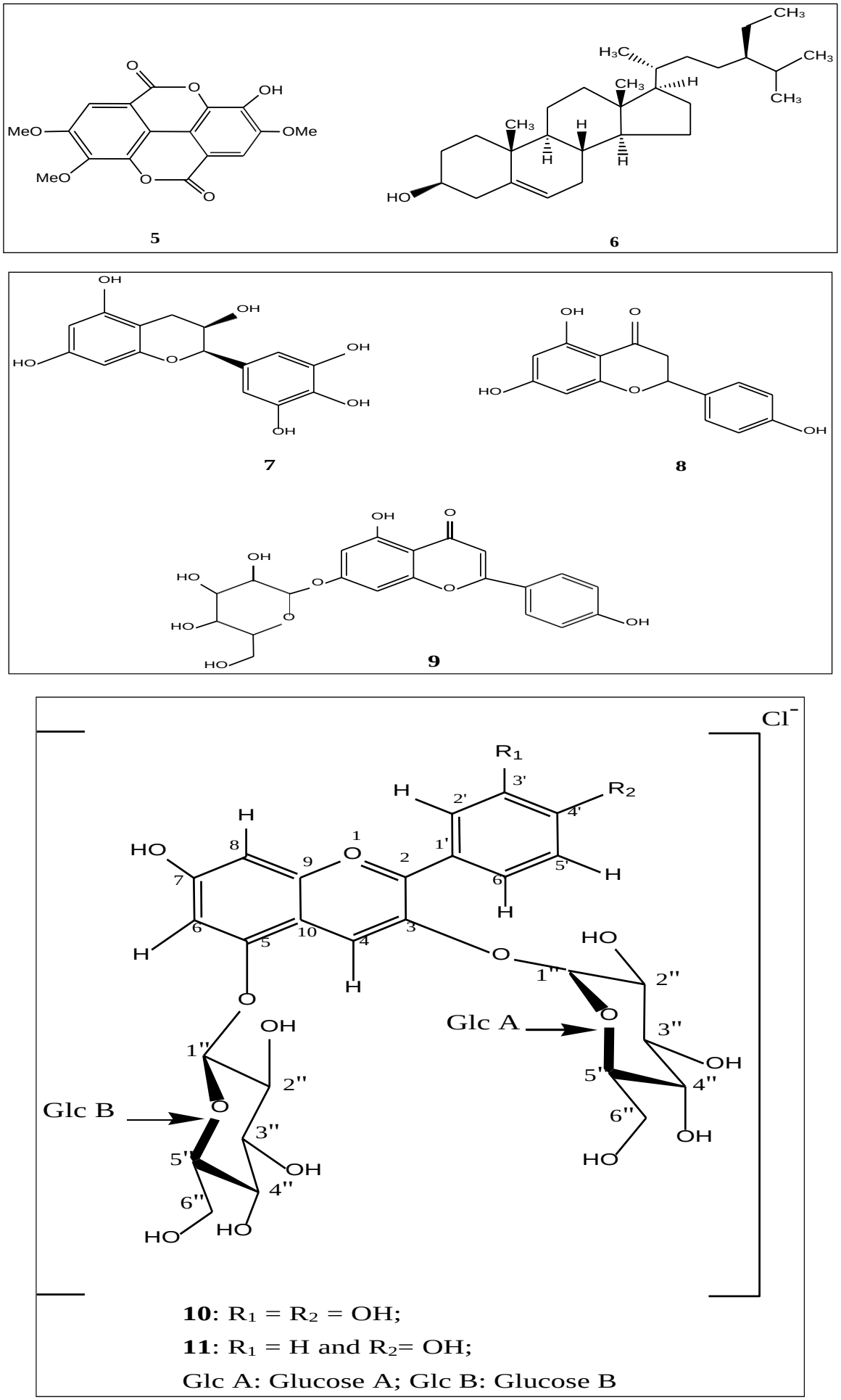



**Fig 1:** Bioactive compounds isolated from *Combretum paniculatum*

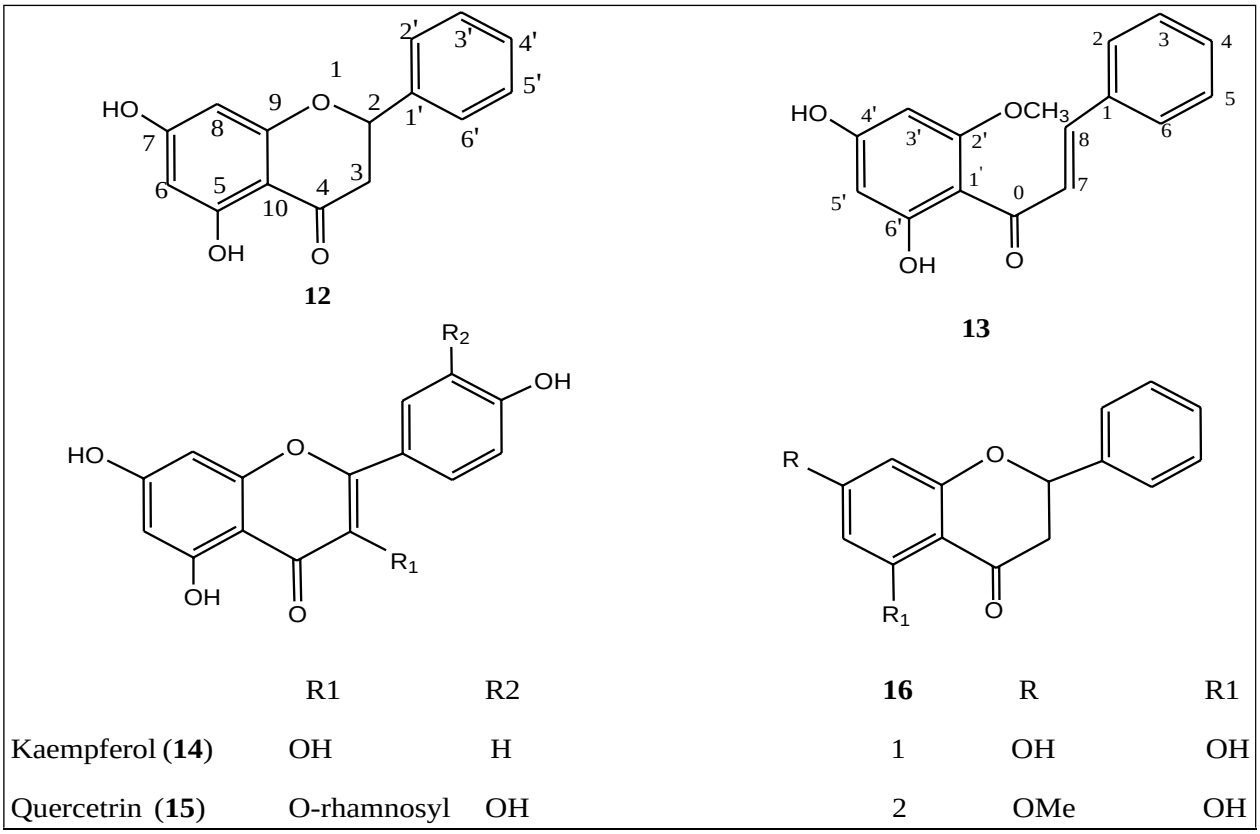
***Combretum apiculatum***

*Combretum apiculatum* is a species of tree in the family *Combretaceae* known by the common name red bush willow. It is native to the mesic to semi-arid savanna regions of Africa, southwards of the equator. It is an attractive, deciduous and small to medium-sized tree which occurs in various savanna regions, often at low altitudes and in rocky areas of well-drained soil. *C. apiculatum* is a single- or multi-stemmed small tree 3-10m high, with a short often curved trunk and spreading irregular canopy. The long slender branches hang low down, giving the tree a willow-like appearance. It grows in higher rainfall regions. The bark on the main stem is grey to dark grey or brownish grey and smooth becoming scaly and rough with age [38].

Its fruit pose a threat to livestock, especially the seeds which are poisonous but eaten by brown-headed parrots.

Medicinally, a decoction of the leaves has been used as a steam bath and as an enema to relieve stomach disorders. As treatment for conjunctivitis, an ash from the burnt stem is mixed with white clay and water and the resulting paste is spread over the face [39].

Leaf extracts of *Combretum apiculatum* subsp. *Apiculatum* had the most antioxidant compounds. This species was consequently selected for phytochemical investigation. A DPPH assay-directed fractionation of the leaf extracts of *C. apiculatum* led to the isolation of four antioxidant compounds from the ethyl acetate and butanol soluble fractions. The structures of the compounds were determined by spectroscopic analyses ($^{1}$H-NMR, $^{13}$C-NMR and MS) and identified as: cardamonin (12), pinocembrin (13), quercetrin (14), kaempferol (15), flavanones (16) (Figure 2) [40].




| | R1 | R2 | **16** | R | R1 |
|---|---|---|---|---|---|
| Kaempferol (**14**) | OH | H | 1 | OH | OH |
| Quercetrin (**15**) | O-rhamnosyl | OH | 2 | OMe | OH |

**Fig 2:** The structures of antioxidant compounds from *Combretum apiculatum*

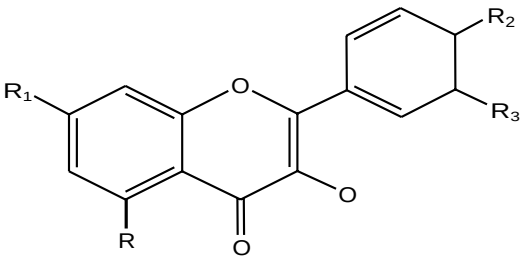
**Combretum *erythrophylum***

*Commbretum erythrophyllum*, commonly known as the river bush willow is a medium-sized to large, spreading tree found in bush along riverbanks in southern Africa. It is planted as a shade and ornamental tree in South Africa and the United States, and is propagated by seed. A medium to large tree 7-12m in height. Straight or multi-stemmed with dense spreading crown. The bark is a smooth pale gray or yellow brown that flakes with age to expose pale bark patches with large lumps which sometimes occur on older trunks and main branches.

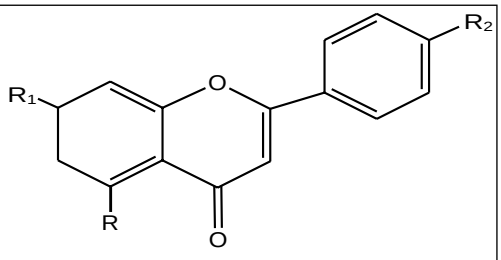
The coarse wood shows little distinction between sapwood and heartwood.

The roots (regarded as poisonous) are used as a purgative and to treat venereal diseases. The bark is mixed with other herbs to make a decoction that is drunk in the morning and evening, quarter of a cup for sores. The fruit are regarded as poisonous and reputedly cause hiccups [41]. Bioactivity directed fractionation of the leaf extracts of *C. erythrophyllum* led to the isolation of seven active compounds, four flavonols: rhamnocitrin (17), kaempferol (18), quercetrin-5, 3-dimethyl ether (19), rhamnazin (20) and three flavones: apigenin (21), genkwanin (22), 5-hydroxy-7, 4-dimethoxyflavone (23) (Martini *et al* 2004b) (Figure 4). All test compounds had good activity against *Vibrio cholera* and *E. faecalis*, with MIC values in the range of 25-50 µg/ml. Rhamnocitrin and quercetrin-5,3-dimethylether showed additional good activity (25 µg/ml) against *Micrococcus luteus* and *Shigellasonei*. Toxicity testing showed little or no toxicity towards human lymphocytes with the exception of 5- Hydroxy-7, 4-dimethoxyflavone.

This compound is potentially toxic to human cells and exhibited the poorest antioxidant activity. Both rhamnocitrin and rhamnazin exhibited strong antioxidant activity with potential anti-inflammatory activity. Although these flavonoids are known, it was the first report of biological activity with some of these compounds [42].




| Compound | R | $R_1$ | $R_2$ | $R_3$ |
|---|---|---|---|---|
| **17** | OH | $OCH_3$ | OH | H |
| **18** | OH | OH | OH | H |
| **19** | $OCH_3$ | OH | OH | $OCH_3$ |
| **20** | OH | $OCH_3$ | OH | $OCH_3$ |



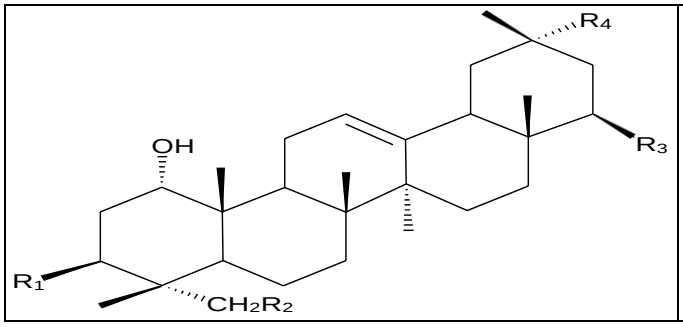

| Compound | R | $R_1$ | $R_2$ |
|---|---|---|---|
| **21** | OH | OH | OH |
| **22** | OH | $OCH_3$ | OH |
| **23** | OH | $OCH_3$ | $OCH_3$ |

**Fig 6:** Compounds isolated from *Combretum erythrophylum*

***Combretum imberbe***

*Combretum imberbe* is a medium to large semi-deciduous tree which grows up to 20m in height. It is the tallest of all the South African *combretum*. It has a spreading canopy and is extremely slow growing. The snakeskin-like bark is one of the main features that make identification easier throughout the season. Dead branches and shoots often remain on a matured tree. The colour of the trunk is pale grey to white. The leathery leaves are arranged opposite each other. The flowers are yellowish cream-colored and have a sweet fragrance. They are produced from November to March. The lead wood produces 4-winged fruit, which are yellowish green and turn pale red when mature from February to June. Parts of this tree are used by various tribes in a number of ways: smoke that comes from the burning leaves has been used to relieve coughs, colds and chest complaints. The flowers can also be used as a cough mixture. The leaves are believed to have magical powers. For treatment of diarrhoea and stomach pains, root decoctions are used. A combination of roots and leaves are taken against bilharzias. Root bark that is boiled in water is used for tanning leather. The gum that exudes from damaged areas on the stem is edible and forms part of the diet of the Bushmen. Leadwood ash is used as toothpaste. The wood is very hard and tough, and burns very slowly with intense heat. The tree has special cultural and religious importance to the Ovambo people of Nambia. The leaves and fruits are used in white magic [43].

A new pentacyclic triterpenoids and four known triterpenoids were reported as the antimicrobial constituents from the leaf extracts of *C. imberbe* (24-28). Two triterpenoids had an MIC of 93µg/ml compared to 63µg/ml for pentacyclic triterpenoids against *S. aureus*. Compound 5 (1α, 23-dihydroxy-12-oleanen-29-oic acid-3β-O-2, 4 diacetyl-L rhamnopyranoside) was (Figure 4) reported for the first time [44].




| Compounds | $R_1$ | $R_2$ | $R_3$ | $R_4$ |
|---|---|---|---|---|
| **24** | OH | H | H | COOH |
| **25** | H | H | H | COOH |
| **26** | H | H | =O | $CH_2OH$ |
| **27** | H | H | OH | COOH |
| **28** | 2, 4-Di-Ac-Rh | OH | H | COOH |

**Fig 4:** A new pentacyclic triterpenoid and four known triterpenoids isolated from *C. imberbe*

**Combretum *woodii***

*Combretum woodii* have 6-10m tall; young stems do not give as much the impression of trying to climb as in *C. kraussii*. Bark grey, smooth at first, later peeling in large sheets or splitting into small rectangular blocks. Leaves alternate to opposite, without stipules, apple green, younger leaves around flower spikes white, elliptical to obovate, dull, hairless, margins wavy and not rolled under, blade often curved upwards. Flowers typical of the genus, in short spikes surrounded by white leaves (October to November). Fruits 4-winged, relatively narrowly ellipsoidal, the wings also quite narrow, the whole yellowish green with a pink (not dark red) tinge. Trees grow slowly and the rarity of this species is debatable, as plants are inconspicuous in the forest except when in flower and more than a few almost inaccessible populations are not yet recorded. There are no reports on the uses of *C. woodii* in traditional medicine and some study suggests that leaves of this species might be used for the treatment of microbial infections in poor communities in South Africa [45].

Dried leaves of *C. woodii* were extracted with ten different solvents to determine the best extractant for subsequent

isolation and characterization of antibacterial compounds. Ethyl acetate was the best extractant with average MIC values of 0.08mg/ml for the four pathogens followed by acetone and DCM with values of 0.14mg/ml. The average MIC values for the positive controls were 0.13 mg/ml (ampicillin) and 0.12mg/ml (chloramphenicol). Acetone extracts of *C. woodii* leaf powder were separated by solvent/solvent partitioning into six fractions. The highest total activity was in the chloroform fraction. This fraction contained mainly one compound active against *Staphylococcus aureus*. This compound was isolated by bioassay-guided fractionation using silica gel open column chromatography and identified by NMR and MS as the stilbene 2, 3, 4-trihydroxyl-3, 5, 4- trimethoxybibenzyl (Combretastin B5) (29) previously isolated from the seeds of *C. kraussii*. It showed significant activity against *Staphylococcus aureus* with an MIC of 16µg/ml but lower activity towards *Pseudomonas aeruginosa* (125µg/ml), *Enterococcus faecalis* (125µg/ml), and slight activity against *Escherichia coli*. This is the first report of the antimicrobial activity of Combretastin B5. Its concentration in the leaves was in the order of 5-10 mg/g which makes the use of non-polar leaf extracts a viable proposition in treating some infections, particularly in resource-poor settings [46].

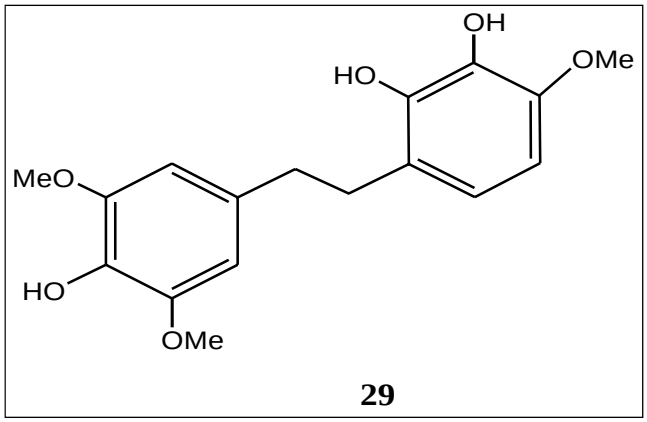



**Fig 5:** Combretastatin B5 isolated from *Combretum woodii*

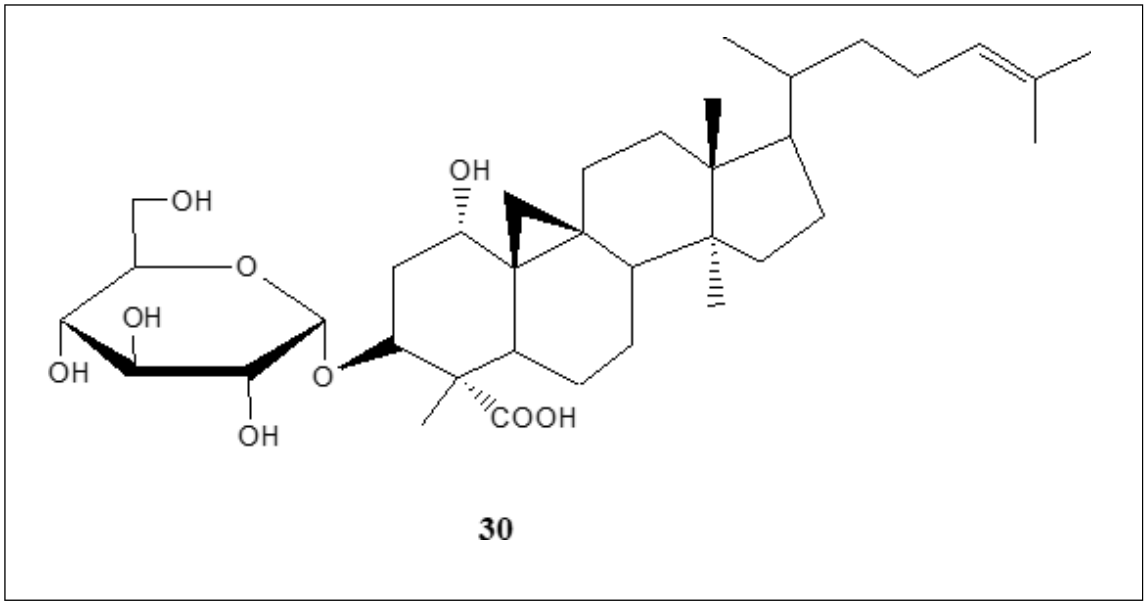
***Combretum molle***

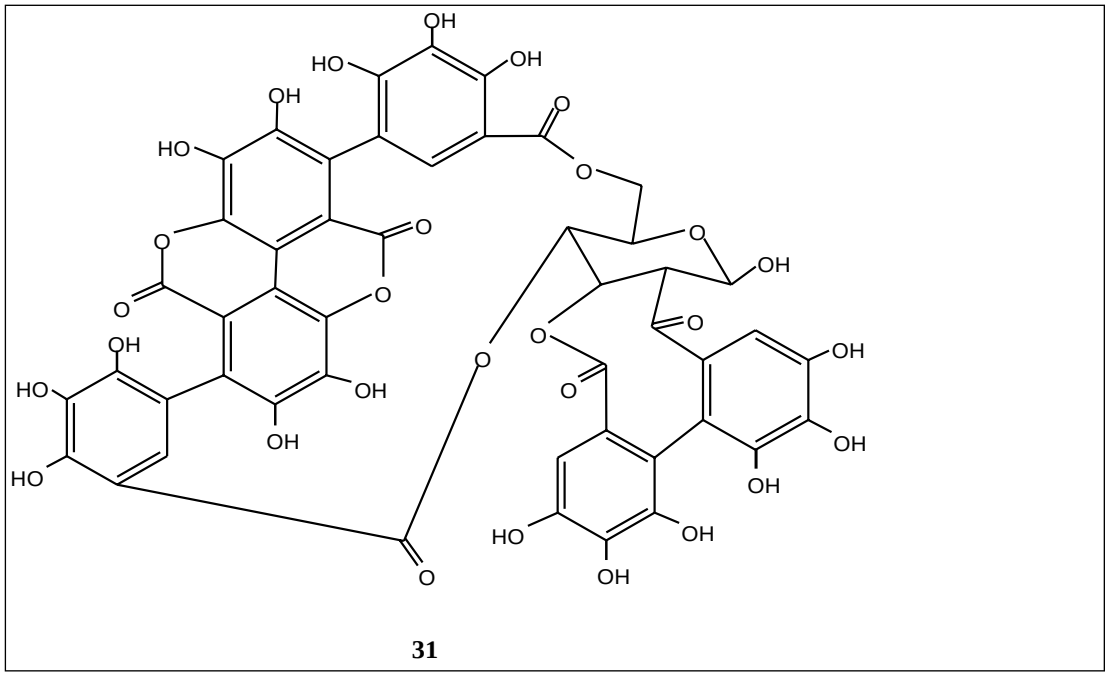
*Combretum molle* is soft-leaved *Combretum*, velvet bush willow which is a tree with a larger, straighter trunk compared to most species of *Combretum*, further distinguished by its rough bark and dense crown. It occurs throughout tropical Africa and in the Arabian Peninsula in areas where woodlands and wooded grasslands predominate, often forming pure stands on hillsides [47].

*C. molle* has been widely used as a medicinal plant to treat various diseases such as parasitic, protozoan and other infectious diseases in East [48-50] and West Africa [51]. Antibacterial studies have demonstrated its activity against *Staphylococcus aureus* and *Helicobacter pylori* at different extract concentrations [52-54].

Methanolic extracts of the roots and leaves (25µg/mL) of *C. molle* showed strong cytotoxic effects against T-24 bladder cancer cells [49]. In addition, the aqueous and methanol extracts of *C. molle* were screened for inhibitory effects against HIV-1 reverse transcriptase. These extracts produced relatively strong inhibition of RNA-dependent-DNA polymerase (RDDP) activity. In the case of compounds obtained from *C. molle*, the analgesic and anti-inflammatory properties of mollic acid glucoside from *C. molle* leaves have been investigated in mice and rats [55].

The result of in vivo activity of the plant extract indicates that MAG (30) possesses analgesic and anti-inflammatory effects in the mammalian models used. The author suggested that MAG possesses both centrally- and peripherally-mediated analgesic effects. *In vitro* anti-HIV activity of two isolated tannins from an acetone fraction, punicalgin (31) (Figure 6) and CM-A was assessed against human immunodeficiency virus type 1 (HIV-1) and type 2 (HIV-2). The results displayed selective inhibition of HIV-1 replication with selective indices (ratio of 50% cytotoxic concentration to 50% effective antiviral concentration) of 16 and 25, respectively and afforded complete cell protection against the virus-induced cytopathic effect when compared to control samples [24].





**31**

**Fig 6:** Compounds isolated from *combretum molle*

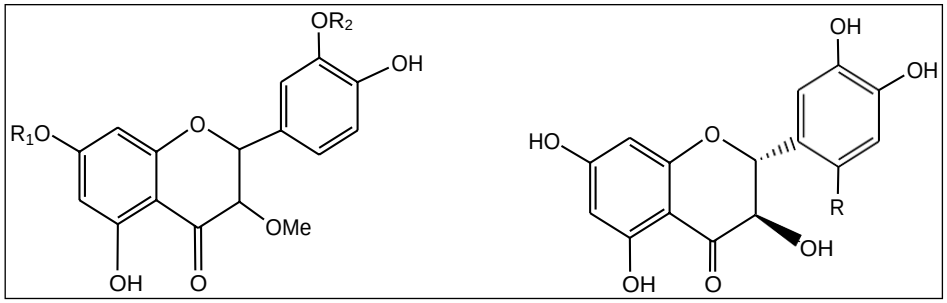
***Combretum quadrangulare***

*Combretum quadrangulare* is a small tree of the family *Combretaceae* which grows up to 10m in height. It grows in the wild or is planted in Vietnam, Cambodia, Laos, Myanmar, and Thailand. *Combretum* is planted along the banks of rivers or arroyos and is found throughout Thailand, especially in open, wet places. You rarely find it at the markets and it is mostly known locally. There is no supplier in the world offering *Combretum*, not even in origin countries, since farmers pick it for themselves. Therapeutic uses of this plant in the country are for anthelmintics (the parts used were seeds, roots and leaves) and curing venereal disease (the parts used are roots and wood). Studies of the chemical constituents of this plant have revealed that alcoholic and other extracts from the roots and seeds could kill earthworms. Extracts from seeds display antibacterial properties [56].

Chemical investigation of the leaves of *C. quadrangulare* resulted in the isolation and structural determination of flavonoids (figure 8). These compounds are kamatakenin (32), isokaempferide (33), 5, 7, 4-trihydroxy-3, 3-diethoxyflavone (34), 5, 4-dihydroxy-3, 7, 3-trimethoxyflavone (35), (+)-catechin (36) [57]. (+)-gallocatechin (37), (-)-epicatechin (38), (-)-epigallocatechin (39), vitexin (40) [58].

5,7,3,5-tetrahydroxy-3, 4-dimethoxyflavone (41), combretol(42), 3,5-dihydroxy-3,4,5,7-tetramethoxyflovone (44), quercetin-3,4-dimethyl ether (45), myricetin-3,3,4-trimethyl ether (46) [59].

A new gallic acid derivative such as *O*-galloyl-6-*O*-(4-hydroxy-3, 5-dimethoxy) benzoyl-*β* D-glucose (47) and the triterpenes of the lupane type, 2*α*, 6β-dihydroxybetulinic acid (48) and 6*β*-hydroxyhovenic acid (49) are also isolated from *C. quadrangulare* (Figure 7 [60].



**32** : $R_1 = CH_3$ $R_2 = H$

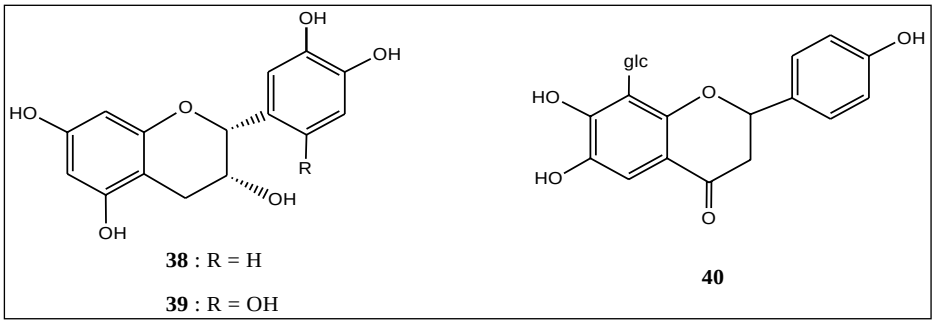
**33** : $R_1 = H$ $R_2 = H$

**34** : $R_1 = H$ $R_2 = CH_3$

**35** : $R_1 = CH_3$ $R_2 = CH_3$

**36** : R = H

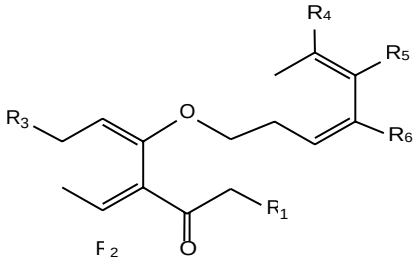
**37** : R = OH




**38** : R = H

**39** : R = OH

**40**



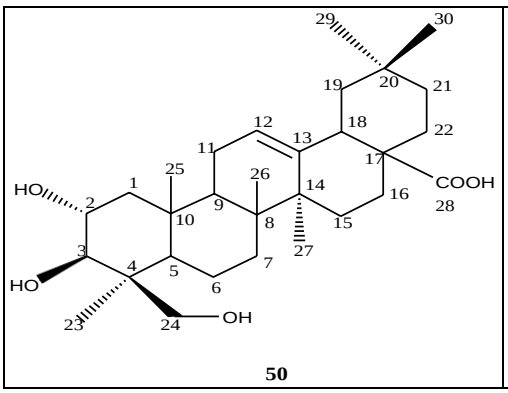

| | | | | | |
|---|---|---|---|---|---|
| **41** : $R_1$ = OMe | $R_2$ = OH | $R_3$ = OH | $R_4$ = OH | $R_5$ = OMe | $R_6$ = OH |
| **42** : $R_1$ = OMe | $R_2$ = OH | $R_3$ = OMe | $R_4$ = OMe | $R_5$ = OMe | $R_6$ = OMe |
| **43** : $R_1$ = OMe | $R_2$ = OH | $R_3$ = OMe | $R_4$ = OH | $R_5$ = OMe | $R_6$ = OMe |
| **44** : $R_1$ = OMe | $R_2$ = OH | $R_3$ = OMe | $R_4$ = OMe | $R_5$ = OH | $R_6$ = H |
| **45**: $R_1$ = OMe | $R_2$ = OH | $R_3$ = OH | $R_4$ = OH | $R_5$ = OMe | $R_6$ = H |
| **46** : $R_1$ = OMe | $R_2$ = OH | $R_3$ = OH | $R_4$ = OMe | $R_5$ = OMe | $R_6$ = OH |

**Fig 7:** Compounds isolated from *Combretum quadrangulare*

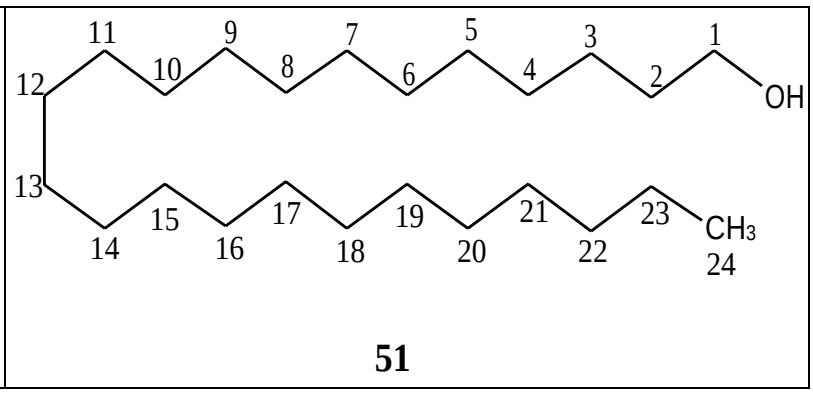
***Combretum microphyllum***

*Combretum microphyllum* is a robust, deciduous climber, sometimes a scrambling shrub or small tree. Masses of small flowers with bright red petals and long stamens form massed sprays which festoon the branches for about three weeks in spring (August to November) before the new leaves appear. The oval leaves are 13-60mm long and 13-50mm wide. The fruit is 4-winged, green tinged with red or pink when young, drying to pale yellowish brown (September to January). The root of this plant was used in traditional medicine by the Venda to expel a retained placenta. Tribes further north were reported as using the ash from the burnt root mixed with other ingredients to treat mental disorders. In recent years the dried fruit have become popular in the curio business, where they are used in flower arrangements [45].

Bioassay-guided liquid-liquid fractionation of the crude methanol extract of the dried leaves of *C. microphyllum* using column chromatography and determining antimutagenic activity yielded three compounds. The first compound was obtained as a powder, the second compound was obtained as a white powder and the third compound was obtained by repeated column chromatography purification until single spots were obtained in TLC. The compounds were identified as n-tetracosanol (50), eicosanoic acid (51) and arjunolic (52) acid using $^{1}H$ and $^{13}C$ NMR spectroscopic analysis (Figure 8) [61].




**50**




**51**

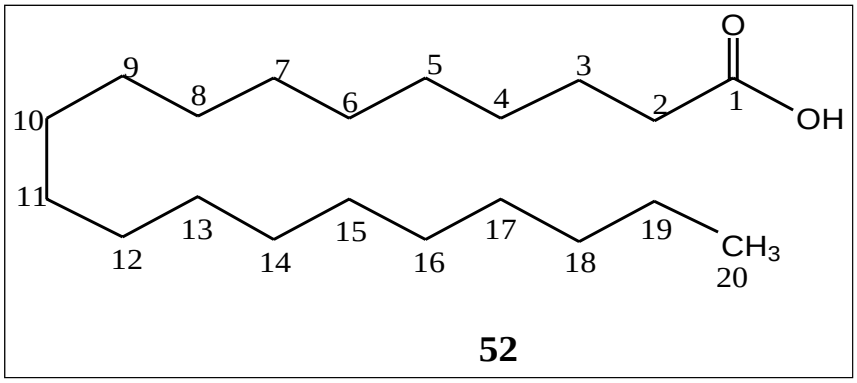



**Fig 8:** Antimutagenic compounds isolated from *Combretum microphyllum*

***Combretum zeyheri***

*Combretum zeyheri* is a deciduous or semi-deciduous tree of up to 10-15m high, with a rounded crown, branched and often with twisted trunks. Bark on younger stem is whitish and hairy; stems have prominently thickened nodes, smooth and flaking; small twigs are reddish and drooping. Leaves are simple, opposite, sometimes is whorls of three on young branches, elliptic to obovate. Young leaves are soft and hairy, rounded with broadly tapering tips and bases. The older leaves are typically larger, bigger than those of any other species of *Combretum*; they are approximately about 80 mm long and 40 mm wide. Margins are entire. Net veining is visible on both surfaces, yellowish green to light green and also with a yellowish autumn colour. The leaves of *C. zeyheri* have been used as herbal medicine and have been reported to have pharmacological activity which includes anti-bacterial, anti-fungal, anticancer and antioxidant properties. The gum of *C. zeyheri* has antibiotic properties. Pounded roots mixed with fats are used for an ointment to relieve haemorrhoids. Powdered roots are taken orally in porridge to stop a bleeding nose and to ease kidney pains. Leaves mixed with oil are used as an embrocation (liquid for rubbing on the body to relieve pain), to ease a stiff neck and backache. Crushed leaves are mixed with water and the resultant fluid is used as an eye lotion. Bark is used for treating gallstones [62].

A total of two pure compounds were isolated from C. *zeyheri* leaf extract. Antifungal compounds5-hydroxy-7, 4-dimethoxyflavone (53) and 3, 5, 7- trihydroxyl-3, 4-dimethoxyflavone (54) were found to be active against *Candida albicans* using broth dilution method (Figure 9). This compound was also found to have synergistic activity on growth of C. *albicans* when combined with miconazole, completely inhibiting growth after only 4 hours of incubation. Analysis of ergosterol content from *Candida albicans* showed a time-dependent decrease to 91% and 63% at 16 and 24 hours respectively, in cells treated with ½MIC of 5-hydroxy-7, 4- dimethoxyflavone. This compound also showed inhibition of both the drug efflux pumps (with IC50= 51.64µg/ml) and the antioxidant enzymes (at 5µM). It may be partly responsible for the reported antifungal activity of *C. zeyheri*, and may serve as a potential source of lead compounds that can be developed as antifungal phytomedicines [63].

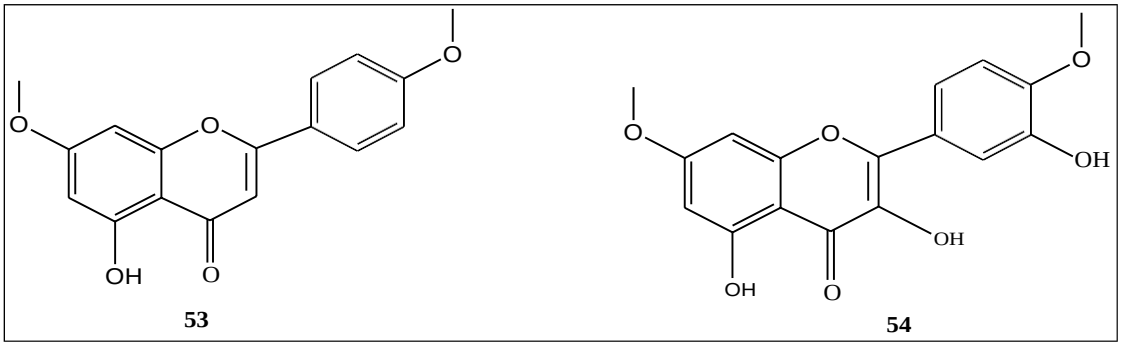



**Fig 9:** Antifungal compounds isolated from *Combretum zeyheri*

***Combretum indicum***

The common name of *Combretum indicum* is Rangoon creeper. *C. indicum* is a ligneous vine that can reach height from 2.5-8m long. The leaves of this plant are elliptical with an acuminate tip and a rounded base. This plant grow from 7-15cm and their arrangement is opposite in direction. The flowers of Rangoon creeper are tubular and fragrant with colour varies from white to pink to red. The fruit of Rangoon creeper is 30-35mm long which is ellipsoidal and it has five prominent wings in nature. The fruit tastes like almonds when it gets mature. The Rangoon creeper plant is used for various medicinal purposes as well as traditional and folk medicine. The roots of these plants are used to treat rheumatism and seed or fruit is used as potent against helmintic activity to expel parasitic worm from the human body. Fruit decoction can also used for gargling and are also used to combat the nephritis. Leaves of these plants are used in treating of relieving pain caused by fever. The juice from the leaves is used to heal boils and ulcers and to treat ringworm infection. The roots are used to relieve cough and hiccups. This plant is used to treat hyper lipidemia, bronchial asthma, abdominal distension, intestinal ascariasis, dandruff. The plant *C. indicum* is used to promoting growth of wild boar or domestic pig hybrid and it's also used to prevent downy mildew of black berry. The various chemical constituents were isolated from the various

parts of the plant *C. indicum* contain asquisqualic acid (55), arachidonic acid (56), linoleic acid (57), rutin (58) and methyl urasolate (59) (Figure 10). Furthermore the main compound of this plant quisqualic acid showed excitatory and anti-helmintic activity on various animal models. It causes various types of limbic seizures and neuronal necrosis [64].

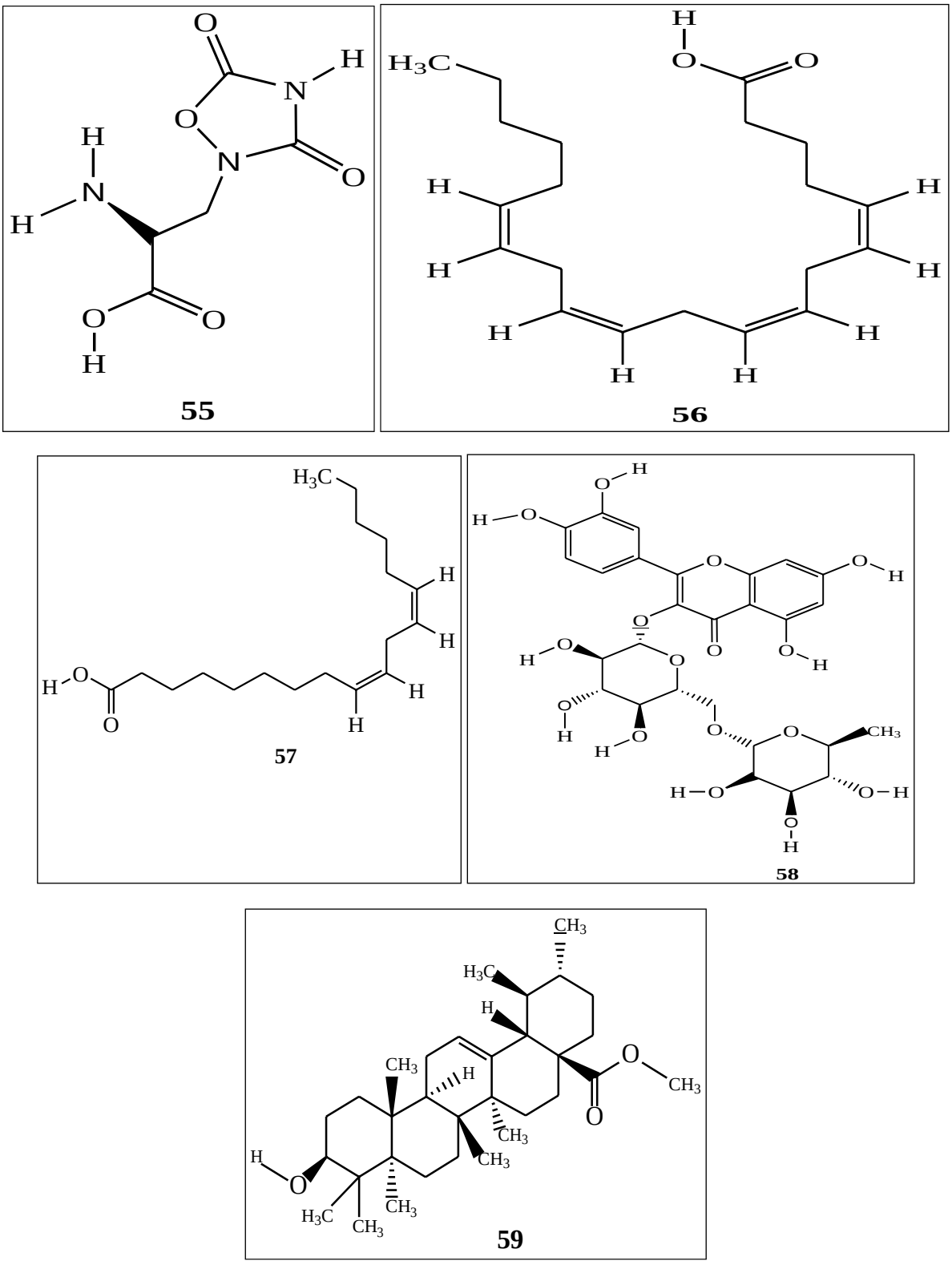



**Fig 10:** Compounds isolated from *Combretum indicum*

**Conclusion**

The genus *Combretum* includes almost 400 species found all across Africa, many of which are widely used in African traditional medicine. *Combretum* species are used in many cultures in folk medicine for treatment of microbial infections and several inflammatory conditions. *Combretum* has shown its potential as a source of various secondary metabolites like alkaloids, flavonoids, phenols, saponins, steroids and tannins. These secondary metabolites from the genus of *combretum* have been reported for their vitro

biological activities such as antibacterial, antifungal, antihyperglycemic, cytotoxicity, anti-inflammatory, anti-snake, antimalarial, anticancer and antioxidant properties. This review specially focuses on about the chemistry of biological active compounds isolated and identified from ten selected species of *combretum*.

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