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Ethnomedicinal application, phytochemistry and therapeutic effects of genus *clerodendrum*

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ABSTRACT

The genus *Clerodendrum* consist of flowering plants, which was once classified as a member of the Verbenaceae family, was recently classified as a member of the Lamiaceae family. Various species of this genus have been generally used for treating several ailments and disorders as well as ornamental plants. Secondary metabolites found in abundance in these species include terpenoids, saponins, carbohydrates, and glucosides as well as alkaloids, flavonoids, and phenolic compounds. Studies conducted so far have shown that the extracts and compounds of the species in this genus exert diverse physiological activities, including anti-inflammatory, anti-diabetic, antihypertensive, anti-allergic, analgesic, hepatoprotective, post-coital antifertility, antimicrobial, anticholinesterase, membrane stabilizing, antihelmitic, hypolipidemic, antitumor, and antimicrobial properties. Medicinal plants in this genus are beneficial, therefore they should be considered as lead in drug discovery and formulation.

Keywords: *Clerodendrum* species, Forkloric uses, Pharmacological application, Phytoconstituents**,** Therapeutics

Graphical Abstract: Analysed the information that has recently become available on the phytochemistry, ethnobotany, and biological activities of various species of *Clerodendrum*.

INTRODUCTION

The genus *Clerodendrum* consist of flowering plants that was once classified as a member of the Verbenaceae family but was recently classified as a member of the Lamiaceae family. Based on phylogenetic analysis of morphological and molecular data, it is currently categorized in the subfamily *Ajugoideae* and is one of the numerous taxa that were shifted from *Verbenaceae* to *Lamiaceae* in the 1990s. A genus of flowering plants in the family Lamiaceae is called *Clerodendrum* [1]. In traditional medicine, the species in the genus is used for a variety of purposes due to its antihypertensive, sedative, analgesic, and anti-inflammatory properties, according to pharmacological research [2,3]. The members of this genus thrive in tropical and warm temperate regions worldwide, with the highest concentration found in tropical Africa and southern Asia. However, there are also a few species that can be found in tropical Americas, northern Australia, and eastern Asia's temperate zone [4]. The estimated number of species has been put at anywhere between 150 and 450. This is partially due to the transfer of about 30 species to Rotheca, 30 more to Volkameria, and 1 to Ovieda [5].

They are small trees, lianas, and shrubs with opposite or whorled leave that typically reach heights of 1 to 12 meters (3 to 39 feet 4 inches). The height of *C. floribundum* can reach 30 m (98 ft). Ants live inside the hollow stems of *Clerodendrum myrmecophila* and *Clerodendrum fistulosum* [4]. *Clerodendrum trichotomum* is a typical ornamental plant found in warmer regions. Eight additional species are also cultivated in the tropics for their abundance of beautiful flowers [6]. One of them, *Clerodendrum macrostegium*, suckers profusely from the roots and frequently becomes a thicket in a few years [6]. Plants of the world online [7] recognized 258 species within this genus. Various species of the genus *Clerodendrum* have been generally used for treating several ailments and disorders as well as ornamental plants. The main objective of this review is to analyse the information that has recently become available on the phytochemistry, ethnobotany, and biological activities of various species of *Clerodendrum*. The publications published by Elsevier, Springer, Taylor and Francis, and some other trustworthy and pertinent English scientific sources (obtained through Scopus database, Google Scholar, and PubMed) were explored (between June and December, 2022) to gather the pertinent original research articles.

METHODOLOGY

The literature for this review paper was found using the search terms "Genus *Clerodendrum*," "*Clerodendrum* species' medicinal application," "pharmacology," "therapeutic uses," and "phytochemistry" in a variety of electronic sources, including Google, Google Scholar, PubMed, Medline, Research Gate, Web of Sciences, and SciFinder. The last access to these sources was made on December 15, 2022. To gather as much material as possible, the search terms were employed independently or in different combinations. To ensure that the results satisfied the requirements for inclusion, they were carefully assessed. For instance, the publications must be written in English and concentrate on ethnobotanical studies, the medicinal benefits of species in the genus *Clerodendrum*, pharmacological activity, and phytochemistry. Articles not fulfilling these criteria were excluded.

ETHNOMEDICINAL USES OF *CLERODENDRUM SPECIES*

Clerodendrum volubile P. Beauv.: *Clerodendrum* volubile P. Beauv. has garnered attention within the realm of medicinal flora due to its exceptional therapeutic properties, possibly owing to its multifaceted significance in traditional medicine and diverse nutritional qualities. It is widely distributed in the warm temperate and tropical regions of the world [8]. It is locally known as 'eweta' or 'marugbo' in Southwestern Nigeria. The leaves of this plant are widely used as a vegetable, often blended with other vegetables to add a sweet aroma and taste. In Nigeria and other West African countries, green leafy vegetables are typically cooked to enhance palatability and improve their edibility, as cooking is a common practice in the region [9].

Clerodendrum violaceum Gurke: *Clerodendrum violaceum* Gurke, commonly called *Clerodendrum* in English, in Southwestern Nigeria, is locally called "Ewe isedun". Leaf decoction is used for the treatment of malaria. It is, therefore, necessary to explore the antimalarial potentials of the *Clerodendrum violaceum* leaf extracts as a potential agent in the fight against malaria infection [10].

Clerodendrum splendens G. Don.: *Clerodendrum* splendens G. Don is a shrub that stands at a height of around 3.7 meters. Its foliage consists of uncomplicated, opposite leaves, displaying a rich, dark green hue. The plant is obtained in the wild and used locally as medicine. It is frequently planted as an ornamental. *Clerodendrum* splendens leaves have long been employed in traditional medicine by local inhabitants to alleviate a range of ailments including shingles, pediatric

spleen disorders, asthma, rheumatism, ulcers, and malaria [11].

Clerodendrum paniculatum L.: *Clerodendrum paniculatum L.*, commonly referred to as the pagoda flower, was initially documented by the Swedish botanist Linnaeus. The species epithet, 'paniculatum,' originates from the extensive clusters of flowers, termed 'panicles,' that characterize this species. It is often cultivated in gardens as an ornamental plant due its showy orange red to scarlet coloured flowers in terminal panicles. This shrub is widely distributed in Australia, China, Taiwan, Laos, Vietnam, Indonesia, India, Sri Lanka, Malaysia, Combodia, and many other Asian countries [12.13]. *Clerodendrum paniculatum* has been reported to have both ethnomedicinal and ornamental uses in some region of the world. In India, China, and Japan, it is traditionally used for treating ulcers, neuralgia, rheumatism, wounds, and inflammation. It is utilized as an antipyretic and anti-inflammatory drug in traditional Thai medicine. *Clerodendrum paniculatum* is used as ornaments in Lao People's Democratic Republic. It is also reported to be medicinal in Indonesia where it is used for treatment of sore eyes in Lombok [14,15]. *Clerodendrum paniculatum* is commonly used in herbal bath preparation by the Yunnanese group in Thailand. The Nicobarese of Nancowry group of Islands in Andaman and Nicobar also utilizes the plant traditionally in the management of body ache, snake bite, wounds, jaundice and giddiness [16].

Clerodendrum polycephalum Baker: *Clerodendrum polycephalum* Baker is a 4 m tall, erect, or scandent shrub or small tree that can be found in the nearby jungle and savannah. The leaves are decussate (whorled), sepals typically connate, and lobes are uneven. It is native to tropical and warm temperate regions globally, with the bulk of the species found in tropical Africa, South Asia, and a few extending north into the temperate zone in eastern Asia [17,18]. This species can also be found in Cameroun, Ghana, Sierra Leone, and Guinea to Southern Nigeria [18]. *C. polycephalum* has various therapeutic values. In Ivory Coast, people who experience dizziness, fainting, or epileptic seizures bathe their faces with the plant's leaf sap [19]. The Yoruba people of Nigeria usually call it "Aporo," which translates to "kills pain" and "as an antidote to venomous stings and bites." It has anti-inflammatory and antinociceptive properties [8]. It is also used as a pain reliever and in medications to treat convulsions, epilepsy, and paralysis [18].

Clerodendrum capitatum (Wild.) Schumach.: *Clerodendrum capitatum* (Wild.) Schumach. is an indigenous tropical plant that can reach heights of 0.5-2 m and grows fast, erect, with many branches, and with a perennial undershrub. The plant is generally known in Nigeria as a medical magical plant and is claimed to mend fractured bones [20], it is also well-known for managing local cases of type 2 diabetes, obesity, and hypertension [21].

Clerodendrum fragrans (Vent.) Wild.: *Clerodendrum fragrans (Vent.) Wild.* is a shrub that attains a height of around 2.5-3 meters. Its leaves, simple and opposite, are broad and oval, measuring between 6-25 cm in length and 5-25 cm in width. The flowers are of a delicate whitish-pink hue, with reddish-purple petals, each blossom spanning 10-15 mm in length. This plant is used traditionally for the treatment of febrifuge, incephalagia, ophthalmia, rheumatism, asthma, and other respiratory diseases [22].

Clerodendrum tricotomum Thunb: *Clerodendrum tricotomum* Thunb is commonly found in East Asia, including China, Taiwan, Korea, and Japan. Traditional medical practitioners have treated a variety of inflammatory conditions, headaches, and hypertension, with its leaves, blossoms, and twigs [23].

Clerodendrum bungei Steud.: *Clerodendrum bungei* Steud. is a shrub that grows one to two meters

tall and has an offensive odor [24]. It is extensively spread throughout much of China, except the northeast. The roots, stems, and leaves of *C. bungei* have also been used as herbal medicine in China to treat swelling, pain, and other conditions in addition to being utilized as an ornamental plant because of its lovely blossoms. The roots are particularly well-known ethnodrug called "Binliang" of the "Dai" people living in Yunnan Province [24].

Clerodendrum phlomidis L.: *Clerodendrum phlomidis* L. is employed in Ayurvedic medicine. It grows up to 9 m high and is a shrub or tree that can be found in Sri Lanka and India [25]. Some plant parts are used to treat conditions like dyspepsia, digestive issues, colic, cholera, dysentery, postpartum fever, and measles while a patient is recovering. Its bitter root and bark are used to cure neurological problems and sluggishness [26]. The herb has long been used to treat dysuria and urine retention. Its leaf extracts have hepatoprotective qualities. The leaf juice possessed anthelmintic and anti-diabetic effects [27].

Clerodendrum serratum (L.) Moon: Traditional medical systems like Ayurveda and Unani have suggested that the roots of *C. serratum* have therapeutic benefits. In English, it is frequently referred to as Blueglory or Beetle killer. Asthma, inflammatory, and viral illnesses have traditionally been treated with *C. serratum*, a traditional medication. Numerous investigations on the roots and formulations of *C. serratum* for their potential as an antiasthmatic in recent years validated the widespread interest in this plant. Numerous phytopharmacological research has been conducted on this plant to support the different traditional applications for it. The bulk of the investigations suggested that the plant's roots and leaves can be used to cure liver diseases, fever, inflammation, and respiratory disorders. Many ethnomedicinal reports have supported *C. serratum* as one of India's promising traditional medicines; it is used for the treatment of liver disease, wounds, snakebites, asthma fever, illnesses, and headache [28].

Clerodendrum viscosum Vent.: *Clerodendrum viscosum* extract was reportedly used in Ayurveda to treat leprosy, worm indigestion, itching, cough, and colds, as well as other ailments. Its leaf juice was particularly effective at treating scorpion stings. It was employed in the Unani system to treat rheumatism and as vermifuge [29]. Indian homeopathy is well known for its use in the treatment of fresh wounds, post-natal problems, and diarrhea [30]. The leaves can also be coated with edible oil and used as a fast pain reliever [31]. The tribal people of the Chotanagpur plateau in eastern India are said to employ numerous plant roots, stems, and leaves as medicines to treat conditions like asthma, cataracts, malaria, and blood, skin, and lung ailments. It is also known that its fresh leaves can be used as a vermifuge and in the preparation of conventional expectorant pills [32]. Similar uses have been documented for leaves and roots in Thailand, where they are used to cure kidney problems and intestinal infections [33]. The leaf juice is applied externally to treat tumors, skin conditions, snake bites, and scorpion stings in Bangladesh, where it is also used as a potent anthelmintic, emetic, moderate laxative, and cholagogue [34].

Clerodendrum myricoides (Hochst.) Vatke: *Clerodendrum myricoides* (Hochst.) Vatke is one of the traditional plants utilized in several regions of Ethiopia. *Clerodendrum myricoides* is a shrub with bluish flowers that has a long history of use in traditional medicine [35]. It is sometimes confused with Rotheca myricoides (Hochst.) Steane & Mabb. Traditional uses of the roots and leaves of Clerodendrum myricoides include treating conditions such as gonorrhea, rabies, measles, glandular tuberculosis, colic, eye diseases, malaria, body swellings, wound dressings, and asthma, as reported by Persson [36]. This herb is also used to cure toothaches, headaches, Qilensa, diuretic, general

malaise (mich), pneumonia, dry cough, and mental disorders [37]. In conventional medicine, it is used to treat cough, spleen enlargement, impotence, sterility, dysentery, diarrhea, and dysentery. Additionally, it has been used to treat cattle with East Coast fever [38].

Clerodendrum cyrtophyllum Turcz: *Clerodendrum cyrtophyllum* Turcz is a perennial herb widely spread in southern China, particularly around the Coast of Hainan Island, which is the most abundant wild source [39]. It primarily grows in tropical and subtropical climates. This herb has a good track record for treating a wide range of human illnesses, including colds, high fevers, throat inflammation, epidemic encephalitis, furuncles, rheumatoid arthritis, carbuncles, and snakebites [40].

Clerodendrum inerme (L.) Gaertn: *Clerodendrum inerme (L.) Gaertn*, a synonym of Volkameria inermis L., is found in the southern regions of China, India, and Southeast Asia, extending to Northern Oceania. Typically thriving on coastal beaches, it serves as a mangrove plant and is employed in coastal afforestation efforts. In combination with other plant leaves, the leaves of *C. inerme* are used in Indian tribal medicine to treat boils, skin rashes, coughs, and fevers. In local medicine, they are also employed to clean the uterus and treat umbilical cord infections. The leaf decoction is employed to alleviate inflammation and has demonstrated efficacy in treating bronchitis, headache, weakness, drowsiness, and digestive issues [41].

Clerodendrum chinense (Osbeck) Mabb.: *Clerodendrum chinense* (Osbeck) Mabb. is an upright, evergreen shrub with strong branches which can reach heights of two meters. The plant uses suckers to spread widely. The plant is collected in the wild and used locally as medicine. It is occasionally grown for medical purposes in China and Vietnam and is frequently planted as an ornamental, with the double-flowered but sterile type being the most popular [42].

Phytochemical screening of *Clerodendrum* species: Phytochemical analysis of Clerodendrum infortunatum root revealed the presence of carbohydrates, starch, mucilage, saponins, flavonoids, tannins, and phenolic compounds [43]. The quantification reveals that the plant's phenol content (64.35 mg/g) was the highest, followed by flavonoid (61.93 mg/g) and alkaloid (13.33 mg/g) [44]. *Clerodendrum* species (*C. inerme, C. peniculatum, C. philippinum, C. phlomidis, C. serratum*, and *C. villosum*) were found to contain glycosides, terpenoids, anthraquinones, flavonoids, saponins, tannins, lignin, phenol, and alkaloids [45].

Clerodendrum infortunatum methanol extract has been discovered to be high in sterols, terpenoids, alkaloids, carbohydrates, tannins, and glycosides [46]. *Clerodendrum philippinum* contains a variety of phytochemicals, including alkaloids, terpenoids, flavonoids, saponins, tannins, phenolics, and glycosides [47]. Carbohydrates, reducing sugar, hexose sugar, cardiac glycosides, saponins, tannins, and phenols were found in the hydroalcoholic extract of *Clerodendrum phlomidis* [48].

Secondary metabolites found in abundance in *Clerodendrum splendens* leaves include Terpenoids, Saponins, carbohydrates, and glucosides. It contains traces of alkaloids, flavonoids and phenolic compounds [49]. The Leaves of *C. colebrookianum* contain alkaloids, flavonoids, saponins, tannins, terpenoids, and steroids, but no anthraquinones [50]. In the pre- and post-flowering stages of *C. volubile*, preliminary phytochemical screening revealed the presence of flavonoids, saponins, tannins, cardiac glycosides, phenol, steroids, and alkaloids. There was no discernible difference in tannin levels between the two growth stages. However, the alkaloid, saponin, and phenol contents increased by 60.5 percent, 5.62 percent, and 660 percent, respectively, in the post-flowering stage in both growth stages. Flavonoid concentrations decreased by 26.2 percent after flowering [51]. Pre-flowering ash, protein, and fat levels were significantly higher, while post-flowering carbohydrate and fiber levels were

significantly higher. Manganese, Iron, Calcium, Potassium, and Magnesium content was significantly higher in the pre-flowering stage, with increases of 27%, 28%, 21%, 14%, and 17%, respectively, while phosphorous was not significantly different during either stage [51].

Many biologically active compounds, such as polyphenols, tannins, alkaloids, terpenoids, and glycosides, are abundant in *Clerodendrum phlomidis* leaf extract [52]. *Clerodendrum volubile* contained flavonoids (34.79 ± 0.37 mg/100 mg dry extract), alkaloids (36.73 ± 0.27 mg/100 mg dry extract), reducing sugars (07.78 ± 0.09 mg/100 mg dry extract), and cardiac glycosides (24.55 ± 0.12 mg/100 mg dry extract) [53].

PHYTOCONSTITUENTS

Clerodendrum splendens G. Don*:* The ethanol extract of the leaves yielded a flavonone diglycoside, 3',5',5-trihydroxy-4'-methoxy flavonone-7-*O*-*β*-*D* gluconopyranosyl methyl glucopyranose [54].

Clerodendrum glabum Meyer: From the hexane extract of *C. glabum* leaves, 3-(1-oxobutyl)-11-hydroxytaraxast-20(30)-ene-24,28-dioc acid (*Clerodendrum*ic acid) and heptadecanoic acid were isolated [55].

Clerodendrum fragrans Wild.: The leaf of *C. fragrans* contained *β*-sitosterol, clerosterol, daucosterol, caffeic acid, kaempferol, 5,4'-dihydroxy-kaempferol-7-*O*-beta-rutinoside, acteoside, and leucoseceptoside A [56].

Clerodendrum tricotomum (L.) Thunberg.: A bitter principle, clerodendrin A (a clerodon-skeletoned diterpene) was isolated from *C. tricotomum* [57]. Ley et al. [58] isolated jionoside D from *C. trichotomum* leaf. Acteoside, isoacteoside, methyl caffeate, 3,4-dihydroxyphenethyl alcohol, 3,4-dihydroxyphenethyl glucoside, chlorogenic acid, 3,4-dihydroxyphenylacetic acid, 3-(3,4-dihydroxyphenyl) alanine, 3,4-dihydroxyphenylamine hydrochloride, ferulic acid, and sinapic acid have also been isolated from the stem [59]. The isolation of three phenylpropanoid compounds was achieved through the chromatographic separation of methanol extract of *Clerodendrum trichotomum* leaves. These compounds are: *β*-(3′,4′-dihydroxyphenyl)ethyl-*O*-*α*-L-rhamnopyranosyl(1→3)-*β*-D-(4-*O*-caffeoyl)-glucopyranoside, acteoside (verbascoside), *β*-(3′,4′-dihydroxyphenyl)ethyl-*O*-*α*-L-rhamnopyranosyl(1→3)-*β*-*D*-(6-*O*-caffeoyl)-glucopyranoside, isoacteoside, *β*-(3′,4′-dihydroxyphenyl) ethyl-*O*-*α*-L-rhamnopyranosyl(1→3)-*β*-D-glucopyranoside, and decaffeoylacteoside [60]. Acteoside, leucosceptoside A, martynoside, acteoside isomer, and isomartynoside were isolated from *C. trichotomum* stem [61]. *Clerodendrum trichotomum* leaves and stems were used to isolate a new fatty acid, (5*E*,7*E*)-9-oxooctadeca-5,7-dienoic acid [62]. Ten compounds were isolated and identified from a petroleum ether extract of the leaves, including four triterpenes (lupeol, friedelin, betulinic acid, and taraxerol), four sterols (22-dehydroclerosterol, clerosterol, stigmasterol, and sitosterol), and one diterpenoid (transphytol) [63]. Five glycosides were isolated from the flowers: four phenylpropanoid glycosides and one monoterpene glycoside. The isolated compounds' structures were confirmed to be acteoside, martynoside, leucosceptoside A, isoacteoside, and neohancoside A [64].

Clerodendrum phlomidis L.: A glycoside, α-*L*-Rhamnopyranosyl-(1→2)-α-D-glycopyranosyl-7-O-naringin-4′-O-α-D-glycopyranoside-5-methyl ether and 2',4'-trihydroxyl-6'-methoxychalcone-4,4'-α-*D*-glycoside were isolated from the flower of *C. phlomidis* [65]. The presence of constituents such as 3,7,11,15-Tetramethyl-2-hexadecen-1-ol, 1-Octadecyne, 1-Octadecyne, Tetraacetyl-d-xylonic nitrile, n-Hexadecanoic acid, Nonadecanoic acid, 3-Decyn-2-ol, *Z,Z*-10,12-Hexadecadien-1-ol acetate, 2-Pentadecyn-1-ol, 19,19-Dimethyl-eicosa-8,11-dienoic acid, Silane, [[(3.beta.)-gorgost-5-en-3-yl]oxy]trimethyl, squalene, silane, [[(3.beta.)-gorgost-5-en-3-yl]oxy]trimethyl, Pseduosarsasapogenin-5,20-dien, (2s,3s)-(-)-3-

Propyloxiranemethanol were revealed by GC-MS analysis of *C. phlomidis* leaf [48].

Clerodendrum japonicum (Thunb.) Sweet: The chemical constituents isolated from ethanol extract of dried aerial parts of this plant includes: 7α-hydroxy syringaresinol, (-)-syringaresinol, (-)-medioresinol, 2″,3″-*O*-acetylmartyonside, 2″-*O*-acetyl-martyonside, martinoside, monoacetyl martinoside, cytochalasin O, 9-epi-blumenol B, (6*R*, 9*S*) and (6*R*,9*R*)-9-hydroxy-4-megastigmen-3-one, (6*R*,9*S*)-3-oxo-α-ionol, (-)-dehydrovomifoliol, megastigm-5-en-3,9-diol, (3*R*,6*E*,10*S*)-2,6,10-trimethyl-3-hydroxydodeca-6,11-diene-2,10-diol, (2*R*)-butylitaconic acid, 3-(3α-hydroxybutyl)-2,4,4-trimethylcyclohexa-2,5-dienone, and (-)-loliolide [66].

Clerodendrum bungei Steudel.: Beta-sitosterol, taraxerol, glochidone, glochidonol, and glochidiol were isolated from the whole plant [56]. Ten compounds isolated from a 95% aqueous ethanol extract of whole plant are 11,12,16*S*-trihydroxy-7-oxo-17(15→16),18(4→3)-diabeo-abieta-3,8,11,13-tetraen-18-oic acid, 12*S**,13*R**-dihydroxy-9-oxo-octadeca-10(*E*)-enoic acid, clerodenoside A, trichotomoside, glycosmisic acid, 4'-O-methylscutellarein, neroplomacrol, butylitaconic acid, hexylitaconic acid and *p*-hydroxybenzonic acid [67].

Clerodendrum infortunatum L.: Three pure compounds isolated from the leaves of *C. infortunatum* were identified as clerodin, 15-methoxy-14, 15-dihydroclerodin, and 15-hydroxy-14,15-dihyroclerodin [68]. This plant's GC-MS analysis revealed fourteen active compounds, including octadecatrienoic acid (3.864%), Ethyl 13-Methyl-Tetradecanoate (3.668 %), neophytadiene (3.372%), tridecanoic acid,12-methyl-Methyl ester (2.588%), methyl 11-Mrthyl-Dodecanoate (1.546%), Phenol,4-(-Methylpropyl) (1.422%), Bis (1,2,2-Trimethylpropyl) Methylphodhonate (1.285%), Benzofuran,2,3-Dihydro (0.909%), Phosphinothioic fluoride (0.883%), Imidazole,4-fluro- (0.604%), Oleic acid (0.595%), 3,7,11,15-Tetramethyl-2-Hexadecen-1-ol (0.456%), 4-cyclopentene-1,3-dione (0.441 %), and Cyclobutanethiol (0.373%) [69]. Limonene, catechol, p-vinylguaiacol, 5,8,11-eicosatriynoic acid, stigmasterol, desulphosinigrin, guaiacol, tyrosol, vaccenic acid, hexadecanoic acid, phytol, betulin, hydroxymethylfurfural, vitamin D; eugenol (phenol, 2,6-dimethoxy-4-(2-propenyl)); cinnamic acid (hydrocinnamic acid; vanillic acid, phytol, 6-oxa-bicyclo [3.1.0] hexan-3-one, 2-myristynoyl pantetheine, 2-methoxy-4-vinylphenol, desulphosinigrin, 4-((1E)-3-Hydroxy-1-propenyl)-2-methoxyphenol, hexadecanoic acid and ascorbic acid have also been reported different parts of *C. infortunatum* [70].

Saponin, alkyl sterols, and enzymes have been found in the plant's leaves as well as 2, -(3,4-dehydroxyphenyl)-ethanol-L-O-α-2-rhamnopyranosyl-(1→3)-*β*-D-(4-O-caffeoyl)-glycolpyranoside (acetoside). The leaves also contain a fixed oil comprising glycerides of linoleic, oleic, stearic, and lignoceric acid. Luperol, *β*-sitosterol, and Clerosterol are the chemical compounds isolated from the roots. Clerosterol was identified as 5, 25- sigmastadien-3*β*-ol, Clerodolone as lup-20(30)-en-3*β*-diol-12-one and clerodone as 3*β*-hydroxylupan-12-one and a steroidal glycoside. Three compounds identified as clerodin, 15-methoxy-14, 15-dihydroclerodin and 15-hydroxy-14,15-dihydroclerodin from this plant have been reported. Furthermore, phenolic (acetoside, fumaric acid, methyl, and ethyl esters of caffeic acid, and so on), flavonoids (Apigenin, acacetin, and methyl esters of acacetin-7-0-glucuronide, cabruvin, quercetin, scutellaren, scutellarein-7-0-*β*-*D*-glucuronide, and hispidulin), Steroids (Clerodolone, Clerodone, Clerodol and a sterol Clerosterol) and Clerodin have also been isolated [22].

Clerodendrum paniculatum L.: The root of this plant contains rutin, quercetin, *β*-sitosterol, *β*-amyrin, lupeol, oleanolic aldehyde acetate, stigmasta-4,25-dien-3-one and (3)-stigmasta-4,22,25-trien-3-ol [16].

Clerodendrum chinense (Osbeck) Mabb.: The methanol extract of *C. chinense* yielded (22E, 24S)-stigmasta-4,22,25-trien-3-one, 7,8,4'-trihydroxyflavone-6-O-*β*-D-glucuronopyranoside, 14,15-dihydro-15ξ-hydroxyclerodendrin A, 2α-acetoxy-14,15-dihydro-15ξ-hydroxyclerodendrin A and 2α-acetoxy-14,15-dihydro-15ξ-methoxyclerodendrin A [71].

Clerodendrum inerme (L.) Geartn.: *Clerodendrum inerme* is rich in apigenin, apigenin-7-0-glucoside, luteolin, luteolin-7-0-glucoside, kaempferol, and scopoletin [72]. Phytochemicals isolated from the aerial parts include B-friedoolean-5-ene-3-b-ol, b-sitosterol, stigmasta-5,22,25-trien-3-b-ol, betulinic acid, and 5-hydroxy-6,7,40-trimethoxyflavone [73]. Apigenin, scutallarin, and pectinolinergenin were also discovered in alcohol fraction of this plant [74]. A tetraterpenoid (*β*-carotene), two phytosterols (22-dehydroclerosterol and 22-dehydroclerosterol-3-O-*β*-D-glucoside), a flavonoid (4'-methyl scutellarein), a diterpenoid (clerodermic acid), and a phenylpropanoid glycoside (verbascoside) were found in the ethanol extract of the whole plant [75].

Clerodendrum serratum (L.) Moon.: Leaves of this plant yielded racemosol (22*E*, 24*ξ*)-24-*n*-propylchlosest-7,22-diene-3*β*-ol, apigenin, 15,18-dihydroxy-8,13*Z*-dienelabdan-8-aldehyde [76]. Serratin as well as lupeol were isolated from the essential oil [77].

Clerodendrum brachyanthum Schauer: Eudesmin, syringaresinol dimethyl ether, kusaginin, and Brachynoside were isolated from the leaves's ethanol extract as well as 2-(3,4-dimethoxyphenyl) ethyl-3-*O*-α-L-rhamnopyranosyl-4-*O*-(3,4-dihydroxycinnamoyl)-*β*-*D*-glucopyranoside [78]

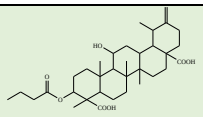
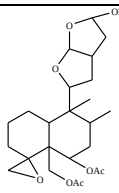
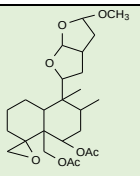
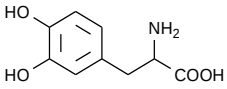
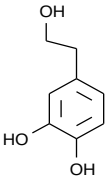
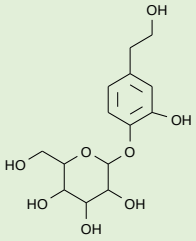
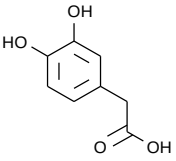
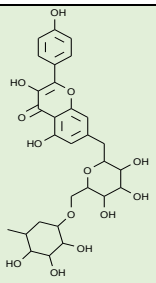
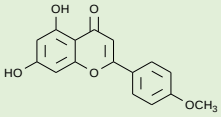
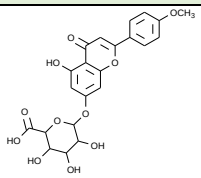
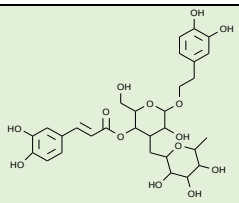
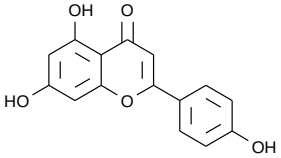
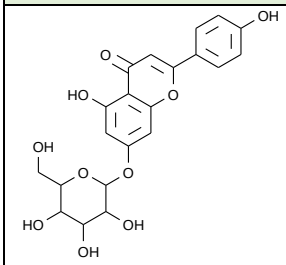
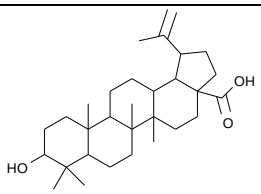
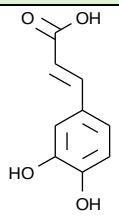
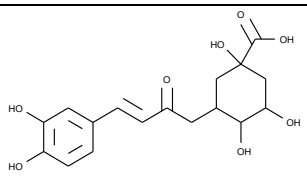
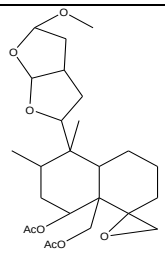
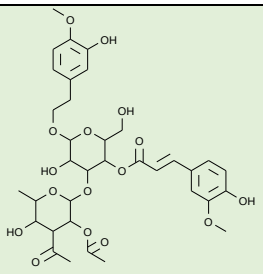
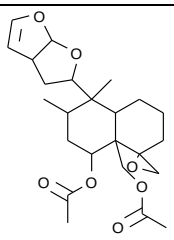
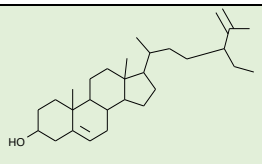
Clerodendrum calamitosum L.: Purpurin 7 dimethyl ester, Pheophorbide A, and (10*S*)-Hydroxypheophorbide A were isolated from the leaves and stems, as were three pheophorbide-related compounds [79].

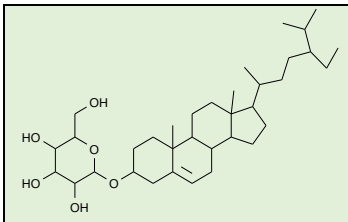
Clerodendrum cyrtophyllum Turcz.: Methyl (10*S*)-hydroxypheophorbide A and the known (10*S*)-hydroxypheophytin A were also isolated from the leaves [79]. The stem yielded two glycosidated coumaramides, clerodendiod A and B [80].

Clerodendrum viscosum Vent.: Some flavonoids, such as apigenin, acacetin, quercetin, scutellarin, hispidulin-7-*O*-glucuronide, cabruvin, as well as terpenoids like clerodin, phenolic compounds like fumeric acid, stearic acid, and caffeic acid, anthraquinones, and alkaloids, have been found in *C. viscosum*. Steroids such as clerodolone, clerodone, clerodol, and clerosterol have been isolated from root extracts of this plant [81,82]. Aside from steroids, a few compounds have been isolated from different parts of this plant, including scutellarin, hispidulin-7-0-glucuronide [83], apigenin, acacetin [84], viscosene [85], and saponin [86].

Clerodendrum myricoides (Hochst.) R. Br. ex Vatke: The root back yielded two new iridoid glycosides, myricoidoside A and myricoidoside B, as well as euphroside and 7-*O*-cinnamoyl-5-hydroxygardaloside [87].

Pharmacological activities of *Clerodendrum* species: Researchers have been driven to explore the pharmacological properties of the Clerodendrum genus and confirm the efficacy of various species as therapeutic remedies, aligning with the extensive clinical applications of traditional Chinese medicine. Multiple studies have shown that extracts or active ingredients from Clerodendrum species exhibit a diverse range of pharmacological activities. Some pharmacological activities of these species are presented in Table 1 while the mechanism of action of the selected *Clerodendrum* species found in literature is presented in Table 2.

 3-(1-oxobutyl)-11-hydroxytaraxast-20(30)-ene-24,28-dioc acid (clerodendrumic acid)	 15-hydroxy-14,15-dihyroclerodin	 15-methoxy-14,15-dihyroclerodin	 3-(3,4-dihydroxyphenyl) alanine
 3,4-dihydroxyphenethyi alcohol	 3,4-dihydroxyphenethyl glucose	 3,4-dihydroxyphenylacetic acid	 5,4'-dihydroxy-kaempferol-7-O-beta-rutinoside
 Acacetin	 Acacetin-7-0-glucuronide	 Acteoside	 Apigenin
 Apigenin-7-0-glucoside	 Betulinic acid	 Caffeic acid	 Chlorogenic acid
 Clerodinin A	 Clerodenoside A	 Clerodin	 Clerosterol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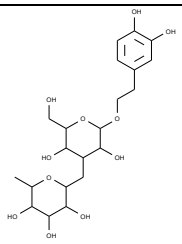
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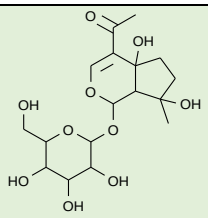
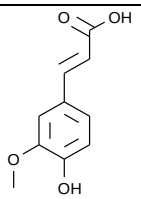

Euphroside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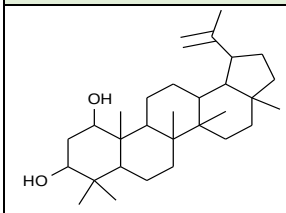
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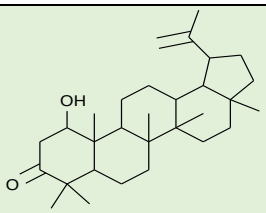
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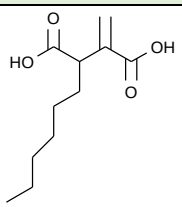
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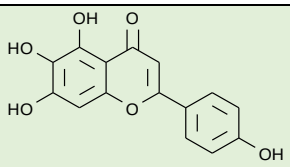
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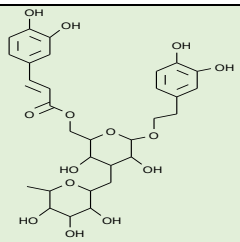
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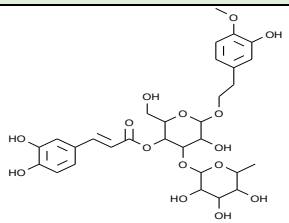
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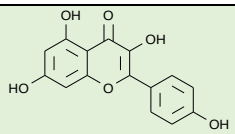
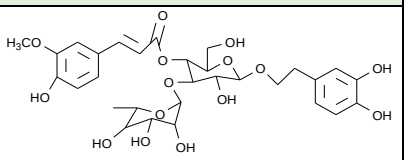

Kaempferol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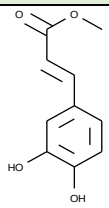
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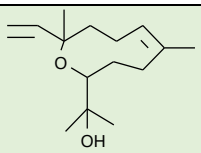
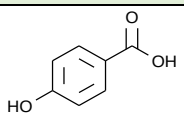

3,10-epoxy-3,7,11-trimethyldodeca-1,6-dien-11-ol (neroplomacrol)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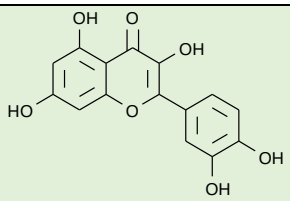
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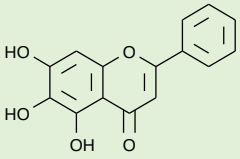
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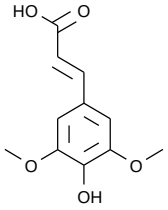
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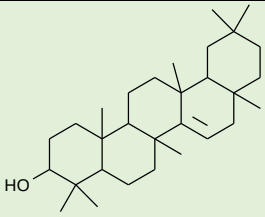
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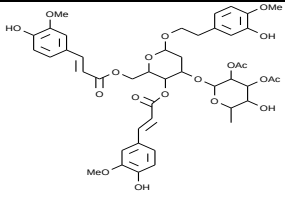
2-(3-hydroxy-4-methoxyphenyl) ethyl 3-0-(2,3-di-O-acetyl-alpha-L-rhamnopyanosyl)-4-0-[(2E)-3-(3-hydroxy-4-methoxyphenyl) prop-2-enoyl]-?-D-glucopyranoside (Trichotomoside)

Figure 1: Chemical structures of compounds from *Clerodendrum* Species

Table 1: Pharmacological investigation of some *Clerodendrum* species

***Clerodendrum* Species**	**Pharmacological activity**	**Tested substance**	**Study model (type of study, duration, standard control)**	**Dose range (route of administration)**	**Efficacy (dosage/ outcome)**	**References**
C. serratum	Anti-allergic activity	Aqueous extract of roots and stems	Milk induced leucocytosis in mice.	Low dose (90 mg/kg) and high dose (180 mg/kg) of root and stem	180 mg/kg	[88]
	Analgesic activity	Ethanolic extract of leaves	Tail flick test (*in vivo*, 7 days, diclofenac sodium 3 mg/kg) Acetic acid induced writhing test (in vivo, 30 min, diclofenac sodium 3 mg/kg)	250 and 500 mg /kg	500 mg/kg	[89]
	Anticancer activity	Methanolic extract	DMBA induced carcinogenicity in Testis, kidney and liver of mice	300, 600, 900 mg/kg, Oral	900 mg/kg	[90]
	Hepatoprotective activity	Aqueous and alcohol extract of root	Rifampicin induced hepatotoxicity in rats (*in vivo,* 10 days, silymarin, (25 mg/kg))	200 mg/kg, Oral	200 mg/kg	[91]
	Anti-inflammatory activity	Aqueous extract of the roots	Rats' granuloma pouch method (*in vivo* 10 days, dexamethasone (0.36 mg/kg))	Low dose (90 mg/kg) and high dose (180 mg/kg), Interperitoneal	180 mg/kg	[88]
***C. chinense* (Osbeck) Mabberley**	Anti-inflammatory activity	Methanol extract of leaves	Carrageenan paw edema test on rat (100 mg/kg) oral	Verbascoside showed significant activity at 25mg/kg after 4h of treatment	77- 89 % activity	[92]
	Analgesic activity		Electrical stimulation of rats' tail using a 515 Master Shocker	100 mg/kg body weight of methanol extract and verascoside (25 mg/kg) showed significant analgesic activities	74-89% after 1 h and 61-73 % after 2h	
***C. infortunatum* L.**	*in vitro* cytotoxic activity	Methanolic extract of leaves	Ehrlich's ascites carcinoma (EAC) in Swiss albino mice	50-500 µg/mL	A reduction in tumor cell volume and an increase in the lifespan of mice.	[93]
	Antibacterial activity	Ethanolic extract of leaf	Disc diffusion and MIC determination method against E. coli, Proteus vulgaris, Bacillus subtilis, Staphylococcus aureus	500 mcg/mL	Ethanolic extract showed significant inhibitory activity with zone of inhibition compared to tetracycline, standard drug	[94]
	Antifungal activity	*n*-hexane, Chloroform, ethyl acetate, ethanol extract of the Leaf	Disc diffusion method using *A. niger, A. flavus*	50, 75, 100 mg/mL	Chloroform extract showed a significant zone of inhibition with a diameter of 10.83 mm	[95]
		Ethanolic extract of the leaf	Disc diffusion method using, *A. niger, A. flavus, F. oxysporum, P. chrysogenum,*	-----	Extract exhibited a significant zone of inhibition against *A. niger* (14.67 mm) a*nd F. oxysporum* (13.00 mm)	[96]

			T. mentagrophytes		respectively	
	Antidiabetic activity	leaf	α-Amylase inhibition assay	Starch-iodine method: 25µL sample (0-1mM) and 50 µL α-Amylase (5 U/mL)	Jionoside D isolated from *C. infortunatum* showed significant activity (IC_{50} 3.4±0.2 µM) greater than standard, Acarbose, (IC_{50} 5.9±0.1 µM)	[97]
	Anticancer activity		Hs578T and MDA-MB-231 cell lines	Cell Viability using MTS Assay Transwell Cell Migration Assay	Compound, jionoside C, Showed cytotoxic effect (IC_{50} 85.3±2.4 µM and 96.5±1.5 µM) against Hs578T and MDA-MB-231 correspondingly	
	Antiproleferative activity		HS578T and MDA-MB-231 cell lines	Colony Formation Assay	Compounds, byzantionoside B and , jionoside C reduced the cell count significantly illustrating the antiproliferative effect of the plant *C. infortunatum*	
			HS578T and MDA-MB-231 cell lines	Cell migration Tumor-Sphere Formation Assay	Compounds, byzantionoside B and , jionoside C inhibited the cancer cell migration leading to reduction in metastasis Jionoside C demonstrated a cancer cell size and number reduction	
	Anticholinesterase activity		AChE		Isolated compounds showed little or no Antocholinesterase enzyme inhibitory activity	
C. viscosum	Thrombolytic	Methanol extract, ethyl acetate, petroleum ether, carbon tetrachloride, chloroform, aqueous soluble fractions	*In vitro* evaluation of blood clot lysis	-----	Ethyl acetate soluble fraction revealed activity of 54.47% as compared to positive control, standard drug, with 69.13% lysis	[98]
	Antibacterial activity	Root	*In vitro* disc diffusion techniques using the Gram positive and gram-negative bacteria strains		Petroleum ether extracts of Cl. viscosum showed the highest activity (zone of inhibition; 18 0.31 mm) against Bacillus cereus in comparison to the standard, 29 ± 0.14	
	Membrane stabilizing		Hypotonic solution and heat induced haemolysis of human erythrocytes		Ethyl acetate soluble fraction showed activity of 60.30 % as compared to ASA, positive control (71.90 %)	
	Antimicrobi	Methanol	Disc diffusion method		Petroleum ether soluble	

	al	extract of root	against *Escherichia coli, Shigella dysentria, Staphylococcus aureus, Bacillus subtilis, Salmonella typhi. Bacillus cereus and Sarcina lutea*		fraction showed highest zone of inhibition of 18 ± 0.31 mm against *B. cereus* compared with standard, ASA, 29 ± 0.41mm	
			Salmonella paratyphi MTCC-3220, *Salmonella enterica typhimurium* MTCC-98, *Salmonella enteric* ser. typhi MTCC-733, *Shigella flexeneri* MTCC-9543, Shigella MTCC-5151, *Escherichia coli* MTCC-118, *Escherichia coli* MTCC-614, *Streptococcus mitis* 2798, *Pseudomonas aeruginosa* 1035, *Bacillus circulans* MTCC-490, *Vibrio cholera* MTCC-3906	1.01-10 mg/mL	Petroleum ether extract of showed highest zone of inhibition against S. enterica typhimurium 98 (18.95±0.81), compared to Ciprofloxacin, CF (21.56±0.82)	[99]
	Antihelmitic efficacy	Ethanol extract of leaf	Worms from freshly slaughtered intestine of domestic fowl	10, 20, 40 and 80 mg/mL concentrations of the crude leaf extracts and 0.0005, 0.001, 0.0025, 0.005 mg/mL concentrations of praziquan-tel (PZQ)	At 10 and 80 mg/mL paralysis was observed at 9.30 ± 0.3 h and 1.30±0.35h respectively while the control drug showed paralysis at 0.17±0.01h, 3.22±0.07 h at 0.005 and 0.0005 mg/mL respectively	[100]
***C. capitatum* (Wild) Schumach et. Thonn.**	Hypoglycemic	Aqueous leaf extract	Fasting plasma glucose were evaluated in young adult male Wistar rats treated extract using glucose oxidase method	0, 100, 400, 800 mg/kg	Rats treated with 800 mg/kg of the extract showed a significant reduction in fasting blood glucose, thus showing the hypoglycaemic property of CC	[101]
***C. volubile P* Beauv.**	Antioxidant activity	DCM fraction of leaf	*In vitro* DPPH assay	15, 30, 60, 120, 240 µg/mL	Free radicals' accumulation as a result of oxidative stress was significantly reduce with an inhibitory concentration of 25.51 µg/mL	[102]
	Enzyme inhibitory activity		Inhibitory effect on pancreatic α-amylase, lipase and α-glucosidase with positive controls acarbose, orlistat and ascorbic acid respectively		Inhibitory effects of the DCM fraction of the leaves were shown enzyme activities of α-glucosidase and lipase with concentration at 4.14 and 0.02 µg/mL correspondingly	
	Anticancer activity	Leaf	Cell proliferation assay using MTT against prostate cancer cell lines, PC3 and DU145	0-100 µg/mL for a period of 24 and 48 hr	Dose- dependent inhibition of growth leading to reduced cell viability	[103]
			Apoptosis monitoring by flow cytometry (Annexin V/ FITC) assay		Result showed an increase in the segment of apoptotic DNA cell	

	Antifungal activity	Extract against *Aspergills flavus*	Well diffusion method and minimum inhibitory assays	25, 12.5, 6.25, and 3.125 mg/ml	Significant zone of inhibition was recorded in Cold water (13.00 mm) and ethanol (15.00 mm) extracts which was further confirmed with the minimum inhibitory concentration of 25 and 50 mg/mL respectively	[104]
	Antidiabetic activity	Leaf extract	α-amylase, α- glycosidase and angiotensin-1	------	Significant inhibition of the α-amylase and α- glycosidase (IC_{50} = 0.40, 0.68 mg/mL) enzyme activities for the hydrolysis carbohydrate, thus, reducing the glucose concentration in the blood stream.	[105]

Table 2: Mechanism of action of selected plants from *Clerodendrum* species

Plant name	Pharmacological activities	Mechanism of action	References
C. *serratum*	Hepatoprotective activity	Inhibition of free radical generated from metabolism of carbon tetrachloride. This thereby reinstates the normal level of liver function markers in the body.	[106]
	Anti-allergic / anti- inflammatory activity	The prevention of inflammatory and pro-inflammatory mediators from being released. There is also a release or enabling entrance of components of the white blood cells such as neutrophils, lymphocyte into the respiratory organ.	[107]
	Anti-inflammatory and anti-arthritic activity	The inhibition of cyclooxygenase (COX-2) and Tumor necrosis factor (TNF-α) for proinflammatory cytokines in immune cell activation	[108]
C. fragans	Cytotoxicity	Inhibition of cell proliferation by action of dehydrogenase in the mitochondria of cell	[109]
C. petasites	Anti-inflammatory and antipyretics	Inhibition of synthesis of prostaglandins	[110]
C. chinense	Diuretic and anti-hypertensive activity	*C. chinense* aqueous extract exhibited a diuretic effect by preventing tubular reabsorption of sodium and water as a direct result of its level of potassium concentration.	[111]
	Cytotoxicity	Verbascoside isolated from *C. chinense* inhibited signalling cascades thereby inducing apoptosis in colorectal cancer cells. Also, isoverbascoside caused an arrest of the G0/G1 cell cycle thereby inhibiting the cell proliferation of MGC 803 gastric cancer	[112 - 114]
C. viscoum	Cytotoxicity	Induction of apoptosis in MCF-7 cancer cell line	[115]
	Antibacterial and antifungal	Inhibition of growth of the organism strains	[116]

CONCLUSION

In conclusion, many phytochemicals from the genus *Clerodendrum* have been identified and isolated"=.

Studies conducted on this genus have revealed a diverse range of biological activities exhibited by its crude extracts and compounds. These activities include anti-inflammatory, anti-diabetic, antihypertensive, analgesic, hepatoprotective, antimicrobial, and antitumor properties, among others. From a phytochemical and biological standpoint, many other species are completely unknown. The toxicity of isolated components has, however, received little attention in the literature, and quantitative data on the species are also scanty. Medicinal plants in this genus are beneficial, therefore they should be considered as lead in drug discovery and formulation.

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