



ISSN 2278-4136
JPP 2014; 3 (2): 181-204
Received: 22-05-2014
Accepted: 23-06-2014

Cinthia C. Lima
Instituto de Química e Biotecnologia,
Universidade Federal de Alagoas,
57072-970, Maceió-AL, Brazil.

Rosângela P. L. Lemos
Instituto do Meio Ambiente do Estado de
Alagoas, 57017-320, Maceió-AL,
Brazil.

Lucia M. Conserva
Instituto de Química e Biotecnologia,
Universidade Federal de Alagoas,
57072-970, Maceió-AL, Brazil.

Dilleniaceae family: an overview of its ethnomedicinal uses, biological and phytochemical profile

Cinthia C. Lima, Rosângela P. L. Lemos, Lucia M. Conserva

Abstract

The family Dilleniaceae consists of 10-14 genera and about 500 species distributed into four subfamilies. It is taxonomically isolated and it is the sole representative of Dilleniales. Some of its species play an important role in traditional medicine and they have been used for the treatment of various diseases and infections, such as arthritis, diabetes, dysentery, hepatitis, blennorrhagia, and to treat gastrointestinal disorders, inflammation, hemorrhoids, wounds, and leishmanial ulcers. Pharmacological studies have confirmed that extracts from these species as well as some of their isolated compounds possess a wide range of biological activities, including anti-hemorrhagic, anti-inflammatory, antioxidant, antimicrobial, antitumoral, anti-ulcer, immunological, and cancer chemoprevention, with flavonoids and terpenoids as the major active principles. To date, more than 130 compounds, distributed in different structural classes (flavonoids, terpenoids, lignans, phenolic derivatives, and other compounds) have been reported from this family. This paper briefly reviews for the first time the ethnomedicinal uses, phytochemical profile and biological activities of some isolated compounds and extracts from Dilleniaceae species.

Keywords: Dilleniaceae, ethnomedicinal uses, biological activities, flavonoids, terpenoids, phenolic derivatives.

1. Introduction

The use of plants as medicines goes back to early man. Certainly the great civilizations of the ancient Chinese, Indians, and North Africans provided written evidence of man's ingenuity in utilizing plants for the treatment of a wide variety of diseases [1]. According to the World Health Organization, more than 80% of the world population depends primarily on plant based medicines for basic healthcare needs [2]. Plants of Dilleniaceae family play an important role in traditional medicine and some of them are used for arthritis, diabetes [3-4], dysentery, hepatitis, blennorrhagia [5], and to treat gastrointestinal disorders, inflammation [6-9], hemorrhoids, wounds [10], and leishmanial ulcers [11]. Studies have shown that extracts from of them as well as their isolated compounds possess diverse biological activities, including anti-hemorrhagic [12], anti-inflammatory, antioxidant, antimicrobial [13-14], antitumoral [15], anti-ulcer, immunological [16], and cancer chemoprevention [17].

Chemical investigations of plants of this family showed that more than 130 compounds distributed in different structural classes have been isolated, with flavonoids and terpenoids as the major classes of active principles. Flavonoids are the most representatives and diversified. Beside common and glycosides aglycones (flavones, flavonols, dihydroflavonols and isoflavones), some O-methylated and sulphates compounds have been found. In addition, plants of this family also contain terpenoids [triterpenoids distributed in different structural skeletons (oleanane, seco-oleanane, lupane, cycloartane, and friedelane), phytosteroids and diterpene] and other classes of compounds like lignans, anthraquinones, phenolic derivatives, and others.

1.1 Botanical description and taxonomic aspects

Dilleniaceae family consists of 10-14 genera and about 500 species, generally shrubs, trees or occasionally lianas or herbs, with a distribution mainly pantropical but a large number of species also occur in subtropical and temperate Australia. Comparatively, this family is rare in Africa, where it is represented only by members of the pantropical genus *Tetracera* [18]. According to Horn [19], this family is best divided into four subfamilies: Delimoideae, comprises only the genus *Tetracera* (ca. 20 species), which represents the sister group to all other subfamilies;

Correspondence:
Lucia M. Conserva
Instituto de Química e
Biotecnologia, Universidade Federal
de Alagoas, 57072-970, Maceió-AL,
Brazil.

Doliocarpoideae, containing the Neotropical endemic genera *Curatella* (1 species), *Davilla* (30), *Doliocarpus* (48), *Neodillenia* (3), *Pinzona* (1) - are sister to a clade containing the Old World genera and form a monophyletic group sister of the subfamilies paleotropica^[6, 18]; Hibbertioideae (*Hibbertia*, *Adrastaea* and *Pachynema* and was treated as an Old World clade), and Dilleniaceae (*Acrotrema*, *Didesmandra*, *Dillenia*, and *Schumacheria*). A group of Australian species with photosynthetic stems, previously recognized as the genus *Pachynema*, have been reclassified by Horn^[18] as a derived subgroup of *Hibbertia*. In Brazil, six genera containing 82 species are present [*Davilla* (30), *Doliocarpus* (34), *Tetracera* (15), *Curatella*, *Neodillenia*, and *Pinzona* (1 species each)]^[20].

The family Dilleniaceae is taxonomically isolated and is the sole representative of Dilleniales. The principal characters used for earlier subdivisions of this family include anther structure and dehiscence, leaf architecture and the degree of carpel fusion. However, molecular phylogenetic data have been informative as to the infrafamilial relationships and the clade containing all genera, exclusive of *Tetracera*, is strongly supported by structural data above^[19]. It shows a remarkable diversity in features (floral symmetry and the number of flower organs such as stamens or carpels) that are relatively stable in other families. Despite this diversity, this family is constant enough in other features that they have been recognized as a unified group. However, the position of this family in the phylogenetic tree and its classification among the other flowering plants is doubtful. The Angiosperm Phylogeny Group II system^[21] recognizes this family, unplaced as to order, assigned to the clade core eudicots (a monophyletic group)^[22] and debates either including it in order Caryophyllales or reinstating the order Dilleniales for just this one family, but decides to leave it unplaced^[23]. Another study has suggested that the core eudicots can be divided into two clades: Pentapetalae and Gunnerales. Pentapetalae can be then divided into three clades: (i) a “superrosid” clade consisting of Rosidae, Vitaceae and Saxifragales; (ii) a “superasterid” clade consisting of Santalales, Berberidopsidales, Caryophyllales and Asteridae; and (iii) Dilleniaceae^[24]. Moreover, there is a growing consensus of molecular data suggesting Dilleniaceae are sister to Caryophyllales. Soltis *et al.*^[25] and Horn^[19] lists a number of features suggesting a relationship between Dilleniaceae and Rhabdodendraceae, probably sister to the rest of Caryophyllales. Using complete plastid genome sequence data, Moore *et al.*^[26] placed Dilleniaceae as sister to Superrosidae, but topology tests did not reject alternative positions of Dilleniaceae as sister to Asteridae or Pentapetalae. Recently Soltis *et al.*^[27] placed the Dilleniaceae as related to the clade of Asteridae + Caryophyllales + Santalales, but other analysts have placed them closer to Rosidae + Saxifragales, or even sister to all other Pentapetalae^[27].

This review reports an account of Dilleniaceae species used in traditional medicine, their phytochemical profile and biological activities of extracts and isolated compounds. For a better understanding and objectivity collected data about each species of the family are discussed below by genera and they are based on papers published up to 2013. All the available information was collected via electronic search (using Chemical Abstracts Service, Google Scholar and Web of Science) and a library search for articles published in peer-reviewed journals.

2. Distribution and ethnomedicinal uses of Dilleniaceae species

2.1 *Acrotrema* species

The genus *Acrotrema* comprises of about 10 species distributed in the Indo-Malayan region, especially in Sri Lanka^[28]. The oil prepared of whole plant of *A. arnottianum*, a small herb endemic to peninsular India, is used by *Malavedan* tribes of Kerala to prevent excessive hair fall and in combination with others ingredients applied external against baldness and fresh leaf paste of the plant to relieve headache^[28].

2.2 *Curatella* species

This genus contains only one species (*C. americana*) in the Neotropical region. This species is an evergreen woody shrub^[3-4] that occurs from Central America to Bolivia and in almost all of Brazil^[29]. It is a medicinal plant used extensively in folk medicine throughout its range. Infusions from the leaves and stems are used for arthritis, diabetes, and to lower blood pressure^[3-4]. Cooked leaves are used to mitigate skin eruptions, for dressing wounds, and the water for purifying blood^[3]. In Brazil, this plant is popularly known as ‘cajueiro-bravo’, ‘sambaiba’ and ‘lixeira’ and used to treat inflammation and gastrointestinal disorders^[6-9], and in Colombia for hypertension^[30].

2.3 *Davilla* species

Davilla is a genus of 30 to 40 species of lianas, vines or erect or shrubs natives to the Neotropics^[31] and distributed from Southern Mexico to South Brazil, Bolivia and Paraguay^[6]. Some of its species are used in traditional medicine as tonics and aphrodisiacs^[32], to treat stomach diseases, diarrhea and swelling, particularly of the lymph nodes and testicles^[33], hemorrhoids, diarrhea, and wounds^[10]. *D. elliptica*, known as “cipó-caboclo and pau-de-bugre” is a shrub used in Brazilian folk medicine as an astringent, tonic, sedative, diuretic, to treat hemorrhoids, hernia, and in topical applications as an antiseptic for cleaning wounds^[34]. *D. rugosa*, known as “cipó-caboclo or cipó-carijó”, is used as tonics, aphrodisiacs and for stomach ailments^[32, 35].

2.4 *Dillenia* species

Dillenia is a genus of about 110 species of trees or shrubs, native to tropical and subtropical regions of southern Asia, Australasia, and the Indian Ocean islands. Some species are used for their edible fruits and medicinal applications^[36-39] or are cultivated as ornamentals^[40]. *D. indica*, the most investigated species of this genus, is an evergreen large shrub or small to medium-sized tree that grows all over the Bangladesh and India. It has been grown in gardens as an ornamental plant^[40] and it is widely used as food and reputed in the folk medicine of Bangladesh and India^[37-38]. Their ripe fruits are used in the flavoring of curries and preparation of jam and jelly and the acidic juice is sweetened with sugar and used as a cooling drink. The fruit possess tonic laxative properties and is used for relieving abdominal pain. The bark and leaves are used as laxative and astringent. Bruised bark is applied as a cataplasm for patients with arthritis^[36, 40]. The mixed juices of bark, leaf and fruits are used for the treatment of cancer and diarrhea^[41]. The fruit juice is used as a cardiogenic and mixed with sugar and water is used as a cooling beverage for fever. It also tones up the nervous system and removes fatigue^[40]. In India, the plant is traditionally used for treatment of diabetes^[39, 42]. Whole plant of *D. indica* used

in case of fever, as an aphrodisiac and also promotes virility; decoction of it can be used as a universal antidote [43]. *D. papuana* is a tree which bark is used in the traditional medicine of Papua, New Guinea to treat asthma, severe chest pains and to assist in child delivery [44].

2.5 *Doliocarpus* species

Doliocarpus is a Neotropical genus of about 50 species, of wide distribution in Central and South Americas, from Mexico to South Brazil, being the Amazon region with greater representation of species [6]. Species of this genus are common lianas (rarely shrubs) and in the folk medicine are used by hunters (sap) for slaking thirst when the rivers are far from the hunting place, leishmanial ulcers (bark) [11] and aphrodisiac [45]. *D. schottianus* is used to treat diabetes mellitus, hypertension and eye diseases [46] and in Peru, the vine water of *D. dentatus* is used to treat malaria [47].

2.6 *Didesmandra*, *Neodillenia* and *Pachynema*

The genus *Didesmandra* is known from only a few populations in Sarawak, Borneo [19] while *Neodillenia* (03 species) has occurrence in the Amazon region (Brazil), Colombia, Ecuador, Peru, and Venezuela [20]. According to Kubitzki [48], the species previously placed in *Pachynema* were transferred to *Hibbertia* [19]. At moment, no information on traditional medicine, biological or phytochemical studies were reported for these genera.

2.7 *Tetracera*

Species of this genus have been used in folk medicine for the treatment of various diseases and infections [49-55]. In traditional Indian medicine, some species have been used against dysentery, hepatitis and blennorrhagia. It has also been utilized as febrifuge and diuretic agent, and has been prescribed for health promotion, alleviation of fatigue and treatment of jaundice [5]. Decoction of the roots of *T. boiviana* is drunk against the influence of "witch craft" and mixed with roots of *Rhynchosia albissima* is drunk to induce labor. A

piece of the roots is tied to the wrist of all members of the family to protect them from influenza or pneumonia when the village is struck by these diseases [56]. Different parts of *T. indica* (syn.: *Assa indica*) have been found to act in the treatment of fever, flue, sinus symptoms, skin rashes, itching, piles, mouth ulcer, diarrhea, diabetes, and insect bites [55]. In Malaysia, decoction of the stems and roots is used to reduce high blood pressure and the leaves, crushed and mixed with water, are applied on the whole body to treat fever [57] and its roots are used to treat high blood pressure and high fever, while leaves and roots pounded together is used to treat skin itching [58]. Moreover, its shoot ground, wrapped in banana leaves are heated then applied to treat headache [55]. Furthermore, this species is also one of the active ingredients in a local herbal medicine (Plantisol) in Malaysia, which is widely prescribed to treat diabetes [55].

3. Biological and phytochemical profile of Dilleniaceae species

3.1 *Acrotrema* species

The genus *Acrotrema* comprises of about 10 species distributed in the Indo-Malayan region, especially in Sri Lanka [28]. From the biological and chemical point of view, only two species (*A. arnotianum* and *A. uniflorum*) have been investigated so far. Antioxidant and antimicrobial activities of the extracts and isolated compounds have been reported [59-60]. Phytochemical investigation of *A. arnotianum* revealed the presence of procyanidin, free and glycosides flavonols, terpenoids, phenolic derivative, alcohol, and carboxylic acid (Tables 1-3; Figs. 1-3) while from the leaves of *A. uniflorum*, beside terpenoids (Table 2; Fig. 2), free and glycosides flavonols, flavanol sulphates like isorhamnetin 3,7,4'-trisulphate (**10**), kaempferol 3,7,4'-trisulphate (**23**), ombuin 3,3'-disulphate (**39**), quercetin 3-sulphate (**49**), and rhamnocitrin 3-sulphate (**53**) also have been found (Table 1; Fig. 1). In this family, with exception of **49** that also occur in the genera *Dillenia*, *Schumacheria* and *Tetracera* and **53** in *Tetracera*, compounds **10**, **23** and **39** is restrict to this genus.

Table 1: Distribution of the flavonoids in the Dilleniaceae species.

| Compound | Source | Plant part/ References |
|--|--|---------------------------------|
| Flavones and Flavonols | | |
| Apigenin (1) | <i>T. mandagascariensis</i> | Leaves [61] |
| Apigenin 7-galactoside sulphate (2) | <i>T. stuhmanniana</i> | Leaves [61-62] |
| Apigenin 7-sulphate (3) | <i>T. mandagascariensis</i> | Leaves [61] |
| Avicularin (4) | <i>C. americana</i> <i>Pinzona coriacea</i> | Leaves [61, 125] Leaves [61] |
| Azaleatin (5) | <i>Dillenia triquetra</i> , <i>T. boiviana</i> , <i>T. breyniana</i> , <i>T. costata</i> , <i>T. oblongata</i> , <i>T. sellowiana</i> , <i>T. tigara</i> , <i>T. volubilis</i> | Leaves [61] |
| 3',5-Dihydroxy-4',3-dimethoxyflavone-7-O-β-D-glucoside (6) | <i>Dillenia indica</i> | Stem barks [126] |
| 5,7-Dihydroxy-4'-methoxyflavone 3-O-β-D-glucopyranoside (7) | <i>Dillenia indica</i> | Stem barks [126] |

| | | |
|---|---|---|
| Dillenetin (8) | <i>Dillenia indica</i> | Pericarp ^[124] |
| Isorhamnetin (9) | <i>Acrotrema uniflorum</i> | Leaves ^[61] |
| | <i>Dillenia indica</i> | Barks, Fruits, Pericarp ^[124] |
| | <i>Dillenia</i> spp. (Huber sn.) | Leaves ^[61] |
| | <i>Doliocarpus amazonicus</i> | Leaves ^[61] |
| Isorhamnetin 3,7,4'-trisulphate (10) | <i>Acrotrema uniflorum</i> | Leaves ^[61-62] |
| Isovitexin (11) | <i>Doliocarpus brevipedicellatus</i> , <i>D. dentatus</i> , <i>D. lacifolius</i> , <i>D. multiflorus</i> , <i>D. paraensis</i> , <i>D. verruculosus</i> | Leaves ^[61] |
| Izalpinin (12), Izalpinin-3-methyl ether (13) | <i>T. asiatica</i> | Leaves ^[117] |
| Kaempferol (14) | <i>Acrotrema arnotianum</i> | Entire plant ^[60] |
| | <i>Acrotrema uniflorum</i> | Entire plant ^[60, 124] |
| | <i>Acrotrema uniflorum</i> , <i>Davilla alata</i> , <i>D. angustifolia</i> , <i>D. cearensis</i> , <i>D. elliptica</i> , <i>D. flexuosa</i> , <i>D. grandiflora</i> , <i>D. kunthii</i> , <i>D. lacunosa</i> , <i>D. macrocarpa</i> , <i>D. rugosa</i> , <i>Dillenia bracteata</i> , <i>D. retusa</i> , <i>D. spp.</i> , <i>D. triquetra</i> , <i>Doliocarpus amazonicus</i> , <i>D. elegans</i> , <i>D. gracilis</i> , <i>D. sellowianus</i> , <i>D. spraguei</i> , <i>D. validus</i> , <i>D. verruculosus</i> , <i>S. angustifolia</i> , <i>T. amazonica</i> , <i>T. alnifolia</i> , <i>T. asperula</i> , <i>T. boiviniana</i> , <i>T. breyniana</i> , <i>T. costata</i> , <i>T. edentata</i> , <i>T. empedoclea</i> , <i>T. lasiocarpa</i> , <i>T. leiocarpa</i> , <i>T. madagascariensis</i> , <i>T. masuiana</i> , <i>T. oblongata</i> , <i>T. poggei</i> , <i>T. rasiflora</i> , <i>T. rutenbergii</i> , <i>T. sarmentosa</i> , <i>T. sellowiana</i> , <i>T. stuhimanniana</i> , <i>T. tigara</i> , <i>T. volubilis</i> , <i>T. willdenowiana</i> | Leaves ^[61] |
| | <i>Dillenia indica</i> , <i>D. retusa</i> | Timber, Fruits ^[124] |
| | <i>H. amplexicaulis</i> , <i>H. alligena</i> , <i>H. banksii</i> , <i>H. billardieri</i> , <i>H. dentata</i> , <i>H. deplancheana</i> , <i>H. lineares</i> , <i>H. salignea</i> , <i>H. stricta</i> , <i>H. vestita</i> , <i>H. volubis</i> | Leaves ^[104] |
| | <i>Wormia burbidgei</i> | Barks ^[124] |
| | <i>Wormia triquetra</i> | Barks, Fruits, Timber ^[124] |
| | <i>T. asiatica</i> | Leaves ^[104] |
| | <i>Dillenia bracteata</i> , <i>D. spp.</i> , <i>S. castaneifolia</i> | Leaves ^[61-62] |
| | <i>Dillenia retusa</i> , <i>T. amazonica</i> , <i>T. empedoclea</i> , <i>T. lasiocarpa</i> , <i>T. masuiana</i> | Leaves ^[61] |
| | <i>Acrotrema arnotianum</i> | Entire plant ^[60] |
| | <i>Dillenia indica</i> | Barks ^[127] |
| | <i>Dillenia indica</i> | Leaves ^[128-129] |
| | <i>Davilla alata</i> , <i>D. angustifolia</i> , <i>D. cearensis</i> , <i>D. elegans</i> , <i>D. grandiflora</i> , <i>D. macrocarpa</i> , <i>Doliocarpus gracilis</i> , <i>D. sellowianus</i> , <i>T. asperula</i> , <i>T. edentata</i> , <i>T. leiocarpa</i> | Leaves ^[61] |
| | <i>Dillenia bracteata</i> , <i>D. spp.</i> , <i>D. triquetra</i> , <i>S. casteinifolia</i> , <i>T. alnifolia</i> , <i>T. boiviniana</i> , <i>T. breyniana</i> , <i>T. costata</i> , <i>T. oblongata</i> , <i>T. rasiflora</i> , <i>T. rutenbergii</i> , <i>T. volubilis</i> , <i>T. willdenowiana</i> | Leaves ^[61] |
| | <i>uniflorum</i> | Leaves ^[61-62] |
| | <i>H. cuneiformis</i> , <i>T. mandagascariensis</i> | Leaves ^[61, 104] |

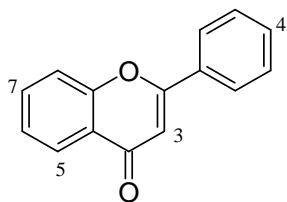
| | | |
|--|---|---|
| Luteolin 7-sulphate (25) | <i>T. stuhimanniana</i> | Leaves [61] |
| Mearnsetin (26) | <i>Doliocarpus spraguei</i> , <i>Hibbertia</i> spp. | Leaves [61] |
| Mearnsetin 3-rhamnoside (27) | <i>Doliocarpus spraguei</i> (Leaves) | [61-62] |
| 5-Methylkaempferol (28) | <i>T. boiviana</i> , <i>T. breyniana</i> , <i>T. costata</i> , <i>T. oblongata</i> , <i>T. sellowiana</i> , <i>T. volubilis</i> | Leaves [61] |
| 7-O-Methylkaempferol (29) | <i>T. breyniana</i> | Stems [122] |
| 7-O-Methylquercetin (30) | <i>T. breyniana</i> | Leaves [122] |
| Myricetin (31) | <i>Davilla alata</i> , <i>D. angustifolia</i> , <i>D. cearensis</i> , <i>D. elliptica</i> , <i>D. flexuosa</i> , <i>D. grandiflora</i> , <i>D. kunthii</i> , <i>D. lacunosa</i> , <i>D. microcarpa</i> , <i>D. nitida</i> , <i>D. rugosa</i> , <i>Doliocarpus amazonicus</i> , <i>D. elegans</i> , <i>D. gracilis</i> , <i>D. major</i> , <i>D. sellowianus</i> , <i>D. spraguei</i> , <i>D. validus</i> , <i>D. verruculosus</i> , <i>S. alnifolia</i> , <i>T. asperula</i> , <i>T. edentata</i> , <i>T. leiocarpa</i> , <i>T. sellowiana</i> , <i>T. tigara</i> , <i>T. willdenowiana</i> <i>Dillenia indica</i> <i>H. amplexicaulis</i> , <i>H. alligena</i> , <i>H. billardieri</i> , <i>H. lineares</i> , <i>H. salignea</i> , <i>H. stricta</i> , <i>H. vestita</i> , <i>H. volubis</i> | Leaves [61] Stem barks [130] Leaves [104] |
| Myricetin 3-arabinoside (32) | <i>Davilla elliptica</i> , <i>D. lacunose</i> , <i>S. alnifolia</i> | Leaves [61] |
| Myricetin 3-O-β-galactopyranoside (33) | <i>Davilla elliptica</i> , <i>D. lacunosa</i> , <i>D. nitida</i> , <i>S. alnifolia</i> , <i>T. sellowiana</i> , <i>T. willdenowiana</i> | Leaves [61, 64] |
| Myricetin-3-O-α-L-rhamnoside (34) | <i>Davilla alata</i> , <i>D. angustifolia</i> , <i>D. cearensis</i> , <i>D. grandiflora</i> , <i>D. kunthii</i> , <i>D. lacunosa</i> , <i>D. microcarpa</i> , <i>D. rugosa</i> , <i>Doliocarpus amazonicus</i> , <i>D. elegans</i> , <i>D. gracilis</i> , <i>D. major</i> , <i>D. sellowianus</i> , <i>D. validus</i> , <i>D. verruculosus</i> , <i>T. edentata</i> , <i>T. leiocarpa</i> , <i>T. stuhimanniana</i> <i>Davilla elliptica</i> <i>Davilla elliptica</i> <i>Davilla flexuosa</i> <i>Davilla nitida</i> <i>Doliocarpus spraguei</i> | Leaves [61] Leaves [15, 33, 61] Aerial parts [131] Leaves [61, 87] Leaves [33, 61] Leaves [61-62] |
| Myricetin-3'-O-α-L-rhamnoside (35) | <i>Davilla flexuosa</i> | Leaves [88] |
| Myricetin-3-O-rhamnoside sulphate (36) | <i>Davilla alata</i> <i>Davilla flexuosa</i> <i>Davilla macrocarpa</i> | Leaves [61] Leaves [61-62] Leaves [62] |
| Myricetin 3,7,3',4'-tetramethyl ether (37) | <i>Doliocarpus amazonicus</i> subsp. <i>duckeanus</i> | Leaves [62] |
| Ombuin (38) | <i>Acrotrema uniflorum</i> | Leaves [61] |
| Ombuin 3,3'-disulphate (39) | <i>Acrotrema uniflorum</i> | Leaves [61-62] |
| Quercetin (40) | <i>Acrotrema arnotianum</i> <i>Acrotrema uniflorum</i> <i>Acrotrema uniflorum</i> , <i>C. americana</i> , <i>Davilla alata</i> , <i>D. angustifolia</i> , <i>D. cearensis</i> , <i>D. grandiflora</i> , <i>D. kunthii</i> , <i>D. lacunosa</i> , <i>D. macrocarpa</i> , <i>D. rugosa</i> , <i>Doliocarpus amazonicus</i> , <i>D. elegans</i> , <i>D. gracilis</i> , <i>D. guianensis</i> , <i>D. macrocarpus</i> , <i>D. major</i> , <i>D. savannarum</i> , <i>D. schottianus</i> , <i>D. sellowianus</i> , <i>D. validus</i> , <i>D. verruculosus</i> <i>Davilla elliptica</i> <i>Davilla flexuosa</i> , <i>D. nitida</i> <i>Davilla rugosa</i> <i>Dillenia bracteata</i> , <i>D. retusa</i> , <i>D. spp.</i> , <i>D. triquetra</i> | Entire plant [60] Entire plant [60, 124] Leaves [61] Leaves [15, 33, 61] Leaves [61, 87] Stems [88] Leaves [61] |

| | | |
|--------------------------------------|--|---|
| | <i>Dillenia indica</i> | Barks ^[127] |
| | <i>Dillenia retusa</i> | Barks, Fruits, Timber ^[124] |
| | <i>Doliocarpus spraguei</i> | Leaves ^[61-62] |
| | <i>H. amplexicaulis, H. alligena, H. banksii, H. billardieri, H. dentata, H. deplancheana, H. hermannifolia, H. lineares, H. lucens, H. pancheri, H. salignea, H. scandens, H. stricta, H. vestita, H. wagapui, H. volubis</i> | Leaves ^[104] |
| | <i>Pinzona coriacea, S. alnifolia, S. casteinifolia, T. alnifolia, T. boiviniana, T. breyniana, T. costata, T. edentata, T. empedoclea, T. lasiocarpa, T. leiocarpa, T. madagascariensis, T. masuiana, T. oblongata, T. rasiflora, T. rutenbergii, T. sarmentosa, T. sellowiana, T. stuhimanniana, T. tigara, T. volubilis, T. willdenowiana</i> | Leaves ^[61] |
| | <i>T. breyniana</i> | Leaves ^[122] |
| | <i>Wormia burbridgei, W. triquetra</i> | Barks ^[124] |
| Quercetin-3-O-arabinopyranoside (41) | <i>Davilla elliptica</i> | Leaves ^[25] |
| Quercetin-3-O-galactopyranoside (42) | <i>C. americana, Davilla alata, D. cearensis</i> | Leaves ^[61] |
| | <i>Davilla elliptica</i> | Leaves ^[25] |
| | <i>Doliocarpus guianensis, D. macrocarpa, D. savannarum, D. schottianus, D. validus, D. verruculosus, Pinzona coriacea, S. alnifolia, T. boiviniana, T. breyniana, T. costata, T. empedoclea, T. lasiocarpa, T. masuiana, T. sellowiana, T. volubilis, T. willdenowiana</i> | Leaves ^[61] |
| Quercetin 3-galactoarabinoside (43) | <i>americana</i> | Leaves ^[61] |
| Quercetin 3-glucoronide (44) | <i>Dillenia retusa, D. spp., T. alnifolia, T. empedoclea, T. lasiocarpa, T. masuiana, T. sarmentosa, T. sellowiana, T. stuhimanniana</i> | Leaves ^[61] |
| Quercetin 3-glucoside (45) | <i>C. americana, Doliocarpus elegans, D. savannarum, S. alnifolia, T. empedoclea, T. lasiocarpa, T. madagascariensis, T. masuiana, T. sarmentosa, T. willdenowiana</i> | Leaves ^[61] |
| Quercetin-3-O-β-D-rhamnoside (46) | <i>Acrotrema arnotianum</i> | Entire plant ^[60] |
| Quercetin-3-O-α-L-rhamnoside (47) | <i>C. americana, Davilla alata, D. angustifolia, D. cearensis, D. grandiflora, D. kunthii, D. lacunosa, D. macrocarpa, D. rugosa</i> | Leaves ^[61] |
| | <i>Davilla elliptica, D. nitida</i> | Leaves ^[33, 61] |
| | <i>elliptica</i> | Leaves ^[15] |
| | <i>D. elliptica</i> | Aerial parts ^[131] |
| | <i>Davilla flexuosa</i> | Leaves ^[61, 88] |
| | <i>Doliocarpus amazonicus, D. elegans, D. gracilis, D. major, D. schottianus, D. sellowianus, D. spraguei, D. validus, Pinzona coriacea, T. asperula, T. edentata, T. leiocarpa, T. madagascariensis, T. sarmentosa, T. stuhimanniana, T. tigara, T. willdenowiana</i> | Leaves ^[61] |
| Quercetin 3-robinobioside (48) | <i>Doliocarpus macrocarpus, D. savannarum</i> | Leaves ^[61] |
| Quercetin 3-sulphate (49) | <i>Acrotrema uniflorum, Dillenia bracteata, D. spp., D. triquetra, S. angustifolia, S. casteinifolia, T. alnifolia, T. boiviniana, T. breyniana, T. costata, T. madagascariensis, T. masuiana, T. oblongata, T. rasiflora, T. rutenbergii, T. sarmentosa, T. sellowiana, T. tigara, T. volubilis, T. willdenowiana</i> | Leaves ^[61] |

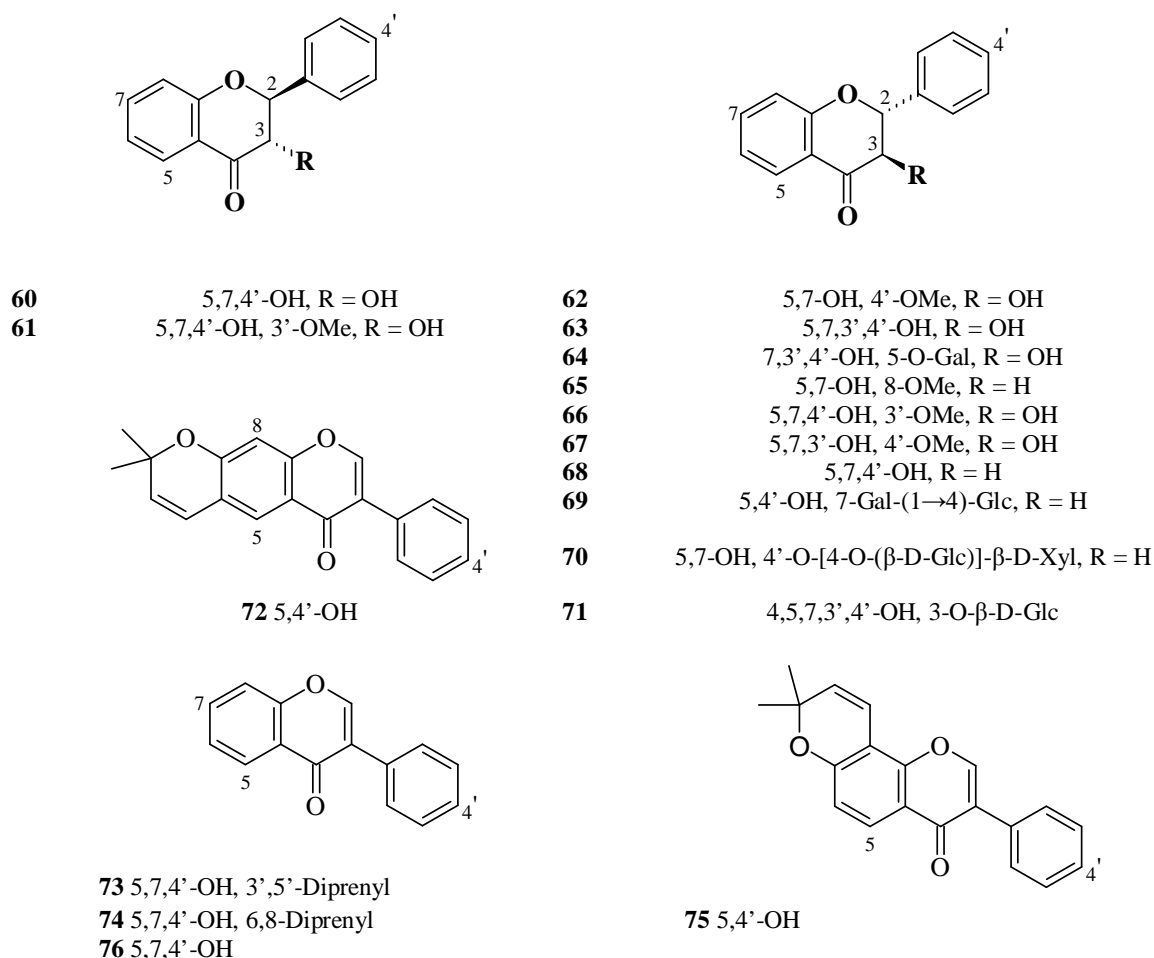
| | | |
|--|--|--|
| Rhamnetin 3-glucoside (50) | <i>Dillenia pentagyna</i> | Stems [132] |
| Rhamnocitrin (51) | <i>T. alnifolia, T. poggei, T. rosiflora, T. rutenbergii</i> | Leaves [61] |
| Rhamnocitrin 3-glucuronide (52) | <i>T. rosiflora, T. rutenbergii</i> | Leaves [61-62] |
| Rhamnocitrin 3-sulphate (53) | <i>Acrotrema uniflorum</i> <i>T. alnifolia, T. puggei, T. rosiflora, T. rutenbergii</i> | Leaves [61] Leaves [61-62] |
| Saponarin (54) | <i>Doliocarpus brevipedicellatus, D. lancifolius, D. multiflorus, D. paraensis</i> | Leaves [61] |
| Tilioside (55) | <i>Dillenia philippinensis</i> | Leaves [70] |
| Vitexin (56) | <i>Dillenia</i> spp., <i>Doliocarpus amazonicus, D. brevipedicellatus, D. dentatus, D. lancifolius, D. multiflorus, D. paraensis</i> | Leaves [61] |
| Wogonin (57) | <i>T. indica</i> <i>T. asiatica</i> | Aerial parts [89] Leaves [117] |
| Wogonin 7-O- β -D-glucuronide methyl ester (58), Wogonin 7-O- β -D-glucuronide (59) | <i>T. asiatica</i> | Leaves [117] |
| Dihydroflavonols | | |
| (+)-Dihydrokaempferol (60) | <i>Dillenia indica</i> <i>Dillenia retusa</i> <i>Wormia triquetra</i> | Timber [124] Barks [124] Barks, Timber [124] |
| (\pm)-Dihydroisorhamnetin (61) | <i>Dillenia indica</i> | Barks [124] |
| Dihydrokaempferide (62) | <i>Dillenia indica</i> | Leaves [129] |
| (+)-Dihydroquercetin (63) | <i>Dillenia indica, D. retusa</i> | Barks, Timber [124] |
| Dihydroquercetin galactoside (64) | <i>Dillenia pentagyna</i> | Stems [132] |
| Dihydrowogonin (65) | <i>T. asiatica</i> | Leaves [117] |
| (+)-3'-Methoxydihydroquercetin (66) | <i>Dillenia indica</i> | Barks [124] |
| 4'-O-Methyltaxifolin (67), Narigenin (68) | <i>Davilla rugosa</i> <i>Dillenia indica</i> <i>Dillenia indica</i> | Stems [88] Leaves [129] Barks [124] |
| Naringenin 7-galactosyl-(1 \rightarrow 4)-glucoside (69), Naringenin-4'-O-[4-O-(β -D-glucopyranosyl)]- β -D-xylopyranoside (70) | <i>Dillenia pentagyna</i> | Stems [132-133] |
| 4,5,7,3',4'-Pentahydroxyflavan-3-O- β -D-glucopyranoside (71) | <i>Dillenia indica</i> | Stem barks [126] |
| Isoflavonoids | | |
| Alpinumisoflavone (72), Derrone (73), 3',5'-Diprenylgenistein (74), 6,8-Di-prenylgenistein (75), Genistein (76) | <i>T. scandens</i> <i>T. scandens</i> | Branch [116] Branch [116] |
| Leucoanthocyanins | | |
| Procyanidin (77) | <i>Acrotrema uniflorum, C. americana, Davilla alata, D.</i> | Leaves [61] |

angustifolia, *D. cearensis*, *D. elliptica*, *D. flexuosa*, *D. grandiflora*, *D. macrocarpa*, *D. nitida*, *D. rugosa*, *Dillenia bracteata*, *D. retusa*, *D. triquetra*, *Doliocarpus amazonicus*, *D. brevipedicellatus*, *D. dentatus*, *D. elegans*, *D. gracilis*, *D. guianensis*, *D. lancifolius*, *D. macrocarpus*, *D. major*, *D. multiflorus*, *D. paraensis*, *D. savannarum*, *D. schottianus*, *D. sellowianus*, *D. spraguei*, *D. validus*, *D. verruculosus*, *H. volubis*, *Pinzona coriacea*, *S. alnifolia*, *S. angustifolia*, *S. casteinifolia*, *T. amazonica*, *T. alnifolia*, *T. breyniana*, *T. empedoclea*, *T. lasiocarpa*, *T. madagascariensis*, *T. masuiana*, *T. oblongata*, *T. poggei*, *T. sarmentosa*, *T. sellowiana*, *T. stuhimanniana*, *T. tigara*, *T. volubilis*, *T. willdenowiana*

| | | |
|----------------------|--|-------------|
| Prodelphinidin (78) | <i>Davilla elliptica</i> , <i>D. macrocarpa</i> , <i>Doliocarpus amazonicus</i> , <i>D. gracilis</i> , <i>D. multiflorus</i> , <i>D. sellowianus</i> , <i>D. spraguei</i> , <i>H. volubis</i> , <i>S. alnifolia</i> , <i>S. angustifolia</i> , <i>S. casteinifolia</i> , <i>T. sellowiana</i> , <i>T. tigara</i> , <i>T. willdenowiana</i> | Leaves [61] |
| Propelargonidin (79) | <i>Davilla flexuosa</i> , <i>Doliocarpus guianensis</i> , <i>D. macrocarpus</i> | Leaves [61] |



| | | | |
|----|---|----|--|
| 1 | 5,7,4'-OH | 30 | 3,7,4'-OH, 5-OMe |
| 2 | 5,4'-OH, 7-Gal-OSO ₃ H | 31 | 3,5,7,3',4',5'-OH |
| 3 | 5,4'-OH, 7-OSO ₃ H | 32 | 5,7,3',4',5'-OH, 3-Ara |
| 4 | 5,7,3',4'-OH, 3- α -L-Ara | 33 | 5,7,3',4',5'-OH, 3-Gal |
| 5 | 3,7,3',4'-OH, 5-OMe | 34 | 5,7,3',4',5'-OH, 3-O- α -L-Rha |
| 6 | 3',5-OH, 4', 3-OMe, 7-O- β -D-Glc | 35 | 3,5,7,4',5'-OH, 3'-O- α -L-Rha |
| 7 | 5,7-OH, 4'-OMe, 3-O- β -D-Glc | 36 | 5,7, 3',4',5'-OH, 3-O- α -L-Rha-SO ₃ H |
| 8 | 3,5,7-OH, 3',4'-OMe | 37 | 5,5'-OH, 3,7,3',4'-OMe |
| 9 | 3,5,7,4'-OH, 3'-OMe | 38 | 3,5,3'-OH, 7,4'-OMe |
| 10 | 5-OH, 3'-OMe, 3,7,4'-OSO ₃ H | 39 | 5-OH, 7,4'-OMe, 3,3'-OSO ₃ H |
| 11 | 5,7,4'-OH, 6-C-Glc | 40 | 3,5,7,3',4'-OH |
| 12 | 3,5-OH, 7-OMe | 41 | 5,7,3',4'-OH 3-O-Ara |
| 13 | 5-OH, 3,7-OMe | 42 | 5,7,3',4'-OH 3-Gal |
| 14 | 3,5,7,4'-OH | 43 | 5,7,3',4'-OH 3-Gal-Ara |
| 15 | 3,5-OH, 7,4'-OMe | 44 | 5,7,3',4'-OH 3-O- β -D-Glu |
| 16 | 5,4'-OH, 3,7-OSO ₃ H | 45 | 5,7,3',4'-OH 3-Glc |
| 17 | 5,7,4'-OH, 3-Gal | 46 | 5,7,3',4'-OH 3-O- β -D-Rha |
| 18 | 3,5,7-OH, 4'-O- β -Glc | 47 | 5,7,3',4'-OH, 3-O- α -L-Rha |
| 19 | 5,7,4'-OH, 3-Glc | 48 | 5,7,3',4'-OH, 3- α -L-Rha-(1 \rightarrow 6)-Gal |
| 20 | 3,5,7-OH, 4'-OMe | 49 | 5,7,3',4'-OH, 3-OSO ₃ H |
| 21 | 5,7,4'-OH, 3-Rha | 50 | 5,3',4'-OH, 7-OMe, 3-Glc |
| 22 | 5,7,4'-OH, 3-OSO ₃ H | 51 | 3,5,4'-OH, 7-OMe |
| 23 | 5-OH, 3,7,4'-OSO ₃ H | 52 | 5,4'-OH, 7-OMe, 3-Glu |
| 24 | 3,5,7,3',4'-OH | 53 | 5,4'-OH, 7-OMe, 3-OSO ₃ H |
| 25 | 3,5,3',4'-OH, 7-OSO ₃ H | 54 | 5,4'-OH, 6-C-Glc, 7-O- β -D-Glc |
| 26 | 3,5,7,3',5'-OH, 4'-OMe | 55 | 5,7,4'-OH, 3-(6-O- <i>p</i> -Cou)- β -D-Glc |
| 27 | 5,7,3',5'-OH, 3-Rha, 4'-OMe | 56 | 5,7,4'-OH, 8-C-Glc |
| 28 | 3,5,4'-OH, 7-OMe | 57 | 5,7-OH, 8-OMe |
| 29 | 3,5,3',4'-OH, 7-OMe | 58 | 5-OH, 7-O- β -D-Glu-(OMe), 8-OMe |
| | | 59 | 5-OH, 7-O- β -D-Glu, 8-OMe |



Ara = Arabinoside; *Cou* = Coumaroyl; *Gal* = Galactopyranoside; *Glc* = Glucopyranoside; *Glu* = Glucoronide; *Rha* = Rhamnopyranoside.

Fig 1: Structures of flavonoids isolated from Dilleniaceae species.

3.2 *Curatella* species

At 20 mg/kg, ethanol extract of *C. americana* showed in vivo antihypertensive activity, and hydroalcoholic extract from the bark showed anti-inflammatory and analgesic activities [7]. The ethanol extract of the bark of this plant also was investigated in vivo models in rodents for their ability to prevent and heal ulceration of the gastric mucosa. This extract significantly decreased the severity of gastric damage formation induced by the combination of several gastroprotective models. It also presented effective healing action in chronic gastric disease [9]. Antimicrobial (*Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Candida albicans*, and *C. parapsilosis*), promastigote forms of *Leishmania amazonensis*, and a poliovirus and cytotoxic activities of crude extract and its ethyl acetate fraction from *C. americana*, obtained using Brazilian cachaca as the extractor liquid, were evaluated. This plant proved to be effective especially as an antifungal (*C. albicans*) and showed potential for antipoliiovirus activity [13]. Another study involving antimicrobial activities ethanol extract from the stem bark showed weak activity against *S. aureus*. Phytochemical screening of this extract showed presence of saponins,

triterpenes, phenolic compounds, steroids, tannins, and catechin [14]. On the other hand, chemical investigation of the leaves of this plant resulted in the isolation of quercetin (40) and five glycosides flavonols (Table 1; Fig. 1), besides triterpenes [β -amyrin (80), betulinic acid (83) and lupeol (99)], gallic acid (119) and foeniculin (128) (Figs. 2-3).

3.3 *Davilla* species

Davilla is a genus of 30 to 40 species of lianas, vines or scandent shrubs natives to the Neotropics [31] and distributed from South Mexico to Brazil, Bolivia and Paraguay [6]. Plants of this genus contain mainly chemical constituents belonging to flavonol free, glycosides and sulphates [61-62], dihydroflavonols (Table 1; Fig. 1), terpenoids and polyphenols (Tables 2-3; Figs. 2-3). Some of its species as well as their chemical constituents possess important biological activities, such as mutagenic and genotoxic [33], antitumoral [15], anti-hemorrhagic [12], anti-ulcer, anti-inflammatory, and immunological [16], antimycobacterial [34], and cancer chemoprevention activities [15].

Methanol extract from leaves of *D. elliptica* and its flavonoids fraction [myricetin (31) and quercetin (40)] showed total

neutralization capacity against local hemorrhages against *Bothrops jararaca* venom^[12]. Phytochemical screening of the leaves showed presence of tannins, coumarins, resins, flavonoids, saponins, steroids, and triterpenes^[10]. Methanol extracts from leaves of *D. elliptica* and *D. nitida* (500 mg/kg) showed anti-ulcer, anti-inflammatory, immunological, and anti-*Helicobacter pylori* activities. The chemical investigation of these extracts showed that both possess phenolic acid derivatives, acylglycoflavonoids and condensed tannins^[16]. In another chemical study of these species led to the isolation of flavonoids (Table 1). Among them, myricetin-3-O- α -L-rhamnopyranoside (**34**) and quercetin-3-O-galactopyranoside (**42**) (Fig. 1) were active as antitumoral and inhibited the release of NO in murine macrophages. Myricetin (**31**) and quercetin (**40**) showed promising activity in the treatment of murine breast cancer by immunomodulatory and antiproliferative activities^[15].

Mutagenic and genotoxic potential of *D. nitida* and *D. elliptica* and its isolated compounds [myricetin (**31**), myricetin-3-O- α -L-rhamnoside (**34**), quercetin (**40**), quercetin-3-O- α -L-rhamnoside (**47**), and gallic acid (**119**) (Figs. 1 and 3)] were evaluated in the *Salmonella typhimurium* assay^[33]. In the assessment of mutagenic potential by the Ames test extracts from both plant species and an ethyl acetate fraction from *D. nitida* induced positive responses. In the presence of metal ion, both species aqueous and ethyl acetate fractions, as well as their isolated compounds, induced single- and double-strand-breaks in plasmid DNA in a cell-free system^[33]. At 50, 150 and 250 μ g/mL, chloroform extract of *D. elliptica* stimulated the production of H₂O₂, NO and TNF- α in peritoneal macrophages cultures. This extract also was active against *Micobacterium tuberculosis* (MIC 62.5 μ g/mL)^[34]. The hydroalcoholic extract from stems of this plant reduced response in the formalin test inflammatory phase in mice. This effect was not reverted by pre-treatment with naloxone and not affected rota-rod and tail-flick performance^[63]. Extracts from *D. elliptica* also were active for cancer chemoprevention^[17]. Ethanol extract from *D. elliptica* leaves guided by an antinociceptive assay^[64] resulted in the isolation of myricetin-3-O- β -galactopyranoside (**33**), which produced significant inhibition on nociception induced by formalin (ID₅₀ 0.26 mg/kg; p.o.)

The hydroalcoholic extract of the stems of *D. rugosa* (7.5, 15, 30 or 60 mg/kg) and its fractions (CHCl₃, CHCl₃-EtOAc, EtOAc, EtOAc-EtOH, EtOH, and EtOH-H₂O; 15 mg/kg) protected animals from developing gastric ulcers induced by HCl/ethanol and immersion-restraint stress. They also showed effects on spontaneous motor activity and elevated plus-maze behavior. An anxiolytic effect was also observed^[65-66]. From stems of this plant flavonoids and terpenoids were isolated (Tables 1 and 2). The hydroalcoholic extract of the aerial parts also presented antioxidant activity and exerted a moderate antiulcer effect in rats. It was screened with regard to their chemical constitution and alkaloids, coumarins, flavonoids, saponins, polyphenols/tannins, and lignans were identified^[32]. Extracts from *D. rugosa* (leaves, fruits and barks) and *D. kunthii* (leaves and barks) showed high antioxidant capacities based either on the capacity to scavenge free radicals (TEAC, ORAC and TRAP) or on the ability to protect biological structures^[65, 67].

3.3.1 Phytochemical profile of *Davilla* species

In this genus, in addition to procyanidin, prodelfinidin and

propelargonidin, a total of fourteen flavonoids [flavonols free (03) and glycosides (09), and dihydroflavonols (02) (Table 1)], three terpenoids (Table 2) and two others compounds (Table 3) were found. Among them, myricetin-3'-O- α -L-rhamnoside (**35**), myricetin rhamnoside sulphate (**36**), quercetin-3-O-arabinopyranoside (**41**), and 4'-O-methyltaxifolin (**67**) occur exclusively in this genus. Other flavonol glycosides like kaempferol 3-rhamnoside (**21**), myricetin 3-arabinoside (**32**), myricetin 3-galactopyranoside (**33**), and myricetin-3-O- α -L-rhamnoside (**34**) co-occur in *Doliocarpus* and *Tetracera* or *Schumacheria* and *Tetracera*.

3.4 *Dillenia* species

Of the total cataloged species, less than 20 of them were investigated under the profile chemical or as biological potential. Some of these species as well as their chemical constituents possess important biological activities, such as antibacterial^[37, 43], antioxidant^[38, 68-69], antitumoral^[70-71], anti-leukemic^[72], and hepatoprotective^[73]. At the dose of 200 and 400 mg/kg, methanol extract from barks of *D. indica* produced an increase in pain threshold in hot plate and tail immersion methods, reduced the writhing caused by acetic acid and the number of licks induced by formalin. Methanol extract from leaves of this plant also showed anti-inflammatory activity and significant activity in acetic acid-induced permeability, in addition to central nervous system depressant activity^[40]. Crude methanol extract of the roots shows analgesic and antidiarrhoeal activities and reduced GI motility in animal models^[74]. In another study this extract and its bioactive EtOAc fraction also showed significant antidiabetic and antihyperlipidemic effects^[75-76] and has also inhibited the histopathological changes of the pancreas and kidney in alloxan induced diabetic rats^[75]. In DPPH (IC₅₀ 12.32 \pm 0.16 μ g/mL) and total reactive oxygen species (IC₅₀ 34.72 \pm 0.48 μ g/mL) this extract also showed antioxidant potentiality and a good reducing power^[68].

Ethanol and methanol extracts from the leaves and fruits of *D. indica* showed, respectively, hepatoprotective^[73] and anti-leukemic activities^[72]. Methanol extract was fractionated and EtOAc fraction showed the highest anti-leukemic activity. From this fraction, betulinic acid (**83**) was isolated. The crude methanol extract and its hexane, CCl₄ and CHCl₃ soluble fractions (500 μ g/disc) from the stems showed moderate antimicrobial activities. These extracts also revealed significant cytotoxic activity when tested by brine shrimp lethality bioassay and exhibited significant free radical scavenging activity^[37, 77]. The alkaline extract from the seeds of this plant exhibited activity against *Vibrio cholerae*, *Salmonella typhi* and *B. anthracis* and yielded saponins, glycosides, proteins, free amino acids, and sugars and the acetone extract exhibited activity against *Collaterotrichum* and *Trichoderma viride*^[78].

Aqueous-acetone extract from the barks and EtOAc, MeOH and H₂O extracts from the fruits of *D. indica* showed *In vitro* potent antioxidant effect (methanol > EtOAc > water)^[79-80]. At 1 mg/mL, ethanol extract showed the highest inhibition of α -amylase activity (60%), inhibited α -glucosidase activity and release of histamine from the peritoneal exudate cells^[81]. A mucoadhesive buccal tablet of oxytocin was prepared with mucilage isolated from edible *D. indica* fruits^[82-83]. After *In vitro* and *in vivo* studies, this product showed 27% bioavailability without damaging the buccal mucosa suggesting its suitability as an alternative to noninvasive

administration of oxytocin [81-83]. A new nasal gel formulation has been developed using this mucoadhesive agent. *In vitro* drug release characteristics using a Franz-diffusion cell and excised bovine nasal membrane was also found to be better in comparison to the synthetic polymers [hydroxyl-propyl-methyl cellulose (HPMC) and carbopol 934] [84]. Phytochemical studies with *D. indica* revealed the occurrence of a number of flavanoids (Table 1; Fig. 1), terpenoids (Table 2; Fig. 2), phenolic derivatives, in addition to alcohol, anthraquinone, dicarboxylic acid 3-deoxytartaric acid (Table 3; Fig. 3).

A chemical study involving seven *Dillenia* species (*D. andamanica*, *D. aurea*, *D. bracteata*, *D. indica*, *D. pentagyna*, *D. retusa*, and *D. scabralla*) showed that triterpenes [betulin (81) betulinic acid (83) and lupeol (99)], along with β -sitosterol (112) are present in all species [86]. Methanol extract of the stem bark of *D. pentagyna* showed antitumor activity *in vivo* against murine ascites Dalton's lymphoma [87]. From the stem and stem bark flavonoid glycosides [88-89], terpenoids [90-91], including a diterpene [92], were isolated (Tables 1-2).

In a preliminary study, the petroleum ether extract of *D. papuana* showed antibacterial activity. Biological activity-guided fractionation yielded four oleanene-type triterpenoids: dillenic acids A-C (90-92), and 3-oxoolean-1,12-dien-30-oic acid (104) (Fig. 2). These compounds and dillenic acids D (93) and E (94), isolated from the leaves and stems of this species, showed antibacterial activities against *B. subtilis*, *E. coli*, and *Micrococcus luteus* [44, 93]. According to Nick *et al.* [93], aside from a double bond in γ - or δ -position to a carboxylic group, a ketone function in ring A of an oleanene-skeleton may be required for this activity.

From the leaves of *D. philippinensis*, a sulphated glucoside [6'-O-sulphate benzyl glucoside (134)], four seco-A-ring oleanane-type triterpenoids (108-111) [2,3-seco-olean-12-ene-2,3,30-trioic acid (108), 2,3-seco-olean-12-ene-2,3,28-trioic acid (109), 2,3-seco-olean-12-ene-2,3-dioic-28-methyl ester (110), and 2,3-seco-olean-12-ene-2,3-dioic-28-butyl ester (111)], a flavonoid glucoside, and other compounds were isolated (Tables 2-3; Figs. 2-3). Triterpenes as 2 α ,3 β -dihydroxyolean-12-en-28-oic acid (88), messagenic acid (101), 2,3-seco-olean-12-ene-2,3-dioic-28-methyl ester (110) and 2,3-seco-olean-12-ene-2,3-dioic-28-butyl ester (111) exhibited moderate activity against *Leishmania major* and A549 human lung adenocarcinoma cells [70].

From the fruits of *D. kerrii*, a synonym of *D. parviflora*, terpenoids and phenolic derivatives were isolated (Tables 2-3;

Figs. 2-3). Among them, betulinol (81), betulinic acid (83), lupeol (99), ethyl gallate (118), and gallic acid (119) inhibited the proliferation of K562 cells. Compounds 118 and 119 also showed the anti-hypoxia effect with no cytotoxicity on anoxic ECV304 cells [72]. Hexane, CH₂Cl₂, EtOAc, MeOH, and aqueous extracts from different parts of *D. suffruticosa*, a plant used to treat cancerous growth, exhibited antimicrobial [94], antioxidant and cytotoxic activities. On the other hand, the CH₂Cl₂ and EtOAc exhibited higher cytotoxic activity to selected cancer cells (HeLa, MCF-7, MDA-MB-231, A549 and HT29) [95]. Phytochemical screening of these extracts suggested the presence of saponins, triterpenes, sterols, and polyphenolic compounds [95].

3.4.1 Phytochemistry profile of *Dillenia* species

From the chemical point of view, *Dillenia* species contain mainly flavonoids and terpenoids, besides other classes of compounds (Tables 1-3; Figs. 1-3) and polysaccharides [96-101]. The flavonoids were found as C-glucosylflavone, flavonols (free, glycosides and sulphates) and dihydroflavonols (Table 1; Fig. 1). Among flavonol glycosides, six of them (6-7, 17,

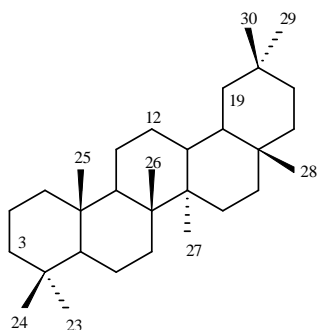
19, 50, and 55) occur exclusively in this genus while three of flavonol sulphates [kaempferol 3,7-disulphate (16), kaempferol 3-sulphate (22) and quercetin 3-sulphate (47)] co-occur in the genera *Schumacheria* and/or *Tetracera*. In relation to dihydroflavonols, with exception of (+)-dihydrokaempferol (60) and narigenin (68) that occur respectively also in *Wormia* (considered a synonymy of *Dillenia*) and *Davilla*, eight of them (61-64, 66 and 69-71) are restricted occurrence in this genus. The presence of flavonol O-methyl ethers has also been reported. Triterpenoids found in this genus possess diversified structural skeletons. They are lupane (81-84, 98-99, 101, and 107), cycloartane (87), oleanane (85, 89-92, 94, and 101-103), nor-lupane (104), and seco-A-ring oleanane-type (93 and 108-110) (Table 2; Fig. 2). This latter type of triterpene, in whole family, has limited occurrence in three species of this genus (*D. papuana*, *D. pentagyna* and *D. philippinensis*). Other compounds found in *Dillenia* species are phenolic derivatives (118-119 and 121-122), sulphated derivatives (124 and 134), anthraquinone glycoside (125), alcohol (129), acid (129), and (3S,5R,6R,7E,9S)-megastigman-7-ene-3,5,6,9-tetraol 3-O- β -D-glucopyranoside (132).

Table 2: Terpenoids isolated from Dilleniaceae species.

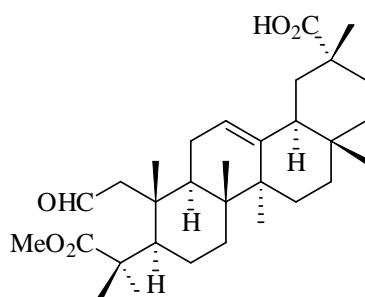
| Compounds | Source | Plant part/ References |
|--------------------------|---|--|
| β -Amyrin (80) | <i>C. americana</i> | Leaves [123] |
| Betulin = betulinol (81) | <i>Dillenia andamanica</i> , <i>D. aurea</i> , <i>D. bracteata</i> , <i>D. indica</i> , <i>D. pentagyna</i> , <i>D. retusa</i> , <i>D. scabralla</i> <i>Dillenia indica</i> <i>Dillenia indica</i> <i>Dillenia indica</i> | Leaves [86] Wood, Fruits [134-135] Stem barks [130] Trunk barks [136] |

| | | |
|--|---|---|
| | <i>Dillenia pentagyna</i> <i>Doliocarpus dentatus</i> <i>T. akara, T. indica, T. sarmentosa, T. scandens</i> | Stem barks ^[90] Stems ^[11] Leaves ^[86] |
| Betulinaldehyde (82) | <i>Dillenia indica</i> <i>Dillenia indica</i> <i>Dillenia papuana</i> <i>Doliocarpus dentatus</i> | Fruits ^[134] Stem barks ^[130] Leaves ^[44] Stems ^[11] |
| Betulinic acid (83) | <i>Acrotrema arnotianum</i> <i>A. uniflorum</i> <i>C. americana</i> <i>Davilla rugosa</i> <i>Dillenia andamanica, D. aurea, D. bracteata,</i> <i>D. indica, D. pentagyna, D. retusa, D. scabralla</i> <i>Dillenia indica</i> <i>Dillenia indica</i> <i>Dillenia indica</i> <i>Dillenia indica</i> <i>Dillenia kerrii</i> <i>Dillenia papuana</i> <i>Dillenia philippinensis</i> <i>Dillenia retusa</i> <i>Doliocarpus dentatus</i> <i>T. asiatica</i> <i>T. akara, T. indica, T. sarmentosa, T. scandens</i> <i>T. boiviniana</i> <i>T. breyniana</i> <i>T. potatoria</i> <i>Wormia burbridgei</i> <i>W. triquetra</i> | Entire plant ^[86] Entire plant ^[137] Leaves ^[123] Stems ^[88] Leaves ^[86] Fruits ^[72, 134] Leaves ^[130] , Stem barks ^[138] Trunk barks ^[136] Barks, Timber, Pericarp ^[137] Fruits ^[71] Stems, Leaves ^[93] Leaves ^[70] Barks, Fruits, Timber ^[137] Stems ^[11] Entire plant ^[117] Leaves ^[86] Twigs, Stem barks ^[115] Leaves ^[122] Roots ^[114] Barks ^[137] Barks, Fruits, Timber, Flowers ^[137] |
| Betulonic acid (84) 3- <i>cis</i> - (85) and 3- <i>trans-p</i> -Coumaroyl maslinic acid (86) | <i>Dillenia pentagyna</i> <i>T. boiviniana</i> | Stem barks ^[90] Twigs, Stem barks ^[115] |
| Cycloartenone (87) | <i>Dillenia indica</i> | Leaves ^[138] |
| Daucosterol (88) 2 α ,3 β -Dihydroxyolean-12-en-28-oic acid (89) | <i>T. asiatica</i> <i>Dillenia philippinensis</i> | Entire plant ^[117] Leaves ^[70] |
| Dillenic acid A (90), Dillenic acid B (91), Dillenic acid C (92) | <i>Dillenia papuana</i> | Aerial parts ^[44] |
| Dillenic acid D (93), Dillenic acid E (94) | <i>Dillenia papuana</i> | Stems, Leaves ^[93] |
| Diploic acid (95) | <i>Dillenia pentagyna</i> | Stems ^[92] |
| 3- <i>trans</i> -Feruloyl maslinic acid (96) | <i>T. asiatica</i> | Entire plant ^[5] |
| Friedelin (97) | <i>Davilla rugosa</i> | Stems ^[88] |
| 3 β -Hydroxylupane-13 β ,28-lactone (98) | <i>Dillenia indica</i> | Stem barks ^[130] |
| Lupeol (99) | <i>Acrotrema arnotianum</i> | Entire plant ^[30, 86] |

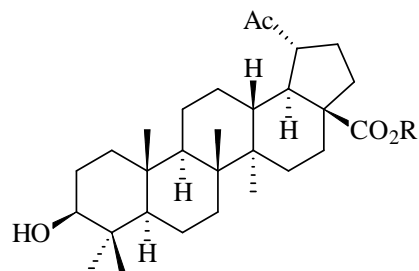
| | | |
|---|---|---|
| | <i>C. americana</i> | Leaves ^[123] |
| | <i>Dillenia andamanica</i> , <i>D. aurea</i> , <i>D. bracteata</i> , <i>D. indica</i> , <i>D. pentagyna</i> , <i>D. retusa</i> , <i>D. scabralla</i> | Leaves ^[86] |
| | <i>Dillenia indica</i> | Stem barks ^[130] |
| | <i>Dillenia kerrii</i> | Fruits ^[69] |
| | <i>Dillenia pentagyna</i> | Stem barks ^[90] |
| | <i>T. akara</i> , <i>T. indica</i> , <i>T. sarmentosa</i> , <i>T. scandens</i> | Leaves ^[86] |
| Lupeol acetate (100) | <i>Acrotrema arnotianum</i> | Entire plant ^[30, 86] |
| Messagenic acid (101) | <i>Dillenia philippinensis</i> | Leaves ^[70] |
| Morolic acid (102) | <i>Dillenia pentagyna</i> | Stem barks ^[90] |
| 3-Oxoolean-12-en-30-oic acid (103) | <i>Dillenia papuana</i> | Stems, Leaves ^[93] |
| 3-Oxoolean-1,12-dien-30-oic acid (104) | <i>Dillenia papuana</i> | Stems, Leaves ^[44] |
| Platanic acid (105), Platanic acid 28- <i>O</i> - β -D-glucopyranosyl ester (106) | <i>T. scandens</i> | Stems ^[120] |
| α -L-Rhamnopyranosyl-3 β -hydroxylup-20(29)-en-28-oic acid (107) | <i>Dillenia pentagyna</i> | Stems ^[90] |
| 2,3-Seco-olean-12-ene-2,3,30-trioic acid (108), 2,3-Seco-olean-12-ene-2,3,28-trioic acid (109), 2,3-Seco-olean-12-ene-2,3-dioic-28-methyl ester (110), 2,3-Seco-olean-12-ene-2,3-dioic-28-butyl ester (111) | <i>Dillenia philippinensis</i> | Leaves ^[70] |
| β -Sitosterol (112) | <i>Acrotrema arnotianum</i> <i>Dillenia andamanica</i> , <i>D. aurea</i> , <i>D. bracteata</i> , <i>D. pentagyna</i> , <i>D. scabralla</i> <i>Dillenia indica</i> | Entire plant ^[30, 86] Leaves ^[86] Leaves ^[138] |
| | <i>Dillenia indica</i> | Stem barks, Wood ^[130] , Fruits ^[135] |
| | <i>Dillenia indica</i> | Barks, Timber, Pericarp ^[85, 137] , Leaves ^[137] |
| | <i>Dillenia kerrii</i> | Fruits ^[71] |
| | <i>Dillenia pentagyna</i> | Leaves ^[86] |
| | <i>Dillenia retusa</i> | Timber ^[86] , Fruits ^[137] |
| | <i>T. asiatica</i> | Entire plant ^[117] |
| | <i>T. akara</i> , <i>T. indica</i> , <i>T. sarmentosa</i> , <i>T. scandens</i> | Leaves ^[86] |
| | <i>T. breyniana</i> | Leaves ^[122] |
| | <i>Wormia burbidgei</i> | Barks ^[137] |
| | <i>Wormia triquetra</i> | Barks, Fruits, Timber ^[137] |
| Sitostenone (113) | <i>Davilla rugosa</i> | Stems ^[88] |



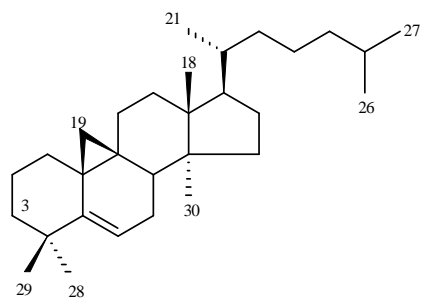
- | | | | |
|-----------|--|------------|--|
| 80 | 3 β -OH, Δ^{12} | 92 | 1 α -OH, 3-Oxo, 29-CO ₂ H, Δ^{12} |
| 85 | 2 α -OH, 3 β -O- <i>cis-p-Cou</i> , 28-CO ₂ H, Δ^{12} | 94 | 1 α ,3 β -OH,29 β -CO ₂ H, Δ^{12} |
| 86 | 2 α -OH, 3 β -O- <i>trans-p-Cou</i> , 28-CO ₂ H, Δ^{12} | 96 | 2 α -OH, 3 β -O- <i>trans-p-Fer</i> , 28-CO ₂ H, Δ^{12} |
| 89 | 2 α ,3 β -OH, 28-CO ₂ H, Δ^{12} | 102 | 3 β -OH,28-CO ₂ H, Δ^{18} |
| 90 | 2 α -OH, 3-Oxo, 29 β -CO ₂ H, Δ^{12} | 103 | 3-Oxo, 30-CO ₂ H, Δ^{12} |
| 91 | 2-Oxo, 3 β -OH, 29 β -CO ₂ H, Δ^{12} | 104 | 3-Oxo, 30-CO ₂ H, $\Delta^{1,12}$ |



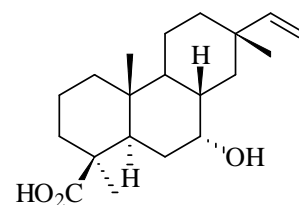
103



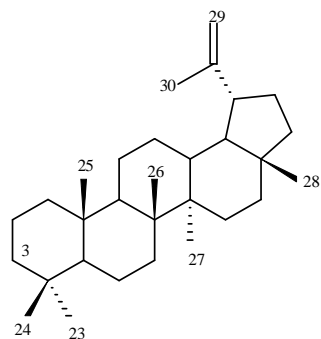
105 R = H
106 R = β -D-Glu



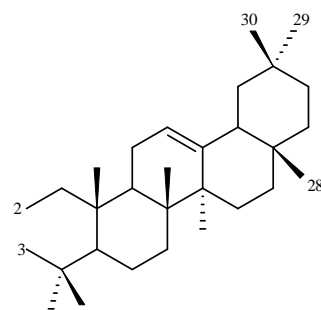
87 3 β -OH



95

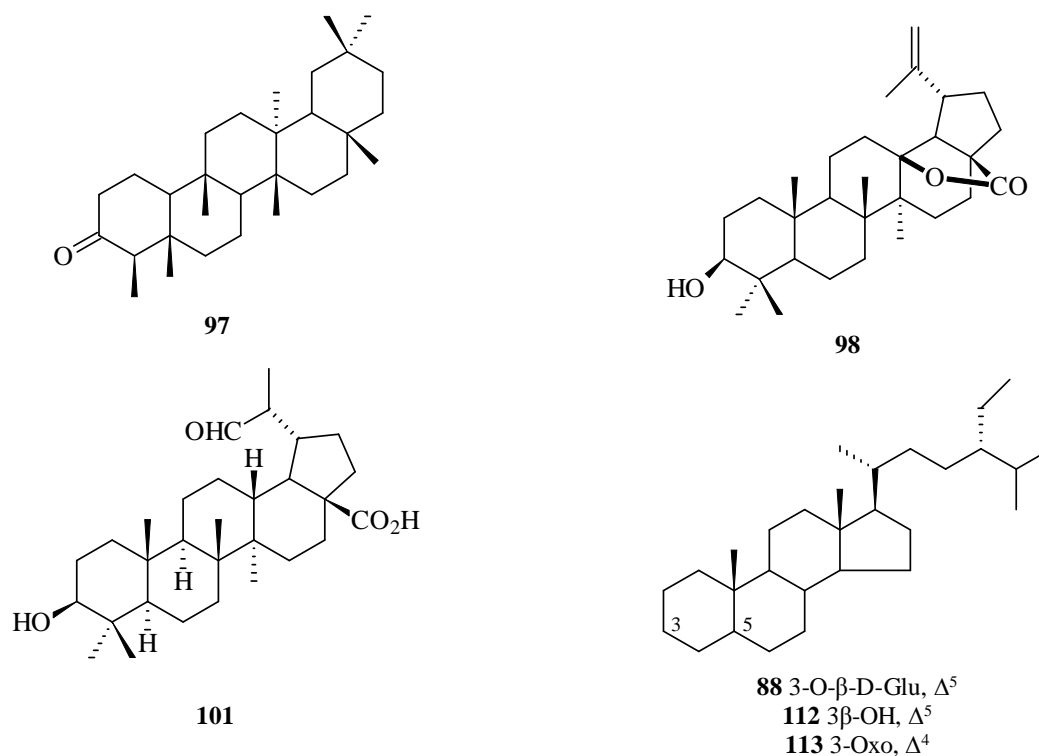


- | | |
|-----------|-------------------------------------|
| 81 | 3 β ,28-CH ₂ OH |
| 82 | 3 β -OH, 28-CHO |
| 83 | 3 β -OH, 28-CO ₂ H |
| 84 | 3-Oxo, 28-CO ₂ H |



- | | |
|------------|---|
| 108 | 2,3,30-CO ₂ H |
| 109 | 2,3,28-CO ₂ H |
| 110 | 2,3-CO ₂ H, 28-CO ₂ Me |
| 111 | 2,3-CO ₂ H, 28-CO ₂ -Bu |

99 3 β -OH
 100 3 β -OAc
 107 3 β -O- α -L-Rha, 28-CO₂H



Cou = Coumaroyl; Fer = Feruloyl.

Fig 2: Structures of terpenoids isolated from Dilleniaceae species.

3.5 *Doliocarpus* species

Antiproliferative bioassay-guided fractionation of the diethyl ether extract of *D. dentatus* led to the isolation of betulinic acid (**83**) as the cytotoxic active metabolite [47]. In addition, other triterpenes (Table 2) and lignans like (-)-lirioresinol B (**114**), (+)-medioresinol (**115**) and (+)-pinioresinol (**116**) also were isolated from stems of this species. Among them, betulinic acid (**82**) and lignans **114** and **115** showed *In vitro* activity against amastigotes of *L. amazonensis* [21]. From the bark, wood and leaves of *D. schottianus* betulinic acid (**83**) was detected and quantified by HPLC. The CH₂Cl₂-MeOH extract from woody stem and stem bark of *D. verruculosus* inhibits both human fibroblast collagenase and stromelysin in the initial screening. Bioassay-guided fractionation of this extract led to the isolation of **83** that also inhibited both activities in a concentration-dependent manner [45-46]. It also was active against human tumor cell lines and *M. tuberculosis* [47].

3.5.1. Phytochemistry profile of *Doliocarpus* species

A total of nineteen species of this genus were studied and the main chemical constituents isolated were flavonoids, triterpenes, lignans and other compounds (Tables 1-3; Figs. 1-3). There is not a single substance which is present in all species; however, flavonoids are present at least one of all studied species and chlorogenic (**123**) and isochlorogenic (**131**) acids occurring in 10 out of 19 species (Table 3).

Among the flavonoids, C-glycosylflavones like isovitexin (**11**), saponarin (**54**) and vitexin (**56**), mostly co-occurring and represented in four to six species. With exception of **56** that also was found in *Dillenia* spp. [61], they seem to be a characteristic feature of the genus because the former were not found in other genera of the family, only in leaves of *D. amazonicus*, *D. brevipedicellatus*, *D. lancifolius*, *D. multiflorus*, and *D. paraensis* (Table 1). In addition, quercetin 3-robinobioside (**48**) occurs only in leaves of *D. macrocarpus* and *D. savannarum* [61], but not in other genera of the family. In the whole family, the occurrence of lignans is limited to one species of this genus (*D. dentatus*) [11].

Kubitzki [102] divided this genus into two sections: *Calinea*, characterized by having leaves with tertiary nerves subparallel, filaments erect-flexuose with anthers, and ovary glabrous or pilose, and *Doliocarpus* having leaves with tertiary nerves reticulate, filaments reflexed with anthers extrorse at anthesis, and the ovary pilose [31]. According to Gurni and Kubitzki [61], phytochemistry gives strong support to the close relationship between the two sections of *Doliocarpus* which chemically cannot be distinguished; this is important because, based on morphology, the homogeneity of the genus could not be established beyond doubt.

3.6 *Hibbertia* species

Hibbertia is a large Australian genus that includes over 150

species of lianas, shrubs, and small trees. Most of them are endemic to Australia, the remainder found in Madagascar, New Caledonia, New Guinea and Fiji [103]. This genus is currently undergoing critical taxonomic revision and the current delineation and identification of some taxa is problematic and species phylogenetic relationships are unknown. Based on floral feature and a molecular phylogenetic study there are four subgenera recognized: *Hibbertia* subg. *Hibbertia*, *Hibbertia* subg. *Adrastea*, *Hibbertia* subg. *Hemistemma*, and *Hibbertia* subg. *Pachynema* [19]. At moment, no information on traditional medicine or biological studies was reported for this genus.

3.6.1 Phytochemistry profile of *Hibbertia* species

Although *Hibbertia*, the largest genus of the family, was not studied in detail because of the lack of modern taxonomic treatment, the distribution of the flavonoids in the leaves of eighteen species was investigated by Kubitzki [103]. Some of them contain myricetin and/or quercetin or both and kaempferol. Luteolin (**24**) was found only in *H. cuneiformis* (Table 1; Fig. 1) and all species investigated contain ellagic acid (Table 3; Fig. 3) and leucoanthocyanans.

3.7 *Pinzona* species

Pinzona is a monotypic genus characterized by one species [*P. coriacea* (syn.: *Doliocarpus calinoides*)] [105]. From the leaves this plant flavonoids like avicularin (**4**), quercetin (**40**), quercetin-3-O-galactopyranoside (**42**), and quercetin-3-O- α -L-rhamnoside (**47**), besides procyanidin were found (Table 1; Fig. 1). *Pinzona* and *Curatella* are genera chemically closely akin. The only difference between them is the presence of quercetin 3-galactoarabinoside (**43**) in *Curatella* which also is not present in any other genus of the family. Among the different compounds common to them, avicularin (**4**) is especially meaningful because this is absent from all other genera of the family.

3.8 *Didesmandra*, *Neodillenia* and *Pachynema*

The genus *Didesmandra* is known from only a few populations in Sarawak, Borneo [19] while *Neodillenia* (03 species) has occurrence in the Amazon region (Brazil), Colombia, Ecuador, Peru, and Venezuela [20]. According to Kubitzki [48], the species previously placed in *Pachynema* were transferred to *Hibbertia* [19]. At moment, no information on traditional medicine, pharmacological or phytochemical studies were reported for these genera.

3.9 *Schumacheria* species

This genus is endemic to Sri Lanka and contains only three species (*S. alnifolia*, *S. angustifolia* and *S. castaneifolia*). Methanol extracts of the stem-bark, root-bark and leaves of *S. castaneifolia* showed antioxidant (DPPH), cytotoxic (brine shrimp assay) and phytotoxic activities [105]. Chemically, these species have been studied and their chemical profile is characterized by the presence of flavonols free and glycosides based on kaempferol, myricetin and quercetin (Table 1). The flavonol glycosides of *S. alnifolia* [myricetin 3-arabinoside (**32**), myricetin 3-galactopyranoside (**33**), quercetin-3-O-galactopyranoside (**42**), and quercetin 3-glucoside (**45**)] are replaced by flavonol sulphates in *S. angustifolia* [quercetin 3-sulphate (**49**)] and *S. castaneifolia* [kaempferol 3,7-disulphate (**16**), kaempferol 3-sulphate (**22**) and quercetin 3-sulphate (**49**)] [61].

3.10 *Tetracera*

Tetracera, the sole genus of subfamily Delimoideae, contains about 45 species with a pantropical distribution, of which 20 occur in the Neotropical area [61]. According Kubitzki [107], this genus presents two sections: *Tetracera* (plants with rough leaves and inflorescence with 12-200 flowers) and *Akara* (with only one species occurring in the America) [108]. A variety of reports are found about biological properties of *Tetracera* species. Some of them were active as antifungal [109], antinociceptive [110], antiplasmodial [49], antimycobacterial [54], anti-HIV and anti-reverse transcriptase [111], anti-hyperglycemic [53], antioxidant [112-113], anti-ulcerogenic [51-52, 114], hepatoprotective [112], DNA polymerase β inhibition [115], glucose-uptake activity [115], and xanthine oxidase inhibition [50].

3.10.1 Phytochemistry profile of *Tetracera* species

Phytochemical investigations on *Tetracera* species showed that flavonoids and terpenoids are the main chemical constituents (Tables 1-2), with many of them actives to most different purposes. Among them, betulinic acid (**83**) from *T. potatoria* significantly reduced induced gastric ulceration in pretreated animals [114]. 3-*Trans*-feruloyl maslinic acid (**96**) from whole plant of *T. asiatica* showed potent anti-cancer, anti-HIV, anti-diabetic, and anti-inflammatory activities [5]. Other chemical constituents such as izalpinin (**12**), izalpinin-3-methyl ether (**13**), kaempferol-4,7-dimethyl ether (**15**), wogonin (**57**), wogonin 7-O- β -D-glucuronide methyl ester (**58**), wogonin 7-O- β -D-glucuronide (**59**), dihydrowogonin (**65**), betulinic acid (**83**), daucosterol (**88**), β -sitosterol (**112**), and stearic acid (**133**) have been also isolated [117].

Bioassay-guided fractionation of an active methyl ethyl ketone extract from twigs and stem bark of *T. boiviana*, using an assay to monitor DNA polymerase β inhibition (98% inhibition at 100 μ g/mL), resulted in the isolation of betulinic acid (**83**), 3-*cis*- (**85**) and 3-*trans*-*p*-coumaroyl maslinic (**86**) acids. These compounds inhibited DNA polymerase β in the presence (IC₅₀ 14, 15, and 4.2 μ M, respectively) and absence of bovine serum albumin (IC₅₀ 6.5, 7.5, and 2.0 μ M, respectively). Further, these compounds potentiated the effects of bleomycin in cultured P-388D1 cells [115].

A screening conducted with methanol extract from leaves of *T. indica* showed antibacterial activity against *B. subtilis*, *S. aureus* and *E. coli* [117] and antihyperglycemic effects [55]. Phytochemical study of this extract revealed the occurrence of terpenoids (Table 2) and a flavonoid [wogonin (**57**)] [89]. Petroleum ether extract from leaves of *T. poggei*, a plant used in the Democratic Republic of Congo for dysentery, hepatitis, gonorrhoea, as febrifuge and diuretic, showed antiplasmodial activity. From this plant was isolated rhamnocitrin 3-sulphate (**53**) [49].

An ethanol extract of *T. scandens* showed anti-HIV and *In vitro* anti-HIV-1 reverse transcriptase (RTase) activities [111]. Methanol extract of this plant also showed protein tyrosine phosphatase 1B inhibitory activity *In vitro* [119] and MeOH-H₂O extract exhibited strong xanthine oxidase inhibitory activity (IC₅₀ 15.6 μ g/mL) [50]. From MeOH extract of the stem of this plant, a *nor*-lupane triterpene, 28-O- β -D-glucopyranosyl ester of platanic acid (**106**), was isolated together with kaempferol (**14**), quercetin (**40**), tiliroside (**55**), betulinic acid (**83**), platanic acid (**105**), and emodin (**127**).

With exception of **55**, all other compounds displayed significant xanthine oxidase inhibitory activity, and compound **127** showed more potent inhibitory activity (IC_{50} 1.9 μ M) than that of a positive control [120]. An EtOAc-soluble partition of the methanol extract of a branch of *T. scandens* showed glucose-uptake activity. From this fraction five isoflavones [alpinumisoflavone (**72**), derrone (**73**), 3',5'-diprenylgenistein (**74**), 6,8-diprenylgenistein (**75**), and genistein (**76**)] were isolated. With exception of **75**, these compounds also

exhibited significant glucose-uptake activity in basal and insulin-stimulated L6 myotubes and inhibited protein tyrosine phosphatase 1B activities. Compounds **74** (IC_{50} 34.27 \pm 0.35 μ M) and **76** (IC_{50} 18.69 \pm 0.19 μ M) reduced muscle cell viability [116].

T. alnifolia var. *podotricha* bark and leaves contain tannins, catechol tannins, flavonoids, and leucoanthocyanin. *T. masuiana* leaves and rhizomes contain tannins and leucoanthocyanin [121]. Hexane fraction from stem of *T. breyniana* was effective (LD_{50} 72.08 μ g/mL) against fourth instar *Aedes aegypti* larvae and EtOAc fractions from the leaves and stem showed moderate ability to scavenge free radicals. From these later fractions were isolated three flavonols [quercetin (**40**), 7-O-methylkaempferol (**28**) and 7-O-methylquercetin (**29**) and two terpenoids [betulinic acid (**83**) and β -sitosterol (**112**)] [122]. In another study was isolated from

the leaves azaleatin (**5**), kaempferol (**14**), kaempferol 3-sulphate (**22**), 5-methylkaempferol (**28**), quercetin (**40**), quercetin-3-O-galactopyranoside (**42**), and quercetin 3-sulphate (**49**) [61].

In this genus, beside procyanidin and prodelfinidin, a total of 35 flavonoids distributed in different structural types (flavones, flavonols, dihydroflavonols, and isoflavones) were found (Table 1). Flavonols are present as galactosides (**2**, **17**, **33**, **42**), glucosides (**45** and **52**), rhamnosides (**21**, **34**, **47**), glucuronides (**44**, **52** and **58-59**), and sulphates (**2-3**, **22**, **25**, **49**, and **53**) (Fig. 1). Flavonol O-methyl ethers (**5**, **12-13**, **15**, **28**, **51-53**, **57-59**) also are frequent occurrence. In whole family, isoflavones (**72-76**) were found only in *T. scandens* [116]. Terpenoids like triterpenes and phytosteroids (Table 2; Fig. 2) as well as other compounds like ellagic acid (**117**), emodin (**127**), foeniculin (**128**), and stearic acid (**133**) (Fig. 3) also were found in this genus.

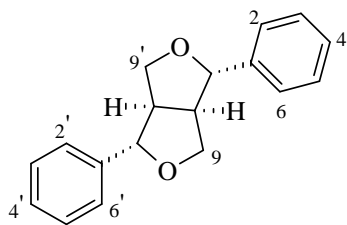
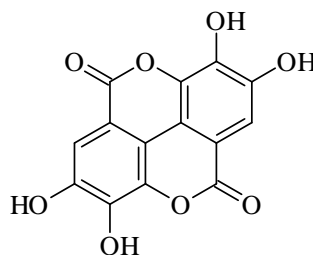
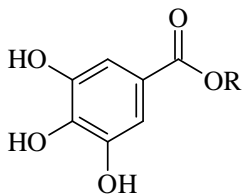
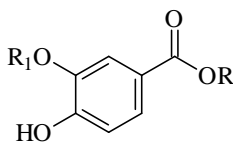
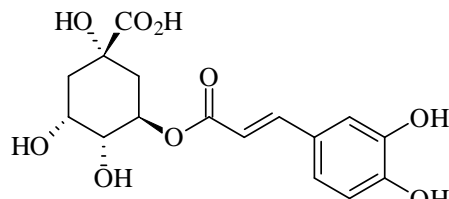
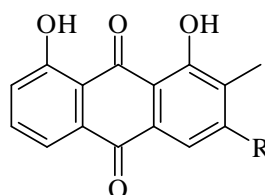
3.11 Wormia species

This genus is considered a synonym of *Dillenia* [123]. Flavonoids (Table 1) and other compounds like sitosterol (**112**) and gallic acid (**119**) were isolated from bark and timber of *W. triquetra*, a synonym of *D. triquetra*, and *W. burbridgei*, a synonym of *D. burbridgei* [124].

Table 3: Other compounds isolated from Dilleniaceae species.

| Compounds | Source | Plant part/References |
|---|---|--|
| <i>Lignans and Phenolic derivatives</i> | | |
| (-)-Lirioresinol B (114), (+)-Medioresinol (115), (+)-Pinioresinol (116) | <i>Doliocarpus dentatus</i> | Stems [11] |
| Ellagic acid (117) | <i>Doliocarpus savannarum</i> , <i>T. madagascariensis</i> , <i>T. poggei</i> , <i>T. rosiflora</i> | Leaves [61] |
| Ethyl gallate (118) | <i>Dillenia kerrii</i> | Fruits [71] |
| Gallic acid (119) | <i>C. americana</i> <i>Davilla elliptica</i> , <i>D. nitida</i> <i>Dillenia kerrii</i> <i>Dillenia indica</i> <i>Dillenia retusa</i> <i>Wormia burbridgei</i> , <i>W. triquetra</i> | Leaves [125] Leaves [33] Fruits [71] Barks [124] Barks [124] |
| 3-Methoxy-4-hydroxybenzoic acid (120) | <i>Acrotrema arnottianum</i> | Leaves [137] |
| Protocatechuic acid (121), Protocatechuic acid methyl ester (122) | <i>Dillenia kerrii</i> | Fruits [71] |
| <i>Other compounds</i> | | |
| Chlorogenic acid (123) | <i>Doliocarpus brevipedicellatus</i> , <i>D. dentatus</i> , <i>D. elegans</i> , <i>D. guianensis</i> , <i>D. lancifolius</i> , <i>D. macrocarpus</i> , <i>D. major</i> , <i>D. multiflorus</i> , <i>D. savannarum</i> , <i>D. sellowianus</i> | Leaves [61] |
| Corchoionoside C6'-O-sulphate (124) | <i>Dillenia philippinensis</i> | Leaves [70] |
| 1,8-Dihydroxy-2-methyl-anthraquinone-3-O- β -D-glucopyranoside (125) | <i>Dillenia indica</i> | Stem barks [125] |

| | | |
|---|--|------------------------------|
| <i>n</i> -Dotriacontanol (126) | <i>Acrotrema arnottianum</i> | Entire plant ^[30] |
| Emodin (127) | <i>T. scandens</i> | Stems ^[120] |
| Foeniculin (128) | <i>C. americana, Davilla alata, Doliocarpus guianensis, D. macrocarpus, D. savannarum, D. schottianus, D. validus, Pinzona coriacea, T. boiviniana, T. breyniana, T. costata, T. volubilis</i> | Leaves ^[61] |
| <i>n</i> -Hentriacontanol (129) | <i>Dillenia indica</i> | Leaves ^[138] |
| 2-Hydroxybutane-1,4-dioic acid (130) | <i>Dillenia indica</i> | Fruits ^[134] |
| Isochlorogenic acid (131) | <i>Doliocarpus brevipedicellatus, D. dentatus, D. elegans, D. guianensis, D. lancifolius, D. macrocarpus, D. major, D. multiflorus, D. savannarum, D. sellowianus</i> | Leaves ^[61] |
| (3 <i>S</i> ,5 <i>R</i> ,6 <i>R</i> ,7 <i>E</i> ,9 <i>S</i>)-Megastigman-7-ene-3, 5,6,9-tetraol 3-O-β-D-glucopyranoside (132) | <i>Dillenia philippinensis</i> | Leaves ^[70] |
| Stearic acid (133) | <i>T. asiatica</i> | Leaves ^[117] |
| 6'-O-Sulphate benzyl glucoside (134) | <i>Dillenia philippinensis</i> | Leaves ^[70] |
| α-Tocopherol (135) | <i>Davilla flexuosa</i> | Leaves ^[88] |
| <i>n</i> -Triacontanoic acid (136) | <i>Acrotrema arnottianum</i> | Entire plant ^[30] |

**114** 4,4'-OH, 3,3',5,5'-OMe**115** 3,3',5'-OMe, 4,4'-OH**116** 4,4'-OH, 3,3'-OMe**117****118** R = Me**119** R = H**120** R = H, R₁ = Me**121** R = R₁ = H**122** R = Me, R₁ = H**123****CH₃(CH₂)₃₀CH₂OH****126**

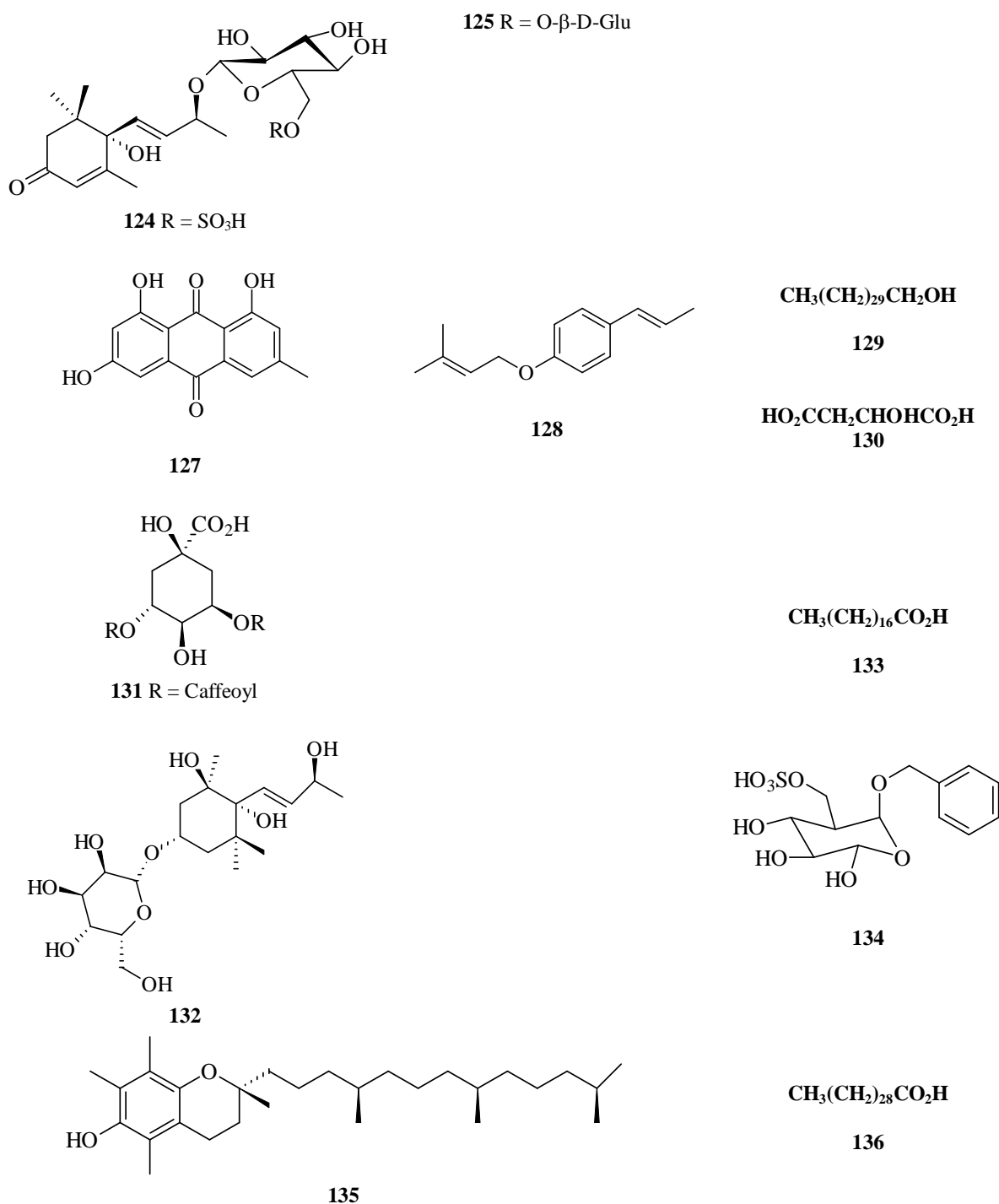


Fig 3: Other compounds isolated from Dilleniaceae species.

4. Conclusion

The extensive literature survey as well as reports on research revealed that Dilleniaceae species are highly regarded to have good potential in the herbal medicine and possess a wide variety of biological properties. The chemical studies of this family deal mainly with flavonoids, triterpenoids, phenolic derivative and other compounds. Comparative analysis of flavonoids of Dilleniaceae species, with particular emphasis on Neotropical genera was previously performed. In this study, the authors found that the distribution of the flavonoids

is reticulate and does not permit the recognition of taxa between the level of genus and family. Currently, the situation does not seem very different. The established occurrence of flavonoids in all genera of Dilleniaceae studied suggests that this class of compounds is a general feature of this family. In this review, more than 130 compounds distributed into different structural classes [flavonoids (76), terpenoids (33), lignans (03), anthraquinone (02), phenolic derivative (07) and others (12)] were found. There are only four structural types of flavonoids reported in this family (flavones, flavonols,

dihydroflavonols, and isoflavones). With exception of isoflavones, flavonoids are present as arabinosides, galactosides, glucuronides, glucosides, rhamnosides, and sulphates. Flavones and flavonols glycosides are present in all genera while flavonoids sulphates were found only in five of them (*Acrotrema*, *Davilla*, *Dillenia*, *Schumacheria*, and *Tetracera*), glucuronides in two (*Dillenia* and *Tetracera*), and dihydroflavonols only in three (*Davilla*, *Dillenia* and *Tetracera*) of the eleven genera studied. In the whole family, the occurrence of lignans is limited to *Doliocarpus dentatus* and there is also an occasional occurrence of isoflavonoids, which in the present instance is limited to one species of the genus *Tetracera*. Almost every species studied contain leucoanthocyanans.

5. Acknowledgements

The authors thank to CNPq, FAPCAL and CAPES for the financial support.

6. References

- Phillipson JD. Phytochemistry and medicinal plants. *Phytochemistry* 2001; 56:237-243.
- Bhat R, Karim AA. Tongkat Ali (*Eurycoma longifolia* Jack): a review on its ethnobotany and pharmacological importance. *Fitoterapia* 2010; 81:669-679.
- Liogier HA. Las Plantas medicinales de Puerto Rico y del Caribe. Iberoamericana de Ediciones. Inc., San Juan, PR: 1990.
- Killeen TJ, García E, Beck SG. Guía de árboles de Bolivia. Missouri Botanical Gardens and Herbario Nacional de Bolivia. La Paz, Bolivia, 1993.
- Subramanyam R, Goud M, Sudhamalla B, Reddeem E, Gollapudi A, Nellaepalli YV. Novel binding studies of human serum albumin with trans-feruloyl maslinic acid. *J Photochem Photobiol B: Biol* 2009; 95:81-88.
- Bruniera CP, Groppo M. Flora da Serra do Cipó, Minas Gerais: Dilleniaceae. *Bol Bot Univ São Paulo* 2010; 28:59-67.
- Alexandre-Moreira MS, Piuvezam MR, Araujo CC, Thomas G. Studies on the anti-inflammatory and analgesic activity of *Curatella americana* L. *J Ethnopharmacol* 1999; 67:171-177.
- Vilar JB, De-Andrade LS, Leite KR, Ferreira HD, Chen LC. Assessment of genotoxicity and cytotoxicity of "lixreira" (*Curatella americana* L.) using the prophage lambda induction test (SOS inductest). *Braz J Pharm Sci* 2009; 45:491-496.
- Hiruma-Lima CA, Rodrigues CM, Kushima H, Moraes TM, Lolis SF, Feitosa SB. The anti-ulcerogenic effects of *Curatella americana* L. *J Ethnopharmacol* 2009; 121:425-432.
- Soares ML, Rezende MH, Ferreira HD, Figueiredo ADL, Bustamante KGL, Bara MTF, Paula JR. Pharmacognostic characterization of leaves of *Davilla elliptica* St.-Hil. (Dilleniaceae). *Rev Bras Farmacogn* 2005; 15:352-360.
- Sauvain M, Kunesch N, Poisson J, Gantier J-C, Gayral P, Dedet J-P. Isolation of leishmanicidal triterpenes and lignans from the Amazonian liana *Doliocarpus dentatus* (Dilleniaceae). *Phytother Res* 1996; 10:1-4.
- Nishijima CM, Rodrigues CM, Silva MA, Lopes-Ferreira M, Vilegas W, Hiruma-Lima CA. Anti-hemorrhagic activity of four Brazilian vegetable species against *Bothrops jararaca* venom. *Molecules* 2009; 14:1072-1080.
- De-Toledo CEM, Britta EA, Ceole LF, Silva ER, De-Mello JCP, Dias Filho BP, Nakamura CV, Ueda-Nakamura T. Antimicrobial and cytotoxic activities of medicinal plants of the Brazilian cerrado, using Brazilian cachaca as extractor liquid. *J Ethnopharmacol* 2011; 133:420-425.
- Costa ES, Hiruma-Lima CA, Lima EO, Sucupira GC, Bertolin AO, Lolis SF. Antimicrobial activity of some medicinal plants of the Cerrado, Brazil. *Phytother Res* 2008; 22:705-707.
- Carli CB, De-Matos DC, Lopes FC, Maia DC, Dias MB, Sannomiya M. Isolated flavonoids against mammary tumour cells LM2. *Z Naturforsch C* 2009; 64:32-36.
- Kushima H, Nishijima CM, Rodrigues CM, Rinaldo D, Sassa MF, Bauab TM *et al.* *Davilla elliptica* and *Davilla nitida*: gastroprotective, anti-inflammatory immunomodulatory and anti-*Helicobacter pylori* action. *J Ethnopharmacol* 2009; 123(3):430-438.
- Endringer DC, Valadares YM, Campana PRV, Campos JJ, Guimaraes KG, Pezzuto JM. Evaluation of Brazilian plants on cancer chemoprevention targets *In vitro*. *Phytother Res* 2010; 24:928-933.
- Horn JW. Phylogenetics of Dilleniaceae using sequence data from four plastid loci (*rbcL*, *infA*, *rps4*, *rpl16* intron). *Int J Plant Sci* 2009; 170:794-813.
- Horn JW. Dilleniaceae. In *Flowering plants. The families and genera of vascular plants*. Kubitzki K, editor. Berlin: Springer Verlag, 2007, 132-154.
- Fraga CN, Stehman JR. Novidades taxonômicas para Dilleniaceae brasileiras. *Rodriguesia* 2010; 61:S01-S06.
- APG II (Angiosperm Phylogeny Group II) An update of the Angiosperm Phylogeny Group classification for the orders and families of flowering plants: APG II. *Bot J Linn Soc* 2003; 141:399-436.
- Worberg A, Quandt D, Barniske AM, Löhne C, Hilu KW, Borsch T. Phylogeny of basal eudicots: insights from non-coding and rapidly evolving DNA. *Org Divers Evol* 2007; 7:55-77.
- APG III (Angiosperm Phylogeny Group III) An update of the Angiosperm Phylogeny Group classification for the orders and families of flowering plants: APG III. *Bot J Linn Soc* 2009; 161:105-121.
- Juan R, Pastor J, Alaiz M, Vioque J. Electrophoretic characterization of *Amaranthus* L. seed proteins and its systematic implication. *Bot J Linn Soc* 2007; 155:57-63.
- Soltis DE, Sinters AE, Zanis MJ, Kim S, Thompson JD, Soltis PS, Ronse De Craene LP, Endress, PK, Farris JS. Gunnerales are sister to other core eudicots: implications for the evolution of pentamery. *American J Bot* 2003; 90:461-470.
- Moore MJ, Soltis PS, Bell CD, Burleigh JG, Soltis DE. Phylogenetic analysis of 83 plastid genes further resolves the early diversification of eudicots. *Proceedings of the National Academy of Sciences of the United States of America* 2010; 107:4623-4628.
- Soltis DE, Smith SA, Cellinese N, Wurdack KJ, Tank DC, Brockington SF *et al.* Angiosperm phylogeny: 17 genes, 640 taxa. *American J Bot* 2011; 98:704-730.
- Kumari JU, Navas M, Dan M, Rajasekharan S. Pharmacognostic studies of *Acrotrema arnottianum* Wight – A promising ethnomedicinal plant. *Indian J Trad Know* 2009; 8:334-339.
- Sarmiento G, Monasterio M. Life forms and phenology.

- In:F. Bourlière, ed. Ecosystems of the World XIII. Tropical savannas. Amsterdam, The Netherlands; Elsevier; 1983, 79-108.
30. Guerrero MF, Puebla P, Carron R, Martin ML, Arteaga L, San Roman L. Assessment of the antihypertensive and vasodilator effects of ethanolic extracts of some Colombian medicinal plants. *J Ethnopharmacol* 2002; 80:37-42.
 31. Aymard GA. Three new species of *Davilla* (Dilleniaceae) from Brazil. *Novon* 2007; 17:282-287.
 32. Mendes FR, Tabach R, Carlini EA. Evaluation of *Baccharis trimera* and *Davilla rugosa* in tests for adaptogen activity. *Phytother Res* 2007; 21:517-522.
 33. Biso FI, Rodrigues CM, Rinaldo D, Bisarro RM, Bernardi CC, Pelielo MsJC *et al.* Assessment of DNA damage induced by extracts, fractions and isolated compounds of *Davilla nitida* and *Davilla elliptica* (Dilleniaceae). *Mutat Res, Gen Toxicol Env Mutag* 2010; 702:92-99.
 34. Lopes FCM, Placeres MCP, Jordao JCM, Higuchi CT, Rinaldo D, Vilegas W *et al.* Immunological and microbiological activity of *Davilla elliptica* St. Hill. (Dilleniaceae) against *Mycobacterium tuberculosis*. *Mem Inst Oswaldo Cruz* 2007; 102:769-772.
 35. Bacchi EM. Ação anti-úlceras e cicatrizante de algumas plantas brasileiras. *Rev Bras Farmacogn* 1986; 1:93-100.
 36. Shome U, Khanna RK, Sharma HP. Pharmacognostic studies on *Dillenia indica* Linn. I. leaf. *Proc Indian Acad Sci* 1979; 88:35-48.
 37. Parvin MN, Rahman MS, Mohammad S, Islam MS, Rashid MA. Chemical and biological investigations of *Dillenia indica* Linn. *Bangladesh J Pharmacol* 2009; 4:122-125.
 38. Kumar S, Kumar V, Prakash O. Antidiabetic and antihyperlipidemic effects of *Dillenia indica* (L.) leaves extract. *Braz Pharm Sci* 2011a; 47:373-378.
 39. Kumar S, Kumar V, Prakash O. Microscopic evaluation and physicochemical analysis of *Dillenia indica* leaf. *Asian Pac J Trop Biomed* 2011b; 1:337-340.
 40. Yeshwante SB, Juvekar AR, Nagmoti DM, Wankhede SS, Shah AS, Pimprikar RB *et al.* Anti-inflammatory activity of methanolic extracts of *Dillenia indica* L. leaves. *Pharmacology* 2009; 1:63-66.
 41. Sharma HK, Chhange L, Dolui AK, Nishikimi M, Rao NA, Yagi K. Traditional medicinal plants in Mizoram, India. *Fitoterapia* 2001; 72:146-161.
 42. Tag H, Kalita P, Dwivedi P, Das AK, Namsa ND. Herbal medicines used in the treatment of diabetes mellitus in Arunachal Himalaya, northeast, India. *J Ethnopharmacol* 2012; 141:786-795.
 43. Gandhi D, Mehta P. *Dillenia indica* Linn. and *Dillenia pentagyna* Roxb.: Pharmacognostic, Phytochemical and Therapeutic aspects. *J Appl Pharm Sci* 2013; 3:134-142.
 44. Nick A, Wright AD, Sticher O, Rali T. Antibacterial triterpenoid acids from *Dillenia papuana*. *J Nat Prod* 1994; 57:1245-1250.
 45. Sun HH, Kaplita PV, Houck DR, Stawicki MB, McGarry R, Wahl RC, Gillum AM, Cooper R. A metalloproteinase inhibitor from *Doliocarpus verruculosus*. *Phytother Res* 1996; 10:194-197.
 46. De-Oliveira BH, Santos CAM, Espindola APDM. Determination of the triterpenoid, betulonic acid, in *Doliocarpus schottianus* by HPLC. *Phytochem Analysis* 2002; 13:95-98.
 47. Aponte JC, Vaisberg AJ, Rojas R, Caviedes L, Lewis WH, Lamas G *et al.* Isolation of cytotoxic metabolites from targeted Peruvian Amazonian medicinal plants. *J Nat Prod* 2008; 71:102-105.
 48. Kubitzki K. Dilleniaceae. In: Smith N. *Flouring Plants of the Neotropics*. New Jersey, Princenton; 2004, 128-130.
 49. Tona L, Cimanga RK, Mesia K, Musuamba CT, De Bruyne T, Apers S *et al.* *In vitro* antiplasmodial activity of extracts and fractions from seven medicinal plants used in the Democratic Republic of Congo. *J Ethnopharmacol* 2004; 93:27-32.
 50. Nguyen MTT, Awale S, Tezuka Y, le-Tran Q, Watanabe H, Kadota S. Xanthine oxidase inhibitory activity of Vietnamese medicinal plants. *Biol Pharm Bull* 2004; 27:1414-1421.
 51. Fenner R, Betti AH, Mentz LA, Rates SMK. Plantas utilizadas na medicina popular brasileira com potencial atividade antifúngica. *Rev Bras Cienc Farmac* 2006; 42, 269-394.
 52. Oluwole FS, Ayo JA, Omoloso BO, Emikpe BO, Adesanwo JK. Methanolic extract of *Tetracera potatoria*, an antiulcer agent increases gastric mucus secretion and endogenous antioxidants. *Nigerian J Physiol Sci* 2008; 23:79-83.
 53. Umar A, Ahmed QU, Muhammad BY, Dogarai BB, Soad SZ. Anti-hyperglycemic activity of the leaves of *Tetracera scandens* Linn. Merr. (Dilleniaceae) in alloxan induced diabetic rats. *J Ethnopharmacol* 2010; 131:140-145.
 54. Lawal TO, Adeniyi BA, Wan B, Franzblau SG, Mahady GB. *In-vitro* susceptibility of *Mycobacterium tuberculosis* to extracts of *Uvaria afzelli* Scott Elliot and *Tetracera alnifolia* Willd. *Afr J Biomed Res* 2011; 14:17-21.
 55. Ahmed QU, Dogarai BBS, Amiroudine MZAM, Taher M, Latip J, Umar A, Muhammad BY. Antidiabetic activity of the leaves of *Tetracera indica* Merr. (Dilleniaceae) in vivo and *In vitro*. *J Med Plants Res* 2012; 6:5912-5922.
 56. Hedberg I, Hedberg O, Madati PO, Mshigeni KE, Mshiiif EN, Samuelsson G. Inventory of plants used in traditional medicine in Tanzania. II. Plants of the families Dilleniaceae-Opliaceae. *J Ethnopharmacol* 1983; 9:106-128.
 57. Ong HC, Nordiana M. Malay ethno-medico botany in Machang, Kelantan, Malaysia. *Fitoterapia* 1999; 70:502-513.
 58. Faridah HI, Nurulhuda H. The use of medicinal plant species by the temuan tribe of Ayer Hitam forest, Selangor peninsular Malaysia. *J Trop Agric Sci* 1999; 22:85-94.
 59. Mathew J, Shiburaj S, George V. Antibacterial activity of *Acrotrema arnotianum* Wight. Proc. Fifteenth Kerala Science Congress, Thiruvananthapuram, 2003, 746.
 60. Mathew J, Georg, V. Bioactive compounds from *Acrotrema arnotianum*. *Asian J Chem* 2006; 18:2747-2755.
 61. Gurni AA, Kubitzki K. Flavonoid chemistry and systematic of the Dilleniaceae. *Biochem Syst Ecol* 1981; 9:109-114.
 62. Gurni AA, König WA, Kubitzki K. Flavonoid glycosides and sulphates from the Dilleniaceae. *Phytochemistry* 1981; 20:1057-1059.
 63. Azevedo AO, Campos JJ, Galdino GS, Braga FC, Duarte IDG, Perez AC. Antinociceptive effect from *Davilla elliptica* hydroalcoholic extract. *J Ethnopharmacol* 2007;

- 113:354-356.
64. Campos J.J., de Oliveira Azevedo A., de Souza Filho J.D., Castro Perez A., Castro Braga F. Bioguided isolation of myricetin-3-O- β -galactopyranoside with antinociceptive activity from the aerial part of *Davilla elliptica* St.-Hil. *J Ethnopharmacol* 2013; 150:270-274.
 65. Silva EM, Souza JNS, Rogez H, Rees JF, Larondelle Y. Antioxidant activities and polyphenolic contents of fifteen selected plant species from the Amazonian region. *Food Chem* 2007; 101:1012-1018.
 66. Guaraldo L, Sertie JA, Bacchi EM. Antiulcer action of the hydroalcoholic extract and fractions of *Davilla rugosa* Poirlet in the rat. *J Ethnopharmacol* 2001; 76:191-195.
 67. Souza JNS, Silva EM, Loir A, Rees J-F, Rogez H, Larondelle Y. Antioxidant capacity of four polyphenol-rich Amazonian plant extracts: a correlation study using chemical and biological *In vitro* assays. *Food Chem* 2008; 106:331-339.
 68. Alam MB, Rahman MS, Hasan M, Khan MM, Nahar K, Sultana S. Antinociceptive and antioxidant activities of the *Dillenia indica* bark. *Int J Pharmacol* 2012; 8:243-251.
 69. Das M, Sarma BP, Ahmed G, Nirmala CB, Choudhury MK. *In vitro* antioxidant activity and total phenolic content of *Dillenia indica* and *Garcinia penducalata*, commonly used fruits in Assamese cuisine. *Free Rad. Antioxidants* 2012; 2:30-36.
 70. Macahig RAS, Matsunami K, Otsuka H, Chemical studies on an endemic Philippine plant: sulfated glucoside and seco-A-ring triterpenoids from *Dillenia philippinensis*. *Chem Pharm Bull* 2011; 59:397-401.
 71. Li X, Li C, Cui C, Li M, Fan M. Chemical constituents of *Dillenia kerrii* and their activities on antitumor and anti-hypoxia *In vitro*. *Zhongguo Yaowu Huaxue Zazhi* 2009; 19:130-134.
 72. Kumar D, Mallick S, Vedasiromoni JR, Pal BC. Anti-leukemic activity of *Dillenia indica* L. fruit extract and quantification of betulinic acid by HPLC. *Phytomedicine* 2010; 17:431-435.
 73. Padhya IP, Choudhary NSK, Padhy SK, Dash S. Effect of *Dillenia indica* leaves against carbon tetrachloride induced hepatotoxicity. *J Pharm Chem* 2008; 2:190-193.
 74. Kumar S, Kumar V, Prakash OM. Free radicals scavenging effect of *Dillenia indica* leaves. *Asian J Pharm Biol Res* 2011c; 1:169-173.
 75. Kumar S, Kumar V, Prakash O. Antidiabetic, hypolipidemic and histopathological analysis of *Dillenia indica* (L.) leaves extract on alloxan induced diabetic rats. *Asian Pac J Trop Med* 2011d; 4:347-352.
 76. Kumar S, Kumar V, Prakash O. Antidiabetic and hypolipidemic activities of *Dillenia indica* extract in diabetic rats. *J Chin Integr Med* 2011e; 9:570-574.
 77. Apu A, Muhit M, Tareq S, Pathan A, Jamaluddin A, Ahmed M. Antimicrobial activity and brine shrimp lethality bioassay of the leaves extract of *Dillenia indica* Linn. *J Young Pharmacists* 2010; 2:50-53.
 78. Uppalapati L, Rao JT. Chemical and antimicrobial studies of the extracts of *Dillenia indica* Linn. *Chem Petro-Chem J* 1979; 10:21-23.
 79. Abdille MH, Singh RP, Jayaprakasha GK, Jena BS. Antioxidant activity of the extracts from *Dillenia indica* fruits. *Food Chem* 2004; 90:891-896.
 80. Deepa N, Jena BS. Antioxidant fraction from bark of *Dillenia indica*. *Int J Food Prop* 2011; 14:1152-1159.
 81. Hossain SJ, Tsujiyama I, Takasugi M, Islam MA, Biswas RS, Aoshima H. Total phenolic content antioxidative anti-amylase, anti-glucosidase, and antihistamine release activities of Bangladeshi fruits. *Food Sci Technol Res* 2008; 14:261-268.
 82. Sharma HK, Sarangi B, Pradhan SP. Preparation and *in vitro* evaluation of mucoadhesive microbeads containing Timolol maleate using mucoadhesive substances of *Dillenia indica* L. *Arch Pharm Sci Res* 2009; 1:181-188.
 83. Sharma HK, Pradhan, SP, Sarangi B. Preparation and *In vitro* evaluation of enteric controlled release pantoprazole loaded microbeads using natural mucoadhesive substance from *Dillenia indica* L. *Int J PharmTech Res* 2010; 2:542-551.
 84. Metia PK, Bandyopadhyay AK. *In vitro* and *in vivo* evaluation of a novel mucoadhesive buccal oxytocin tablet prepared with *Dillenia indica* fruit mucilage. *Pharmazie* 2008; 63:270-274.
 85. Kuotsu K, Bandyopadhyay AK. Development of oxytocin nasal gel using natural mucoadhesive agent obtained from the fruits of *Dillenia indica* L. *ScienceAsia* 2007; 33:57-60.
 86. Dan S, Dan SS. Triterpenoids of Indian Dilleniaceae. *J Indian Chem Soc* 1980; 57:760.
 87. Rosangkima G, Prasad SB. Antitumor activity of some plants from Meghalaya and Mizoram against murine ascites Dalton's lymphoma. *Indian J Exp Biol* 2004; 42:981-988.
 88. David JM, Souza JC, Silva Guedes ML, David JP. Phytochemical study of *Davilla rugosa*: flavonoids and terpenoids. *Rev Bras Farmacogn* 2006; 16:105-108.
 89. Harrison LJ, Sia GL, Sim KY. 5,7-Dihydroxy-8-methoxyflavone from *Tetracera indica*. *Planta Med* 1994; 60:493-494.
 90. Tiwari KP, Srivastava SD, Srivastava SK. α -L-Rhamnopyranosyl-3 β -hydroxy-lup-20(29)-en-28-oic acid from the stem of *Dillenia pentagyna*. *Phytochemistry* 1980; 19:980-981.
 91. Tiwari KP, Srivastava SD, Srivastava SK. Triterpenoids from *Dillenia pentagyna*. *J Indian Chem Soc* 1981; 58:817.
 92. Srivastava SK, Srivastava SD. A new diterpene, dipoloic acid from the stem of *Dillenia pentagyna*. *Curr Sci* 1984; 53:646-647.
 93. Nick A, Wright AD, Rali T, Sticher O. Antibacterial triterpenoids from *Dillenia papuana* and their structure-activity relationships. *Phytochemistry* 1995; 40:1691-1695.
 94. Wiert C, Mogana S, Khalifah S, Mahan M, Ismail S, Buckle M, Narayana AK, Sulaiman M. Antimicrobial screening of plants used for traditional medicine in the state of Perak, Peninsular Malaysia. *Fitoterapia* 2004; 75:68-73.
 95. Armania N, Yazan LS, Musa SN, Ismail IS, Foo JB, Wei CK, Noreen H, Hisyam A H, Zulfahmi S, Ismail M. *Dillenia suffruticosa* exhibited antioxidant and cytotoxic activity through induction of apoptosis and G(2)/M cell cycle arrest. *J Ethnopharmacol* 2013; 146:525-535.
 96. Haq QN, Gomes J. Arabino-galactan from the fruits of *Dillenia indica*. *Bangladesh J Sci Ind Res* 1974; 19:184-190.
 97. Srivastava BK, Pande CS. Structure of a polysaccharide from the fruits of *Dillenia indica*. *Indian J Chem, Sect B*

- 1978; 16B:662-664.
98. Rahman ML, Haq QN, Ahmed M. Structural studies on polysaccharides of fruits of *Dillenia indica* Linn. Part I. Isolation of a neutral polysaccharide and its fractionation and methylation studies. *Bangladesh J Sci Ind Res* 1981a; 16:81-89.
 99. Rahman ML, Haq QN, Ahmed M. Structural studies on polysaccharides of fruits of *Dillenia indica* Linn. Part II. Partial hydrolysis and Smith degradation of the neutral polysaccharide. *Bangladesh J Sci Ind Res* 1981b; 16:90-98.
 100. Rahman ML, Haq QN, Ahmed M. Structural studies on polysaccharides of fruits of *Dillenia indica* Linn. Part III. Isolation of an acidic polysaccharide and its fractionation and methylation studies. *Bangladesh J Sci Ind Res* 1981c; 16:119-124.
 101. Rahman ML, Haq QN, Ahmed M. Structural studies on polysaccharides of fruits of *Dillenia indica* Linn. Part IV. Partial hydrolysis and Smith degradation of the acidic polysaccharide. *Bangladesh J Sci Ind Res* 1981d; 16:125-133.
 102. Kubitzki K. *Doliocarpus*, *Davilla*, und verwandte Gattungen (Dilleniaceae). *Mitt Bot Staatssamml München* 1971; 9:1-105.
 103. Tucker SC, Bernhardt P. Floral ontogeny, pattern formation and evolution in *Hibbertia* and *Adrastaea* (Dilleniaceae). *American J Bot* 2000; 87:1915-1936.
 104. Kubitzki K. Flavonoids and systematics of the Dilleniaceae. *Ber Dtsch Bot Ges* 1968; 81:238-251.
 105. Pereira IM, Gomes-Klein VL. Taxonomia e ecologia da família Dilleniaceae nos Estados de Goiás e Tocantins. *Rev Bras Biocienc* 2007; 5:975-977.
 106. Bandara RM CJ, Abeykoon DMB, Bandara BMR, Wickramasinghe A, Wijesundara DSA, Karunaratne DN, Karunaratne V. Antioxidant, cytotoxic and phytotoxic activities of *Schumacheria castaneifolia*, a plant endemic to Sri Lanka. *Proceedings of the Peradeniya University Research Sessions (PURSE)*, Sri Lanka, 2011; 16:156.
 107. Kubitzki K. Die gattung *Tetracera* (Dilleniaceae). *Mitt Bot Staatssamml München* 1970; 9:1-98.
 108. Fraga CN, Aymard C GA. *Tetracera forzzae* (Dilleniaceae), uma nova espécie para a Zona da Mata de Minas Gerais, Brasil. *Novon* 2007; 17:433-436.
 109. Adenkunle AA, Duru C, Odufuwa OM. Antifungal activity and phytochemical screening of the crude extracts of *Khaya ivorensis* Juss (Meliaceae) and *Tetracera potatoria* L. (Dilleniaceae). *South Afr J Bot* 2003; 69:568-571.
 110. Fernando TRGW, Ratnasooriva WD, Deraniyagala AS. Antinociceptive activity of aqueous leaf extract of *Tetracera sarmentosa* L. in rats. *Phcog Res* 2009; 1:381-386.
 111. Kwon HS, Park JA, Kim J-H, You JC. Identification of anti-HIV and anti-Reverse Transcriptase activity from *Tetracera scandens*. *BMB reports* 2012; 45:165-170.
 112. Kukongviriyapan V, Janyacharoen T, Kukongviriyapan U, Laupattarakasae P, Kanokmedhakul S, Chantaranothai P. Hepatoprotective and antioxidant activities of *Tetracera loureiri*. *Phytother Res* 2003; 17:717-721.
 113. Lock O, Castillo P, Doroteo V, Rojas R. Antioxidant activity *In vitro* of selected Peruvian medicinal plants. *Acta Horticulturæ (Proceedings of WOCMAP III: The IIIrd World Congress on Medicinal and Aromatic Plants)* 2005; (675):103-106.
 114. Adesanwo JK, Ekundayo O, Oluwole FS, Olajide OA, van den Berge AJJ, Findlay JA. The effect of *Tetracera potatoria* and its constituent betulinic acid on gastric acid secretion and experimentally-induced gastric ulceration. *Nigerian J Physiol Sci* 2003; 18:21-26.
 115. Ma J, Starck SR, Hecht SM. DNA Polymerase α inhibitors from *Tetracera boivianiana*. *J Nat Prod* 1999; 62:1660-1663.
 116. Lee MS, Kim CH, Hoang DM, Kim BY, Sohn CB, Kim MR, Ahn JS. Genistein-derivatives from *Tetracera scandens* stimulate glucose-uptake in L6 myotubes. *Biol Pharm Bull* 2009; 32:504-508.
 117. Na Z, Li C, Zheng H, Sun H. Chemical constituents from *Tetracera asiatica*. *Yunnan Zhiwu Yanjiu* 2001; 23:400-402.
 118. Liliwirianis N, Zain WZWM, Kassim J, Abdul Karim S. Antimicrobial activity of plant extracts against *Bacillus subtilis*, *Staphylococcus aureus* and *Escherichia coli*. *E-Journal Chem* 2011; 8:S282-S284.
 119. Hoang DM, Trung TN, Hien PTT, Ha DT, Van Luong H, Lee M, Bae K. Screening of protein tyrosine phosphatase 1B inhibitory activity from some Vietnamese medicinal plants. *Nat Prod Sci* 2010; 16:239-244.
 120. Nguyen MTT, Nguyen NT. A new lupane triterpene from *Tetracera scandens* L., xanthine oxidase inhibitor. *Nat Prod Res* 2013; 27:61-67.
 121. Kankonde M. Contribution to the study of traditional pharmacopeia in Zaire. I. Medicinal Dilleniaceae of western Kasai. *Bull Soc Roy Sci Liege* 1982; 51:282-286.
 122. Lima CC, Lemos RPL, Conserva LM. Chemical constituents, larvicidal effects and radical scavenging activity of *Tetracera breyniana* Schltdl. (Dilleniaceae). *J Appl Pharm Sci* 2013; 3:14-18.
 123. Souza MP, Matos FJA, Alencar JW, Rouquayrol PA. Triterpenoids of plants in northeast Brazil. *Byrsonima sericea*, *Crataeva tapia*, and *Curatella americana*. *Rev Bras Farm* 1970; 51:67-70.
 124. Pavanadasivan G, Sultanbawa MUS. Flavonoids of some Dilleniaceae species. *Phytochemistry* 1975; 14:1127-1128.
 125. El-Azizi MM, Ateya AM, Svoboda GH, Schiff PL Jr, Slatkin DJ, Knapp JE. Chemical constituents of *Curatella americana* (Dilleniaceae). *J Pharm Sci* 1980; 69:360-361.
 126. Tiwari KP, Srivastava SD. Pigments from the stem bark of *Dillenia indica*. *Planta Med* 1979; 35:188-190.
 127. Srivastava BK, Pande CS. Chemical examination of the bark of *Dillenia indica*. *Acta Cienc Indica, Chem* 1981; 7:170-174.
 128. Lebreton P, Bouchez MP. Chemotaxonomic investigation of vascular plants. V. Distribution of polyphenols in the Parietales. *Phytochemistry* 1967; 6:1601-1608.
 129. Bate-Smith EC, Harborne JB. Differences in flavonoid content between fresh and herbarium leaf tissue in *Dillenia*. *Phytochemistry* 1971; 10:1055-1058.
 130. Banerji N, Majumder P, Dutta NL. A new pentacyclic triterpene lactone from *Dillenia indica*. *Phytochemistry* 1975; 12:1447-1448.
 131. Rinaldo D, Silva MA, Rodrigues CM, Calvo TR, Sannomiya M, Campaner dos Santos L, Vilegas W, Kushima H, Hiruma-Lima CA, Brito ARMS. Preparative separation of flavonoids from the medicinal plant *Davilla*

- elliptica St. Hill. by high-speed counter-current chromatography. *Quim Nova* 2006; 29:947-949.
132. Srivastava SD. Flavonoids from the stem of *Dillenia pentagyna*. *Phytochemistry* 1981; 20:2445.
133. Tiwari KP, Srivastava SD, Srivastava SK. Naringenin-4'-O-[4-O-(β -D-glucopyranosyl)]- β -D-xylopyranoside from *Dillenia pentagyna*. *Chem Scripta* 1979; 13:191-192.
134. Chowdhury TA, Halder S, Guha SK, Mosihuzzaman M. Isolation and characterization of three triterpenoids and a dicarboxylic acid from the fruit pulp of *Dillenia indica*. *J Bangladesh Chem Soc* 1998; 11:89-96.
135. Sundararamaiah T, Ramraj SK, Rao KL, Vimalabai MV. Isolation of the lupeol group of triterpenes from *Dillenia indica* Linn. and *Diospyros perigrina*. *J Indian Chem Soc* 1976; 53:638.
136. Bhattacharjee SR, Chatterjee A. Betulic acid and betulin, the triterpenoid constituents of *Dillenia indica*. *J Indian Chem Soc* 1962; 39:276-284.
137. Pavanasivam G, Sultanbawa MUS. Chemical investigation of ceylonese plants. IX. Betulinic acid in the Dilleniaceae and a review of its natural distribution. *Phytochemistry* 1974; 13:2002-2006.
138. Mukherjee KS, Badruddoza S. Chemical constituents of *Dillenia indica* Linn. and *Vitex negundo* Linn. *J Indian Chem Soc* 1981; 58:97-98.