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

Cinthia C. Lima, Rosangela 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 Dilleniaceae. 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, lignoids, 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, ethnomedical 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, sec-oleanane, lupane, cycloartenane, and friedelane), phytosteroids and diterpenes) 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;
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 paleotropical [6, 18], Hibbertioidae (Hibbertia, Adrustaea and Pachyrena and was treated as an Old World clade), and Dillenioidae (Acrotera, Didesmandra, Dillenia, and Schumacheria). A group of Australian species with photosynthetic stems, previously recognized as the genus Pachyrena, 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 Dilleniaceae 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 then be 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 Acrotera species

The genus Acrotera 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 [1-4]. 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-carjô”, 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 [36-38] 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 and diabetes and 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 Dolioecarpus species
Dolioecarpus 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 [48]. 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 Sara wak, Borneo [19] while Neodillenia (03 species) has occurrence in the Amazon region (Brazil), Colombia, Ecuador, Peru, and Venezuela [20]. According to Kubitzki [49], 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 blemorrhagia. 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, flu, 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. arnottiannum 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. arnottiannum 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 (0), 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.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Source</th>
<th>Plant part/ References</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Flavones and Flavonols</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apigenin (1)</td>
<td>T. mandagascariensis</td>
<td>Leaves [61]</td>
</tr>
<tr>
<td>Apigenin 7-galactoside sulphate (2)</td>
<td>T. stuhmanniana</td>
<td>Leaves [61-62]</td>
</tr>
<tr>
<td>Apigenin 7-sulphate (3)</td>
<td>T. mandagascariensis</td>
<td>Leaves [61]</td>
</tr>
<tr>
<td>Avicularin (4)</td>
<td>C. americana</td>
<td>Leaves [61]</td>
</tr>
<tr>
<td></td>
<td>Pinzona coriacea</td>
<td>Leaves [61, 125]</td>
</tr>
<tr>
<td>3',5-Dihydroxy-4',3-dimethoxyflavone-7-O-β-D-glucoside (6)</td>
<td>Dillenia indica</td>
<td>Stem barks [126]</td>
</tr>
<tr>
<td>5,7-Dihydroxy-4'-methoxyflavone 3-O-β-D-glucopyranoside (7)</td>
<td>Dillenia indica</td>
<td>Stem barks [126]</td>
</tr>
<tr>
<td>Luteolin (24)</td>
<td>H. cuneiformis, T. mandagascariensis</td>
<td>Leaves&lt;sup&gt;[61, 104]&lt;/sup&gt;</td>
</tr>
<tr>
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</tr>
<tr>
<td>Isorhamnetin (9)</td>
<td>Acrotema uniflorum, Dillenia indica, Dillenia spp. (Huber sn.)</td>
<td>Barks, Fruits, Pericarp&lt;sup&gt;[124]&lt;/sup&gt;</td>
</tr>
<tr>
<td>Isorhamnetin 3,7,4′-trisulphate (10)</td>
<td>Acrotema uniflorum, Dillenia indica</td>
<td>Leaves&lt;sup&gt;[61-62]&lt;/sup&gt;</td>
</tr>
<tr>
<td>Isorhamnetin 3,7,4′-methyl ether (13)</td>
<td>Acrotema arnottianum, Dillenia indica, Dillenia bracteata, D. retusa, D. spp., D. triqueta, Doliocarpus amazonicus</td>
<td>Entire plant&lt;sup&gt;[60]&lt;/sup&gt;</td>
</tr>
<tr>
<td>Kaempferol 4′,7-dimethyl ether (15)</td>
<td>T. asiatica</td>
<td>Leaves&lt;sup&gt;[104]&lt;/sup&gt;</td>
</tr>
<tr>
<td>Kaempferol 3,7-disulphate (16)</td>
<td>Dillenia bracteata, D. spp., S. castaneifolia</td>
<td>Leaves&lt;sup&gt;[61-62]&lt;/sup&gt;</td>
</tr>
<tr>
<td>Kaempferol 3-galactoside (17)</td>
<td>Dillenia retusa, T. amazonica, T. empedoclea, T. lasiocarpa, T. musauana</td>
<td>Leaves&lt;sup&gt;[61]&lt;/sup&gt;</td>
</tr>
<tr>
<td>Kaempferol-4′-O-β-glucopyranoside (18)</td>
<td>Acrotema arnottianum, Entire plant&lt;sup&gt;[60]&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Kaempferol 3-glucoside (19)</td>
<td>Dillenia indica</td>
<td>Barks&lt;sup&gt;[127]&lt;/sup&gt;</td>
</tr>
<tr>
<td>Kaempferol 4′-methyl ether (20)</td>
<td>Dillenia indica</td>
<td>Leaves&lt;sup&gt;[128-129]&lt;/sup&gt;</td>
</tr>
<tr>
<td>Kaempferol 3,7,4′-tri-sulphate (23)</td>
<td>uniflorum</td>
<td>Leaves&lt;sup&gt;[61-62]&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

*Note: The table represents a summary of phytochemicals and their sources from the Journal of Pharmacognosy and Phytochemistry.*
Luteolin 7-sulphate (25)  
Mearnssetin (26)  
Mearnssetin 3-rhamnoside (27)  
5-Methylkaempferol (28)  
7-O-Methylkaempferol (29)  
7-O-Methylquercetin (30)  
Myricetin (31)  
Myricetin 3-arabinoside (32)  
Myricetin 3-O-β-galactopyranoside (33)  
Myricetin-3-O-α-L-rhamnoside (34)  
Myricetin-3′-O-α-L-rhamnoside (35)  
Myricetin-3-O-rhamnoside sulphate (36)  
Myricetin 3,7,3′,4′-tetramethyl ether (37)  
Ombuin (38)  
Ombuin 3,3′-disulphate (39)  
Quercetin (40)  

T. stuhimanniana  
Doliocarpus spraguei, Hibbertia spp.  
Doliocarpus spraguei (Leaves)  
T. boiviana, T. breyniana, T. costata, T. oblongata, T. sellowiana, T. volubilis  
T. breyniana  
Dillenia indica  
H. amplexicaulis, H. alligena, H. billardieri, H. lineares, H. salignea, H. stricta, H. vestita, H. volubis  
Davilla elliptica, D. lacunose, S. alnifolia  
Davilla elliptica, D. lacunosa, D. nitida, S. alnifolia, T. sellowiana, T. willdenowiana  
Davilla elliptica  
Davilla elliptica  
Davilla flexuosa  
Davilla nitida  
Doliocarpus spraguei  
Davilla flexuosa  
Davilla alata  
Davilla macrocarpa  
Doliocarpus amazonicus subsp. ducceanus  
Acrotrema uniflorum  
Acrotrema uniflorum  
Davilla elliptica  
Davilla flexuosa, D. nitida  
Davilla rugosa  
Dillenia bracteata, D. retusa, D. spp., D. triqueta
Dillenia indica
Dillenia retusa
Doliocarpus spraguei
T. brenyiana
Wormia burbidgei, W. triqueta

Quercetin-3-O-arabinopyranoside (41)
Davilla elliptica
Quercetin-3-O-galactopyranoside (42)
C. americana, Davilla alata, D. cearensis
Davilla elliptica
Quercetin 3-galactoarabinoside (43)
americana
Quercetin 3-glucoronide (44)
Quercetin 3-glucoside (45)
Quercetin-3-O-β-D-rhamnoside (46)
Acrotema arnottianum
Entire plant
Quercetin-3-O-α-L-rhamnoside (47)
C. americana, Davilla alata, D. angustifolia, D. cearensis, D. grandiflora, D. kunthii, D. lacunosa, D. macrocarpa, D. rugosa
Davilla elliptica, D. niitida
elliptica
D. elliptica
Davilla flexuosa
Doliocarpus amazzonicus, 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
Quercetin 3-robinobioside (48)
Doliocarpus macrocarpus, D. savannarum
Quercetin 3-sulphate (49)
Leaves
Rhamnetin 3-glucoside (50) | Dillenia pentagyna | Stems [132]
Rhamnocitrin (51) | T. alnifolia, T. poggei, T. rosiiflora, T. rutenbergii | Leaves [61]
Rhamnocitrin 3-glucuronide (52) | T. rosiiflora, T. rutenbergii | Leaves [61-62]
Rhamnocitrin 3-sulphate (53) | Acrotema uniflorum, T. alnifolia, T. poggei, T. rosiiflora, T. rutenbergii | Leaves [61-62]
Saponarin (54) | Doliocarpus brevipedicellatus, D. lancifolius, D. multiflorus, D. paraensis | Leaves [61]
Tiliroside (55) | Dillenia philippinensis | Leaves [70]
Wogonin (57) | T. indica, T. asiatica | Aerial parts [89]
Wogonin 7-O-β-D-glucuronide methyl ester (58), Wogonin 7-O-β-D-glucuronide (59) | T. asiatica | Leaves [117]

**Dihydroflavonols**
(+)-Dihydrokaempferol (60) | Dillenia indica, Dillenia retusa, Wormia triguetra | Timber [124]
(±)-Dihydroisorhamnetin (61) | Dillenia indica | Barks, Barks, Timber [124]
Dihydrokaempferide (62) | Dillenia indica | Barks [124]
(+)-Dihydroquercetin (63) | Dillenia indica, D. retusa | Barks, Timber [124]
Dihydroquercetin galactoside (64) | Dillenia pentagyna | Stems [132]
Dihydrowogonin (65) | T. asiatica | Leaves [117]
(+)-3'-Methoxydihydroquercetin (66) | Dillenia indica | Barks [124]
4'-O-Methyltaxifolin (67), Narigenin (68) | Davilla rugosa, Dillenia indica | Stems [88], Leaves [129], Barks [124]
Naringenin 7-galactosyl-(1→4)-glucoside (69), Naringenin-4''-O-[4-O-(β-D-glucopyranosyl)]-β-D-xylopyranoside (70) | Dillenia pentagyna | Stems [132-133]
4,5,7,3',4'-Pentahydroxyflavan-3-O-β-D-glucopyranoside (71) | Dillenia indica | Stem barks [126]

**Isoflavonoids**
Alpinumisoflavone (72), Derrone (73), 3',5'-Diprenylgenistein (74), 6,8-Di-prenylgenistein (75), Genistein (76) | T. scandens, T. scandens | Branch [116], Branch [116]

**Leucoanthocyanins**
Procyanidin (77) | Acrotema uniflorum, C. americana, Davilla alata, D. indica, D. americana | Leaves [61]


Davilla flexuosa, Doliocarpus guianensis, D. macrocarpus

<table>
<thead>
<tr>
<th>Prodelphinidin (78)</th>
<th>Leaves [61]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 5,7,4'-OH</td>
<td>30 3,7,4'-OH, 5-OMe</td>
</tr>
<tr>
<td>2 5,4'-OH, 7-Gal-OSO-H</td>
<td>31 3,5,7,3',4,5-OMe</td>
</tr>
<tr>
<td>3 5,4'-OH, 7-OSO-H</td>
<td>32 5,7,3',4,5'-OH, 3-Ara</td>
</tr>
<tr>
<td>4 5,7,3',4'-OH, 3-α-L-Ara</td>
<td>33 5,7,3',4,5'-OH, 3-Gal</td>
</tr>
<tr>
<td>5 3,7,3',4'-OH, 5-OMe</td>
<td>34 5,7,3',4,5'-OH, 3-O-α-L-Rha</td>
</tr>
<tr>
<td>6 3',5-OH, 4', 3-OMe, 7-O-β-D-Glc</td>
<td>35 3,5,7,4',5'-OH, 3'-O-α-L-Rha</td>
</tr>
<tr>
<td>7 5,7-OH, 4'-OMe, 3-O-β-D-Glc</td>
<td>36 5,7, 3',4,5'-OH, 3-O-α-L-Rha-OSO-H</td>
</tr>
<tr>
<td>8 3,5,7-OH, 3',4'-OMe</td>
<td>37 5,5'-OH, 3,7,3',4'-OMe</td>
</tr>
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<td>9 3,5,7,4'-OH, 3'-OMe</td>
<td>38 3,5,3'-OH, 7,4'-OMe</td>
</tr>
<tr>
<td>10 5-OH, 3'-OMe, 3,7,4'-OSO,H</td>
<td>39 5-OH, 7,4'-OMe, 3,3'-OSO,H</td>
</tr>
<tr>
<td>11 5,7,4'-OH, 6-C-Glc</td>
<td>40 3,5,7,3',4'-OH</td>
</tr>
<tr>
<td>12 3,5-OH, 7-Ome</td>
<td>41 5,7,3',4'-OH 3-O-Ara</td>
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<tr>
<td>13 5-OH, 3,7-Ome</td>
<td>42 5,7,3',4'-OH 3-Gal</td>
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<td>14 3,5,7,4'-OH</td>
<td>43 5,7,3',4'-OH 3-Gal-Ara</td>
</tr>
<tr>
<td>15 3,5-OH, 7,4'-OMe</td>
<td>44 5,7,3',4'-OH 3-O-β-D-Glu</td>
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<td>16 5,4'-OH, 3,7-OSO,H</td>
<td>45 5,7,3',4'-OH 3-Glc</td>
</tr>
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<td>17 5,7,4'-OH, 3-Gal</td>
<td>46 5,7,3',4'-OH 3-O-β-D-Rha</td>
</tr>
<tr>
<td>18 3,5,7-OH, 4'-O-β-Glc</td>
<td>47 5,7,3',4'-OH 3-O-α-L-Rha</td>
</tr>
<tr>
<td>19 5,7,4'-OH, 3-Glc</td>
<td>48 5,7,3',4'-OH, 3-α-L-Rha-(1→6)-Gal</td>
</tr>
<tr>
<td>20 3,5,7-OH, 4'-OMe</td>
<td>49 5,7,3',4'-OH, 3-OSO,H</td>
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<tr>
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<td>50 5,3',4'-OH, 7-Ome, 3-Glc</td>
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<td>52 5,4'-OH, 7-Ome, 3-Glu</td>
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<tr>
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<tr>
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<td>54 5,4'-OH, 6-C-Glc, 7-O-β-D-Glc</td>
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<tr>
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</tr>
<tr>
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<td>28 3,5,4'-OH, 7-Ome</td>
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</tr>
<tr>
<td>29 3,5,3',4'-OH, 7-Ome</td>
<td>58 5-OH, 7-O-β-D-Glu-(OMe), 8-Ome</td>
</tr>
<tr>
<td>30 3,7,4'-OH, 5-OMe</td>
<td>59 5-OH, 7-O-β-D-Glu, 8-Ome</td>
</tr>
</tbody>
</table>
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 antipoliovirus 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), betulenic 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 [33] 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-inflammatory [12], anti-ulcer, anti-infectious, and immunological [16], antifungal [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-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 Tetracerus or Schucharderia and Tetracerus.

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], antileukemic [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 anti diabetic and anti hyperlipidemic 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 ± 0.16 µg/mL) and total reactive oxygen species (IC50 34.72 ± 0.48 µg/mL) this extract also showed antioxidant potentiality and a good reducing power [69].

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, CHCl3 and CHCl3 soluble fractions (500 µg/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 scavenging activity [35, 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 Collatotrichum 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 mucosal adhesive buccal tablet of oxytixon was prepared with muclilage 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-deoxytartraric 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. scabrilla) showed that triterpenes [betulin (81) betulinic acid (83) and lupeol (99)], along with \(\beta\)-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 oleanane-type triterpenoids:dillenic acids A-C (90-92), and 3-oxool-12,15-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 \(\gamma\)- or \(\delta\)-position to a carbonyl 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-triic acid (108), 2,3-seco-olean-12-ene-2,3,28-triic acid (109), 2,3-seco-olean-12-ene-2,3,30-dioic-28-methyl ester (110), and 2,3-seco-olean-12-ene-2,3,28-dioic-28-butyI ester (111)], a flavonoid glucoside, and other compounds were isolated (Tables 2-3; Figs. 2-3). Triterpenes as 2\(\alpha\),3\(\beta\)-dihydroxyolean-12-ene-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-butyI ester (111) exhibited moderate activity against Leishmania major and A549 human lung adenocarcinoma cells \[90\]. From the fruits of D. kerri, 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, CHCl\(_3\), EtOAc, MeOH, and aqueous extracts from different parts of D. suffruticosas, a plant used to treat cancerous growth, exhibited antimicrobial \[94\], antioxidiant and cytotoxic activities. On the other hand, the \(\text{CHCl}_3\) and EtOAc exhibited higher cytotoxic activity to selected cancer cells (HeLa, MCF-7, MBA-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 flavanoids and terpenoids, besides other classes of compounds (Tables 1-3; Figs. 1-3) and polysaccharides \[96-101\]. The flavanoids were found as C-glycosyflavone, 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 flavon sulphates [kaempferol 3,7-disulphate (16), kaempferol 3-sulphate (22) and quercetin 3-sulphate (47)] co-occur in the genera Schumacheria and/or Tetracerana. In relation to dihydroflavonols, with exception of (+)-dihydrokaempferol (60) and narigenin (68), which occur repeatedly 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), oleane (85, 89-92, 94, and 101-103), nor-lupane (104), and seco-A-ring oleane-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-\(\beta\)-D-glucopyranoside (132).

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<tr>
<th>Compounds</th>
<th>Source</th>
<th>Plant part/References</th>
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<td>(\beta)-Amyrin (80)</td>
<td>C. americana</td>
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<tr>
<td></td>
<td>Dillenia indica</td>
<td>Wood, Fruits[134-135]</td>
</tr>
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<td></td>
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<td>Stem barks[130]</td>
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<tr>
<td></td>
<td>Dillenia indica</td>
<td>Trunk barks[136]</td>
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</table>

References [86, 90-91, 93-95, 125-136].
### Betulinaldehyde (82)
- **Dillenia pentagyna**
- **Doliocarpus dentatus**
- **T. akara, T. indica, T. sarmentosa, T. scandens**

### Betulinic acid (83)
- **Dillenia indica**
- **Dillenia indica**
- **Dillenia papuana**
- **Doliocarpus dentatus**

### Betulonic acid (84)
- **3-cis-** (85) and **3-trans-p-Coumaroyl maslinic acid** (86)

### Cycloartenone (87)
- **Dillenia indica**

### Daucosterol (88)
- **2α,3β-Dihydroxyolean-12-en-28-oic acid** (89)

### Dillenic acid A (90), Dillenic acid B (91), Dillenic acid C (92)

### Dillenic acid D (93), Dillenic acid E (94)

### Dipoloic acid (95)
- **Dillenia pentagyna**

### 3-trans-Feruloyl maslinic acid (96)
- **T. asiatica**

### Friedelin (97)
- **Dillenia indica**

### 3β-Hydroxyxypiane-13β,28-lactone (98)
- **Dillenia indica**

### Lupeol (99)
- **Acrotrema arnottianum**

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- **Stem barks** (90)
- **Stems** (11)
- **Leaves** (86)
- **Fruits** (134)
- **Stem barks** (130)
- **Leaves** (44)
- **Stems** (11)
- **Entire plant** (86)
- **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** (137)
- **Stems, Leaves** (93)
- **Twigs, Stem barks** (115)
- **Leaves** (138)
- **Entire plant** (117)
- **Leaves** (70)
- **Aerial parts** (44)
- **Stems, Leaves** (93)
- **Stems** (92)
- **Entire plant** (5)
- **Stems** (88)
- **Stem barks** (130)
- **Entire plant** (30, 86)
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<th>Part(s)</th>
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<td>Messagenic acid (101)</td>
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<td>Morolic acid (102)</td>
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<tr>
<td>3-Oxoolean-12-en-30-oic acid (103)</td>
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</tr>
<tr>
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<td>Dillenia papuana</td>
<td>Stems, Leaves [44]</td>
</tr>
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<td>α-L-Rhamnopyranosyl-3β-hydroxy-lup-20(29)-en-28-oic acid (107)</td>
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<td>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)</td>
<td>Dillenia philippinensis</td>
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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 (+)-pinoresinol (116) also were isolated from stems of this species. Among them, betulinaldehyde (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. [60], 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 [113]. 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. Adrustea, 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 leucoanthocyanins.

3.7 Pinzonea species
Pinzonea is a monotypic genus characterized by one species [P. coriacea (syn.: Dolioarpus calinoides)] [105]. From the leaves this plant flavonoids like avicularin (4), quercetin (40), quercetin-3-O-galactopyranoside (42), and quercetin-3-O-a-L-rhamnoside (47), besides procyanidin were found (Table 1; Fig. 1). Pinzonea and Caratella are genera chemically closely akin. The only difference between them is the presence of quercetin 3-galactoarabinoside (43) in Caratella 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 Sara wak, Borneo [19] while Neodillenia (03 species) has occurrence in the Amazon region (Brazil), Colombia, Ecuador, Peru, and Venezuela [20]. According to Kubitzki [103], 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 antiinflammatory [109], antinociceptive [110], antiplasmodial [49], antimiycobacterial [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 active to most different purposes. Among them, betulinic acid (83) from T. potatoria significantly reduced induced gastric ulceration in pretreated animals [114]. 3-Trans-furuloyl maslinic acid (96) from whole plant of T. asiatica showed potent anti-cancer, anti-HIV, anti-diabetic, and anti-inflammatory activities [15]. Other chemical constituents such as izalpin (12), izalpin-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 also been 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 μg/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 μM, respectively) and absence of bovine serum albumin (IC50 6.5, 7.5, and 2.0 μM, respectively). Further, these compounds potentiated the effects of bleomycin in cultured P-388D1 cells [119]. 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, gonorrhea, as febrifuge and diuretic, showed antiplasmodial activity. From this plant was isolated rhamnocitrin 3-glucoside methyl ester (63) [102]. 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 μg/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 (IC₅₀ 1.9 μM) 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 (IC₅₀ 34.27 ± 0.35 μM) and 76 (IC₅₀ 18.69 ± 0.19 μM) 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 [123]. Hexane fraction from stem of T. breyniana was effective (LD₅₀ 72.08 μg/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 flavonoids [quercetin (40), 7-O-methylkaempferol (28) and 7-O-methylquercetin (29) and two terpenoids [betulonic 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 prodelphinidin, 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. triqueta, and W. burbridgei, a synonym of D. burbridgei [124].

### Table 3: Other compounds isolated from Dilleniaceae species.

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Source</th>
<th>Plant part/ References</th>
</tr>
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<tbody>
<tr>
<td><strong>Lignans and Phenolic derivatives</strong></td>
<td></td>
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<tr>
<td>(-)-Liroioresinol B (114), (+)-Medioresinol (115),</td>
<td>Doliocarpus dentatus</td>
<td>Stems [11]</td>
</tr>
<tr>
<td>(+)-Pinoresinol (116)</td>
<td></td>
<td></td>
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<tr>
<td>Ellagic acid (117)</td>
<td>Doliocarpus savannarum, T. madagascariensis,</td>
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<tr>
<td></td>
<td>T. poggei, T. rosiflora</td>
<td></td>
</tr>
<tr>
<td>Ethyl gallate (118)</td>
<td>Dillenia kerri</td>
<td>Fruits [71]</td>
</tr>
<tr>
<td>Gallic acid (119)</td>
<td>C. americana</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Davilla elliptica, D. nitida</td>
<td>Leaves [125]</td>
</tr>
<tr>
<td></td>
<td>Dillenia kerri</td>
<td>Leaves [33]</td>
</tr>
<tr>
<td></td>
<td>Dillenia indica</td>
<td>Fruits [71]</td>
</tr>
<tr>
<td></td>
<td>Dillenia retusa</td>
<td>Barks [124]</td>
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<tr>
<td></td>
<td>Wormia burbridgei, W. triqueta</td>
<td>Barks [124]</td>
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<tr>
<td>3-Methoxy-4-hydroxybenzoic acid (120)</td>
<td>Acrotrema arnottianum</td>
<td></td>
</tr>
<tr>
<td>Protocatechuic acid (121), Protocatechuic acid</td>
<td>Dillenia kerri</td>
<td>Fruits [71]</td>
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<tr>
<td>methyl ester (122)</td>
<td></td>
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<tr>
<td><strong>Other compounds</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chlorogenic acid (123)</td>
<td>Doliocarpus brevipedicellatus, D. dentatus,</td>
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<td></td>
<td>D. elegans, D. guianensis, D. lancifolius,</td>
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<td></td>
<td>D. macrocarpus, D. major, D. multiflorus,</td>
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<td></td>
<td>D. savannarum, D. sellowianus</td>
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<tr>
<td>Corchoionoside C6’-O-sulphate (124)</td>
<td>Dillenia philippinensis</td>
<td></td>
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<tr>
<td>1,8-Dihydoxy-2-methyl-anthraquinone-3-O-β-D-glucopyranoside (125)</td>
<td>Dillenia indica</td>
<td>Stem barks [125]</td>
</tr>
</tbody>
</table>
n-Dotriacontanol \((\text{126})\)

Emodin \((\text{127})\)

Foeniculin \((\text{128})\)

\(n\)-Hentriacontanol \((\text{129})\)

2-Hydroxybutane-1,4-dioic acid \((\text{130})\)

Isochlorogenic acid \((\text{131})\)

\((3S,5R,6R,7E,9S)\)-Megastigman-7-ene-3, 5,6,9-tetraol 3-O-\(\beta\)-D-glucopyranoside \((\text{132})\)

Stearic acid \((\text{133})\)

6’-O-Sulphate benzyl glucoside \((\text{134})\)

\(\alpha\)-Tocopherol \((\text{135})\)

\(n\)-Triacontanoic acid \((\text{136})\)

\(\alpha\)-Tocopherol \((\text{135})\)

\(\alpha\)-Tocopherol \((\text{135})\)
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 flavonoids glycosides are present in all genera while flavonoids sulphates were found only in five of them (Acrotrema, Davilla, Dillenia, Schumacheria, and Tetraceria), glucuronicides in two (Dillenia and Tetraceria), and dihydroflavonols only in three (Davilla, Dillenia and Tetraceria) 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 Tetraceria. Almost every species studied contain leucoanthocyanins.

5. Acknowledgements
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6. References


113:354-356.


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