Review on Phytochemistry and Pharmacology of the Genus *Licaria* (Lauraceae)

Wan Mohd Nuzul Hakimi Wan SALLEH, Farediah AHMAD

**ABSTRACT**

The genus *Licaria* (Lauraceae) is a flowering plant genus, comprises 40 species and endemic to Central and South America. Most of the species have been used as traditional medicine. Phytochemicals isolated from *Licaria* species are lignans, neolignans, alkaloids, lactones, triterpenes, and arylpropanoids. The purpose of this review is to examine in detail from a phytochemical and pharmacological point of view what is reported in the past and current literature obtained from plants belonging to the *Licaria* genus.

**Keywords**: *Licaria*, Lauraceae, Phytochemistry, Pharmacology, Neolignans

**INTRODUCTION**

The genus *Licaria* (Lauraceae) is a Neotropical genus consisting of 40 species distributed from southern Florida, Mexico to the south of Brazil and Bolivia. In Brazil, the occurrence of 20 species and two subspecies, mostly in the Amazon region. These trees have a resilient wood, useful as timber for construction and as firewood (1). The genus evergreen monoecious, hermaphrodite, trees or rarely bushes. It is characterized by the combination of flowers with three 2-locellate stamens, a well-developed cupule, often with a double margin and alternate and opposite leaves. The fruit is a bay with tepals deciduous and an underlying dome double border (2). Most of *Licaria* species have ben used in the ethnomedical folk traditions of indigenous Central and South America for various ailments such as indigestion (3), diarrhea (4), stomachache (5), and as stimulant (3). To date, comparative phytochemical data are available for only eleven *Licaria* species. Several bioactive substances including lignans, neolignans, alkaloids, lactones, triterpenes, essential oils, arylpropanoids, and other components, have been isolated from different species of *Licaria*. Literature reviews show that several of them have been reported with
interesting pharmacological activities such as cytotoxicity (6), antibacterial (7), antimalarial (8), anti-leishmanial (4), antioxidant, and antiplatelet inhibitory activities (9). The aim of this review is to examine from phytochemical and pharmacological perspectives the different Licaria species for which the extraction, isolation, structural characterization and description of the biological activity of individual compounds are reported in the literature. In addition, the chemical compositions of the essential oils of Licaria species are also reported. A substructure search performed using the SciFinder Scholar database and searches by keywords in PubMed, Medline, and Scopus, indicated that to date 14 species have been cited in this perspective. The discussion on phytochemistry, pharmacology and essential oils compositions of each plant is provided.

PHYTOCHEMISTRY AND PHARMACOLOGY

A review on the literatures revealed that few phytochemical studies have been carried out on Licaria species prior to the current study. Phytochemical investigations have been conducted on eleven species species of Licaria which are L. aritu Ducke, L. armeniaca (Nees) Kosterm., L. aurea (Huber) Kosterm. L. brasiliensis (Nees) Kosterm., L. canella (Meisn.) Kosterm., L. chrysophylla (Meisn.) Kosterm., L. macrophylla (A.C. Smith) Kosterm., L. mahuba (A. Samp.) Kosterm., L. puchury-major (Mart.) Kosterm., L. rigida Kosterm., and L. triandra (Sw.) Kosterm. The studies have reported the presence of several classes of natural products including lignans, neolignans, alkaloids, lactones, triterpenes, and arylpropanoids. The phytochemical studies of Licaria species are listed in Table 1 and the chemical structures are shown in Figure 1.

Table 1. Chemical constituents isolated from the genus Licaria

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Species</th>
<th>Part</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neolignans</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Licarin A 1</td>
<td>L. aritu</td>
<td>Wood</td>
</tr>
<tr>
<td>Licarin B 2</td>
<td>L. aritu</td>
<td>Wood</td>
</tr>
<tr>
<td>(2S,3S,3aR,5R)-3α-Allyl-5-methoxy-2-(3ʹ,4ʹ-methylenedioxyphenyl)-3-methyl-2,3,3a,4,5,6-hexahydro-6-oxo-benzofuran 3</td>
<td>L. armeniaca</td>
<td>Trunk wood</td>
</tr>
<tr>
<td>(2S,3S,3aR,5R)-3α-Allyl-5,7-dimethoxy-2-(3ʹ,4ʹ-methylenedioxy-phenyl)-3-methyl-2,3,3a,4,5,6-hexahydro-6-oxo-benzofuran 4</td>
<td>L. armeniaca</td>
<td>Trunk wood</td>
</tr>
<tr>
<td>Armenin A 7</td>
<td>L. armeniaca</td>
<td>Trunk wood</td>
</tr>
<tr>
<td>Armenin B 8</td>
<td>L. armeniaca</td>
<td>Trunk wood</td>
</tr>
<tr>
<td>(7S,8R,1ʹS,2ʹS,3ʹS)-2ʹ-Acetoxyl-1ʹ-allyl-3ʹ,5ʹ-dimethoxy-8-methyl-7-piperonyl-bicyclo [3.2.1]-oct-5ʹ-en-4ʹ-one 9</td>
<td>L. armeniaca</td>
<td>Trunk wood</td>
</tr>
<tr>
<td>3a-allyl-5-methoxy-3-methyl-2,3,3a,4,5,6-hexahydro-6-oxobenzofuran 12</td>
<td>L. armeniaca</td>
<td>Trunk wood</td>
</tr>
<tr>
<td>Dimethoxy-2-(3,4-methylenedioxyphenyl)-3-methyl-2,3,3a,4,5,6-hexahydro-6-oxobenzofuran 13</td>
<td>L. armeniaca</td>
<td>Trunk wood</td>
</tr>
<tr>
<td>(1S,5R,6S,7R,8R)-8-acetoxyl-1-allyl-3,5-dimethoxy-7-methyl-6-(3ʹ-methoxy-4ʹ,5ʹ-methylenedioxyphenyl)-4-oxobicyclo [3.2.1]-oct-2-ene 17</td>
<td>L. armeniaca</td>
<td>Fruits</td>
</tr>
<tr>
<td>(1S,5R,6S,7R)-1-Allyl-3-methoxy-7-methyl-6-(3ʹ-methoxy-4ʹ,5ʹ-methylenedioxyphenyl)-4,8-dioxobicyclo[3.2.1]oct-2-ene 18</td>
<td>L. armeniaca</td>
<td>Fruits</td>
</tr>
<tr>
<td>(1S,5R,6S,7R)-1-Allyl-3-methoxy-7-methyl-6-(3ʹ,4ʹ,5ʹ-trimethoxyphenyl)-4,8-dioxobicyclo[3.2.1]oct-2-ene 19</td>
<td>L. armeniaca</td>
<td>Fruits</td>
</tr>
<tr>
<td>Grandisin 20</td>
<td>L. aurea</td>
<td>Fruits</td>
</tr>
<tr>
<td>de-O-Methylgrandisin 21</td>
<td>L. aurea</td>
<td>Fruits</td>
</tr>
<tr>
<td>dide-O-Methylgrandisins 22</td>
<td>L. aurea</td>
<td>Fruits</td>
</tr>
<tr>
<td>Virolongin A 23</td>
<td>L. aurea</td>
<td>Fruits</td>
</tr>
<tr>
<td>Virolongin B 24</td>
<td>L. aurea</td>
<td>Fruits</td>
</tr>
<tr>
<td>Eusiderin A 27</td>
<td>L. chrysophylla</td>
<td>Bark/fruits calyx</td>
</tr>
<tr>
<td>Formula</td>
<td>Name</td>
<td>Source</td>
</tr>
<tr>
<td>---------</td>
<td>------</td>
<td>--------</td>
</tr>
<tr>
<td>rel-(7S,8R,1'S,4'S,5'R)-4'-Hydroxy-3,4,5,3',5'-pentamethoxy-6'-oxo-Δ-1,3,5,2',8'-8.1',7.5'-neolignan 29</td>
<td>L. brasiliensis</td>
<td>Trunk wood</td>
</tr>
<tr>
<td>rel-(7S,8R,1'S,4'R,5'R)-4'-Hydroxy-3,4,5,3',5'-pentamethoxy-6'-oxo-Δ-1,3,5,2',8'-8.1',7.5'-neolignan 30</td>
<td>L. brasiliensis</td>
<td>Trunk wood</td>
</tr>
<tr>
<td>rel-(7S,8R,1'S,5'S,6'S)-6-Acetoxy-3'-hydroxy-3,5'-dimethoxy-4,5-methylenedioxy-4'-oxo-Δ-1,3,5,2',8'-8.1',7.5'-neolignan 31</td>
<td>L. brasiliensis</td>
<td>Trunk wood</td>
</tr>
<tr>
<td>rel-(7R,8S,1'S,5'S,6'S)-6-Acetoxy-3,4,5,3',5'-pentamethoxy-4'-oxo-Δ-1,3,5,2',8'-8.1',7.5'-neolignan 32</td>
<td>L. brasiliensis</td>
<td>Trunk wood</td>
</tr>
<tr>
<td>rel-(7S,8R,1'S,4'R,5'R,6'R)-6'-Hydroxy-3,4,5,3',5'-pentamethoxy-4'-oxo-Δ-1,3,5,2',8'-8.1',7.5'-neolignan 33</td>
<td>L. brasiliensis</td>
<td>Trunk wood</td>
</tr>
<tr>
<td>Canellin A 35</td>
<td>L. canella</td>
<td>Trunk wood</td>
</tr>
<tr>
<td>Canellin B 36</td>
<td>L. canella</td>
<td>Trunk wood</td>
</tr>
<tr>
<td>Canellin C 37</td>
<td>L. canella</td>
<td>Trunk wood</td>
</tr>
<tr>
<td>Chrysophyllin A 40</td>
<td>L. chrysophylla</td>
<td>Trunk wood</td>
</tr>
<tr>
<td>Chrysophyllin B 41</td>
<td>L. chrysophylla</td>
<td>Trunk wood</td>
</tr>
<tr>
<td>Chrysophyllon I-A 42</td>
<td>L. chrysophylla</td>
<td>Trunk wood</td>
</tr>
<tr>
<td>Chrysophyllon I-B 43</td>
<td>L. chrysophylla</td>
<td>Trunk wood</td>
</tr>
<tr>
<td>Chrysophyllon II-A 44</td>
<td>L. chrysophylla</td>
<td>Trunk wood</td>
</tr>
<tr>
<td>Chrysophyllon II-B 45</td>
<td>L. chrysophylla</td>
<td>Trunk wood</td>
</tr>
<tr>
<td>Chrysophyllon III-A 46</td>
<td>L. chrysophylla</td>
<td>Trunk wood</td>
</tr>
<tr>
<td>Chrysophyllon III-B 47</td>
<td>L. chrysophylla</td>
<td>Trunk wood</td>
</tr>
<tr>
<td>Eusiderin I 51</td>
<td>L. chrysophylla</td>
<td>Bark/fruits calyx</td>
</tr>
<tr>
<td>Eusiderin J 52</td>
<td>L. chrysophylla</td>
<td>Bark/fruits calyx</td>
</tr>
<tr>
<td>Eusiderin K 53</td>
<td>L. chrysophylla</td>
<td>Bark/fruits calyx</td>
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<td>Eusiderin L 54</td>
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<td>L. chrysophylla</td>
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<td>Virolongin E 56</td>
<td>L. chrysophylla</td>
<td>Bark/fruits calyx</td>
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<td>Virolongin F 57</td>
<td>L. chrysophylla</td>
<td>Bark/fruits calyx</td>
</tr>
<tr>
<td>Virolongin G 58</td>
<td>L. chrysophylla</td>
<td>Bark/fruits calyx</td>
</tr>
<tr>
<td>Chrysophyllon IV-B 59</td>
<td>L. chrysophylla</td>
<td>Bark</td>
</tr>
<tr>
<td>Chrysophyllon V1-B 60</td>
<td>L. chrysophylla</td>
<td>Bark</td>
</tr>
<tr>
<td>Macrophyllin 61</td>
<td>L. macrophylla</td>
<td>Trunk wood</td>
</tr>
<tr>
<td>Aurein 67</td>
<td>Licaria sp.</td>
<td>Wood</td>
</tr>
<tr>
<td>Eusiderin 68</td>
<td>Licaria sp.</td>
<td>Wood</td>
</tr>
<tr>
<td></td>
<td>L. rigida</td>
<td>Trunk wood</td>
</tr>
</tbody>
</table>
**(7S,8S)-Δ'2,'6'-Dimethoxy-3,4-methylenedioxy-7.0.3,'8.4,'1.0.7'-neolignan 75**  
* L. puchury-major  
  Seeds  

**Ferrearin B 76**  
* L. puchury-major  
  Seeds  

**Ferrearin C 77**  
* L. puchury-major  
  Seeds  

**rel-(7S,8S,1'R,2'S)-2'-Hydroxy-3,4-dimethoxy-3'-oxo-Δ4',8'-8.1',7.0.2'-neolignan 78**  
* L. puchury-major  
  Seeds  

**Ferrearin G 79**  
* L. puchury-major  
  Seeds  

**Oxaguanin 80**  
* L. puchury-major  
  Seeds  

**rel-(7S,8S,1'R,5'R)-5'-Methoxy-3,4-methylenedioxy-4'-oxo-Δ2',8'-8.1',7.0.2'-neolignan 81**  
* L. puchury-major  
  Seeds  

**3'-Methoxyburchellin 82**  
* L. puchury-major  
  Seeds  

**Eusiderin B 93**  
* L. rigida  
  Trunk wood  

**Triandrin A 94**  
* L. triandra  
  Seeds  

**Triandrin B 95**  
* L. triandra  
  Seeds  

**Burchellin 96**  
* L. triandra  
  Seeds  

**Lignans**  
- **Magnolin 11**  
  * L. armeniaca  
  Trunk wood  

**Alkaloids**  
- **tri-O-Methylmoschatoline 10**  
  * L. armeniaca  
  Trunk wood  

**Bracteoline 14**  
* L. armeniaca  
  Trunk wood  

**O-Methylbracteoline 15**  
* L. armeniaca  
  Trunk wood  

**α-Dehydroreticuline 16**  
* L. armeniaca  
  Trunk wood  

**Reticuline 83**  
* L. puchury-major  
  Seeds  

**Orientaline 84**  
* L. puchury-major  
  Seeds  

**Coclaurine 85**  
* L. puchury-major  
  Seeds  

**N-methylcoclaurine 86**  
* L. puchury-major  
  Seeds  

**Norjuziphine 87**  
* L. puchury-major  
  Seeds  

**Norisoboldine 88**  
* L. puchury-major  
  Seeds  

**Isoboldine 89**  
* L. puchury-major  
  Seeds  

**Glaziovine 90**  
* L. puchury-major  
  Seeds  

**Reticuline N-oxide [91 N-Me (S)]**  
* L. puchury-major  
  Seeds  

**Reticuline N-oxide [92 N-Me (R)]**  
* L. puchury-major  
  Seeds  

**Lactones**  
- **(-)-Dihydromahubanolide B 65**  
  * L. mahuba  
  Trunk wood  

- **(-)-iso-Dihydromahubanolide B 66**  
  * L. mahuba  
  Trunk wood  

**Miscellaneous compounds**  
- **Sitosterol 5**  
  * L. armeniaca  
  Trunk wood  

- **Elemicin 39**  
  * L. canella  
  Trunk wood  

- **2,3,4,5-Tetramethoxycinnamyl alcohol 49**  
  * L. chrysophylla  
  Trunk wood  

- **2,3,4,5-Tetramethoxycinnamaldehyde 50**  
  * L. chrysophylla  
  Trunk wood  

- **Borneol 62**  
  * L. macrophylla  
  Trunk wood  

- **Elemol 63**  
  * L. macrophylla  
  Trunk wood  

- **Nerolidol 64**  
  * L. macrophylla  
  Trunk wood  

- **Eugenol 69**  
  * L. puchury-major  
  Trunk wood  

- **Safrole 70**  
  * L. puchury-major  
  Trunk wood  

- **Syringic aldehyde 71**  
  * L. puchury-major  
  Trunk wood  

- **3,4-Methylenedioxyxannaldehyde 72**  
  * L. puchury-major  
  Trunk wood  

- **3,4-Methylenedioxyxannal alcohol 73**  
  * L. puchury-major  
  Trunk wood
Salleh and Ahmad

*L. aritu* Ducke

*L. aritu* is an arboreous Lauraceae species which occurs along the Manaus-Itacoatiara road, Amazonas State. The only literature report refers to the isolation from the benzene extract of the wood have characterize licarin A 1 and B 2 (10).

*L. armeniaca* (Nees) Kosterm.

*L. armeniaca* is a tree up to 7 m, widely distributed in the Amazonian rainforest, Brazil. Four studies have been reported from this species. The first report was published in 1978 by Alba and co-workers (11). These authors isolated two novel benzofuranoid neolignans, namely (2S,3S,3aR,5R)-3a-allyl-5-methoxy-2-(3′,4′-methyleneoxyphenyl)-3-methyl-2,3,3a,4,5,6-hexahydro-6-oxo-benzofuran 3 and (2S,3S,3aR,5R)-3a-allyl-5,7-dimethoxy-2-(3′,4′-methyleneoxy-phenyl)-3-methyl-2,3,3a,4,5,6-hexahydro-6-oxo-benzofuran 4, together with sitosterol 5,6,7-dimethoxycoumarin 6, armenin A 7, and armenin B 8 from the benzene extract of trunk wood. Purification of the benzene/ethanol extract of the trunk wood by Alegrio et al. (12) have reported to have a novel neolignan (7S,8R, 1′S,2′S, 3′S)-2′-acetoxy-1′-allyl-3′,5′-dimethoxy-7-piperonyl-bicyclo[3.2.1]oct-5′-en-4′-one 9, including sitosterol 5,6,7-dimethoxycoumarin 6, tri-O-methylmoschatoline 10 and magnolin 11. In addition, Abdel-Hafiz and co-workers (13) have successfully isolated two neolignans, 3a-allyl-5-methoxy-3-methyl-2,3,3a,4,5,6-hexahydro-6-oxo-benzofuran 12 and dimethoxy-2-(3,4-methylenedioxyphenyl)-3-methyl-2,3,3a,4,5,6-hexahydro-6-oxo-benzofuran 13, including three alkaloids, bracteoline 14, O-methylbracteoline 15 and a-dehydrocreticuline 16. Barbosa-Filho and co-workers (14) have studied on the fruit extracts. The isolation on ethanol/water extract have found that is three novel neolignans (1S,5R,6S,7R,8R)-8-acetoxy-1-allyl-3,5-dimethoxy-7-methyl-6-(3′-methoxy-4′,5′-methylenedioxyphenyl)-4-oxobicyclo[3.2.1]oct-2-ene 17, (1S,5R,6S,7R)-1-allyl-3-methoxy-7-methyl-6-(3′-methoxy-4′,5′-methylenedioxyphenyl)-4,8-dioxobicyclo[3.2.1]oct-2-ene 18, and (1S,5R,6S,7R)-1-allyl-3-methoxy-7-methyl-6-(3′,4′,5′-trimethoxyphenyl)-4,8-dioxobicyclo[3.2.1]oct-2-ene 19.

*L. aurea* (Huber) Kosterm.

*L. aurea* is a tree widely distributed in the Amazonian rainforest, Brazil. The ethanolic fruit extract of L. aurea have found to contain the diaryltetrahydrofuran type neolignans, grandisin 20, de-O-methylgrandisin 21 and dide-O-methylgrandisin 22, as well as virolongin A 23 and virolongin B 24, as reported by Barbosa-Filho and co-workers (15). Bezerra and co-workers (16) also successfully isolated grandisin 20 from this species. Three years later, Marques et al. (17) were studied on wood part and successfully identified as aurein A-B 25-26, eusiderin A 27, virolongin B 24 and virolongin C 28.

*L. brasiliensis* (Nees) Kosterm.

*L. brasiliensis* is a tree popularly known as 'louro capitu', grows wild in the Forest Reserve of Jari, Municipality of Almerim, Brazil (18). Phytochemical studies on the hexane extract of the trunk wood of this species have led to the isolation of six novel bicyclo[3.2.1]octanoid neolignans, identified as rel-(7S,8R,1′S,4′S,5′R)-4′-Hydroxy-3,4,5,3′,5′-pentamethoxy-6′-oxo-Δ-1,3,5,2′,8′-8.1′,7.5′-neolignan 29, rel-(7S,8R,1′S,4′R,5′R)-4′-Hydroxy-3,4,5,3′,5′-pentamethoxy-6′-oxo-Δ-1,3,5,2′,8′-8.1′,7.5′-neolignan 30, rel-(7S,8R,1′S,5′S,6′S)-6-acetoxy-3′,5′-dimethoxy-4,5-methylenedioxy-4′-oxo-Δ-1,3,5,2′,8′-8.1′,7.5′-neolignan31, rel-(7R,8S,1′S,5′S,6′S)-6-acetoxy-3,4,5,3′,5′-pentamethoxy-4′-oxo-Δ-1,3,5,2′,8′-8.1′,7.5′-neolignan 32, rel-(7R,8S,1′S,5′S,6′S)-6′-hydroxy-3,4,5,3′,5′-pentamethoxy-4′-oxo-Δ-1,3,5,2′,8′-8.1′,7.5′-neolignan 33, and rel-(7S,8R,1′S,4′R,5′S,6′S)-6′-acetoxy-4′-hydroxy-3′,3′,5′-trimethoxy-4,5-methylenedioxy-Δ-1,3,5,2′,8′-8.1′,7.5′-neolignan 34 (18).

*L. canella* (Meisn.) Kosterm.

*L. canella* is a botanical species popularly known as 'louro pirarucu'. Within the ethnic group Tacana of the Amazonian region, this species has the same name and use as *Aniba canellila*, probably due to their aromatic barks. The barks of both species have ethnopharmacological uses to alleviate abdominal pain, intestinal cramps or discomfort, without diarrhea (8). The ethanol extract of the bark of this species showed activity in vitro against chloroquine sensitive Plasmodium falciparum (IC50 value of 3.8 µg/mL) and also resistant strains (IC10 value of 3.2 µg/mL). The extract of the stem demonstrated low activity against human myeloma cell line, RPMI 8226 cancer cells (8). Giesbrecht and co-workers (19) have reported the benzene/ethanol extract of the trunk wood to have three neolignans, canellin A 35, B 36 and C 37, as well as dillapiol 38, elemicin 39 and sitosterol 5.

*L. chrysophylla* (Meisn.) Kosterm.

*L. chrysophylla* is a tree growing in Amazonian rainforest,
Brazil. The first and up to now, four studies have been reported from this species. Ferreira and co-workers (20) have isolated chrysophyllin A 40 and B 41 from petroleum extract of the trunk wood. Both compounds were also found from the same species, reported by Lopes et al. (21). They also managed to obtain chrysophyllon I-A 42, chrysophyllon I-B 43, chrysophyllon II-A 44, chrysophyllon II-B 45, chrysophyllon III-A 46, chrysophyllon III-B 47, 2,3,4,5-tetramethoxyallylbenzene 48, 2,3,4,5-tetramethoxychinnamyl alcohol 49 and 2,3,4,5-tetramethoxychinnamaldehyde 50 from the petroleum extract of trunk wood. Furthermore, Silva and co-workers (22) have reported on the other parts of this species which are from the bark and fruits calyx ethanolic extract. They found five new benzodioxane neolignans, eusiderin I-M 51-55, three new β-aryloxy-arylpropane type neolignan, virolongin E-G 56-58, together with known compounds, eusiderin A 27 and virolongin B 24. In addition, Bezerra et al. (16) have studied on the bark extract of this species and successfully isolated chrysophyllon IV-B 59, chrysophyllon V1-B 60, chrysophyllon I-B 43, chrysophyllon II-A 44, chrysophyllon II-B 45, chrysophyllon III-B 47. They also found that the isolated compound have strong inhibition of supercoiled DNA relaxation induced by topo II-a at a concentration of 100 µM. These results indicate that no obvious correlation can be derived between the structure of these compounds and the inhibitory activity of DNA relaxation by DNA topoisomerase II.

*L. macrophylla* (A.C. Smith) Kosterm.

*L. macrophylla* is a tree which grows in the Amazon region, Brazil (23). Only one study has been reported in the literature about this plant in 1974, when Franca and coworkers (23) described the isolation and characterization of a novel neolignan, macrophyllin 61 from the trunk wood extracts. Besides, they also managed to get sitosterol 5, borneol 62, elemol 63, and nerolidol 64.

*L. mahuba* (A. Samp.) Kosterm.

*L. mahuba*, an Amazonian Lauraceae has been reported to have (−)-dihydromahubanolide B 65 and (−)-*iso*-dihydromahubanolide B 66. Synthesis of both compounds was achieved starting from (−)-methyl 5-hydroxymethyl-2,2-dimethyl-1,3-dioxolane-4-carboxylate which was readily available from L-(+)-tartaric acid, as published by Tanaka and Yamashita (24). Gottlieb and co-workers (25) also reported the phytochemical study from the wood of a *Licaria* sp. They were successfully identified two neolignans, namely aurein 67 and eusiderin 68.

**L. puchury-major** (Mart.) Kosterm.

*L. puchury-major* is popularly known in Brazil as ‘puchuri’ or ‘pixuri’. Their seeds are used in folk medicine for stomach and intestinal ailments and also as a calming agent in adults and children to treat insomnia, nervousness and irritability (26). The first phytochemical study of this species appeared in the literature in 1973 when Leao da Silva and co-workers (27) isolated and structurally characterized sitosterol 5, eugenol 69, safrole 70, syringic aldehyde 71, 3,4-methylenedioxychinnamaldehyde 72 and 3,4-methylenedioxychinnamyl alcohol 73 from trunk wood extract. In addition, Uchiyama and co-workers (28) have reported that the EtOH extract of the seeds of *L. puchury-major* showed the growth inhibitory activity against human leukemia Jurkat cells (53.3% inhibition at 30 µg/mL). Besides, acetone fraction was found to be the most active (82.7% inhibition at 30 µg/mL) and induced early apoptosis at 30 µg/mL within 24 h against Jurkat cells. Bioassay-guided fractionation of the ethanol extracts led to the isolation of one phenylpropanoid and ten neolignans. They were identified as apiole 74, (7S,8S)-Δ4′-2′,6′-dimethoxy-3,4-methylenedioxy-7.O.3′,8′.4′,1′.O.7′-neolignan 75, ferrearin B 76, ferrearin C 77, licarin A 1, rel-(7S,8S,1′R,2′S)-2′-hydroxy-3,4-dimethoxy-3′-oxo-Δ4′,8′-8′-1′,7′.O.2′-neolignan 78, ferrearin G 79, oxaguianin 80, rel-(7S,8S,1′R,5′R)-5′-methoxy-3,4-methylenedioxy-4′-oxo-Δ2′,8′-8′,1′,7′.O.2′-neolignan 81, armenin B 8, and 3′-methoxyburchellin 82. The cytotoxic activity of isolated compounds against Jurkat was tested by MTT assay and found that compounds 76, 77, 78 and 79 having furanocyclohexenone structure with hemiacetal in the molecule showed cytotoxic activity at 10 µM. These four neolignans induced early apoptosis at 10 µM within 24 h, while compound 75 also induced apoptosis at 100 µM within 48 h. Studies on this species was continued by Ohaski and co-workers (6) and successfully isolated ten alkaloids from the seeds extract. They were identified as reticuline 83, orientaline 84, coclaurine 85, N-methylcoclaurine 86, norjuziphine 87, norisoboldine 88, isoboldine 87, glaziovine 90 and reticule N-oxide [91 N-Me (S); 92 N-Me (R)]. The cytotoxicity of the obtained compounds was evaluated against vincristine-sensitive and -resistant P388 cells in the presence of P388/VCR(+) or the absence of P388/VCR(-) of low levels of vincristine. Norjuziphine 87, norisoboldine 88, and isoboldine 89 exhibited potent cytotoxic activity in the presence of vincristine P388/VCR(+).
Figure 1. Chemical structures of the compounds isolated from the genus Licaria
Table 2. Essential oils compositions from the genus *Licaria*

<table>
<thead>
<tr>
<th>Species</th>
<th>Locality</th>
<th>Parts/Major components</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>L. canella</em></td>
<td>Brazil</td>
<td><strong>Leaves:</strong> Benzyl Benzoate (69.7-73.0%), α-copaene (4.5-4.9%), α-phellandrene (3.3-4.2%), α-pinene (3.0-3.5%) (4)</td>
</tr>
<tr>
<td><em>L. excelsa</em></td>
<td>Costa Rica</td>
<td><strong>Leaves:</strong> α-Pinene (42.9%), β-pinene (22.0%) (31)</td>
</tr>
<tr>
<td><em>L. macrophylla</em></td>
<td>Brazil</td>
<td><strong>Wood:</strong> Elemol (25.0%), nerolidol (5.0%), borneol (3.0%) (27)</td>
</tr>
<tr>
<td><em>L. martiniana</em></td>
<td>Brazil</td>
<td><strong>Leaves:</strong> β-Caryophyllene (41.7%), β-selinene (7.9%), isovalerate linalool (5.9%), linalool (5.3%) (9)</td>
</tr>
<tr>
<td></td>
<td>Brazil</td>
<td><strong>Stems:</strong> β-Caryophyllene (21.4%), spathulenol (11.5%), linalool (6.5%), α-cadinol (5.9%), γ-cadinene (5.7%) (9)</td>
</tr>
<tr>
<td><em>L. puchury-major</em></td>
<td>Brazil</td>
<td><strong>Twigs:</strong> Eugenol (61.0%), safrole (20.1%), eucalyptol (10.8%), α-terpineol (6.8%) (32)</td>
</tr>
<tr>
<td><em>L. salicifolia</em></td>
<td>France</td>
<td><strong>Leaves:</strong> α-Phellandrene (17.2-22.0%), α-santalene (0.8-20.3%), p-cymene (1.5-17.4%), β-santalene (0.2-7.0%) (35)</td>
</tr>
<tr>
<td></td>
<td>France</td>
<td><strong>Bark:</strong> p-Cymene (10.1-13.0%), α-phellandrene (5.3-8.1%), 7-epi-α-santalene (7.3-7.6%), α-cadinol (4.5-6.5%), caryophyllene oxide (4.3-6.2%) (35)</td>
</tr>
<tr>
<td><em>L. triandra</em></td>
<td>Cuba</td>
<td><strong>Leaves:</strong> Selin-11-en-4α-ol (15.1%), β-pinene (10.6%), β-caryophyllene (9.5%), spathulenol (5.6%) (29)</td>
</tr>
<tr>
<td></td>
<td>Costa Rica</td>
<td><strong>Leaves:</strong> β-Eudesmol (11.4%), caryophyllene oxide (3.0%) (29)</td>
</tr>
</tbody>
</table>

*L. rigida* Kosterm.

*L. rigida*, collected at the Ducke Forest Reserve, near Manaus, Amazonas State, have been investigated by Fo et al. (7). They managed to isolate three neolignans from the trunk wood extract, namely eusiderin 68, eusiderin B 93, canellin A 35 and canellin C 37.

*L. triandra* (Sw.) Kosterm.

*L. triandra* is a tree 7-16 m high. It is frequent in woodlands on limestone or shale, 100-1000 m, flowering in September-November, fructifying in January-September. It grows wild in Florida and West Indies southward to Martinique (29). The leaves are used locally as folk medicine such as against indigestion, stomachache and as stimulant (3). Phytochemical investigation from the seeds of this species have afforded two new neolignans, identified as triandrin A-B 94-95 (18) as well as a known benzofuranoid neolignan, burchellin 96 as reported by Castro and Ulate (30).

Literatures revealed that few essential oils studies have been carried out on *Licaria* species. The chemical compositions of the essential oils of *Licaria* species have been conducted on seven species, which are *L. canella* (4), *L. excelsa* (31), *L. macrophylla* (27), *L. martiniana* (9), *L. puchury-major* (5,32,33,34), *L. salicifolia* (35), and *L. triandra* (29,31,36). The major components of the essential oil compositions from *Licaria* species are tabulated in Table 2. Monoterpenes hydrocarbon was found as the major group components, in the essential oil of *L. triandra* (Cuba: 42.9%; Costa Rica: 77.7%) (29,31). Meanwhile, oxygenated monoterpenes and benzenoids were found from the essential oil of *L. puchury-major* (seeds: 34.3%) (5) and *L. canella* (leaves: 71.3-74.9%) (4), respectively. In addition, sesquiterpenes hydrocarbons were found from the essential oil of *L. martiniana* (47.0-65.8%) (9). Benzyl benzoate, eugenol, and safrole were the major components identified with more than 50% in the essential oils of *Licaria* species. Benzyl benzoate was found in 69.7-73.0% from the leaves oil of *L. canella* (4). Other studies have demonstrated that benzyl benzoate is effective at denaturing dust mite allergen (37) and can eradicate mites and reduce their populations (38). In addition, eugenol presented 61.0% from the twigs oil of *L.
puchury-major (32). It has been shown in the pharmacological studies that eugenol demonstrated anesthetic, hypothermic, muscle-relaxant, antistress effect and anticonvulsant activities (39, 40). Besides, the seeds oil from the same species has successfully found saffrole in 51.3% (33) and 58.4% (5). Studies have revealed the genotoxic (41) and carcinogenic (42) potentials of saffrole. The study of Taiwanese oral cancer patients suggests that saffrole may form stable saffrole-DNA adducts in human oral tissues following betel quid chewing, which may contribute to oral carcinogenesis (43).

The in vitro antibacterial activity of the essential oil of L. triandra was studied against five bacteria strains (Bacillus cereus, Staphylococcus aureus, Listeria monocytogenes, Bacillus subtilis and Escherichia coli) using the disc diffusion method. The essential oil showed weak activity against the bacteria tested (29). Palazzo and co-workers (31) have evaluated in vitro cytotoxicity activity of the essential oils of L. excelsa and L. triandra against human breast adenocarcinoma cells (MDA-MB-231/MDA-MB-231) and human breast ductal carcinoma cells (Hs 578T). The essential oil of L. triandra was found weak activity with 25% kill at 100 μg/mL, while L. excelsa oil found to be inactive. The evaluation of the anti-leishmanial activity of the essential oil of L. canella indicated moderate activity against Leishmania amazonensis with IC₅₀ value of 19 μg/mL. Meanwhile, the essential oil displayed low cytotoxicity against Artemia salina with LC₅₀ value of 5.25 μg/mL (4). Besides, the essential oils of L. martiniana showed weak antioxidant (DPPH >1000 μg/mL) and antiplatelet inhibitory activities (leaves 4.2%; stems 36.9%) at quantitative spectrometric assays (9).

CONCLUSION

In this review, we summarized the secondary metabolites isolated from the genus Licaria and their pharmacological properties. Most of the species produced lignans and neolignans. Apart from that, further phytochemical studies need to be carried out in the near future to provide a more detailed pattern of the natural constituents and of the biologically active principles in extracts. As a conclusion, it is evident that the genus Licaria comprises therapeutically promising and valuable plants, some of which are used in the traditional medicine of indigenous populations. Meanwhile, there are only few studies describing their pharmacological properties, this genus merits more attention in the on-going search for new bioactive compounds.

ACKNOWLEDGMENTS

The authors thank to Research University Grant (GUP-Q/130000.2526.03H93) for financial support and the Department of Chemistry, Faculty of Science, Universiti Teknologi Malaysia (UTM) for research facilities.

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