Research Article

Phytochemical Analysis, Anti-inflammatory, and Antioxidant Activities of Dendropanax dentiger Roots

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Dendropanax dentiger root is a traditional medicinal plant in China and used to treat inflammatory diseases for centuries, but its phytochemical profiling and biological functions are still unknown. Thus, a rapid, efficient, and precise method based on ultra high-performance liquid chromatography coupled with quadrupole time-of-flight tandem mass spectrometry (UHPLC-Q-TOF-MS/MS) was applied to rapidly analyse the phytochemical profiling of D. dentiger with anti-inflammatory and antioxidant activities in vitro. As a result, a total of 78 chemical compositions, including 15 phenylpropanoids, 15 alkaloids, 14 flavonoids, 14 fatty acids, 7 phenols, 4 steroids, 4 cyclic peptides, 3 terpenoids, and 2 others, were identified or tentatively characterized in the roots of D. dentiger. Moreover, alkaloid and cyclic peptide were reported from D. dentiger for the first time. In addition, the ethanol crude extract of D. dentiger roots exhibited remarkable anti-inflammatory activity against cyclooxygenase- (COX-) 2 inhibitory and antioxidant activities in vitro. This study is the first to explore the phytochemical analysis and COX-2 inhibitory activity of D. dentiger. This study can provide important phytochemical profiles and biological functions for the application of D. dentiger roots as a new source of natural COX-2 inhibitors and antioxidants in pharmaceutical industry.

1. Introduction

Over the past few years, secondary metabolites from natural products play an important role in the development of new drugs [1]. Higher plants represent sources of abundant phytochemicals with a wide range of biological effects and have attracted more attention in the past decades [2–6]. Consequently, most medicinal plants belong to higher plants have been widely to treat many human diseases in traditional folk medicine [1, 7–9]. Although numerous studies on the medicinal plants used as traditional Chinese medicines (TCMs), problems of chemical compositions and biological properties remained the main barriers in the development of modern traditional medicines or new drugs.

The genus Dendropanax (Araliaceae), known as “Shushen” in Chinese, comprises about 80 known species in tropical America and eastern Asia. In China, 16 native species have been found, which were widely cultivated in parks and/or used as folk medicine [10]. D. dentiger (Harms) Merr. is native to China and widely distributed in Guangxi, Jiangxi, Yunnan, and Guangdong provinces. In TCM, the roots of D. dentiger have been used as an important folk medicine for the treatment of inflammatory diseases [11]. Due to its potential pharmaceutical industry promoting effects, D. dentiger afforded structurally diverse and biologically active compounds, such as steroids, alkaloids, flavonoids, and monoterpenes; some of them showed potential anti-inflammatory, cytotoxic, and antioxidant activities [12, 13]. Although lots of chemical compositions report on D. dentiger, the full chemical profiling and COX-2 inhibitory activity of this plant have not yet been studied so far.
This study was the first time to determine the phytochemical profiling and COX-2 inhibitory activity. In addition, it was also to evaluate the antioxidant activity, including DPPH and ABTS assays in vitro. This finding may contribute to the processing and utility of *D. dentiger*.

2. Materials and Methods

2.1. Chemicals and Reagents. The COX-2 inhibitor screening assay kit was purchased from Beyotime Biotechnology (Shanghai, China). 2,2-Diphenyl-1-picrylhydrazyl (DPPH), celecoxib were purchased from Sigma-Aldrich (St. Louis, MO, USA). L-Ascorbic acid (Vc) was purchased from Aladin (Shanghai, China). Acetonitrile and formic acid (LC-MS grade) were purchased from Fisher Scientific (Pittsburgh, PA, USA). HPLC grade water was deionized using a Milli-Q ultrapure water system (Merck Millipore, Milford, MA, USA).

2.2. Plant Material. The roots of *D. dentiger* were collected in the town of Baidu, Baise City, Guangxi, China, in October 2016. A botanical voucher specimen of this plant (No. DDD20161022) was deposited at authors’ laboratory and was identified by one of the authors Ronghua Liu [10].

2.3. Extraction Procedure. The dried and powdered roots of *D. dentiger* (10.0 kg) were extracted with 95% EtOH (60 L × 3) and subsequently 50% EtOH (60 L × 3) by maceration at room temperature for seven days. All filtrates were combined and evaporated under reduced pressure (EYELA, Tokyo, Japan) to obtain the ethanol crude extract of *D. dentiger* (DD, 1275 g, 12.75%).

2.4. UHPLC-Q-TOF-MS/MS. The UHPLC-Q-TOF-MS/MS was provided in our previously published article [14]. Chromatographic separation was conducted on a Luna Omega C18 (100 × 2.1 mm, 1.6 μm, Phenomenex Inc., CA, USA) keeping at 40°C. 0.1% aqueous formic acid (v/v) A) and acetonitrile (B) were used as mobile phases. The gradient elution with the flow rate of 0.3 mL/min was performed as follows: 0-15 min, 25% B; 15-18 min, 25%-55% B; 18-40 min, 55%-95% B; 40-42 min, 95% B for column cleaning, and a conditioning cycle time of 3 min with the same initial conditions of 5% B. The sample inject volume was 3 μL.

2.5. COX-2 Inhibitory Assay. The anti-inflammatory effect of the sample against COX-2 inhibition was determined using colorimetric COX-2 inhibitor screening assay kit (no. S0168) and using celecoxib as the positive drug [2–4]. Briefly, 75 μL of assay buffer, 5 μL of cofactor working solution, and 5 μL of working solution were mixed with 5 μL of the sample at different concentrations and then incubated at 37°C. After 10 min, 5 μL of probe and 5 μL of substrate were added in all wells and then incubated at 37°C for 5 min, and the absorbance was determined (Asample). The absorbance of a blank (Ablank) and control (Acontrol) composed of only the sample and COX-2 enzyme solutions was also determined, respectively. The COX–2 inhibitory activity (%) = [(Acontrol − Asample)/(Acontrol − Ablank)] × 100%.

2.6. Antioxidant Assay

2.6.1. DPPH Radical Scavenging Activity. The DPPH radical scavenging activity of the sample was provided in our previously published article [2–4]. Briefly, 150 μL of DPPH solution (dissolved 0.2 mM in methanol) was mixed with 50 μL of the sample at different concentrations. The mixture was stirred and incubated in the dark at 30°C for 30 min, and the absorbance was determined at 517 nm (Asample). The absorbance of a blank (Ablank) and negative control (Acontrol) composed of only the sample and DPPH solutions was also determined, respectively. The DPPH radical scavenging activity of the sample was calculated by the following equation:

DPPH scavenging activity = [1 − (Asample − Ablank)/Acontrol] × 100%. Vc was used as a positive control in this experiment.

2.6.2. ABTS Radical Scavenging Activity. The ABTS radical scavenging activity of the sample was carried out using the method reported by Sun et al. with minor modification [15]. Briefly, 1.76 mL of K3S2O8 (140 mM) and 100 mL of ABTS solution (7 mM) were mixed and stored in the dark at 25°C for 12 h. Then, the ABTS stock solution was diluted with PBS (0.1 M, pH7.4) until an absorbance value of 0.70 ± 0.02 was reached at 734 nm to obtain the diluted ABTS’ radical solution. Subsequently, 10 μL of the sample was mixed with 195 μL the diluted ABTS’ radical solution and incubated in the dark at 25°C for 106 min, and the absorbance of the sample at 734 nm (Asample) was measured. The absorbance of a blank (Ablank) and negative control (Acontrol) composed of only the sample and diluted ABTS’ radical solutions was also determined, respectively. The ABTS radical scavenging activity of the sample was calculated by the following equation: ABTS scavenging activity = [1 − (Asample − Ablank)/Acontrol] × 100%. Vc was used as a positive control in this experiment.

2.7. Statistical Analysis. Graphpad Prism 6 was used for statistical analysis, and the data were presented as the means ± standard deviation (SD). One-way analysis of variance (ANOVA) and Tukey’s test were used for comparison of differences in groups. Differences with *p* < 0.05 indicated statistical significance.

3. Results and Discussion

3.1. Identification of Main Constituents in *D. dentiger* Root Extract. In the present study, the phytochemical compositions were identified using UHPLC-Q-TOF-MS/MS based on the existing literatures and public databases, including ChemSpider, Massbank PubChem, and mzCloud, and summarized and described in Table 1 [16–44]. The base peak chromatograms of *D. dentiger* roots extract in positive and negative ion modes were presented in Figure 1. A total of 78 compounds, including 15 phenylpropanoids, 15 alkaloids, 14 flavonoids, 14 fatty acids, 7 phenols, 4 steroids, 4 cyclic peptides, 3 terpenoids, and 2 others, were identified. The molecular formula was accurately assigned within mass error of 5 ppm. Then, the fragment ions were
### Table 1: Compounds identified from the roots of D. dentiger by UHPLC-Q-TOF-MS/MS in positive/negative ion mode.

| No. | RT (min) | Ion mode | Molecular weight | Measured mass | Error (ppm) | Molecular formula | Fragments | Identification | Reference |
|-----|----------|-----------|------------------|---------------|-------------|-------------------|-----------|----------------|-----------|
|     |          |           |                  |               |             |                   |           |                |           |
| **Phenylpropanoids** |          |           |                  |               |             |                   |           |                |           |
| 17  | 5.03     | [M-H]    | 342.09508        | 341.08806     | 0.7         | C_{15}H_{18}O_{9} | 191.0568\(^a\), 179.0351, 173.0458, 135.0467, 93.0375 | Caffeoyl hexose | 16         |
| 18  | 5.23     | [M-H]    | 354.09508        | 353.08806     | 0.7         | C_{16}H_{18}O_{9} | 353.0872, 191.0571\(^a\), 179.0356, 161.0254 | Chlorogenic acid | 16         |
| 19  | 5.59     | [M-H]    | 326.10017        | 325.09321     | 1           | C_{15}H_{18}O_{8} | 176.0497, 163.0405, 145.0302, 119.0524\(^a\), 114.0389, 59.0167 | Coumaric acid glucoside | 17         |
| 21  | 5.91     | [M-H]    | 180.04226        | 179.03629     | 4.3         | C_{9}H_{8}O_{4}   | 135.0461\(^a\), 134.0386, 89.0430 | Caffeic acid | 18         |
| 22  | 6.89     | [M-H]    | 338.10017        | 337.0932      | 0.9         | C_{16}H_{18}O_{8} | 191.0574\(^a\), 173.0460, 163.0410, 119.0529, 93.0385 | 3-p-COQA | 19         |
| 26  | 7.93     | [M-H]    | 368.11073        | 367.10358     | 0.3         | C_{17}H_{20}O_{9} | 193.0511, 191.0567\(^a\), 134.0389, 93.0377 | Methyl 4-caffeylquininate | 19         |
| 27  | 8.12     | [M-H]    | 504.18429        | 503.17658     | -0.9        | C_{22}H_{32}O_{11}| 503.1761\(^a\), 341.1243, 221.0673, 161.0474, 101.0269 | Tinoscorside D | 20         |
| 31  | 9.56     | [M-H]    | 742.26842        | 741.26178     | -0.9        | C_{34}H_{46}O_{18}| 417.1571\(^a\), 402.1310, 181.0524, 166.0289 | Syringaresinol-4,4'-bis-O-β-D-glucopyranoside | 21         |
| 36  | 10.77    | [M-H]    | 472.19446        | 471.18683     | -0.8        | C_{22}H_{32}O_{13}| 189.0565, 163.0773, 134.0381, 105.0375\(^a\), 89.0250, 71.0169 | Eugenol rutinoside | 22         |
| 38  | 11.00    | [M-H]    | 624.20542        | 623.19799     | -0.3        | C_{29}H_{36}O_{15}| 623.1974\(^a\), 461.1662, 179.0354, 161.0254\(^a\), 135.0459 | Verbasconside | 23         |
| 40  | 12.49    | [M-H]    | 580.21559        | 579.20843     | 0.2         | C_{28}H_{36}O_{13}| 417.1550, 402.1323, 387.1019, 181.0516\(^a\), 166.0279, 151.0047 | Syringaresinol-4'-O-β-D-glucopyranoside | 21         |
| 42  | 13.18    | [M-H]    | 516.12678        | 515.11912     | -0.7        | C_{23}H_{24}O_{12}| 353.0878, 191.0566, 179.0359, 173.0466\(^a\), 161.0255, 135.0467 | 3,5-di-O-Caffeoylquinic acid | 24         |
| 50  | 15.03    | [M-H]    | 500.13186        | 499.12418     | -0.8        | C_{23}H_{24}O_{11}| 353.0878, 337.0925, 191.0569, 179.0361, 173.0467\(^a\), 135.0463 | 4-PCO-5-CQA | 19         |
| 54  | 16.76    | [M-H]    | 208.07356        | 207.06732     | 5           | C_{11}H_{16}O_{4} | 161.0258, 135.0466, 133.0313\(^a\) | Caffeic acid ethyl ester | 21         |
| 55  | 17.52    | [M-H]    | 524.22576        | 523.21801     | -0.9        | C_{28}H_{36}O_{11}| 361.1659\(^a\), 346.1430, 317.1404, 231.0668, 161.0257 | Secoisolariciresinol hexose | 16         |
| **Alkaloids** |          |           |                  |               |             |                   |           |                |           |
| 2   | 1.51     | [M+H]\(^+\) | 135.0545        | 136.06184     | 0.5         | C_{6}H_{8}N_{5}   | 136.0627, 119.0356\(^a\), 107.0489, 92.0260, 91.0554\(^a\), 65.0414 | Adenine | 18         |
| 3   | 1.54     | [M+H]\(^+\) | 181.07389       | 182.08102     | -0.8        | C_{6}H_{11}NO_{3} | 119.0492, 91.0561\(^a\), 77.0414, 65.0423 | Tyrosine | 25         |
| 4   | 1.59     | [M+H]\(^+\) | 267.09675       | 268.10379     | -0.9        | C_{10}H_{13}N_{5}O_{4} | 136.0622\(^a\), 119.0360 | Adenosine | 18         |
| 5   | 1.65     | [M+H]\(^+\) | 283.09167       | 284.09882     | -0.5        | C_{10}H_{13}N_{5}O_{5} | 152.0569\(^a\), 135.0308, 110.0364 | Guanosine | 25         |
| 6   | 1.71     | [M+H]\(^+\) | 131.09463       | 132.10211     | 1.5         | C_{6}H_{13}NO_{2} | 86.0987\(^a\), 72.9415, 69.0718, 57.0693, 55.9383, 55.0230 | Isoleucine | 25         |
| No. | RT (min) | Ion mode | Molecular weight | Measured mass | Error (ppm) | Molecular formula | Fragments | Identification | Reference |
|-----|---------|----------|------------------|---------------|-------------|------------------|-----------|---------------|-----------|
| 7   | 1.72    | [M + H]^+ | 275.13689        | 276.14402     | -0.5        | C_{12}H_{21}NO_{6} | 276.1431, 258.1327, 230.1383^a, 212.1256, 87.0330 | Glutarylcarnitine | 26 |
| 9   | 2.55    | [M + H]^+ | 165.07898        | 166.08619     | -0.4        | C_{6}H_{11}NO_{2}  | 120.0811, 13.0550, 77.0412^a | Phenylalanine | 27 |
| 23  | 7.16    | [M + H]^+ | 341.16271        | 342.17031     | 1           | C_{20}H_{23}NO_{4} | 342.1718, 297.1133, 282.0899, 265.0867^a, 222.0899, 58.0696 | Magnoflorine | 26 |
| 24  | 7.31    | [M + H]^+ | 327.14706        | 328.15459     | 0.8         | C_{19}H_{21}NO_{4} | 328.1557, 178.0862^a, 163.0627, 151.0759 | Stepholidine | 28 |
| 37  | 10.85   | [M + H]^+ | 277.11028        | 278.11756     | 0           | C_{18}H_{15}NO_{2} | 278.1183, 263.0948, 220.1129, 204.0813^a | Dehydroeroemerine | 27 |
| 44  | 13.79   | [M + H]^+ | 589.2887         | 590.29653     | 0.9         | C_{31}H_{43}NO_{10} | 590.2971^a, 572.2870, 558.2670, 540.2608, 508.2340 | Benzoylmesaconine | 26 |
| 48  | 14.94   | [M + H]^+ | 603.30435        | 604.31125     | -0.6        | C_{32}H_{45}NO_{10} | 604.3141^a, 554.2761, 242.1194 | Benzoylaconine | 26 |
| 49  | 15.00   | [M + H]^+ | 335.11576        | 336.1233      | 0.8         | C_{20}H_{17}NO_{4} | 336.1244, 321.1012, 320.0937^a, 306.0774, 292.0981, 278.0822 | Berberine | 26 |
| 52  | 15.83   | [M + H]^+ | 573.29378        | 574.30155     | 0.9         | C_{31}H_{43}NO_{9} | 574.3045^a, 542.2772, 510.2458, 105.0336 | Benzoylhypaconine | 26 |
| 57  | 17.95   | [M + H]^+ | 615.30435        | 616.31177     | 0.2         | C_{33}H_{45}NO_{10} | 616.3162^a, 556.2911, 524.2635, 338.1757, 161.0597 | Hypeaconitine | 26 |

Flavonoids

| No. | RT (min) | Ion mode | Molecular weight | Measured mass | Error (ppm) | Molecular formula | Fragments | Identification | Reference |
|-----|---------|----------|------------------|---------------|-------------|------------------|-----------|---------------|-----------|
| 25  | 7.41    | [M-H]^−  | 594.15847        | 593.15094     | -0.4        | C_{27}H_{30}O_{15} | 593.1523, 503.1208, 473.1098, 433.0778, 353.0675^a, 297.0772 | Apigenin-6,8-di-C-glucoside | 17 |
| 29  | 8.66    | [M-H]^−  | 564.14791        | 563.14072     | 0.2         | C_{26}H_{28}O_{14} | 563.1414, 545.1304, 503.1196, 473.1092, 443.0980, 383.0781, 353.0676^a, 297.0786, 173.0466, 93.0369 | Schaftoside | 19 |
| 30  | 8.91    | [M-H]^−  | 448.10056        | 447.09339     | 0.2         | C_{21}H_{20}O_{11} | 435.0627, 339.0514, 327.0523^a, 299.0569, 297.0410, 133.0307 | Isoorientin | 19 |
| 32  | 10.07   | [M-H]^−  | 432.10565        | 431.09862     | 0.6         | C_{21}H_{20}O_{10} | 431.0991, 341.0666, 311.0567, 293.0454, 283.0616^a, 161.0247, 117.0365 | Vitexin | 19 |
| 33  | 10.11   | [M-H]^−  | 610.15339        | 609.14652     | 0.7         | C_{27}H_{30}O_{16} | 609.1490, 447.1153, 301.0363, 300.0284^a, 271.0259, 255.0310, 161.0249 | Rutin | 19 |
| 34  | 10.15   | [M+H]^+ | 464.09548        | 465.10317     | 0.9         | C_{26}H_{26}O_{12} | 303.0504^a, 257.0444, 201.0546, 85.0309 | Myricitrin | 29 |
| 35  | 10.34   | [M-H]^−  | 580.14282        | 579.13562     | 0.1         | C_{26}H_{26}O_{15} | 579.1365, 285.0411^a | Luteolin-7-O-xylosyl-glucoside | 19 |
| 39  | 11.76   | [M-H]^−  | 462.11621        | 461.10885     | -0.2        | C_{22}H_{22}O_{11} | 461.1063, 299.0560^a, 284.0334, 256.0375 | 5,7,2′-Trihydroxy-6-methoxyllavone | 30 |
| 45  | 14.18   | [M-H]^−  | 492.12678        | 491.11956     | 0.1         | C_{23}H_{24}O_{12} | 491.1189^a, 459.0923, 323.0771, 315.0732, 314.0442, 179.0361, | Tricin 5-glucoside/tricin 7-glucoside | 17 |
| No. | RT (min) | Ion mode | Molecular weight | Measured mass | Error (ppm) | Molecular formula | Fragments | Identification | Reference |
|-----|---------|----------|------------------|---------------|-------------|-----------------|-----------|---------------|-----------|
| 47  | 14.88   | [M-H]^- | 446.08491        | 445.07734     | -0.7        | C$_{21}$H$_{18}$O$_{11}$ | 269.0451a | Baicalin       | 30        |
| 53  | 16.06   | [M-H]^- | 286.04774        | 285.04067     | 0.7         | C$_{15}$H$_{10}$O$_{6}$ |           | Luteolin      | 17        |
| 56  | 17.84   | [M-H]^- | 300.06339        | 299.05669     | 1.9         | C$_{16}$H$_{12}$O$_{6}$ | 284.0313a, 256.0382, 227.0343, 151.0067 | Diosmetin | 19        |
| 61  | 19.12   | [M+H]^+ | 402.13147        | 403.13883     | 0.2         | C$_{21}$H$_{22}$O$_{8}$ | 342.1110  | Nobiletin     | 31        |
| 66  | 20.54   | [M-H]^- | 270.05282        | 269.04576     | 0.8         | C$_{15}$H$_{10}$O$_{5}$ | 403.1397, 388.1151, 373.0922a, 269.0467a, 241.0515, 225.0568, 213.0563, 197.0617, 181.0660, 171.0458 | Apigenin  | 32        |
| 61  | 19.12   | [M+H]^+ | 402.13147        | 403.13883     | 0.2         | C$_{21}$H$_{22}$O$_{8}$ | 342.1110  | Nobiletin     | 31        |
| 66  | 20.54   | [M-H]^- | 270.05282        | 269.04576     | 0.8         | C$_{15}$H$_{10}$O$_{5}$ | 403.1397, 388.1151, 373.0922a, 269.0467a, 241.0515, 225.0568, 213.0563, 197.0617, 181.0660, 171.0458 | Apigenin  | 32        |

**Fatty acids**

| No. | RT (min) | Ion mode | Molecular weight | Measured mass | Error (ppm) | Molecular formula | Fragments | Identification | Reference |
|-----|---------|----------|------------------|---------------|-------------|-----------------|-----------|---------------|-----------|
| 16  | 4.98    | [M-H]^- | 176.06847        | 175.06192     | 4.1         | C$_{7}$H$_{12}$O$_{3}$ | 115.0411, 113.0637, 85.0689a | Hydroxy-methylglutaric acid | 33        |
| 58  | 18.28   | [M-H]^- | 228.13616        | 227.12906     | 0.8         | C$_{12}$H$_{20}$O$_{4}$ | 329.2329, 229.1451, 211.1348, 209.1191, 171.1038a, 139.1141, 127.1144 | Dihydroxy dodecadienoic acid | 34        |
| 59  | 18.40   | [M-H]^- | 329.23349        | 329.2336      | 0.8         | C$_{18}$H$_{34}$O$_{5}$ | 209.1192a, 207.1408, 185.1193, 163.1139, 137.0985, 125.0991, 99.0849, 97.0682, 57.0403 | Trihydroxy-octadecenoic acid | 35        |
| 62  | 19.55   | [M-H]^- | 310.21441        | 309.20744     | 1           | C$_{18}$H$_{30}$O$_{4}$ | 313.2389, 277.2178, 201.1139a, 199.0981, 171.1029, 127.1142, 125.0980 | Dihydroxy-octadecatrienoic acid | 35        |
| 65  | 20.54   | [M-H]^- | 314.24571        | 313.23872     | 0.9         | C$_{18}$H$_{34}$O$_{4}$ | 311.2234, 293.2129, 275.2005, 211.1353, 201.1141, 185.1188, 171.1040a, 139.1145, 127.1155 | Dihydroxy-octadecadienoic acid | 35        |
| 67  | 20.72   | [M-H]^- | 312.23006        | 311.22326     | 1.5         | C$_{18}$H$_{32}$O$_{4}$ | 261.2204, 187.1461, 145.1020, 131.0859, 107.0870, 93.0718, 81.0721a, 67.0580 | Dihydroxy-octadecadienoic acid | 35        |
| 68  | 21.47   | [M+H]^+ | 352.26136        | 353.26862     | -0.1        | C$_{21}$H$_{36}$O$_{4}$ | 293.2114a, 249.2220, 197.1180, 185.1186, 125.0981, 113.0987 | Glyceryl linolenate | 36        |
| 69  | 23.75   | [M-H]^- | 294.2195         | 293.21295     | 2.5         | C$_{18}$H$_{32}$O$_{3}$ | 337.2750, 263.2377, 245.2258, 175.1478, 161.1327, 147.1159, 109.1017, 95.0862, 81.0720a | Hydroxy-octadecatrienoic acid | 35        |
| 71  | 28.55   | [M+H]^+ | 354.27701        | 355.28463     | 1           | C$_{21}$H$_{36}$O$_{4}$ | 261.2204, 187.1461, 145.1020, 131.0859, 107.0870, 93.0718, 81.0721a, 67.0580 | Glyceryl linoleate | 36        |
| No. | RT (min) | Ion mode | Molecular weight | Measured mass | Error (ppm) | Molecular formula | Fragments | Identification | Reference |
|-----|----------|-----------|------------------|---------------|-------------|------------------|-----------|----------------|-----------|
| 72  | 29.08    | [M-H]^-   | 356.29266        | 355.28536     | -0.1        | C_{21}H_{40}O_{4} | 355.2758, 355.2918, 293.2837, 295.0241, 240.9931 | Monoolein | 22 |
| 74  | 30.78    | [M + H]^+ | 330.27701        | 331.28412     | -0.5        | C_{19}H_{36}O_{4} | 313.2738, 109.1018, 95.0863, 85.1026, 81.0716, 71.0880, 57.0740 | Glycerin palmitate | 36 |
| 75  | 37.15    | [M-H]^-   | 284.27153        | 283.2645      | 0.9         | C_{18}H_{32}O_{2} | 283.2631, 282.3573, 265.2527, 199.8494 | Tearic acid or its isomer | 35 |
| 77  | 40.40    | [M-H]^-   | 312.30283        | 311.29527     | -0.9        | C_{20}H_{40}O_{2} | 311.2948, 311.1673, 293.2749, 184.0163, 183.0121 | Arachidic acid/eicosanoic acid | 37 |
| 78  | 43.36    | [M-H]^-   | 340.33413        | 339.32722     | 1.1         | C_{22}H_{44}O_{2} | 339.1992, 338.0199, 368.0127, 119.0516 | Behenic acid | 22 |
| 7  | 1.93     | [M-H]^-   | 170.02152        | 169.0152      | 4.6         | C_{7}H_{6}O_{5}  | 125.0254, 124.0202, 97.0341, 79.0239, 69.0410 | Gallic acid | 38 |
| 10  | 2.80     | [M-H]^-   | 316.07943        | 315.07253     | 1.2         | C_{13}H_{14}O_{5} | 153.0201, 152.0127, 108.0246 | 3-Carboxy-4-hydroxyphenoxy glucoside | 19 |
| 11  | 2.94     | [M-H]^-   | 330.09508        | 329.08808     | 0.8         | C_{14}H_{16}O_{6} | 167.0359, 152.0128, 123.0474, 108.0251 | Vanillic acid hexose | 16 |
| 12  | 3.47     | [M + H]^+ | 198.05282        | 199.05998     | -0.6        | C_{9}H_{14}O_{3} | 197.0465, 182.0234, 167.0000, 138.0344, 123.0112, 95.0176 | Syringic acid | 25 |
| 13  | 3.50     | [M-H]^-   | 360.10565        | 359.0987      | 0.9         | C_{15}H_{20}O_{10} | 225.0399, 196.0402, 181.0514, 163.0405, 148.0190, 135.0469, 120.0222, 109.0389, 95.0205 | Methoxypolygoacetophenoside | 33 |
| 14  | 3.82     | [M-H]^-   | 256.0583         | 255.05159     | 2.2         | C_{11}H_{12}O_{4} | 140.0463, 125.0236, 95.0504, 77.0414, 65.0421 | Piscidic acid | 39 |
| 28  | 8.55     | [M + H]^+ | 182.05791        | 183.06503     | -0.8        | C_{9}H_{14}O_{4} | 25(27)-ene-Timosaponin AIII | 783.4257, 737.4121 | 25 |
| 63  | 19.56    | [M + HCOO]^+ | 738.41904 | 783.41695 | 1           | C_{39}H_{62}O_{13} | 783.4257, 737.4121 | 25(27)-ene-Timosaponin AIII | 35 |
| 64  | 19.91    | [M + HCOO]^+ | 1050.52469      | 1095.52283    | 0.9         | C_{50}H_{82}O_{23} | 917.4771, 887.4673, 593.3684 | F-Gitonin | 35 |
| 73  | 30.23    | [M-H]^-   | 340.24023        | 339.23303     | 0.2         | C_{23}H_{32}O_{2} | 339.2323, 163.1143 | Dimethisterone | 35 |
| 76  | 38.29    | [M + H]^+ | 412.37052        | 413.37809     | 0.7         | C_{20}H_{40}O_{2} | 413.3786, 395.3701, 255.2108, 213.1639, 173.1328, 159.1170, 145.1017, 109.0658 | α-Spinasterol | 40 |
| 41  | 12.63    | [M + H]^+ | 678.50438        | 679.51224     | 0.8         | C_{36}H_{56}O_{6} | 679.5139, 661.5044, 566.4337, 548.4185, 486.2149, 435.3332, 322.2482, 209.1660, 114.0932 | Cyclo hexaleucyl (or isoleucyl) | 35 |
3.1.1. Phenylpropanoids. Phenylpropanoids were widely distributed in medicinal plants and its structures containing one or more C₆-C₃ units, which include three structure types, including simple phenylpropanoids, coumarins, and lignans [14]. A total of 15 phenylpropanoids in the roots of D. dentiger extract were identified in negative ion mode, including 12 simple phenylpropanoids and 3 lignans (Figure 2).

Compounds 17-19, 21, 22, 26, 27, 36, 38, 42, 50, and 54 were simple phenylpropanoids, while compounds 27 and 36 were phenylpropanol and phenylpropene, respectively. Moreover, compounds 17, 18, 21, 26, 38, 42, 50, and 54 were caffeic acid derivatives, including 4 caffeoylquinic acid derivatives (18, 26, 42, 50). They combine by the quinic acid and caffeic acid with ester linkage and have similar cleavage pathways. The typical neutral losses of caffeoyl, quinine, H₂O, and CO₂ were the major cleavage pathway of such compounds. Taking compound 18 as an example, it gave the same MS² base peak at m/z 191.0571 due to the loss of caffeic acid and a relatively intense secondary ion at m/z 179.0356 resulting from the loss of a hexosyl residue and was tentatively assigned as secoisolariciresinol hexose.

Table 1: Continued.

| No. | RT (min) | Ion mode | Molecular weight | Measured mass | Error (ppm) | Molecular formula | Fragments | Identification | Reference |
|-----|----------|----------|------------------|---------------|-------------|------------------|-----------|---------------|-----------|
| 43  | 13.71    | [M + H]^+ | 791.58845        | 792.59618     | 0.6         | C_{42}H_{77}N_{17}O_{7} | 792.5976, 774.5873, 679.5137, 661.5069, 566.4308, 548.4199, 453.3648, 435.3336, 340.2605, 322.2510, 227.1767, 209.1654 | Cyclo hetaleucyl (or isoleucyl) | 35 |
| 46  | 14.58    | [M + H]^+ | 904.67251        | 905.68109     | 1.4         | C_{48}H_{88}N_{8}O_{8} | 905.6811, 887.6715, 869.6634, 774.5847, 548.4196, 435.3333 | Cyclo octaleucyl (or isoleucyl) | 35 |
| 51  | 15.33    | [M + H]^+ | 1017.75658       | 1018.76517    | 1.3         | C_{54}H_{99}N_{9}O_{9} | 1018.7684, 1000.7590, 887.6637 | Cyclo nonaleucyl (or isoleucyl) | 35 |
| 15  | 4.70     | [M-H]^-  | 376.13695        | 375.12984     | 0.5         | C_{16}H_{24}O_{10} | 375.1307, 213.0777, 169.0879, 151.0776, 113.0265 | Mussaenosid acid | 18 |
| 20  | 5.79     | [M-H]^-  | 390.11621        | 389.10865     | -0.7        | C_{16}H_{22}O_{11} | 389.1098, 345.1181, 209.0459, 183.0691, 165.0554, 139.0781, 121.0672, 95.0526, 69.0405 | Oleoside | 41 |
| 60  | 18.59    | [M-H]^-  | 822.40379        | 821.39586     | -0.8        | C_{42}H_{62}O_{16} | 821.3970, 351.0564, 310.1458, 289.1346, 248.1234, 217.1122, 186.1010, 155.0901, 124.0804 | Glycyrrhizin | 42 |
| 1   | 0.90     | [M-H]^-  | 342.11621        | 341.10951     | 1.7         | C_{12}H_{22}O_{11} | 179.0573, 161.0463, 119.0376, 113.0272, 89.0287, 71.0195, 59.0207 | Sucrose | 43 |
| 70  | 24.37    | [M + H]^+ | 278.15181        | 279.1589      | -0.7        | C_{16}H_{24}O_{4} | 149.0233, 121.0287, 56.0190, 38.0093, 20.0000 | Dibutyl phthalate | 44 |

*aBase peak. RT: retention time; 3-p-COQA: 3-O-trans-coumaroylquinic acid; 4-PCO-5-CQA: 4-O-feruloyl-5-coumaroylquinic acid.

used to further confirm the chemical structure. Furthermore, the fragmentation pathways of some representative compounds were proposed in order to facilitate structural identification. Among them, compounds 7, 10, 11, 13-32, 34-39, 41, 43-46, 48, 50-59, 61-65, 67-69, and 71-77 were reported for the first time in the Araliaceae family. Moreover, this is the first report on compounds 1-3, 5, 6, 9, 12, 40, 42, 47, 49, 60, 66, and 78 from the genus *Dendropanax* and compounds 4, 8, 33, and 70 from *Dendropanax dentiger* [12, 13].

3.1.2. Alkaloids. In this study, a total of 15 alkaloids (Figure 3) in the roots of *D. dentiger* extract were identified, including 4 diterpenoid alkaloids (44, 48, 52, and 57), 4 isoquinoline alkaloids (23, 24, 37, and 49), 3 purine alkaloids (2, 4, and 5), 3 amino acid (3, 6, and 9), and 1 other alkaloid (7).
Compounds 44, 48, 52, and 57 were diterpenoid alkaloids, which were belonging to aconitum alkaloids. In tandem mass spectrum of aconitum alkaloids commonly observe the neutral losses of H_2O (18 Da), MeOH (32 Da), CO_2 (44 Da), and PhCOOH (122 Da). Take the case of the 52, it gave fragment ions at m/z 574.3045, 542.2772, 510.2458, and 105.0336 in the positive mode were corresponding to [M + H]^+, [M + H – CH_4]^+, and [M + H – 2CH_3OH]^+, respectively. Compared with literature data, compound 52 was identified as benzoylhyaconine, and the possible fragmentation mechanism was depicted in Figure S2.

Compounds 23, 24, 37, and 49 were isoquinoline alkaloids, which were widely distributed in medicinal plants and have high medicinal value. Compound 23 gave fragment ions at m/z 342.1718, 297.1133, 282.0899, and 265.0867 in the positive mode were corresponding to [M + H]^+, [M + H – C_2H_5N]^+, [M + H – C_2H_5N – CH_3]^+, and [M + H – C_2H_5N – CH_3OH]^+, respectively, of which ring B lost a C_2H_5N by a cleavage and formed a Cp-ring; then, the ring A lost a methoxy at C-6 and formed an epoxy between C-6 and C-7. The tandem mass pattern of this compound was similar with magnoflorine. Thus, it could be identified as magnoflorine. The ESI–MS spectra of compound 24 exhibited similar quasi-molecular ions peak [M + H]^+ at m/z 328.1557; their MS^2 generated fragments at m/z 178.0862 and m/z 151.0759 by splitting of RDA on C-ring. Hence, compound 24 was tentatively identified as stepholidine. The [M + H]^+ ion of compound 37 at m/z 278.1183 had a similar mass and fragmentation pathway to the dehydrooroemerine, according to the characteristic ions at m/z 263.0948 [M + H – CH_5]^+, m/z 220.1129 [M + H – CH_2O – CO]^+, and m/z 204.0813 [M + H – CH_2 – CH_2 – CH_2 – CH_2 – CO]^+. For compound 49, the positive mode MS^2 spectrum showed the parent ion at m/z 336.1233 [M + H]^+, and MS^3 spectrum showed the fragment ions at m/z 321.1012 [M + H – CH_5]^+, 320.0937 [M + H – CH_5]^+, 306.0774 [M + H – 2CH_5]^+, 292.0981 [M + H – CH_5 – CO]^+, and 278.0822 [M + H – 2CH_5 – CO]^+. Compared with literature data, compound 49 was identified as berberine, and the possible fragmentation mechanism was depicted in Figure S3.

Moreover, other 7 alkaloid compounds 2, 3, 4, 5, 6, 7, and 9 were identified as adenine, tyrosine, adenosine, guanosine, isoleucine, glutarylcarcinitine, and phenylalanine, respectively. To the best of our knowledge, alkaloid was reported from D. dentiger for the first time.

3.1.3. Flavonoids. The mass spectra fragmentation patterns were widely used to provide the structural characterization of flavonoids in relation to the flavonoid aglycone and flavonoids glycoside. Moreover, the identification of the flavonoid aglycone was based on fragmentations, which related to the lost small neutral molecules and radicals (CH_3, H_2O, CO, and CO_2), as well as the loss of a glucuronic acid (176 Da), hexose residue (162 Da), and apiose residue (132 Da) for flavonoids glycoside [14].

In this study, 5 flavonoids (39, 53, 56, 61, and 66) and 9 flavonoid glycosides (25, 29, 30, 32, 33, 34, 35, 45, and 47) in the roots of D. dentiger extract were identified based on the molecular weight and fragmentation information (Figure 4). Compounds 39, 53, 56, 61, and 66 were belonging to flavonoids, which considered as 5,7,2'-trihydroxy-6-methoxyflavone, luteolin, diosmetin, nobiletin, and apigenin, respectively. The MS^2 spectrum of 66 shown in Figure S4 was a representative example, which showed a [M – H]^- ion at m/z 269.0467, in accordance with the elemental composition of C_{15}H_{16}O_{5}.

Compounds 25, 29, 30, 32, 33, 34, 35, 45, and 47 were flavonoid glycosides, which considered as apigenin-6,8-di-C-glucoside, schaftoside, isoorientin, vitexin, rutin, myricitrin, luteolin-7-O-xilosyl-glucoside, tricin 5-glucoside, and baicalin, respectively. Compound 29 was C-glycosides, which the disaccharide substitution continuously loses 60, 90, and 120 Da fragment ions. Compound 29 showed a [M – H]^+ ion at m/z 563.1414, C-6 substituted hexose broke up in 0.4X0, 0.3X1 and 0.2X1 to get 503.1196, 473.1092, and 443.0980 fragment ions, respectively, after that C-8 site pentose frustrated at 0.3X1 and 0.2X1 to get 383.0781 and 353.0676, because
Figure 2: Chemical structures of phenylpropanoids from *D. dentiger* roots.

Figure 3: Chemical structures of alkaloids from *D. dentiger* roots.
the C-6 substituent glycosyl groups were superior to the C-8 replacement fracture. According to the characteristics of the fragment ions, compound 29 was easily confirmed as schafotoside. However, compound 33 was O-glycosides, which typically lost the entire sugar neutral molecule with significant loss of 132, 146, 162, and 192 Da fragments. Compound 33 [M−H]−609.1490 was rutin, which could be detected aglycone ion [Y0]−301.0363 and radical aglycone ion [Y0−H]−300.0284 after losing carbohydrate continuously in the negative ion mode, and the possible fragmentation mechanism was depicted in Figure S5.

3.1.4. Fatty Acids. In our study, a total of 14 fatty acids (peaks 16, 58-59, 62, 65, 67-69, 71, 72, 74, 75, 77, and 78) were identified based on the reference mass spectra and databases.

3.1.5. Phenols. A total of 7 phenols were identified in this study. Compounds 8, 10, 11, 12, 13, 14, and 28 were considered as gallic acid, 3-carboxy-4-hydroxy-phenoxy glucoside, vanillic acid hexose, syringic acid, methoxypolygoacetophenoside, piscidic acid, and syringaldehyde, respectively.

Take compound 11 as an example, its fragment ions at m/z 167.0359, 152.0128, 123.0474, and 108.0251 were identified as vanillic acid hexose. The ion at m/z 167.0359 was obtained by the loss of hexose, while the ion at m/z 123.0474 was produced by continuous loss of CO2. Meanwhile, the ion at m/z 152.0128 was obtained by the loss of CH3 from the precursor ion at m/z 167.0359, while the ion at m/z 108.0251 was produced by continuous loss of CO2. Based on the above fragment ions, which was obtained in the MS2 spectrum, the structure of compound 11 was easily confirmed as vanillic acid hexose.

3.1.6. Steroids. Four steroids (peaks 63, 64, 73, and 76) were identified in this study. Peaks 63 and 64 generated [M+HCOO]− ions at m/z 783.41695 and 1095.52283 in negative mode were unequivocally determined to be 25(27)-ene-timosaponin AIII and F-gitonin by comparison with the reference data. Peak 73 produced [M−H]− ions at

![Chemical structures of flavonoids from D. dentiger roots.](image-url)
m/z 339.2323 in ESI− mode. By comparing the quasi-molecular ions and fragmentations with MassBank and reference mass spectra data, peak 73 was tentatively identified as dimethisterone. Compound 76 had [M+H]+ ion at m/z 413.3789, and its fragments were at m/z 395.3701 [M+H–H2O]+, 255.2108 [M+H–C10H20–H2O]+, 213.1639 [M+H–C10H20H2O–C6H5]+, 173.1328 [M+H–C10H20–H2O–2C3H4]+, and 159.1170 [M+H–C10H20H2O–2C3H4–CH2]+, and was identified as α-spinasterol.

3.1.7. Cyclic Peptides. A total of 4 cyclic peptides (peaks 41, 43, 46, and 51) were identified in this study, and the compounds 41, 43, 46, and 51 showed [M+H]+ ion at m/z 679.51224, 792.59618, 905.68109, and 1018.76517, respectively. They have similar fragmentation pathways [14]. This is the first time to report the cyclic peptide from D. dentiger.

3.1.8. Terpenoids. In current work, 3 terpenoids (peaks 15, 20, and 60) were identified in negative ion mode.

Compound 15 had [M–H]− ion at m/z 375.1307, and its fragments were at m/z 213.0777 [M–H–Glc]−, 169.0879 [M–H–Glc–CO2]−, and 151.0776 [M–H–Glc–CO2–H2O]−. Its fragmentation process was the same as the literature. Therefore, compound 15 was identified as mussaenosidic acid. Compound 20 exhibited a pseudomolecular ion at m/z 389.1098 [M–H]− and fragment ions at m/z 345.1181 [M–H–CO2]− corresponding to decarboxylation and m/z 165.0554 [M–H–CO2–C6H3O]− corresponding to the cleavage of enolic acid moiety. Meanwhile, fragment ion at m/z 69.0405 was corresponding to the propionic acid. Compound 20 was tentatively identified as oleoside. Compound 60 showed [M–H]− ion at m/z 821.3970 and the fragment ions at m/z 351.0564 were corresponding to [2GluA–H2O]−, which the fragmentation pathways were similar with glycyrrhizin.

3.1.9. Others. Compounds 1 and 70 were given [M + H]+ ions at m/z 341.10951 and 279.1589 and identified as sucrose and dibutyl phthalate, respectively, by comparing with literature.

3.2. COX-2 Inhibitory Assay. COX-2 is one of the most important proinflammatory enzyme of action for anti-inflammatory drugs, and celecoxib was a COX-2 selective inhibitor in clinical practice [2]. As observed in Table 2, the ethanol crude extract of D. dentiger roots showed significant COX-2 inhibitory effect with an IC50 value of 77.2 ± 4.2 μg/mL; however, there was an indicated remarkable difference (p < 0.01) in comparison with that of celecoxib with an IC50 value of 22.4 ± 1.4 ng/mL. To the best of our knowledge, this study was the first time to determine the COX-2 inhibitory activity for D. dentiger [12, 13].

3.3. Antioxidant Activity. The DPPH and ABTS free radical scavenging activity assays were mostly used to evaluate the antioxidant effect of natural antioxidants [2]. Hence, the antioxidant activity of the D. dentiger roots ethanol crude extract was evaluated using ABTS and DPPH assays, and the results are shown in Table 2. The ethanol crude extract of D. dentiger roots showed the outstanding antioxidant activity, with IC50 values of 255.8 ± 10.3 μg/mL for DPPH assay and 151.9 ± 6.5 μg/mL for ABTS assay; however, there were exhibited significant differences (p < 0.01) comparable to those of the positive control Vc with IC50 values of 6.0 ± 0.2 and 1.2 ± 0.1 μg/mL, respectively.

To date, only one paper was reported the antioxidant activity of D. dentiger, and its ethyl acetate and n-butanol fractions showed significant against DPPH free radical scavenging activity [45]. Moreover, 7 phenolic compounds were isolated from the extract of D. dentiger and showed moderate or significant against DPPH free radical scavenging activity, with IC50 values of 0.038-0.741 μM, comparable to that of Vc with an IC50 value of 0.059 μM [45]. Therefore, this observed antioxidant activity could be due to the greater presence of secondary bioactive metabolites belonging to the flavonoids or phenolics noticed in ethanol crude extract of D. dentiger roots.

4. Conclusions

To summarize our findings, this study revealed that the root of D. dentiger was rich in phenylpropanoids, alkaloids, and flavonoids by UHPLC-Q-TOF-MS/MS and showed significant anti-inflammatory and antioxidant activities. This is the first study to describe the phytochemical profiling and COX-2 inhibitory activity of this plant [12, 13]. This study can provide important chemical information for the application of D. dentiger as a new source of natural COX-2 inhibitors and antioxidants in health food and pharmaceutical industry.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that they have no conflict of interest.

Acknowledgments

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Supplementary Materials

Fig. S1: tandem mass spectra and its fragmentation of chlorogenic acid in negative ion mode. Figure S2: tandem mass spectra and its fragmentation of benzoylhypaconine in positive ion mode. Figure S3: tandem mass spectra and its fragmentation of berberine in positive ion mode. Figure S4: tandem mass spectra and its fragmentation of apigenin in positive ion mode. Figure S5: tandem mass spectra and its fragmentation of rutin in positive ion mode. (Supplementary Materials)

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