

OCCURRENCE, BIOLOGICAL ACTIVITIES AND <sup>13</sup>C NMR DATA OF AMIDES FROM *Piper* (Piperaceae)<sup>#</sup>

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This manuscript describes an update review with up to 285 references concerning the occurrence of amides from a variety of species of the genus *Piper* (Piperaceae). Besides addressing occurrence, this review also describes the biological activities attributed to extracts and pure compounds, a compiled <sup>13</sup>C NMR data set, the main correlations between structural and NMR spectroscopic data of these compounds, and employment of hyphenated techniques such as LC-MS, GC-MS and NMR for analysis of amides from biological samples and crude *Piper* extracts.

Keywords: *Piper*; <sup>13</sup>C NMR compilation; amides.

## INTRODUCTION

Piperaceae is one of the largest families among the basal Angiosperms, with approximately 3,000 species described to date.<sup>1</sup> The family is currently divided into five genera: *Macropiper*, *Zippelia*, *Piper*, *Peperomia* and *Manekia*,<sup>2</sup> consisting of a wide variety of species found commonly around the world. *Piper*, *Peperomia* and *Manekia* occur in Brazil, mainly in the Amazonian and Atlantic forests.<sup>3</sup> *Piper* is the largest genus of this family, including more than 1,000 species, and can also be considered the largest genus of the basal angiosperms.<sup>4</sup>

Amides are the major constituents of several species of *Piper*. Currently, they can be considered alkaloids in accordance with the modern definition by Pelletier.<sup>5</sup> Natural amides can be classified as open-chain alkamides, aristolactams, 4,5-dioxoaporphines, ceramides, amides with pyrrolidine, piperidone and piperidine groups, cyclobutanamides and cyclohexanamides. The term piperamide is restricted to describe all compounds carrying an aromatic group and an amide group.

In 1997, a review of this genus was published<sup>6</sup> dealing with chemical distribution and biological activities of amides. In the present review, an update with new chemical constituents of this genus is described and a compilation of <sup>13</sup>C NMR data and biological activities of these compounds are provided.

*Piper* SPECIES, TRADITIONAL USES AND BIOLOGICAL ACTIVITIES

Despite the large number of species of *Piper*, the use of these plants in folk medicine remains limited. One of the most well-known *Piper* Brazilian medicinal plants is *P. corcovadensis*, commonly found in North and Northeast regions, and popularly known as “João-brandinho”. The leaves of this plant are used for the treatment of rheumatism in the form of poultice and infusions as well for flu and cough. In the Southeast region, the roots and branches of this specie are chewed to relieve toothache due to its anesthetic action on the mucous membrane.<sup>7</sup>

In China, the use of leaves of *P. futokasura* is recommended in the treatment of cardiac arrhythmias and asthma. In Jamaica, stomach pains are treated with an infusion of leaves from *P. aduncum* and *P. hispidum*. Leaves from *P. amalago* are also employed in Mexico and Brazil for stomach pains and for the treatment of various infections.<sup>8</sup> Leaves and stems of *P. marginatum* and *P. tuberculatum* are used in Brazil, especially in Paraíba State (Brazil) against snake bite and as a sedative.<sup>9</sup>

The roots from *P. sarmentosum* are used in Thailand as a carminative and digestive. In Malaysia and Indonesia however, the leaves and roots of this plant are used for the treatment of toothache, foot dermatitis, cough and asthma.<sup>10</sup>

The genus *Piper* is also known to produce compounds with insecticidal activity.<sup>11</sup> In addition, several others activities are attributed to the species of this genus. The literature reports fungicidal,<sup>12</sup> antinociceptive,<sup>13</sup> anti-inflammatory,<sup>14</sup> enzymatic inhibition,<sup>15</sup> antiplatelet aggregation,<sup>16</sup> trypanocidal,<sup>17</sup> piscicidal,<sup>18</sup> anticancer,<sup>19</sup> antioxidant,<sup>20</sup> allelopathic,<sup>21</sup> antiphidic,<sup>22</sup> antimicrobial,<sup>23</sup> antiplasmodial (antimalarial),<sup>24</sup> antileishmanial,<sup>25</sup> anxiolytic/antidepressant,<sup>26</sup> antituberculosis,<sup>27</sup> antidiabetic,<sup>28</sup> adipogenesis,<sup>29</sup> nematocidal,<sup>30</sup> herbicidal,<sup>31</sup> hepatoprotective,<sup>32</sup> and antisecretory and anti-*Helicobacter pylori*<sup>33</sup> activities.

CHEMISTRY OF *Piper*

The variability of the chemical constituents of Piperaceae is considerable. Species of this genus produce different metabolic classes such as neolignans,<sup>34</sup> lignans,<sup>35</sup> lactones,<sup>36</sup> terpenes,<sup>37</sup> phenylalkanoids/benzenoids,<sup>38</sup> hydroquinones,<sup>39</sup> alkaloids/amides,<sup>40</sup> steroids,<sup>41</sup> chalcones/dihydrochalcones,<sup>42</sup> chromones,<sup>43</sup> fatty acids,<sup>44</sup> ceramides<sup>45</sup> and flavonoids.<sup>46</sup> Essential oils of *Piper* spp. are mainly composed of phenylpropanoids (e.g.: *trans*-anethole, elemicin, chavicol), monoterpene hydrocarbons (e.g.:  $\alpha$ -pinene, myrcene, limonene), sesquiterpene hydrocarbons, (e.g.:  $\alpha$ -caryophyllene, germacrene D, bicyclogermacrene) and oxygenated monoterpenes (e.g.: 1,8-cineole, linalool, terpinen-4-ol) and sesquiterpenes (spathulenol, *E*-nerolidol, caryophyllene oxide).<sup>47</sup>

Among the major classes of natural compounds, amides isolated from *Piper* present broad structural diversity (Figure 1). Aromatic or

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aliphatic open chain amides, aristolactams, ceramides, 4,5-dioxoaporphines, amides with pyrrol, pyrrolidine, piperidone and piperidine groups are biosynthesized from cinnamic acid derivatives and some aminoacids.<sup>48</sup> However, the compounds of the cyclobutanamide and cyclohexanamide types are probably formed from cycloaddition reactions.<sup>49</sup>

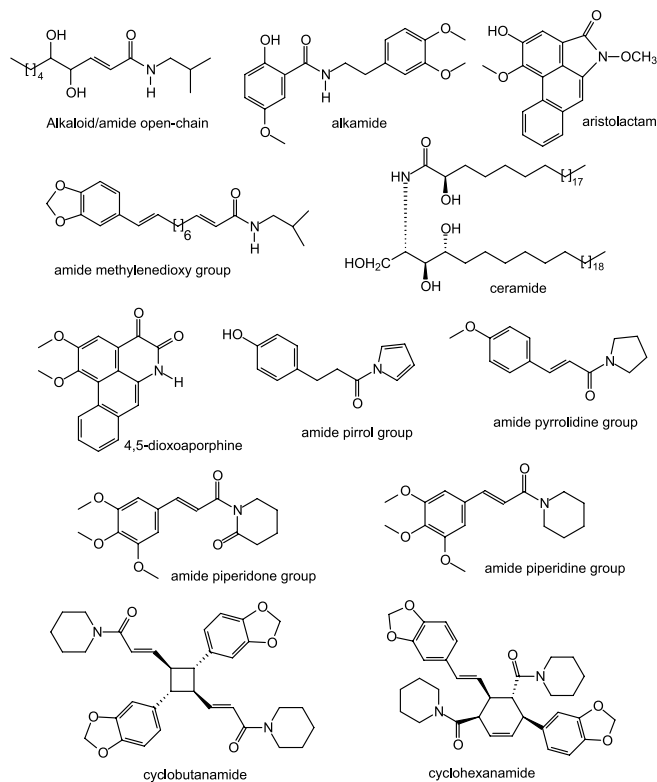


Figure 1. Structural diversity of amides

### Occurrence of amides in *Piper* spp.

Parmar *et al.*<sup>6</sup> previously published a review describing the occurrence of amides updated through to 1997. The cited review described the chemical composition of 90 species of *Piper*. The occurrence of 144 different amides present in 67 *Piper* species was also described (represented in Table 2 by the symbol &). In the present review, the results of a study of 158 species are described, corresponding to approximately 16% of the genus. Thus, since 1997, 68 new species have been investigated for their chemical (Table 1) and biological activities. These updated studies described the isolation of 133 new compounds in this genus, which corresponds to an increase of around 92% in the number of these metabolites found in the *Piper* genus, which presently numbers 277 amides (Table 2). Among these new compounds, the isolation of 22 cyclohexanamides,<sup>49</sup> two new ceramides<sup>45</sup> and 15 cyclobutanamides,<sup>50</sup> is noteworthy, all of which present unique skeletal complexes. Comparison of the compounds isolated in the last decade with those previously described by Parmar *et al.*<sup>6</sup> indicates increased structural diversity of piperamides, probably due to advances in instrumental techniques of isolation and chemical identification.

### Compilation of C-13 NMR data of amides from *Piper*

In Supplementary Material, a Table containing a  $^{13}\text{C}$  NMR data compilation of 182 amides isolated from the genus *Piper* can be found. Prior to the 1990's, there was scant  $^{13}\text{C}$  NMR data described

Table 1. New species of *Piper* studied since 1996

<i>Piper</i> species	Ref.	<i>Piper</i> species	Ref.
<i>P. abutiloides</i>	51	<i>P. hostmannianum</i>	52
<i>P. aequale</i>	53	<i>P. holtonii</i>	54
<i>P. amplum</i>	55	<i>P. imperiale</i>	56
<i>P. ananofolium</i>	57	<i>P. klotzschianum</i>	58
<i>P. aleyreanum</i>	59	<i>P. laetispicum</i>	60
<i>P. arieianum</i>	61	<i>P. lanceaefolium</i>	62
<i>P. augustum</i>	63	<i>P. lhotzkyanum</i>	64
<i>P. bavinum</i>	65	<i>P. longicaudatum</i>	66
<i>P. betel</i>	67	<i>P. loretoanum</i>	68
<i>P. bogotense</i>	69	<i>P. magnibacum</i>	70
<i>P. caldense</i>	71	<i>P. malacophyllum</i>	72
<i>P. caninum</i>	73	<i>P. mollicomum</i>	74
<i>P. carniconnectivum</i>	75	<i>P. mollissimum</i>	76
<i>P. carpunya</i>	33, 77	<i>P. mullesua</i>	78
<i>P. cenocladum</i>	79	<i>P. multiplinervium</i>	80
<i>P. cernuum</i>	81	<i>P. obliquum</i>	82
<i>P. colubrinum</i>	83	<i>P. ossanum</i>	84
<i>P. coruscans</i>	85	<i>P. peltatum</i>	22
<i>P. cumanense</i>	24	<i>P. permucronatum</i>	86
<i>P. crassinervium</i>	39	<i>P. porphyrophyllum</i>	87
<i>P. cyrtopodon</i>	88	<i>P. pseudolindenii</i>	89
<i>P. darienense</i>	90	<i>P. regnellii</i>	91
<i>P. diospyrifolium</i>	92	<i>P. renitens</i>	93
<i>P. dumosum</i>	94	<i>P. reticulatum</i>	95
<i>P. elongatum</i>	96	<i>P. rusbyi</i>	97
<i>P. fimbriulatum</i>	98	<i>P. saltuum</i>	99
<i>P. friedrichsthalii</i>	100	<i>P. sanctifelicis</i>	101
<i>P. fulvescen</i>	102	<i>P. sanguineispicum</i>	73
<i>P. galeatum</i>	103	<i>P. sintenense</i>	104
<i>P. gibbilimbium</i>	105	<i>P. solmsianum</i>	106
<i>P. glandulosissimum</i>	107	<i>P. tricuspe</i>	108
<i>P. guanacastensis</i>	109	<i>P. ungaromense</i>	110
<i>P. heterophyllum</i>	111	<i>P. vicosanum</i>	112
<i>P. hoffmanseggianum</i>	113	<i>P. xylostoides</i>	114

for these compounds. Moreover, in the previously published data there were a considerable number of signals equivocally assigned. As an example of this observation, the C-2 signal of compound **70** suggests it must be reattributed given it seems to be changed with the C-5'. The same mistake may have occurred with C-6' and C-8' since heteronuclear bidimensional correlation techniques such as HMQC and HMBC were not employed for unequivocal attribution of these compounds.

The  $\beta$ -carbons of conjugated amides are deshielded in comparison to  $\alpha$ -carbon due to resonance effects such as those observed for **31**, **33**, **34**, **74** and **107** (Supplementary Material). This effect is also responsible for the acyl carbon resonances which are found to be shielded. The peak of the carbonyl group in piplartine (**60**) is unshielded ( $\delta$  169.2) compared with the acyl group ( $\delta$  175.5) of **61** ( $\Delta\delta$  6.3 ppm). The chemical shift in the acyl groups of amides ranges from  $\delta$  156.5 to 175.6 ppm. These values are dependent on the present substituents bearing C-2'. For example, the chemical shifts in the acyl groups of **1** and **7** are  $\delta$  169.6 and the resonances of the same carbon in **2** and **3** are approximately  $\delta$  165.0. This protective effect is due to the methoxyl group which donates electrons more than hydroxyl groups. Therefore, these values may be indicative of the location of these groups at C-2' of amides.

The  $\delta$   $^{13}\text{C}$  assignments reported for the carbon atoms C-1''/C-4'',

**Table 2.** Amides from the genus *Piper*: Structure, occurrence and biological activity

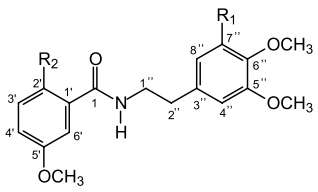
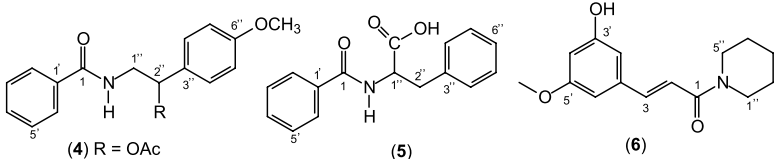
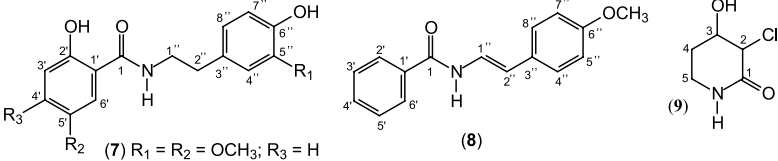
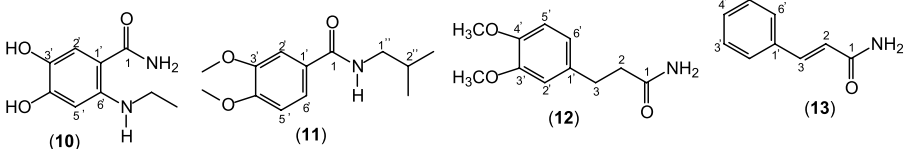
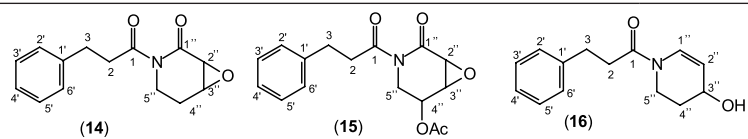
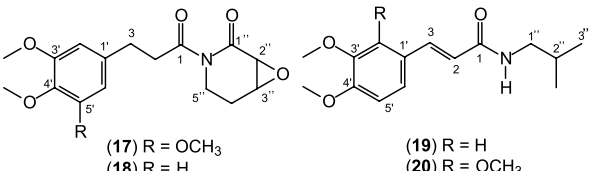
N <sup>o</sup>	Compounds	Species	Biological activity	Ref.
	 <p>(1) R<sub>1</sub> = H; R<sub>2</sub> = OH  (2) R<sub>1</sub> = H; R<sub>2</sub> = OCH<sub>3</sub>  (3) R<sub>1</sub> = R<sub>2</sub> = OCH<sub>3</sub></p>			
1	taiwanamide A			
2	taiwanamide B	<i>P. taiwanense</i>	anti-platelet aggregation	16
3	taiwanamide C			
	 <p>(4) R = OAc      (5)      (6)</p>			
4	tembamide acetate	<i>P. guayranum</i>	-	115
5	<i>N</i> -benzoylphenylalanine	<i>P. aurantiacum</i>	-	116
6	1-(3'-Hydroxy-5'-methoxycinnamoyl)-piperidine	<i>P. galeatum</i>	antiinflammatory	117
	 <p>(7) R<sub>1</sub> = R<sub>2</sub> = OCH<sub>3</sub>; R<sub>3</sub> = H      (8)      (9)</p>			
7	aduncamide	<i>P. aduncum</i>	-	118
8	alatomide	<i>P. guayranum</i>	-	115
9	2-chloro-3-hidroxy-1-piperidone	<i>P. hancei</i>	-	119
	 <p>(10)      (11)      (12)      (13)</p>			
10	3',4'-dihydroxy-6'-( <i>N</i> -ethylamine)benzamide	<i>P. nigrum</i>	antioxidant	120
11	<i>N</i> -isobutyl(3',4'-dimethoxy)benzamide	<i>P. amalago</i>	-	121
12	3-(3',4'-dimethoxyphenyl)-propanamide	<i>P. aboricola</i>	-	122
13	<i>trans</i> -cinnamamide	<i>P. taiwanense</i>	-	123
	 <p>(14)      (15)      (16)</p>			
14	kaosine	<i>P. capense</i>	antiplasmodial	124
15	2'' $\alpha$ ,3'' $\beta$ -epoxy-pipermethystine	<i>P. methysticum</i>	-	125
16	awaine			
	 <p>(17) R = OCH<sub>3</sub>  (18) R = H      (19) R = H  (20) R = OCH<sub>3</sub></p>			
17	2'',3''-epoxy-2,3-dihydropiartine	<i>P. verrucosum</i>	-	126
18	piplaroxide	<i>P. tuberculatum</i>	insecticide	127
19	<i>N-trans</i> -(3',4'-dimethoxycinnamoyl)isobutylamine	<i>P. amalago</i>	-	121
20	<i>N-trans</i> -(2',3',4'-trimethoxycinnamoyl)isobutylamine			

Table 2. continuation

N <sup>o</sup>	Compounds	Species	Biological activity	Ref.
	<p>(21) R = R<sub>1</sub> = R<sub>2</sub> = OCH<sub>3</sub>  (22) R = R<sub>1</sub> = R<sub>2</sub> = H  (23) R = H  (24) R = OCH<sub>3</sub>  (25)</p>			
21	<i>N</i> -(3',4',5'-trimethoxydihydroxycinnamoyl) 2''-pyrrolidin-1''-one	<i>P. demeraranum</i>	-	128
22	sarmentamide A	<i>P. sarmentosum</i>	-	10
23	piperlotine F			
24	piperlotine G	<i>P. lolot</i>	-	121
25	piperlotine H			
	<p>(26)  (27) R<sub>1</sub> = R<sub>2</sub> = OCH<sub>3</sub>  (28) R<sub>1</sub> = OH; R<sub>2</sub> = H  (29) R<sub>1</sub> = R<sub>2</sub> = H</p>			
26	<i>N</i> - <i>trans</i> -cinnamoylpyrrole	<i>P. argyrophyllum</i>	-	129
27	<i>N</i> -[3-(3',4'-dimethoxyphenyl)propaneyl]pyrrole	<i>P. brachystachyum</i>	-	130
28	piperlotine E	<i>P. lolot</i>	anti-platelet aggregation	131
29	<i>N</i> -(3-phenylpropanoyl)pyrrole	<i>P. sarmentosum</i>	-	132
	<p>(30)  (31)</p>			
30	<i>N</i> -(2 <i>Z</i> )-[3-(2'-ethoxy-4',5'-methylenedioxyphenyl)prop-2-enoyl]pyrrolidine	<i>P. tuberculatum</i>	Antifungal	133
31	<i>N</i> - <i>trans</i> -cinnamoyl-1''-methoxypyrrrolidine	<i>P. lolot</i>	-	131
	<p>(32) R=R<sub>1</sub>=R<sub>2</sub>=H; R<sub>3</sub>=OCH<sub>3</sub>  (33) R<sub>1</sub>=R<sub>2</sub>=R<sub>3</sub>=H; R=OCH<sub>3</sub>  (34) R=R<sub>2</sub>=R<sub>3</sub>=H; R<sub>1</sub>=OCH<sub>3</sub>  (35) R=R<sub>2</sub>=R<sub>3</sub>=H; R<sub>1</sub>=OCH<sub>3</sub>  (36) R=R<sub>1</sub>=R<sub>2</sub>=R<sub>3</sub>=H  (37) R=R<sub>1</sub>=R<sub>2</sub>=R<sub>3</sub>=H  (38) R=R<sub>1</sub>=R<sub>2</sub>=OCH<sub>3</sub>; R<sub>3</sub>=H  (39) R=R<sub>1</sub>=R<sub>2</sub>=OCH<sub>3</sub>; R<sub>3</sub>=H  (40) R<sub>1</sub>=R<sub>2</sub>=R<sub>3</sub>=OCH<sub>3</sub>; R=H  (41) R<sub>1</sub>=R<sub>3</sub>=H; R=R<sub>2</sub>=OCH<sub>3</sub>  (42) R=H; R<sub>1</sub> + R<sub>2</sub>=OCH<sub>2</sub>O; R<sub>3</sub>=OCH<sub>3</sub>  (43) R=H; R<sub>1</sub> + R<sub>2</sub>=OCH<sub>2</sub>O; R<sub>3</sub>=OCH<sub>3</sub>  (44) R + R<sub>1</sub>=OCH<sub>2</sub>O; R<sub>2</sub>=OCH<sub>3</sub>; R<sub>3</sub>=H  (45) R=R<sub>3</sub>=H; R<sub>1</sub> + R<sub>2</sub>=OCH<sub>2</sub>O  (46) R=R<sub>3</sub>=OCH<sub>3</sub>; R<sub>1</sub> + R<sub>2</sub>=OCH<sub>2</sub>O</p>			
32	<i>N</i> - <i>trans</i> -( <i>o</i> -methoxycinnamoyl)pyrrolidine	<i>P. methysticum</i>	-	134
33	<i>N</i> - <i>trans</i> -( <i>m</i> -methoxycinnamoyl)pyrrolidine	<i>P. methysticum</i> , <i>P. taiwanense</i> and <i>P. philippinum</i>	anti-platelet aggregation	16,135,136
34	<i>N</i> - <i>trans</i> -( <i>p</i> -methoxycinnamoyl)pyrrolidine / piperlotine A		anti-platelet aggregation	
35	<i>N</i> -(2 <i>Z</i> )-[3-(4'-methoxyphenyl)propa-2-enoyl]pyrrolidine	<i>P. lolot</i>	-	131
36	<i>N</i> - <i>trans</i> -cinnamoylpyrrolidine	<i>P. taiwanense</i> , <i>P. marginatum</i> , <i>P. argyrophyllum</i> , <i>P. shimidtii</i> , <i>P. wightii</i> and <i>P. lolot</i>	anti-platelet aggregation	16, 131, 136-139
37	<i>N</i> - <i>cis</i> -cinnamoylpyrrolidine	<i>P. lolot</i>	-	131
38	<i>N</i> -(2 <i>E</i> )-[3-(3',4',5'-trimethoxyphenyl)prop-2-enoyl]pyrrolidine	<i>P. sarmentosum</i> , <i>P. amalago</i> and <i>P. lolot</i>	anti-platelet aggregation	27, 121, 131
39	<i>N</i> -(2 <i>Z</i> )-[3-(3',4',5'-trimethoxyphenyl)prop-2-enoyl]pyrrolidine	<i>P. lolot</i>	anti-platelet aggregation	131
40	<i>N</i> - <i>trans</i> -2',4',5'-trimethoxycinnamoylpyrrolidine	<i>P. sarmentosum</i>		10
41	<i>N</i> - <i>trans</i> -(3',5'-dimethoxycinnamoyl)pyrrolidine	<i>P. amalago</i> , <i>P. philippinum</i> and <i>P. taiwanense</i>	-	121, 123, 135
42	<i>N</i> - <i>trans</i> -(2'-methoxy-4',5'-methylenedioxcinnamoyl)pyrrolidine	<i>P. amalago</i> and <i>P. peepuloides</i>		140, 141
43	<i>N</i> - <i>cis</i> -(2'-methoxy-4',5'-methylenedioxcinnamoyl)pyrrolidine	<i>P. peepuloides</i> and <i>P. hispidum</i>	antifungal	133, 141, 142
44	<i>N</i> - <i>trans</i> -(5'-methoxy-3',4'-methylenedioxcinnamoyl)pyrrolidine	<i>P. amalago</i>	-	121
45	<i>N</i> - <i>trans</i> -(3',4'-methylenedioxcinnamoyl)pyrrolidine	<i>P. peepuloides</i>	-	141

Table 2. continuation

N <sup>o</sup>	Compounds	Species	Biological activity	Ref.
47	sarmentamide B	<i>P. sarmentosum</i>	-	10
48	piperlotine J			
49	piperlotine K	<i>P. lolot</i>	-	131
50	piperlotine L			
51	<i>N-trans</i> -(3',4'-methylenedioxcinnamoyl)isobutylamine	<i>P. arboreum</i> , <i>P. amalago</i> and <i>P. nigrum</i>	antifungal	121, 143- 145
52	<i>N-trans</i> -(3',4'-methylenedioxy-5'-methoxycinnamoyl)isobutylamine			
53	<i>N-trans</i> -(3',4'-methylenedioxcinnamoyl)isopentylamine	<i>P. amalago</i>	-	121
54	<i>N-trans</i> -(3',4'-methylenedioxcinnamoyl)n-pentylamine			
55	<i>N-trans</i> -(3',4'-methylenedioxcinnamoyl)piperidine	<i>P. novae hollandiae</i> and <i>P. nigrum</i>	enzymatic	143, 146-148
56	<i>N-cis</i> -(2'-methoxy-4',5'-methylenedioxcinnamoyl)piperidine	<i>P. peepuloides</i> and <i>P. capense</i>		123, 149
57	<i>N-trans</i> -(2'-methoxy-4',5'-methylenedioxcinnamoyl)piperidine	<i>P. amalago</i> and <i>P. peepuloides</i>		140, 150
58	<i>N</i> -(2 <i>E</i> )-[3-(3',4',5'-trimethoxyphenyl)prop-2-enoyl]piperidine	<i>P. puberullum</i>	antiplasmodial	151
59	<i>N</i> -(2 <i>Z</i> )-[3-(3',4'-methylenedioxy-5'-methoxyphenyl)prop-2-enoyl]piperidine	<i>P. nigrum</i>		145
60	<i>N-trans</i> -(3',4',5'-trimethoxycinnamoyl) $\Delta^{2''}$ -pyridin-1''-one / pipartine	<i>P. arboreum</i> , <i>P. alatabaccum</i> , <i>P. tuberculatum</i> , <i>P. callosum</i> , <i>P. longum</i> , <i>P. retrofractum</i> , <i>P. sylvaticum</i> , <i>P. chaba</i> and <i>P. aborescens</i>	antifungal, cytotoxic, anxiolytic/antidepressant, potential mutagenic, anticancerous, antileishmanial and schistosomicidal	25, 26, 58, 118, 133, 145, 152-159
61	2,3-dihydropipltartine	<i>P. arboreum</i> , <i>P. puberullum</i> , <i>P. alatabaccum</i> , <i>P. rugosum</i> , <i>P. tuberculatum</i> and <i>bartlingianum</i>	antifungal	133, 145, 151, 152, 160-162
62	4'-desmethylpipltartine	<i>P. cenocladum</i>	-	79
63	<i>N-cis</i> -(3',4',5'-trimethoxycinnamoyl) $\Delta^{2''}$ -pyridin-1''-one	<i>P. arboreum</i> and <i>tuberculatum</i>	antifungal	118, 128
64	demethoxypipltartine	<i>P. aborescens</i> and <i>P. tuberculatum</i>	insecticide	127, 158, 163
65	<i>N-trans</i> -(4',5'-methylenedioxy-3'-methoxycinnamoyl) $\Delta^{2''}$ -pyridin-1''-one			
66	<i>N-trans</i> -(4',5'-methylenedioxy-3'-methoxydihydrocinnamoyl) $\Delta^{2''}$ -pyridin-1''-one	<i>P. aborescens</i>	cytotoxic	157, 163
67	cenocladamide	<i>P. cenocladum</i>	-	79

Table 2. continuation

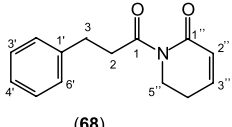
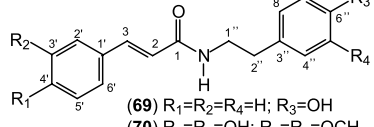
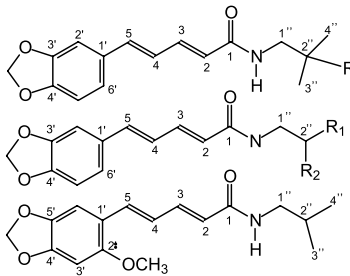
N <sup>o</sup>	Compounds	Species	Biological activity	Ref.
	 (68)			
	 (69) R <sub>1</sub> =R <sub>2</sub> =R <sub>4</sub> =H; R <sub>3</sub> =OH (70) R <sub>1</sub> =R <sub>3</sub> =OH; R <sub>2</sub> =R <sub>4</sub> =OCH <sub>3</sub> (71) R <sub>1</sub> =R <sub>3</sub> =OH; R <sub>2</sub> =R <sub>4</sub> =H (72) R <sub>1</sub> =R <sub>3</sub> =OH; R <sub>2</sub> =OCH <sub>3</sub> ; R <sub>4</sub> =H (73) R <sub>1</sub> =R <sub>3</sub> =OH; R <sub>2</sub> =OCH <sub>3</sub> ; R <sub>4</sub> =H			
68	piperchabamide A	<i>P. chaba</i>	hepatoprotective	33, 164
69	<i>N-trans</i> -cinnamoyltiramine	<i>P. steerni</i> and <i>P. taiwanense</i>	enzymatic	123, 165, 166
70	<i>N-trans</i> -feruloyl-3-O-methyldopamine			
71	<i>N-trans</i> -p-coumaroyltiramine	<i>P. philippinum</i>	-	135, 167
	<i>P. umbellatum</i> , <i>P. argyrophyllum</i> , <i>P. kadsura</i> and <i>P. sanctum</i>	antioxidant, anti-inflammatory, anti-cancerous, enzymatic and antimicrobial		14, 15, 135, 166, 168, 169
72	<i>N-trans</i> -feruloyltiramine	<i>P. argyrophyllum</i> , <i>P. nigrum</i> and <i>P. sanctum</i>	anti-cancerous, melanin biosynthesis inhibition and enzymatic	19, 137, 170-173
73	<i>N-cis</i> -feruloyltiramine	<i>P. argyrophyllum</i>	-	137, 174
	 (74) R=H (79) R=OAc (75) R=OAc (80) R=H (76) R=H (81) R=OAc (77) R=OAc (82) R=H (78) R=H (83) R=H (84) R <sub>2</sub> =CH <sub>3</sub> ; R <sub>1</sub> =-CH <sub>2</sub> CH <sub>3</sub> (86) R <sub>2</sub> =H; R <sub>1</sub> =-CH(CH <sub>3</sub> ) <sub>2</sub> (85)			
74	(2 <i>E</i> ,4 <i>Z</i> ) - scutifoliamide A			
75	(2 <i>E</i> ,4 <i>Z</i> ) - scutifoliamide B	<i>P. scutifolium</i>		
76	(2 <i>Z</i> ,4 <i>E</i> ) -hoffmannseggiamide A		antifungal	114
77	(2 <i>Z</i> ,4 <i>E</i> ) - hoffmannseggiamide B	<i>P. hoffmannseggianum</i>		
78	(2 <i>E</i> ,4 <i>E</i> )- <i>N</i> -isobutyl-5-(3',4'-methylenedioxyphenyl)-penta-2,4-dienamide / piperlonguminine	<i>P. scutifolium</i> , <i>P. ovatum</i> , <i>P. longum</i> , <i>P. acutislegium</i> , <i>P. amalago</i> , <i>P. attenuatum</i> , <i>P. betle</i> , <i>P. chaba</i> , <i>P. guineense</i> , <i>P. hancei</i> , <i>P. klasiana</i> , <i>P. nepalense</i> , <i>P. novae hollandiae</i> , <i>P. pedicelloseum</i> , <i>P. sylvaticum</i> , <i>P. corcovadensis</i> and <i>martiana</i>	antifungal, anti-inflammatory, hepatoprotective and gastroprotective	6, 21, 32, 121, 114, 119, 130, 148, 164, 171-179
79	(2 <i>E</i> ,4 <i>E</i> ) - corcovadine	<i>P. scutifolium</i> , <i>P. corcovadensis</i>	antifungal	114, 179
80	(2 <i>Z</i> ,4 <i>Z</i> ) - isopiperlonguminine	<i>P. scutifolium</i> , <i>P. hoffmannseggianum</i> and <i>P. corcovadensis</i>	antifungal, allelopathic and antimicrobial	21, 114, 178
81	(2 <i>Z</i> ,4 <i>Z</i> )- <i>N</i> -2''-acetoxy-2''-methylpropyl-5-(3',4'-methylenedioxyphenyl)penta-2,4-dienamide		antifungal	114, 178
82	tetrahydropiperlonguminine	<i>P. klotzschianum</i>	-	57
83	(2 <i>E</i> )- <i>N</i> -isobutyl-5-(3',4'-methylenedioxyphenyl)penta-2-enamide /4,5-dihydropiperlonguminine	<i>P. guineense</i> , <i>P. tuberculatum</i> , <i>P. longum</i> and <i>P. chaba</i>	Antifungal and hepatoprotective	27, 133, 164, 180-182
84	piperchabamide E	<i>P. chaba</i>	hepatoprotective	32
85	(2 <i>E</i> ,4 <i>E</i> )- <i>N</i> -isobutyl-5-(4',5'-methylenedioxy-2'-methoxyphenyl)penta-2,4-dienamide / 2'-methoxypiperoylisobutylamine	<i>P. amalago</i>	-	121, 183
86	piperoylisopentylamine			

Table 2. continuation

N <sup>o</sup>	Compounds	Species	Biological activity	Ref.
87	(2 <i>E</i> ,4 <i>E</i> )- <i>N</i> -[5-(3',4'-methylenedioxyphenyl)penta-2,4-dienoyl]pyrrolidine / piperiline	<i>P. arboreum</i> , <i>P. amalago</i> , <i>P. guineense</i> , <i>P. macropodium</i> , <i>P. nigrum</i> and <i>P. trichostachyon</i>	antifungal and enzymatic	121, 145, 146, 175,184,185
88	(2 <i>E</i> )- <i>N</i> -[5-(3',4'-methylenedioxyphenyl)penta-2-enoyl]pyrrolidine	<i>P. arboreum</i> , <i>P. hispidum</i> , <i>P. chaba</i> and <i>P. nigrum</i>	antifungal	133, 142, 144, 145,186
89	(2 <i>Z</i> ,4 <i>E</i> )- <i>N</i> -[5-(3',4'-methylenedioxyphenyl)penta2,4-dienoyl]-pyrrolidine	<i>P. nigrum</i>	-	144
90	(2 <i>E</i> ,4 <i>Z</i> )- <i>N</i> -[5-(3',4'-methylenedioxyphenyl)penta-2,4-dienoyl]pyrrolidine	<i>P. arboreum</i>	antifungal	145
91	Wisanidine	<i>P. amalago</i> and <i>P. guineense</i>	-	187, 188
92	2( <i>E</i> )-[5-(4',5'-methylenedioxy-2-methoxyphenyl)penta-2-enoyl]pyrrolidine/ $\Delta^{\alpha\beta}$ -dihydrowisanidine	<i>P. guineense</i>	-	187
93	n=10, m=4; <i>N</i> -(2 <i>E</i> ,14 <i>E</i> )-eicosa-2,14-dienoylpiperidine	<i>P. retrofractum</i>	-	189
94	wisanine			121
95	$\Delta^{\alpha\beta}$ -dihydrowisanine	<i>P. guineense</i>	-	190
96	piperine	<i>P. nigrum</i> , <i>P. tuberculatum</i> , <i>P. longum</i> , <i>P. acutisleginum</i> , <i>P. album</i> , <i>P. betle</i> , <i>P. argyrophyllum</i> , <i>P. attenuatum</i> , <i>P. aurantiacum</i> , <i>P. chaba</i> , <i>P. guineense</i> , <i>P. hancei</i> , <i>P. khasiana</i> , <i>P. macropodium</i> , <i>P. nepalense</i> , <i>P. novaehollandiae</i> , <i>P. peepuloides</i> , <i>P. sylvaticum</i> and <i>cubeba</i>	antifungal, hepatoprotective, gastroprotective and enzymatic	6, 32, 119, 130, 133, 146, 150, 164, 172-175, 184, 191-200
97	tetrahydropiperine	<i>P. longum</i>	insecticidal	201
98	$\Delta^{\alpha\beta}$ -dihydropiperine/ piperanine	<i>P. arboreum</i> , <i>P. tuberculatum</i> , <i>P. guineense</i> and <i>P. chaba</i>	antifungal, hepatoprotective and gastroprotective	32, 133, 145, 168, 196
99	(2 <i>E</i> ,4 <i>E</i> )- <i>N</i> -[5-(4'-hydroxyphenyl)penta-2,4-dienoyl]piperidine	<i>P. nigrum</i>	Antifungal	133, 191
100	sylvatine	<i>P. aurantiacum</i> , <i>P. brachystachyum</i> , <i>P. chaba</i> , <i>P. guineense</i> , <i>P. longum</i> , <i>P. sylvaticum</i> and <i>P. retrofractum</i>	-	173, 180, 194, 201-204
101	(2 <i>E</i> ,4 <i>E</i> )- <i>N</i> -isobutyl-6-(4'-methoxyphenyl)hex-2,4-dienamide/ piperovatine	<i>P. scutifolium</i> , <i>P. ovatum</i> , <i>P. alatabaccum</i> , <i>P. piscatorum</i> , <i>P. callossum</i> ; <i>P. corcovadensis</i> , <i>P. vahlii</i> , <i>P. propinqua</i> and <i>P. martiana</i>	antifungal, allelopathic, antimicrobial and anti- inflammatory	7, 12, 21, 152, 171, 205-208

Table 2. continuation

N <sup>o</sup>	Compounds	Species	Biological activity	Ref.
102	(2 <i>E</i> ,4 <i>E</i> )- <i>N</i> -isobutyl-7-(3',4'-methylenedioxyphenyl)hept-2,4-dienamide	<i>P. corcovadensis</i> , <i>P. austrosinense</i> and <i>P. falconere</i>	-	7, 209, 210
103	(2 <i>Z</i> ,4 <i>Z</i> )- <i>N</i> -isobutyl-7-(3',4'-methylenedioxyphenyl)hept-2,4-dienamide	<i>P. hispidum</i>	antifungal	133
104	(2 <i>E</i> )- <i>N</i> -isobutyl-7-(3',4'-methylenedioxyphenyl)hept-2-enamide	<i>P. callosum</i>	-	208
105	futoamide	<i>P. futokadsura</i> and <i>P. hancei</i>	-	211, 212
106	(2 <i>E</i> ,4 <i>E</i> ,6 <i>E</i> )- <i>N</i> -[7-(3',4'-methylenedioxyphenyl)hept-2,4,6-trienoyl]piperidine	<i>P. sarmentosum</i> and <i>P. trichostachyon</i>	antituberculosis and antiplasmodial	27, 213
107	(2 <i>Z</i> ,4 <i>Z</i> )- <i>N</i> -[7-(3',4'-methylenedioxyphenyl)hept-2,4-dienoyl]piperidine	<i>P. hispidum</i>	antifungal	142
108	piperetine	<i>P. tuberculatum</i> , <i>P. aurantiacum</i> and <i>P. nigrum</i>	insecticidal	118, 194, 199, 215
109	(2 <i>E</i> ,4 <i>E</i> )- <i>N</i> -[7-(3',4'-methylenedioxyphenyl)hept-2,4-dienoyl]piperidine	<i>P. tuberculatum</i> and <i>P. sintense</i>	-	103, 197
110	(2 <i>E</i> )- <i>N</i> -[7-(3',4'-methylenedioxyphenyl)hept-2-enoyl]piperidine	<i>P. puberullum</i> and <i>P. tuberculatum</i>	-	148,162
111	n=4; (2 <i>E</i> ,8 <i>E</i> )- <i>N</i> -isobutyl-9-(3',4'-methylenedioxyphenyl)non-2,8-dienamide / retrofractamide C	<i>P. retrofractum</i>	hepatoprotective and adipogenesis	29, 32, 203, 215
112	n=4; (8 <i>E</i> )- <i>N</i> -isobutyl-9-(3',4'-methylenedioxyphenyl)non-8-enamide / dihydroretrofractamide C	<i>P. nigrum</i>	enzymatic (ACAT)	216
113	n=4; brachiamide B	<i>P. brachystachyum</i> , <i>P. nigrum</i> and <i>P. sarmentosum</i>	larvicidal, antituberculosis and antifungal	10, 27, 185, 217
114	n=2; sarmentosine	<i>P. sarmentosum</i> and <i>P. nigrum</i>	antituberculosis, larvicidal, antiplasmodial and antifungal	10, 27, 132, 185
115	n=14; (16 <i>E</i> )- <i>N</i> -[17-(3',4'-methylenedioxyphenyl)heptadec-16-enoyl]piperidine	<i>P. amalago</i>	-	121
116	n=12; (14 <i>E</i> )- <i>N</i> -[15-(3',4'-methylenedioxyphenyl)pentadec-14-enoyl]piperidine			
117	n=6; (8 <i>E</i> )- <i>N</i> -[9-(3',4'-methylenedioxyphenyl)non-8-enoyl]piperidine	<i>P. nigrum</i> , <i>P. trichostachyon</i> and <i>boehmeriaefolium</i>	larvicidal, enzymatic and anti- cancerous	24, 146, 171, 185
118	n=7; (9 <i>E</i> )- <i>N</i> -[10-(3',4'-methylenedioxyphenyl)dec-9-enoyl]piperidine		-	218
119	n=4; (6 <i>E</i> )- <i>N</i> -[7-(3',4'-methylenedioxyphenyl)hept-6-enoyl]piperidine	<i>P. nigrum</i>	larvicidal	185
120	n=3 – piperoleine A		enzymatic	146
121	n=5 – piperoleine B	<i>P. nigrum</i> and <i>P. chaba</i>	larvicidal, cell adhesion inhibition, hepatoprotective and enzymatic	32, 146, 164, 185, 219-221



Table 2. continuation

N <sup>o</sup>	Compounds	Species	Biological activity	Ref.
122	(2 <i>E</i> ,4 <i>Z</i> ,8 <i>E</i> )- <i>N</i> -[9-(3',4'-methylenedioxyphenyl)non-2,4,8-trienoyl]piperidine	<i>P. longum</i> and <i>P. nigrum</i>	cell adhesion inhibition and enzymatic	220, 222
123	(2 <i>E</i> ,4 <i>E</i> ,8 <i>E</i> )- <i>N</i> -[9-(3',4'-methylenedioxyphenyl)non-2,4,8-trienoyl]piperidine	<i>P. longum</i> , <i>P. chaba</i> and <i>P. nigrum</i>	cell adhesion inhibition, enzymatic and gastroprotective	166, 216, 220-222
124	n=1; (2 <i>E</i> ,8 <i>E</i> )- <i>N</i> -[9-(3',4'-methylenedioxyphenyl)non-2,8-dienoyl]piperidine	<i>P. longum</i> , <i>P. nigrum</i> , <i>P. retrofractum</i> and <i>P. chaba</i>	insecticidal, hepatoprotective, gastroprotective and enzymatic	32, 164, 182, 195, 201, 220-223
125	n=3; (2 <i>E</i> ,10 <i>E</i> )- <i>N</i> -[11-(3',4'-methylenedioxyphenyl)undec-2,10-dienoyl]piperidine	<i>P. chaba</i>	hepatoprotective	32, 164
126	n=2; retrofractamide A	<i>P. brachystachyum</i> , <i>P. longum</i> , <i>P. nigrum</i> , <i>P. retrofractum</i> and <i>P. ridleyi</i>	hepatoprotective, adipogenesis, enzymatic and larvicidal	29, 32, 130, 185, 215-217, 223, 224
127	n=3; retrofractamide D	<i>P. retrofractum</i>	-	205
128	n=4; phelipinamide	<i>P. philippinum</i>	-	137
129	n=4; retrofractamide B / piperide	<i>P. brachystachyum</i> , <i>P. guineense</i> , <i>P. longum</i> , <i>P. nigrum</i> and <i>P. chaba</i>	insecticidal, hepatoprotective, gastroprotective, adipogenesis and enzymatic	29, 32, 164, 182, 185, 216, 217, 223, 225, 226
130	n=6; guineensine	<i>P. brachystachyum</i> , <i>P. sarmentosum</i> , <i>P. guineense</i> , <i>P. longum</i> , <i>P. attenuatum</i> , <i>P. hancei</i> , <i>P. nigrum</i> , <i>P. officinarum</i> , <i>P. retrofractum</i> , <i>P. sylvaticum</i> and <i>P. chaba</i>	antituberculosis, insecticidal, hepatoprotective and gastroprotective	27, 32, 119, 156, 164, 174, 172, 195, 200, 215, 217, 223, 226, 227
131	n=8; brachistamide B	<i>P. brachystachyum</i> , <i>P. longum</i> , <i>P. sarmentosum</i> and <i>P. chaba</i>	hepatoprotective	27, 32, 174, 200, 228
132	n=9; brachistamide D	<i>P. brachystachyum</i>	-	203
133	n=2; pipercollosine	<i>P. callosum</i> and <i>P. interruptum</i>	-	209, 229
134	n=4; dihydropipericide	<i>P. nigrum</i>	-	174
135	n=8; brachistamide A	<i>P. brachystachyum</i>	-	228
136	n=9; brachistamide E			203
137	n=5; (2 <i>E</i> ,4 <i>E</i> ,11 <i>E</i> )- <i>N</i> -isobutyl-12-(3',4'-methylenedioxyphenyl)dodec-2,4,11-trienamide	<i>P. nigrum</i>	larvicidal	230
138	piperstachine	<i>P. trichostachyum</i>	-	231
139	(12 <i>E</i> ); ridleiamide	<i>P. ridleyi</i>	-	223
140	(13 <i>E</i> ); brachistamide C	<i>P. brachystachyum</i>	-	203
141	piperchabamide D	<i>P. nigrum</i> and <i>P. chaba</i>	cell adhesion inhibition, enzymatic and hepatoprotective	32, 164, 216, 221

Table 2. continuation

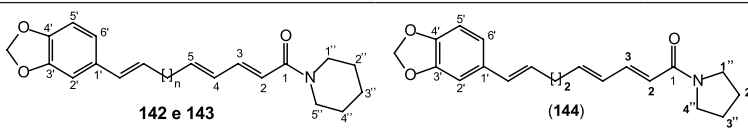
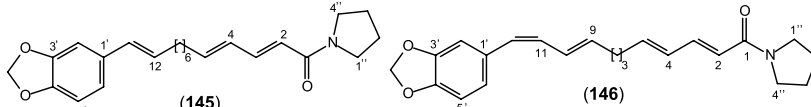
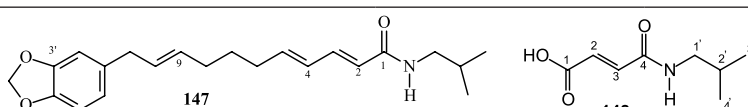
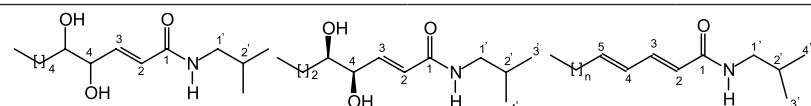
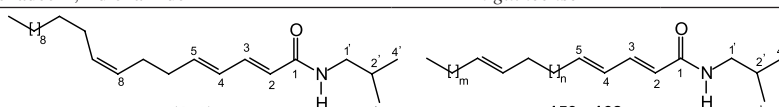
N <sup>o</sup>	Compounds	Species	Biological activity	Ref.
				
142	n=4; (2 <i>E</i> ,4 <i>E</i> ,10 <i>E</i> )- <i>N</i> -[11-(3',4'-methylenedioxyphenyl)undec-2,4,10-trienoyl]piperidine	<i>P. nigrum</i> and <i>P. chaba</i>	hepatoprotective	32, 182
143	n=6; (2 <i>E</i> ,4 <i>E</i> ,12 <i>E</i> )- <i>N</i> -[13-(3',4'-methylenedioxyphenyl)tridec-2,4,12-trienoyl]piperidine	<i>P. chaba</i>		32, 164
144	(2 <i>E</i> ,4 <i>E</i> ,8 <i>E</i> )- <i>N</i> -[9-(3',4'-methylenedioxyphenyl)-non-2,4,8-trienoyl]pyrrolidine	<i>P. nigrum</i> and <i>P. sarmentosum</i>	antimycobacterial and enzymatic	10, 146, 185
				
145	brachiamide A	<i>P. brachystachyum</i> and <i>P. nigrum</i>	enzymatic	146, 217
146	(2 <i>E</i> ,4 <i>E</i> ,9 <i>E</i> ,11 <i>Z</i> )- <i>N</i> -[12-(3',4'-methylenedioxyphenyl)dodec-2,4,9,11-tetraenoyl]pyrrolidine	<i>P. guineense</i>	-	224
				
147	laetispicine	<i>P. laetispicum</i>	antidepressant and antinociceptive	119
148	acid (2 <i>E</i> )- <i>N</i> -isobutyltylamine-4-oxo-but-2-en-1-oic	<i>P. hancei</i>	-	120
				
149	sylvamide	<i>P. sylvaticum</i>	-	232
150	(±)-threo-(2 <i>E</i> )- <i>N</i> -isobutyl-4,5-dihydroxy-oct-2-enamide	<i>P. nigrum</i>	-	145
151	n=2; (2 <i>E</i> ,4 <i>E</i> )- <i>N</i> -isobutyloct-2,4-dienamide	<i>P. marginatum</i> , <i>P. novaehollandiae</i> , <i>P. banksii</i> and <i>P. nigrum</i>	-	148, 233-235
152	n=4; (2 <i>E</i> ,4 <i>E</i> )- <i>N</i> -isobutyldec-2,4-dienamide / pelitorine	<i>P. tuberculatum</i> , <i>P. arboreum</i> , <i>P. sarmentosum</i> , <i>P. longum</i> , <i>P. pedicellosum</i> , <i>P. attenuatum</i> , <i>P. chaba</i> , <i>P. guineense</i> , <i>P. hancei</i> , <i>P. nepalense</i> , <i>P. nigrum</i> , <i>P. peepuloides</i> , <i>P. ribesoides</i> , <i>P. silvaticum</i> , <i>P. wallichii</i> and <i>retrofractum</i>	antifungal, antituberculosis, cell adhesion inhibition, insecticidal, anti-platelet aggregation and enzymatic	25, 27, 44, 130-132, 144, 172, 174, 186, 193, 216, 221, 223, 225, 226, 236-238
153	n=12; (2 <i>E</i> ,4 <i>Z</i> )- <i>N</i> -isobutyloctadec-2,4-dienamide / pipericine	<i>P. nigrum</i>	-	191
154	n=12; (2 <i>E</i> ,4 <i>E</i> )- <i>N</i> -isobutyloctadec-2,4-dienamide	<i>P. longum</i> , <i>P. argyrophyllum</i> , <i>P. guineense</i> and <i>chaba</i>	gastroprotective and hepatoprotective	32, 164, 182, 193, 239
155	n=6; (2 <i>E</i> ,4 <i>E</i> )- <i>N</i> -isobutyl-dodec-2,4-dienamide	<i>P. guineense</i> , <i>P. peepuloides</i> and <i>P. chaba</i>	hepatoprotective	32, 198, 225
156	n=14 (2 <i>E</i> ,4 <i>E</i> )- <i>N</i> -isobutyleicos-2,4-dienamide	<i>P. guineense</i> , <i>P. longum</i> , <i>P. macropodium</i> and <i>P. nigrum</i>	-	182, 196, 240
157	n=10 (2 <i>E</i> ,4 <i>E</i> )- <i>N</i> -isobutylexadec-2,4-dienamide	<i>P. guineense</i>	-	175
				
158	(2 <i>E</i> ,4 <i>E</i> ,8 <i>Z</i> )- <i>N</i> -isobutyleicos-2,4,8-trienamide	<i>P. longum</i> , <i>P. nigrum</i> and <i>P. officinarum</i>	-	182, 235, 241
159	n=5 m=4; (2 <i>E</i> ,4 <i>E</i> ,12 <i>E</i> )- <i>N</i> -isobutyloctadec-2,4,12-trienamide	<i>P. retrofractum</i>	-	189
160	n=7 m=4; (2 <i>E</i> ,4 <i>E</i> ,14 <i>E</i> )- <i>N</i> -isobutyleicos-2,4,14-trienamide	<i>P. retrofractum</i>	-	189
161	n=7 m=4; (2 <i>E</i> ,4 <i>E</i> ,14 <i>Z</i> )- <i>N</i> -isobutyleicos-2,4,14-trienamide	<i>P. retrofractum</i> and <i>P. chaba</i>	gastroprotective and hepatoprotective	32, 164, 191

Table 2. continuation

N <sup>o</sup>	Compounds	Species	Biological activity	Ref.
162	n=3 m=10 (2 <i>E</i> ,4 <i>E</i> ,10 <i>E</i> )- <i>N</i> -isobutyldocos-2,4,10-trienamide	<i>P. officinarum</i>	-	227
163	<i>N</i> -isobutyl-4-hexanoyl-4-hydroxypyrrolidin-1-one	<i>P. nigrum</i>	-	146
164	n=24; <i>N</i> -isobutylhexacosanamide	<i>P. longum</i>	-	217
165	n=16; (2 <i>E</i> )- <i>N</i> -eicos-2-enoylpyrrolidine			
166	n=14; (2 <i>E</i> )- <i>N</i> -octadec-2-enoylpyrrolidine			
167	n=12; (2 <i>E</i> )- <i>N</i> -hexadec-2-enoylpyrrolidine	<i>P. amalago</i>	-	121
168	(9 <i>E</i> )- <i>N</i> -octadec-9-enoylpyrrolidine			
169	n=m=7; (2 <i>E</i> ,11 <i>E</i> )- <i>N</i> -eicos-2,11-dienoylpyrrolidine			
170	n=8; (3 <i>E</i> ,6 <i>E</i> )- <i>N</i> -hexadec-3,6-dienoylpyrrolidine			
171	n=10; (3 <i>E</i> ,6 <i>E</i> )- <i>N</i> -octadec-3,6-dienoylpyrrolidine			
172	n=12; (3 <i>E</i> ,6 <i>E</i> )- <i>N</i> -eicos-3,6-dienoylpyrrolidine	<i>P. amalago</i>	-	121
173	n=14; <i>N</i> -hexadecanoylpyrrolidine			
174	n=16; <i>N</i> -octadecanoylpyrrolidine			
175	n=18; <i>N</i> -eicosanoylpyrrolidine			
176	(2 <i>E</i> ,9 <i>Z</i> )- <i>N</i> -nonadec-2,9-dienoylpyrrolidine / brachistine	<i>P. brachystachyum</i>	-	217
177	n=4; (2 <i>E</i> ,4 <i>E</i> )- <i>N</i> -dec-2,4-dienoylpyrrolidine / sarmentine	<i>P. sarmentosum</i> , <i>P. nigrum</i> and <i>P. lolot</i>	larvicidal, antituberculosis anti-platelet aggregation, herbicidal and antiplasmodial	10, 27, 131, 185
178	n=6; (2 <i>E</i> ,4 <i>E</i> )- <i>N</i> -dodec-2,4-dienoylpyrrolidine	<i>P. nigrum</i>	larvicidal	186
179	n=8; (2 <i>E</i> ,4 <i>E</i> )- <i>N</i> -tetradec-2,4-dienoylpyrrolidine	<i>P. amalago</i>	-	121
180	n=14; (2 <i>E</i> ,4 <i>E</i> )- <i>N</i> -eicos-2,4-dienoylpyrrolidine / trichonine	<i>P. trichostachyon</i>		242
181	(2 <i>E</i> ,4 <i>E</i> )- <i>N</i> -dec-2,4-dienoylpiperidine	<i>P. tuberculatum</i> and <i>P. chaba</i>	-	186, 236
182	(2 <i>E</i> ,4 <i>E</i> )- <i>N</i> -6-oxo-dec-2,4-dienoylpiperidine	<i>P. nigrum</i>	-	145
183	(±)-eritro-(2 <i>E</i> )- <i>N</i> -4,5-dihydroxy-dec-2-enoylpiperidine	<i>P. nigrum</i>	-	145
184	(±)-threo-(2 <i>E</i> )- <i>N</i> -4,5-dihydroxy-dec-2-enoylpiperidine			
185	n=12; (2 <i>E</i> ,4 <i>E</i> )- <i>N</i> -octadec-2,4-dienoylpiperidine	<i>P. retrofractum</i>	-	189
186	n=14; (2 <i>E</i> ,4 <i>E</i> )- <i>N</i> -eicos-2,4-dienoylpiperidine			
187	n=6, m=4; (2 <i>E</i> ,4 <i>E</i> ,12 <i>E</i> )- <i>N</i> -octadec-2,4,12-trienoylpiperidine			
188	n=10, m=2; (2 <i>E</i> ,4 <i>E</i> ,16 <i>Z</i> )- <i>N</i> -eicos-2,4,16-trienoylpiperidine	189, 195		
189	n=8, m=2; (2 <i>E</i> ,4 <i>E</i> ,14 <i>Z</i> )- <i>N</i> -octadec-2,4,12-trienoylpiperidine	<i>P. retrofractum</i> and <i>P. longum</i>	insecticidal and acaricidal	195, 223

Table 2. continuation

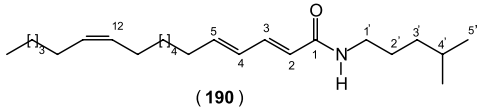
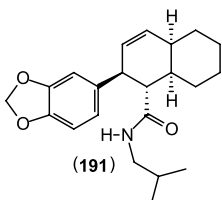
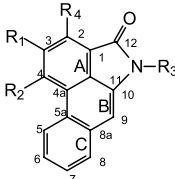
N <sup>o</sup>	Compounds	Species	Biological activity	Ref.	
					
					
190	n=5; pipinoohine	<i>P. nigrum</i>	larvicidal	191	
191	ciclopiperstachine	<i>P. trichostachyon</i>	-	243	
	<p>(192) R<sub>1</sub>=R<sub>2</sub>=R<sub>4</sub>=OCH<sub>3</sub>; R<sub>3</sub>=CH<sub>3</sub>            (193) R<sub>1</sub>=OH; R<sub>2</sub>=H; R<sub>3</sub>=CH<sub>3</sub>; R<sub>4</sub>=OCH<sub>3</sub>            (194) R<sub>1</sub>=R<sub>2</sub>=OCH<sub>3</sub>; R<sub>3</sub>=OH; R<sub>4</sub>=H            (195) R<sub>1</sub>=OCH<sub>3</sub>; R<sub>2</sub>=R<sub>3</sub>=OH; R<sub>4</sub>=H            (196) R<sub>1</sub>=R<sub>2</sub>=OH; R<sub>3</sub>=OCH<sub>3</sub>; R<sub>4</sub>=H            (197) R<sub>1</sub>+R<sub>2</sub>=-OCH<sub>2</sub>O-; R<sub>3</sub>=OCH<sub>3</sub>; R<sub>4</sub>=H            (198) R<sub>1</sub>+R<sub>2</sub>=-OCH<sub>2</sub>O-; R<sub>3</sub>=OH; R<sub>4</sub>=H            (199) R<sub>1</sub>=OH; R<sub>2</sub>=R<sub>3</sub>=OCH<sub>3</sub>; R<sub>4</sub>=H            (200) R<sub>1</sub>=R<sub>2</sub>=OCH<sub>3</sub>; R<sub>3</sub>=R<sub>4</sub>=H</p>		<p>(201) R<sub>1</sub>=R<sub>2</sub>=R<sub>4</sub>=OCH<sub>3</sub>; R<sub>3</sub>=H            (202) R<sub>1</sub>=OH; R<sub>2</sub>=OCH<sub>3</sub>; R<sub>3</sub>=R<sub>4</sub>=H            (203) R<sub>1</sub>=OCH<sub>3</sub>; R<sub>2</sub>=OH; R<sub>3</sub>=R<sub>4</sub>=H            (204) R<sub>1</sub>=R<sub>2</sub>=OCH<sub>3</sub>; R<sub>3</sub>=H; R<sub>4</sub>=OH            (205) R<sub>1</sub>=R<sub>4</sub>=OCH<sub>3</sub>; R<sub>2</sub>=OH; R<sub>3</sub>=H            (206) R<sub>1</sub>=R<sub>4</sub>=OCH<sub>3</sub>; R<sub>2</sub>=OH; R<sub>3</sub>=CH<sub>3</sub>            (207) R<sub>1</sub>=R<sub>4</sub>=OCH<sub>3</sub>; R<sub>2</sub>=OCOCH<sub>3</sub>; R<sub>3</sub>=COCH<sub>3</sub>            (208) R<sub>1</sub>=OCH<sub>3</sub>; R<sub>2</sub>=OH; R<sub>3</sub>=CH<sub>3</sub>; R<sub>4</sub>=H</p>		
192	2,3,4-trimethoxy- <i>N</i> -methylaristolactame	<i>P. crassinervium</i>	-	81	
193	3-hidroxy-2-metoxi- <i>N</i> -methylaristolactam				
194	piperumbellactam A		enzymatic inhibition		
195	piperumbellactam B		antioxidant		
196	piperumbellactam C	<i>P. umbellatum</i>		15	
197	piperumbellactam D		antifungal		
198	<i>N</i> -hidroxyaristolam II				
199	piperlactam S	<i>P. puberulum</i> and <i>P. kadsura</i>	Anti-inflammatory	14, 151	
200	cepharanone B	<i>P. tuberculatum</i> , <i>P. arginatum</i> , <i>P. attenuatum</i> , <i>P. longum</i> , <i>P. chiadoense</i> , <i>P. argyrophyllum</i> , <i>P. boehimerifolium</i> , <i>P. taiwanense</i> , <i>P. augustum</i> <i>P. wightii</i> and <i>P. sanctum</i>	anti-platelet aggregation and antimycobacterial	9, 63, 123, 137, 138, 168, 244-248	
201	piperolactam C	<i>P. scutifolium</i> , <i>P. argyrophyllum</i> , <i>P. boehimerifolium</i> , <i>P. longum</i> , <i>P. wightii</i> and <i>P. taiwanense</i>	antifungal and anti-platelet aggregation	12, 123, 137, 138, 245	
202	aristolactam A II	<i>P. attenuatum</i>	-	244	
203	piperolactam A	<i>P. argyrophyllum</i> , <i>P. marginatum</i> , <i>P. boehimerifolium</i> , <i>P. longum</i> , <i>P. atenuatum</i> , <i>P. hamiltonii</i> , <i>P. wightii</i> , <i>P. philippinum</i> , <i>taiwanense</i> and <i>P. sanctum</i>	anti-platelet aggregation and antimycobacterial	9, 123, 135, 137, 138, 169, 244, 245	
204	piperolactam B	<i>P. argyrophyllum</i> , <i>P. acutisleginum</i> , <i>P. boehimerifolium</i> and <i>P. longum</i>	-	137, 244, 245, 249	
205	piperolactam D	<i>P. argyrophyllum</i> , <i>P. acutisleginum</i> , <i>P. boehimerifolium</i> , <i>P. taiwanense</i> and <i>P. bogotense</i>	anti-platelet aggregation	69, 123, 137, 249, 250	
206	piperolactam E	<i>P. taiwanense</i>		123	
207	10-acetylamine-4-acetoxi-2,3-dimetoxifenantrene-lactam	<i>P. argyrophyllum</i>		137	
208	<i>N</i> -methylpiperolactam	<i>P. ribesoides</i> and <i>P. taiwanense</i>	-	137, 251	

Table 2. continuation

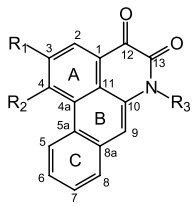
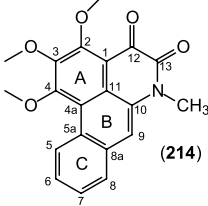
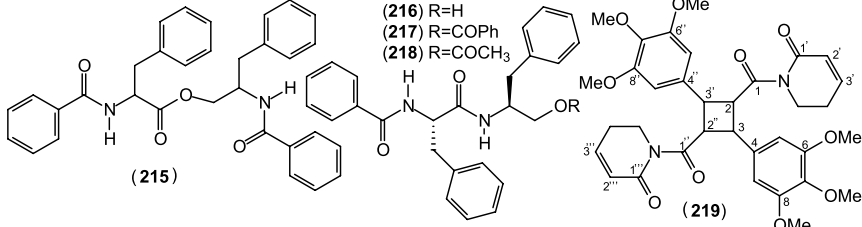
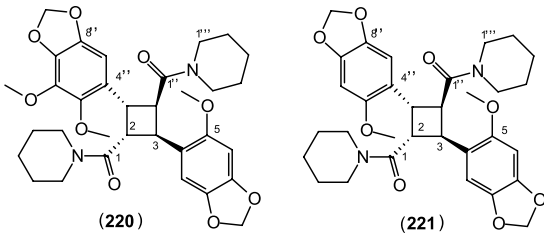
N <sup>o</sup>	Compounds	Species	Biological activity	Ref.
	 <p>(209) R<sub>1</sub>=R<sub>2</sub>=OCH<sub>3</sub>; R<sub>3</sub>=H  (210) R<sub>1</sub>=R<sub>2</sub>=OCH<sub>3</sub>; R<sub>3</sub>=CH<sub>3</sub>  (211) R<sub>1</sub>+R<sub>2</sub>=-OCH<sub>2</sub>O-; R<sub>3</sub>=CH<sub>3</sub>  (212) R<sub>1</sub>=OH; R<sub>2</sub>=OCH<sub>3</sub>; R<sub>3</sub>=H  (213) R<sub>1</sub>=OH; R<sub>2</sub>=OCH<sub>3</sub>; R<sub>3</sub>=CH<sub>3</sub></p>	 <p>(214)</p>		
209	norcepharadione B	<i>P. attenuatum</i> , <i>P. boehimerifolium</i> , <i>P. hamiltonii</i> and <i>P. longum</i>	anti-platelet aggregation	244, 245, 248, 252
210	cepharadione B	<i>P. aborescens</i> , <i>P. argyrophyllum</i> , <i>P. attenuatum</i> , <i>P. auritum</i> , <i>P. boehimerifolium</i> , <i>P. hamiltonii</i> , <i>P. longum</i> , <i>P. sanctum</i> , <i>P. wightii</i> and <i>P. sanctum</i>	-	137, 138, 168, 244, 252-255, 257
211	cepharadione A	<i>P. argyrophyllum</i> , <i>P. attenuatum</i> , <i>P. auritum</i> , <i>P. boehimerifolium</i> , <i>P. hamiltonii</i> , <i>P. longum</i> , <i>P. manauasense</i> , <i>P. methysticum</i> , <i>P. pedicellosum</i> , <i>P. sanctum</i> , <i>P. wighti</i> , <i>taiwanense</i> and <i>P. caninum</i>	cytotoxicity	123, 130, 137, 138, 201, 245, 251-256
212	noraristolodione	<i>P. attenuatum</i> , <i>P. boehimerifolium</i> , <i>P. longum</i> and <i>taiwanense</i>	anti-platelet aggregation	123, 243, 245, 248, 252
213	piperadione	<i>P. attenuatum</i> , <i>P. hamiltonii</i> and <i>P. longum</i> ,	-	244, 245
214	2,3,4-trimethoxy-12,13-dioxo-6a,7-dihydroaporphine	<i>P. aborescens</i>	-	157
	 <p>(215)</p> <p>(216) R=H  (217) R=COPh  (218) R=COCH<sub>3</sub></p> <p>(219)</p>			
215	auranamide	<i>P. aurantiacum</i>	-	257
216	aurantiamide			258
217	aurantiamide benzoate			259
218	aurantiamide acetate	<i>P. aurantiacum</i> and <i>P. sylvaticum</i>	-	115, 259
219	piplartine dimer A	<i>P. tuberculatum</i> , <i>P. retrofractum</i> , <i>P. sylvaticum</i> , <i>P. aborescens</i> and <i>P. rugosum</i>	cytotoxicity	153, 154, 156, 160, 163
	 <p>(220)</p> <p>(221)</p>			
220	cyclobutane-3-(7,8-methylenedioxy-5-methoxyphenyl)-3''-7'',8''-methylenedioxy-5'',6''-dimethoxyphenyl)-2,2''-dicarboxapiperidine	<i>P. peepuloides</i>	-	260
221	cyclobutane-3-(7,8-methylenedioxy-5-methoxyphenyl)-3''-(7'',8''-methylenedioxy-5''-methoxyphenyl)-2,2''-dicarboxapiperidine			

Table 2. continuation

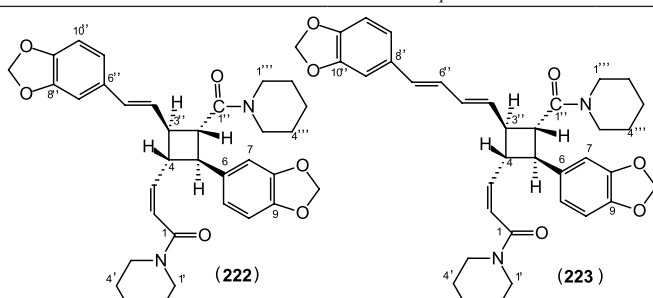
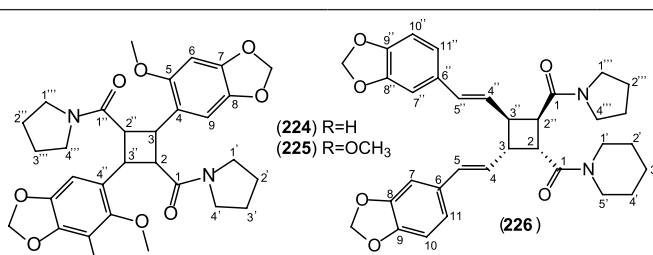
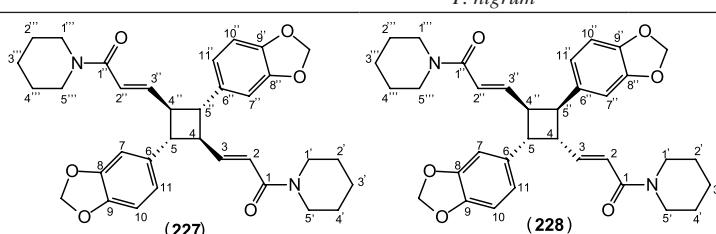
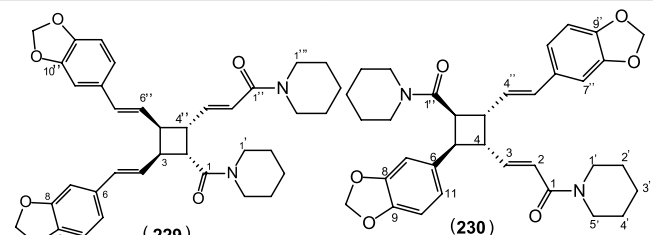
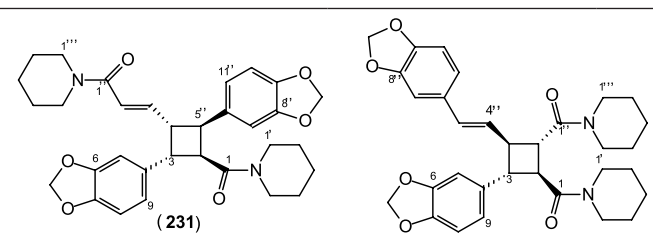
N <sup>o</sup>	Compounds	Species	Biological activity	Ref.
				
222	pipericyclutanamide A	<i>P. nigrum</i>	-	261
223	pipericyclutanamide B			
				
224	cyclobutane-3-(7,8-methylenedioxy-5-methoxyphenyl)-3''-(7'',8''-methylenedioxy-5''-methoxyphenyl)-2,2''-dicarboxypyrrolidine	<i>P. peepuloides</i>	-	262
225	cyclobutane-3-(7,8-methylenedioxy-5-methoxyphenyl)-3''-(7'',8''-methylenedioxy-5'',6''-dimethoxyphenyl)-2,2''-dicarboxypyrrolidine			
226	dipiperamide C	<i>P. nigrum</i>	enzymatic	146, 263
				
227	dipiperamide A	<i>P. nigrum</i>	enzymatic	146, 264
228	dipiperamide B			
				
229	dipiperamide D	<i>P. nigrum</i>	enzymatic	146
230	dipiperamide E			
				
231	nigramide P	<i>P. nigrum</i>	-	145
232	nigramide Q			

Table 2. continuation

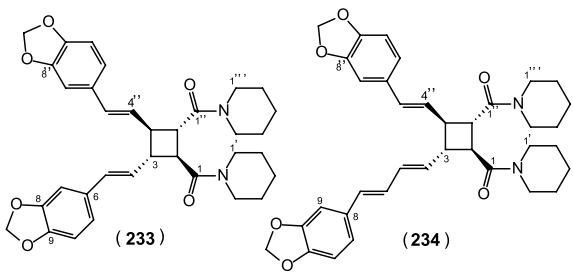
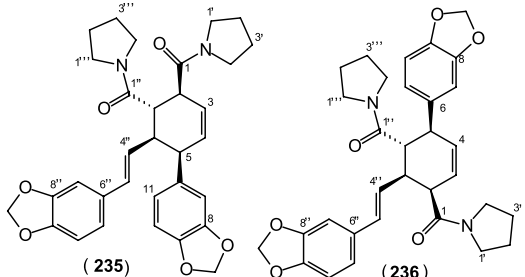
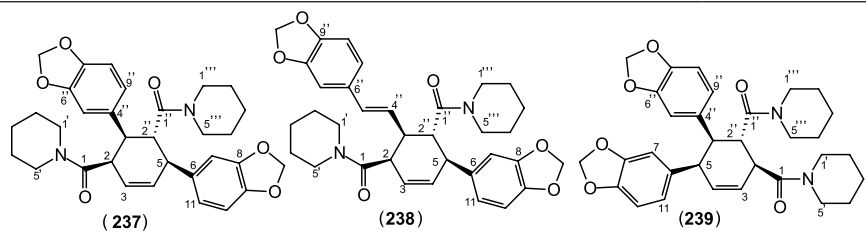
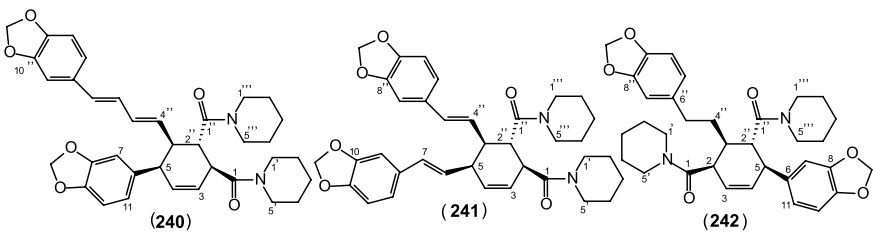
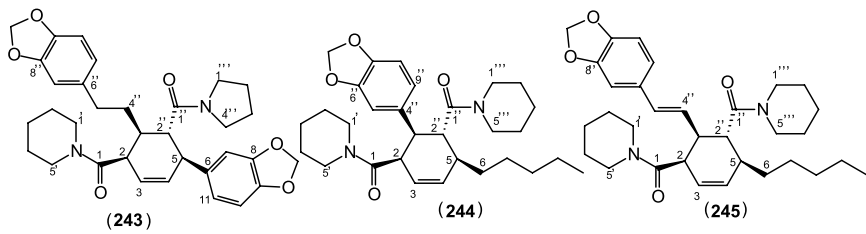
N <sup>o</sup>	Compounds	Species	Biological activity	Ref.
				
233	nigramide R	<i>P. nigrum</i>	-	145
234	nigramide S			
				
235	chabamide F	<i>P. chaba</i>	-	200
236	chabamide G			
				
237	nigramide A	<i>P. nigrum</i>	-	145
238	nigramide B			
239	nigramide C			
				
240	nigramide D	<i>P. nigrum</i>	-	145
241	nigramide E			
242	nigramide F			
				
243	nigramide G	<i>P. nigrum</i>	-	145
244	nigramide H			
245	nigramide I			

Table 2. continuation

N <sup>o</sup>	Compounds	Species	Biological activity	Ref.
246	nigramide J			
247	nigramide K	<i>P. nigrum</i>	-	145
248	nigramide L			
249	nigramide M			
250	nigramide N	<i>P. nigrum</i>	-	145
251	nigramide O			
252	piperchabamide G			
253	piperchabamide H	<i>P. chaba</i>	-	264
254	cycloperstachine A			
255	cycloperstachine B	<i>P. trichostachyon</i>	-	243, 265
256	arboreumine	<i>P. arboreum</i>	antifungal	144
257	pipermethystine	<i>P. methysticum</i>	-	125
258	piperchabamide F			
259	piperchabamide G	<i>P. chaba</i>	-	266
260	piperchabamide H			



Table 2. continuation

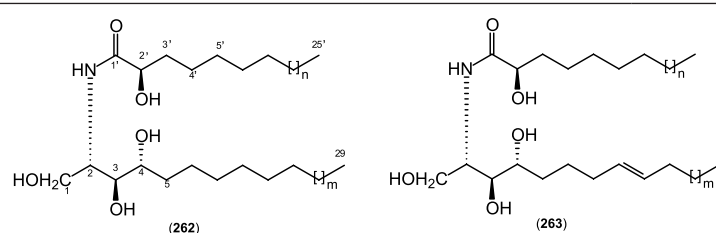
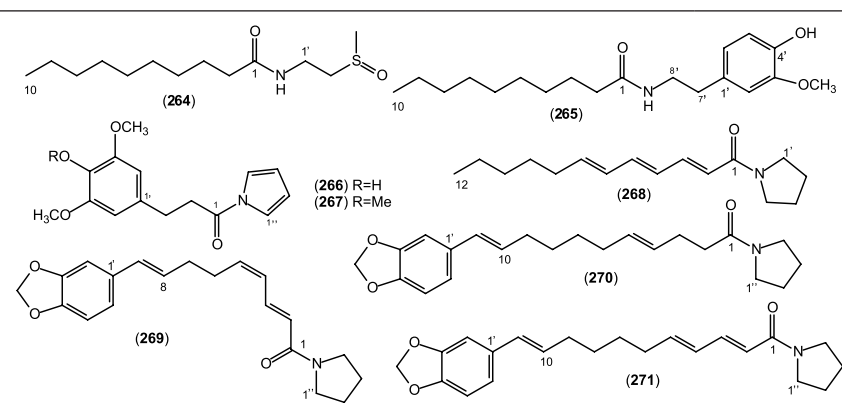
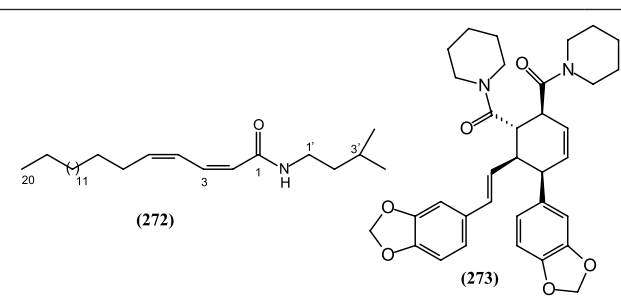
N <sup>o</sup>	Compounds	Species	Biological activity	Ref.
259	( <i>E</i> ) and ( <i>Z</i> ) formouragines	<i>P. argyrophyllum</i>	-	137
260	( <i>E</i> ) and ( <i>Z</i> )- <i>N</i> -formylnormuciferines			
261	<i>N</i> -formylpiperidine	<i>P. nigrum</i>	-	267
				
262	(2 <i>S</i> ,3 <i>S</i> ,4 <i>R</i> )-2- <i>N</i> -[(2' <i>R</i> )-2'-hydroxypentacosanoylamino]-nonacosane-1,3,4-triol	<i>P. betle</i>	-	41
263	(2 <i>S</i> ,3 <i>S</i> ,4 <i>R</i> ,8 <i>E</i> )-2- <i>N</i> -[(2' <i>R</i> )-2'-hydroxytetracosanoylamino]-8-icosylene-1,3,4-triol			
				
264	(2 <i>E</i> ,4 <i>E</i> )- <i>N</i> -[2'-(methylsulfinyl)ethyl]dec-2,4-dienamide			
265	(2 <i>E</i> ,4 <i>E</i> )- <i>N</i> -[4'-hydroxy-3'-methoxyphenyl]ethyl]dec-2,4-dienamide			
266	3-(4'-hydroxy-3',5'-dimethoxyphenyl)propanoylpyrrole			
267	3-(3',4',5'-trimethoxyphenyl)propanoylpyrrole			
268	(2 <i>E</i> ,4 <i>E</i> ,6 <i>E</i> )- <i>N</i> -dodec-2,4,6-trienoylpyrrolidine	<i>P. boehmeriaefolium</i>	-	268
269	(2 <i>E</i> ,4 <i>Z</i> ,8 <i>E</i> )-[9-(3',4'-methylenedioxyphenyl)non-2,4,8-trienoyl]pyrrolidine			
270	(2 <i>E</i> ,4 <i>E</i> ,10 <i>E</i> )-[11-(3',4'-methylenedioxyphenyl)undec-2,4,10-trienoyl]pyrrolidine			
271	(4 <i>E</i> ,10 <i>E</i> )-[11-(3',4'-methylenedioxyphenyl)undec-4,10-dienoyl]pyrrolidine			
				
272	(2 <i>Z</i> ,4 <i>Z</i> )- <i>N</i> -(3'-methylbutyl)-eicos-2,4-dienamide	<i>P. nigrum</i>	-	269
273	chabamide	<i>P. chaba</i>	cytotoxicity	270, 271

Table 2. continuation

N <sup>o</sup>	Compounds	Species	Biological activity	Ref.
274	chabamide H			
275	chabamide I			
276	chabamide J	<i>P. chaba</i>	cytotoxicity	271
277	chabamide K			

C-1''/C5''; or C-2''/C3'', C-2''/C-4'' for pyrrolidine and piperidine alkamides (Figure 2) has indicated the shifts are different, despite the similarity of the carbons. This fact can be observed in compounds **36**,<sup>16</sup> **38**,<sup>131</sup> **44**, **45**,<sup>121</sup> **47**,<sup>10</sup> **97**<sup>272</sup> and **125**<sup>273</sup> (all values given in Table 1S, Supplementary Material, are consistent with those found in the respective articles). Thus, the C-1'' chemical shift is shielded in comparison with C-4'', and the same observation can be made for C-2'' in relation to C-3'' in pyrrolidine derivatives. The same effect is observed for six member rings.<sup>274</sup> In some nigramides (**237-246**)<sup>49</sup>, changes in these values are also seen, indicating the NMR data for these carbons were equivocally attributed. This statement can be explained by the double bond characteristic of the C-N bond. This structural characteristic interferes in the rotational barrier which changes the magnetic shield of C-1' and C-4' (C-5' in six membered rings) of these compounds. A large compression of the carbon electrons located in *syn* to the acyl group may be due to the repulsion of the electrons of oxygen atom. This compression renders C-1' more shielded in comparison to C-4'.

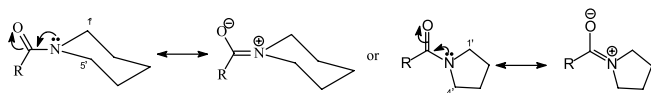


Figure 2. Resonance structures of some amides

## CONCLUDING REMARKS AND FUTURE PERSPECTIVES

Previously, a review of natural and synthetic amides with insecticidal activity was published.<sup>214</sup> This showed that some specific amides can be used, alone or in combination, as insecticides, substituting neurotoxic compounds such as carbamates, organophosphates and pyrethroids. In the present review, we reported a wide range of other biological activity attributed to amides isolated from the genus *Piper* (Table 2). Piperonaline (**124**) showed excellent larvicidal activity against *Aedes aegypti*, comparable to pirimiphos-methyl, the insecticide commonly used,<sup>201</sup> retrofractamide A (**126**) offered satisfactory adipogenic activity, can be considered a promising candidate for the development of antidiabetic agents,<sup>28</sup> and the *N*-[*trans*-cinnamoyl] pyrrolidine (**36**) inhibitor of platelet aggregation with IC<sub>50</sub> of 7.3 mg/mL, comparable with aspirin (IC<sub>50</sub> 5.5 mg/mL), an anti-clotting agent used clinically to combat the formation of thrombi.<sup>131</sup> Data demonstrated the biological and medicinal importance of pipartine

isolated from the roots of *P. chaba*, and indicated that *E*-pipartine may be a promising candidate for use in combinatorial treatments to combat cancer.<sup>275</sup>

To date, the presence of 277 amides from *Piper* has been reported while data from chemical shifts in  $^{13}\text{C}$  NMR is available for 182 compounds. From a phytochemical perspective, approximately 84% of species of *Piper* have not been investigated. Due to its diverse chemical, biological and structural variability, it is important to conduct regular literature reviews on the subject. Advances in hyphenated techniques such as GC/MS/MS have permitted the simultaneous identification and quantification of amides. These techniques can be used as pharmacologically active analytic markers to standardize extracts or herbs with culinary and medicinal properties such as *P. sarmentosum*. These methods can also be used for the determination of new constituents present in the volatile oil;<sup>276</sup> however, for the identification of new compounds by mass spectra fragments, confirmation of their structures by synthesis or employment of standards in the analysis is mandatory.

The development of an interface between HPLC and mass detectors has permitted analysis of mixtures of non-volatile metabolites in different extracts of various parts of plants. The employment of HPLC-APCIMS for determination and quantification of amides and piperamides in economically important *Piper* species, such as *P. nigrum*, has allowed rapid and accurate determination of unsaturated amides, or piperamides, in black pepper and other wild species. APCI allows smooth ionization (in positive or negative scan mode) and also shows some key fragmentations which facilitate the identification of the metabolites. A limitation of this technique is the need for comparison with standards which must be synthesized in some cases.<sup>277</sup> This limitation could be resolved by liquid chromatography coupled with the tandem multistage mass spectrometry (MS/MS) method. The application of ion trap MS<sup>n</sup> in direct structural elucidation is based on characteristic fragmentations and can be used for structural elucidation especially for the minor components in unpurified complex extracts, for which standards are not available. Sun *et al.* employed this technique for the characterization of amides from the extracts of *P. longum*. Upon collisional activation of the [M+H]<sup>+</sup> ion of all the HPLC amide peaks, cleavage of the amide bond can result in losses of the neutral amine moiety (either piperidine or isobutylamine) with subsequent loss of CO to form alkenyl ions. The unique loss of the neutral fragments of 85 and 113 Da would be characteristic for piperidine derived amides. These cleavages with other specific

fragmentations have enabled the identification of 43 known amides present in this plant with only a single chromatographic run. However, for the nine new compounds identified, HRMS data were necessary.<sup>278</sup> Besides the structural feature advantages which HPLC-MS/MS offers, it can also be used as a sensitive and accurate method for the determination of alkaloid amides in plasma. Determination of pipartine (**60**) in rat plasma is important to gain a better understanding of its biological effects. The presence of the protonated molecular ion in  $m/z$  317 and the ion fragment observed in  $m/z$  221 permitted the reliable identification of pipartine in estimating concentration in rat plasma of up to 2.0 ng mL<sup>-1</sup> with high reproducibility.<sup>279</sup> On the other hand, hyphenated techniques allow conclusive determination of the presence of different metabolites in extracts without previous fractionation, sample treatment, synthesis of standards or compound isolation. Even the use of equipment separately can provide data which indicate the different classes of metabolites present or specific compounds. From crude extract NMR and LC-ESIMS analysis of different *Piper* species, Yamaguchi *et al.* confirmed that lignans and other phenolic compounds are present in different contents in adult leaves and seedling leaves. However, the amides showed a similar profile during the developmental stage. In this case, the application of multivariate analysis, such as principal component analysis (PCA) or hierarchical cluster analysis (HCA), is essential.<sup>280</sup>

#### SUPPLEMENTARY MATERIAL

Supplementary material as <sup>13</sup>C NMR data of amides from *Piper* are available free of charge as PDF file at quimicanova.sbgq.org.br.

#### ACKNOWLEDGMENTS

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OCCURRENCE, BIOLOGICAL ACTIVITIES AND  $^{13}\text{C}$  NMR DATA OF AMIDES FROM *Piper* (Piperaceae)<sup>#</sup>

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Table 1S.  $^{13}\text{C}$  NMR data on piperamides found in the genus *Piper* [ $\delta$  (ppm)]

$^{13}\text{C}$	1 <sup>a</sup>	2 <sup>a</sup>	3 <sup>a</sup>	4 <sup>a</sup>	5 <sup>a</sup>	7 <sup>a</sup>	8 <sup>a</sup>	14 <sup>a</sup>	15 <sup>b</sup>	16 <sup>b</sup>	17 <sup>a</sup>	18 <sup>a</sup>	21 <sup>c</sup>
1	169.6	165.0	165.0	168.5	168.8	169.6	165.5	174.7	175.0	170.1	174.6	174.8	172.9*
2	-	-	-	-	119.8	-	-	41.1	41.7	35.3	41.2	41.2	37.8
3	-	-	-	-	142.0	-	-	30.8	31.3	31.5	31.2	30.4	30.2
1'	114.2	122.1	121.9	135.5	137.7	114.2	134.9	140.9	142.1	142.4	136.6	133.5	137.0
2'	155.3	151.8	151.7	129.7	106.2	155.5*	128.7*	128.4	129.3	129.3	105.4	111.3	105.8
3'	119.3	112.9	112.9	129.2*	161.3	119.3	127.0	128.5	129.1	129.1	153.1	148.8	153.5
4'	120.8	119.2	119.3	132.6	101.9	120.9	131.9	126.1	126.8	126.7	136.3	147.4	137.0
5'	151.7	153.9	153.9	129.2	164.9	146.8*	127.0	128.5	129.1	129.1	153.1	112.0	153.5
6'	109.7	115.6	115.5	129.7	106.2	109.6	128.7	128.4	129.3	129.3	105.4	120.3	105.8
1''	40.8	41.1	41.0	45.0	46.4	40.9	123.6	169.6	169.2	127.3	169.6	169.6	170.5*
2''	35.0	35.2	36.0	75.0	24.6	35.1	113.4	52.3	52.5	110.6	52.3	52.3	128.0
3''	130.9	131.9	135.1	130.8	26.5	130.3	130.1	53.4	53.4	61.4	53.4	53.3	147.0
4''	111.9	112.2	105.7	128.0*	26.5	111.2	128.3*	23.8	66.8	32.0	23.8	23.8	50.4
5''	149.2	149.0	153.2	115.3	46.9	144.5*	114.7	35.6	41.8	36.9	35.6	35.6	-
6''	147.9	147.7	136.5	161.0	-	151.8*	159.0	-	-	-	-	-	-
7''	111.5	111.4	153.2	115.3	-	114.6	114.7	-	-	-	-	-	-
8''	120.7	120.8	105.7	128.0	-	121.4	128.3	-	-	-	-	-	-
-OC=O	-	-	-	172.0	-	-	-	-	170.0	-	-	-	-
O=CCH <sub>3</sub>	-	-	-	21.5	-	-	-	-	20.6	-	-	-	-
5''-CH <sub>3</sub>	55.8	55.8	56.1	-	-	59.9*	-	-	-	-	-	-	-
6''-OCH <sub>3</sub>	55.9	56.0	60.8	55.6	-	-	55.2	-	-	-	-	-	-
7''-OCH <sub>3</sub>	-	-	56.1	-	-	-	-	-	-	-	-	-	-
2'-OCH <sub>3</sub>	-	56.3	56.2	-	-	-	-	-	-	-	-	-	-
3'-OCH <sub>3</sub>	-	-	-	-	-	-	-	-	-	-	56.0	55.9	56.1
4'-OCH <sub>3</sub>	-	-	-	-	-	-	-	-	-	-	60.8	55.8	60.5
5'-OCH <sub>3</sub>	56.0	55.8	55.8	-	55.7	60.0*	-	-	-	-	56.0	-	56.1

<sup>a</sup>CDCl<sub>3</sub>; <sup>b</sup>(CD<sub>3</sub>)<sub>2</sub>CO and <sup>c</sup>CD<sub>3</sub>OD

\* may be interchangeable within the same column

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<sup>#</sup>Artigo em homenagem ao Prof. Otto R. Gottlieb (31/8/1920-19/6/2011)

**Table 1S.**  $^{13}\text{C}$  NMR data on piperamides found in the genus *Piper* [ $\delta$  (ppm)]

$^{13}\text{C}$	22 <sup>a</sup>	23 <sup>b</sup>	27 <sup>a</sup>	28 <sup>b</sup>	29 <sup>a</sup>	31 <sup>b</sup>	33 <sup>a</sup>	34 <sup>a</sup>	36 <sup>a</sup>	38 <sup>b</sup>	40 <sup>a</sup>	44 <sup>a</sup>	45 <sup>a</sup>
1	172.5	166.3	169.6	170.2	164.6	164.4	164.6	165.7	164.7	163.9	163.9	168.4	164.8
2	38.1	119.0	36.5	36.3	36.4	122.4	119.1	117.0	118.8	119.3	118.1	117.6	117.0
3	30.3	144.0	29.9	29.5	30.4	139.2	141.6	141.9	141.7	140.9	141.8	141.5	141.3
1'	141.8	134.4	132.7	131.6	140.2	135.7	136.8	129.9	135.3	131.4	130.9	130.3	129.8
2'	128.4	128.3	111.4	112.7*	128.7	104.4	113.2	128.6	127.8	105.7	140.0	109.5	106.5
3'	128.6	128.3	148.9	129.6	128.4	129.0*	159.8	114.7	128.7	139.9	105.2	143.7	148.9
4'	126.1	129.2	147.6	156.0	126.5	127.7	115.0	161.4	129.5	153.9	153.4	130.3	148.2
5'	128.6	128.3	111.7	129.6	128.4	129.4*	129.7	114.7	128.7	139.9	153.4	149.4	108.5
6'	128.4	128.3	120.1	112.7	128.7	104.4	120.4	128.6	127.8	105.7	105.2	100.8	123.8
1''	170.0	175.7	118.8	119.2	118.9	52.2	46.6	46.9	46.6	46.3	46.3	46.1*	46.0*
2''	127.7	33.6	113.0	115.4*	113.2	25.0	26.1	26.4	26.1	26.1	24.4	24.4*	24.4*
3''	146.6	17.2	113.0	115.4	113.2	30.1	24.3	24.6	24.3	24.3	26.2	26.2*	26.2*
4''	50.7	45.8	118.8	119.2	118.9	39.0	46.1	46.3	46.0	45.7	47.0	46.6*	46.6*
OCH <sub>2</sub> O	-	-	-	-	-	-	-	-	-	-	-	101.8	101.4
1''-OCH <sub>3</sub>	-	-	-	-	-	52.2	-	-	-	-	-	-	-
2'-OCH <sub>3</sub>	-	-	-	-	-	-	-	-	-	-	56.1	-	-
3'-OCH <sub>3</sub>	-	-	55.8*	-	-	-	55.3	-	-	55.8	-	-	-
4'-OCH <sub>3</sub>	-	-	55.7*	-	-	-	-	55.7	-	59.9	60.9	-	-
5'-OCH <sub>3</sub>	-	-	-	-	-	-	-	-	-	55.8	56.2	56.8	-

<sup>a</sup>CDCl<sub>3</sub> and <sup>b</sup>(CD<sub>3</sub>)<sub>2</sub>CO

\* may be interchangeable within the same column

**Table 1S.**  $^{13}\text{C}$  NMR data on piperamides found in the genus *Piper* [ $\delta$  (ppm)]

$^{13}\text{C}$	47 <sup>a</sup>	48 <sup>c</sup>	49 <sup>b</sup>	50 <sup>a</sup>	51 <sup>a</sup>	55 <sup>a</sup>	56 <sup>a</sup>	58 <sup>a</sup>	59 <sup>a</sup>	60 <sup>a</sup>	61 <sup>a</sup>	62 <sup>a</sup>	63 <sup>a</sup>	66 <sup>a</sup>
1	165.1	166.1	164.4	166.3	166.2	165.0	167.3	165.7	167.4	166.2	175.5	169.3*	165.7	166.2
2	117.6	118.0	119.8	120.3	119.0	116.0	121.9	118.3	122.5	121.5	40.8	119.8	124.5	41.5
3	143.1	142.6	141.0	141.9	140.5	142.3	132.3	142.3	132.4	144.2	24.5	144.6	136.7	31.5
1'	134.9	135.1	135.8	134.9	129.3	130.3	129.8	132.1	130.3	131.0	136.8	126.9	131.1	134.2
2'	128.0	128.0	128.1	128.1	106.3	106.7	108.2	105.4	108.4	105.9	105.4	105.5	106.6	108.2
3'	128.9	129.8	129.6	130.0	148.9	149.2	147.8	154.5	148.9	153.7	153.1	147.5	152.0	149.4
4'	130.0	128.8	129.0	129.1	148.2	148.5	147.6	140.5	143.5	140.4	136.2	137.5	145.5	136.4
5'	128.9	129.8	129.6	130.0	108.5	108.8	108.2	154.2	135.4	153.7	153.1	147.5	152.8	144.1
6'	128.0	128.0	128.1	128.1	123.7	123.9	123.1	105.4	102.4	105.9	105.4	105.5	106.6	103.2
1''	50.6	44.7	44.5	43.4	47.1	47.3	47.3	47.2	47.3	169.2	165.3	166.0*	168.1	176.3
2''	75.3	52.3	54.8	60.5	28.7	26.1	26.1	27.5	26.2	126.2	125.6	126.1	125.5	126.5
3''	73.5	29.7	34.5	31.2	20.2	25.0	24.4	25.3	24.5	145.9	145.2	145.6	145.4	146.0
4''	50.1	74.1	70.7	70.7	20.2	27.1	25.2	26.4	25.3	25.2	31.5	24.5	24.8	25.0
5''	-	-	-	-	-	43.7	42.0	43.7	42.0	42.0	41.0	41.4	41.1	41.5
OCH <sub>2</sub> O	-	-	-	-	101.4	101.8	101.1	-	101.6	-	-	-	-	101.8
2''-OC=O	170.2	171.0	-	171.2	-	-	-	-	-	-	-	-	-	-
2''-O=CCH <sub>3</sub>	20.8	19.7	-	21.1	-	-	-	-	-	-	-	-	-	-
3''-O=CCH <sub>3</sub>	20.8	-	-	-	-	-	-	-	-	-	-	-	-	-
3''-OC=O	170.2	-	-	-	-	-	-	-	-	-	-	-	-	-
4''-OC=O	-	-	-	171.4	-	-	-	-	-	-	-	-	-	-
4''-O=CCH <sub>3</sub>	-	-	-	21.3	-	-	-	-	-	-	-	-	-	-
3'-OCH <sub>3</sub>	-	-	-	-	-	-	-	56.5	-	56.6	56.0	56.2	56.1	57.0
4'-OCH <sub>3</sub>	-	-	-	-	-	-	-	60.6	-	61.3	60.7	-	60.7	-
5'-OCH <sub>3</sub>	-	-	-	-	-	-	-	56.5	56.5	56.6	56.0	56.2	56.1	-

<sup>a</sup>CDCl<sub>3</sub>; <sup>b</sup>(CD<sub>3</sub>)<sub>2</sub>CO and <sup>c</sup>CD<sub>3</sub>OD

\* may be interchangeable within the same column

**Table 1S.**  $^{13}\text{C}$  NMR data on piperamides found in the genus *Piper* [ $\delta$  (ppm)]

$^{13}\text{C}$	67 <sup>a</sup>	68 <sup>a</sup>	70 <sup>b</sup>	71 <sup>f</sup>	72 <sup>a</sup>	73 <sup>a</sup>	74 <sup>a</sup>	75 <sup>a</sup>	76 <sup>a</sup>	77 <sup>a</sup>	78 <sup>a</sup>	82 <sup>a</sup>	83 <sup>a</sup>	84 <sup>a</sup>
1	165.9	175.6	166.4	166.8	169.2	166.2	166.2	166.1	165.1	165.5	166.6	172.8	166.0	166.2
2	112.2	40.8	115.7*	119.5	118.6	136.7	123.5	123.6	118.3	118.3	122.7	31.1	120.8	123.3
3	147.9	31.1	140.3	140.3	142.1	114.2	136.7	137.1	138.9	138.6	140.0	25.2	142.6	140.9
4	-	-	-	-	-	-	126.4	126.4	123.7	123.8	123.4	35.2	33.8	124.7
5	-	-	-	-	-	-	136.1	136.3	140.5	140.7	139.0	36.5	34.1	138.8
1'	125.9	141.1	128.3	127.1	128.0	147.3	130.6	130.6	131.2	130.1	130.9	135.9	134.6	130.9
2'	105.6	128.4	111.2	130.1	111.5	120.9*	108.4	108.4	107.2	105.2	105.7	107.9	107.9	105.7
3'	147.7	128.6	149.0	116.4	149.4	126.7	147.9	147.9	147.1	148.2	148.3	145.3	145.5	148.2
4'	138.2	126.0	146.2	160.5	150.2	146.8	147.8	147.9	147.0	148.1	148.3	147.3	147.5	148.2
5'	147.7	128.6	116.0*	116.4	116.5	114.8	109.2	109.3	107.5	108.5	108.1	108.6	108.4	108.5
6'	105.6	128.4	122.0*	130.1	123.3	124.2*	125.8	125.6	122.1	122.7	124.4	120.0	124.2	122.6
1''	143.3	165.3	41.9	42.01	42.5	40.6	47.0	48.2	45.9	46.7	47.3	46.7	46.7	45.3
2''	108.2	125.9	36.1	35.8*	35.8	34.2	28.6	82.3	28.6	81.3	28.7	28.3	28.3	35.1
3''	194.1	145.1	131.8	130.6*	131.3	129.3	20.1	24.1	19.2	23.1	20.3	19.9	19.9	27.1
4''	35.7	24.6	113.1	130.5*	130.7	129.3	20.1	24.1	19.2	23.1	20.3	19.9	19.9	11.3
5''	42.2	41.0	145.8	116.8	116.3	114.8	-	-	-	-	-	-	-	17.2
6''	-	-	148.6	157.4	156.9	155.2	-	-	-	-	-	-	-	-
7''	-	-	120.1	116.8	116.3	114.8	-	-	-	-	-	-	-	-
8''	-	-	122.5*	130.5	130.7	129.3	-	-	-	-	-	-	-	-
-OC=O	-	-	-	-	-	-	-	170.9	-	169.8	-	-	-	-
O=CCH <sub>3</sub>	-	-	-	-	-	-	-	22.4	-	21.3	-	-	-	-
OCH <sub>2</sub> O	-	-	-	-	-	-	101.2	101.2	100.2	100.2	101.4	101.0	100.5	101.3
3'-OCH <sub>3</sub>	56.3	-	56.1	-	56.3	55.5	-	-	-	-	-	-	-	-
5'-OCH <sub>3</sub>	56.3	-	-	-	-	-	-	-	-	-	-	-	-	-
5''-OCH <sub>3</sub>	-	-	56.1	-	-	-	-	-	-	-	-	-	-	-

<sup>a</sup>CDCl<sub>3</sub>; <sup>b</sup>(CD<sub>3</sub>)<sub>2</sub>CO and <sup>c</sup>C<sub>3</sub>D<sub>5</sub>N

\*\* may be interchangeable within the same column

**Table 1S.**  $^{13}\text{C}$  NMR data on piperamides found in the genus *Piper* [ $\delta$  (ppm)]

$^{13}\text{C}$	85 <sup>a</sup>	86 <sup>a</sup>	87 <sup>a</sup>	88 <sup>a</sup>	89 <sup>a</sup>	90 <sup>a</sup>	96 <sup>a</sup>	97 <sup>a</sup>	98 <sup>a</sup>	101 <sup>a</sup>	102 <sup>a</sup>	103 <sup>a</sup>	107 <sup>a</sup>	108 <sup>a</sup>
1	166.4	166.5	165.0	164.7	165.6	164.8	165.2	171.8	165.5	166.5	166.6	166.5	165.6	165.5
2	118.8	123.7	121.5	122.3	118.5	121.1	120.0	33.1	121.1	122.9	122.5	118.9	118.1	120.2
3	141.8	141.3	141.8	144.2	139.1	144.4	142.3	24.8	144.0	141.2	141.3	141.3	140.4	142.4
4	122.6	125.1	125.3	34.4	124.2	121.1	125.3	31.3	34.4	129.3	129.1	127.5	127.9	130.5
5	133.7	139.2	138.7	34.5	140.9	134.9	138.0	35.3	34.5	140.9	141.7	141.3	141.6	139.6
6	-	-	-	-	-	-	-	-	-	38.5	35.2	34.9	34.9	126.8
7	-	-	-	-	-	-	-	-	-	-	35.2	35.1	35.0	135.4
1'	124.6	130.9	131.0	135.0	131.4	127.0	130.9	136.0	134.9	131.3	135.3	135.4	135.4	131.6
2'	153.6	106.1	105.8	108.1	106.4	108.1	105.5	107.9	108.8	129.8	109.0*	108.1	108.1	105.6
3'	95.0	148.6	148.3	145.4	148.2	145.6	148.1	147.4	147.5	114.2	147.8	145.6	145.6	147.9
4'	149.1	148.6	148.3	147.5	148.1	147.5	148.0	145.6	145.7	158.4	145.9	147.5	147.5	147.9
5'	141.8	108.9	108.5	108.8	108.3	108.7	108.3	108.7	108.1	114.2	108.9*	108.8	108.8	108.6
6'	105.4	123.0	122.6	121.2	122.6	122.1	122.3	120.9	121.3	129.8	121.4	121.1	121.1	122.1
1''	47.1	39.0	46.5	46.5	46.9	45.8	47.1	46.5*	46.8	47.2	47.2	46.7	46.8	43.4
2''	28.7	38.4	26.2	26.1	26.3	26.0	26.9	26.4*	26.7	28.8	28.8	28.6	26.2	25.7
3''	20.2	26.3	24.4	24.3	24.4	24.2	24.5	24.4	24.6	20.3	20.3	20.1	24.3	24.8
4''	20.2	22.9	45.9	45.8	45.6	46.5	25.7	25.4*	25.5	20.3	20.3	20.1	45.5	26.8
5''	-	22.9	-	-	-	-	43.0	42.5*	43.0	-	-	-	-	47.0
OCH <sub>2</sub> O	101.4	101.7	101.3	100.8	101.0	100.7	101.2	100.5	100.7	-	101.0	100.7	100.7	101.3
2'-OCH <sub>3</sub>	56.7	-	-	-	-	-	-	-	-	-	-	-	-	-
4'-OCH <sub>3</sub>	-	-	-	-	-	-	-	-	-	55.5	-	-	-	-

<sup>a</sup>CDCl<sub>3</sub> and <sup>b</sup>(CD<sub>3</sub>)<sub>2</sub>O

\*\* may be interchangeable within the same column

**Table 1S.**  $^{13}\text{C}$  NMR data on piperamides found in the genus *Piper* [ $\delta$  (ppm)]

$^{13}\text{C}$	109 <sup>a</sup>	110 <sup>a</sup>	111 <sup>a</sup>	112 <sup>a</sup>	113 <sup>a</sup>	114 <sup>a</sup>	117 <sup>a</sup>	118 <sup>a</sup>	119 <sup>a</sup>	121 <sup>a</sup>	122 <sup>a</sup>	123 <sup>a</sup>	124 <sup>a</sup>	125 <sup>a</sup>	126 <sup>a</sup>
1	165.8	165.6	166.3	172.9	165.0	164.7	171.4	171.7	171.5	171.3	165.8	165.6	165.2	165.6	166.3
2	119.3	121.8	123.7	36.9	121.8	120.3	33.4	34.8	34.6	33.4	121.3	119.1	120.5	120.3	122.3
3	142.7	145.5	143.9	25.8	145.6	144.4	25.3	24.4	24.4	25.4	137.3	141.1	145.2	145.9	140.5
4	129.4	32.5	32.4	29.2	32.8	32.2	26.5	29.0	29.3	29.0	120.6	127.8	32.2	32.5	127.4
5	141.1	28.6	27.6	28.9	29.4	31.6	28.9	29.3	32.7	29.3	138.4	142.5	27.9	28.3*	141.2
6	35.2	31.8	28.7	29.2	28.4	130.2	29.3	29.4	128.9	29.4	28.1	32.2	28.9	28.9*	32.6
7	35.2	35.8	31.6	32.8	32.2	127.5	29.7	32.8	129.5	32.8	32.9	32.8	32.6	29.0*	35.9
8	-	-	129.4*	129.2	128.8	-	32.8	129.2	-	129.2	121.3	129.4	128.6	29.3*	128.7
9	-	-	128.7*	129.3	131.4	-	128.0	129.3	-	129.3	130.4	130.1	129.5	32.8	130.0
10	-	-	-	-	-	-	129.2	-	-	-	-	-	-	129.3	-
11	-	-	-	-	-	-	-	-	-	-	-	-	-	129.3	-
1'	135.4	137.2	131.9	132.4	128.4	132.0	132.4	132.4	132.4	132.4	132.4	132.1	132.2	132.4	131.9
2'	109.0	109.4	105.2	105.4	105.4	105.3	105.6	105.4	105.4	105.4	105.7	105.4	105.2	105.3	105.2
3'	147.8	148.4	147.7	147.9	148.0	147.9	146.4	146.5	146.5	147.9	146.9	146.7	146.5	147.9	147.7
4'	145.9	146.4	146.4	146.5	147.8	146.7	147.8	147.9	147.9	146.5	148.1	147.9	147.9	146.5	146.4
5'	108.4	108.6	108.0	108.2	108.9	108.1	108.5	108.1	108.1	108.1	108.4	108.2	108.0	108.2	108.0
6'	121.4	121.8	120.0	120.2	120.2	122.2	119.6	120.1	120.2	120.1	120.6	120.4	120.1	120.1	120.1
1''	47.1	47.1	46.8	46.8	46.0	46.4	46.6	46.6	45.6	46.7	47.1	46.7	46.6	43.0*	46.8
2''	26.9	27.2	28.4	28.5	26.0	26.0	25.4	26.1	24.5	26.6	26.9	26.8	26.5	25.5 <sup>#</sup>	28.4
3''	24.9	25.2	19.9	20.1	24.6	24.2	24.5	24.8	26.1	24.6	24.9	24.7	24.6	24.6	19.9
4''	25.7	26.3	19.9	20.1	46.0	45.7	42.5	45.6	46.6	25.6	25.8	25.6	25.6	26.6 <sup>#</sup>	19.9
5''	43.4	43.8	-	-	-	-	-	-	-	42.6	43.3	43.2	42.9	46.8*	-
OCH <sub>2</sub> O	101.0	101.5	100.7	100.9	100.8	100.9	100.8	100.8	100.8	100.8	101.1	100.9	100.8	100.9	100.7

<sup>a</sup>CDCl<sub>3</sub>

\*#\* may be interchangeable within the same column

**Table 1S.**  $^{13}\text{C}$  NMR data on piperamides found in the genus *Piper* [ $\delta$  (ppm)]

$^{13}\text{C}$	127 <sup>a</sup>	128 <sup>a</sup>	129 <sup>a</sup>	130 <sup>a</sup>	131 <sup>a</sup>	132 <sup>a</sup>	135 <sup>a</sup>	136 <sup>a</sup>	137 <sup>a</sup>	139 <sup>a</sup>	140 <sup>a</sup>	141 <sup>a</sup>	142 <sup>a</sup>	143 <sup>a</sup>	144 <sup>a</sup>	145 <sup>a</sup>
1	166.3	166.3	166.3	166.4	166.4	166.4	166.4	166.4	164.9	166.4	166.4	166.2	165.5	165.7	165.1	157.0
2	122.3	121.8	121.9	121.7	121.8	121.9	121.8	121.9	120.9	121.8	121.8	123.9	118.7	118.6	120.3	121.8
3	141.0	141.2	141.2	141.3	143.0	143.0	143.1	143.0	141.9	143.2	143.1	144.7	142.0	142.8	142.0	145.6
4	127.4	142.8	128.4	129.4	128.3	128.4	128.3	128.4	127.5	128.2	128.3	32.1	128.9	128.9	130.2	129.5
5	143.6	128.4	142.8	143.1	141.2	141.2	141.2	141.2	139.8	141.4	141.2	28.2*	142.6	142.5	141.8	142.0
6	31.4	32.8*	32.8	32.9	32.9	32.5	32.9	32.5	32.7	33.0	32.9	28.9*	32.6*	32.9	32.2	32.5
7	28.6	29.0*	28.3	29.0	29.5*	29.4*	29.8*	29.4*	28.7	29.4*	29.5*	29.0*	28.8*	28.8*	32.9	28.5
8	32.2	28.6*	28.9	28.7	28.6*	28.8*	28.6*	28.8*	28.7	28.8*	29.4*	29.3*	28.9*	29.0*	127.7	29.3
9	129.6	32.7*	32.7	28.9	28.6*	28.8*	28.6*	28.8*	31.5	28.8*	29.2*	32.9	32.7*	29.0*	129.2	29.5
10	128.9	128.5	129.0	29.3	28.6*	28.8*	28.6*	28.8*	31.9	29.4*	29.1*	129.3	129.0	29.3*	-	29.7
11	-	129.3	129.5	32.9	28.6*	28.8*	28.6*	28.8*	128.9*	32.5	29.0*	129.3	129.5	32.9	-	33.4
12	-	-	-	129.3	29.5*	28.8*	28.6*	28.8*	129.1*	129.3	33.8	-	-	129.3	-	128.8
13	-	-	-	129.4	32.8	29.4*	29.8*	29.4*	-	131.2	129.5	-	-	129.3	-	129.5
14	-	-	-	-	129.3	32.9	31.7	32.9	-	34.7	132.0	-	-	-	-	-
15	-	-	-	-	129.4	129.3	35.7	31.6	-	35.9	38.7	-	-	-	-	-
16	-	-	-	-	-	129.5	-	35.6	-	-	-	-	-	-	-	-
1'	131.9	130.6	132.3	132.5	132.6	132.6	136.8	136.8	131.9	136.1	136.8	132.5	132.3	132.5	132.1	132.0
2'	105.2	127.0	105.4	105.4	105.5	108.1	108.0	108.0	104.9	108.1	108.1	105.2	105.3	105.4	105.4	105.5
3'	147.7	113.9	147.9	146.5	148.0	147.9	147.5	147.3	146.5	147.5	147.5	147.9	146.5	147.9	147.9	146.5
4'	146.4	158.6	146.6	149.9	146.6	145.5	145.4	145.4	145.3	145.5	145.4	146.6	147.8	146.5	146.7	148.0
5'	108.0	113.9	108.2	108.2	108.2	108.4	108.9	108.8	107.8	109.0	109.0	108.0	108.1	108.2	108.2	108.3
6'	120.1	127.0	120.2	120.2	120.2	120.1	121.0	121.0	119.7	121.2	121.1	120.2	120.1	120.2	120.1	120.0
1''	46.8	46.9	46.9	46.9	47.0	47.0	47.0	47.0	46.5	47.0	47.0	46.9	43.2	43.2*	46.2	46.5
2''	28.4	28.3	28.6	28.3	28.6	28.6	28.6	28.6	31.5	28.7	28.6	28.6	26.6	25.6 <sup>#</sup>	25.2	24.5
3''	19.9	20.1	20.1	20.1	20.7	20.1	20.1	20.1	28.7	20.2	20.1	20.1	24.5	24.7	25.2	26.0
4''	19.9	20.4	20.1	20.1	20.7	20.1	20.1	20.1	19.9	20.2	20.1	20.1	25.0	26.7 <sup>#</sup>	46.2	45.7
5''	-	-	-	-	-	-	-	-	19.9	-	-	-	46.8	46.9*	-	-
OCH <sub>2</sub> O	100.7	-	100.9	100.9	100.9	100.8	100.7	100.8	100.7	100.7	100.7	100.9	100.8	100.9	100.9	100.7
4'-OCH <sub>3</sub>	-	55.3	-	-	-	-	-	-	-	-	-	-	-	-	-	-

<sup>a</sup>CDCl<sub>3</sub>

\*#\* may be interchangeable within the same column

**Table 1S.** <sup>13</sup>C NMR data on piperamides found in the genus *Piper* [ $\delta$  (ppm)]

<sup>13</sup> C	150 <sup>a</sup>	151 <sup>a</sup>	152 <sup>a</sup>	153 <sup>a</sup>	154 <sup>a</sup>	156 <sup>a</sup>	158 <sup>a</sup>	163 <sup>a</sup>	173 <sup>a</sup>	176 <sup>a</sup>	177 <sup>a</sup>	181 <sup>a</sup>	182 <sup>a</sup>	183 <sup>a</sup>	184 <sup>a</sup>	190 <sup>a</sup>
1	165.6	166.4	166.7	166.0	166.3	166.2	166.5	175.1	172.3	167.0	165.2	165.7	164.3	165.8	165.6	164.7
2	124.7	121.7	122.4	120.0	121.9	121.7	121.9	29.3	35.3	119.8	119.8	118.5	129.0	121.8	121.4	120.9
3	142.8	141.3	140.6	139.0	141.0	141.1	141.1	30.4	25.4	144.1	143.1	142.9	139.2	142.8	144.3	142.1
4	74.2	128.4	128.5	124.0	128.2	128.2	128.3	92.8	30.0	32.6	128.6	128.8	139.1	74.6	74.3	127.3
5	74.0	142.9	142.4	114.5	142.8	143.0	142.9	209.3	29.9	27.3	142.2	142.6	133.8	74.5	74.0	140.5
6	35.2	35.0	32.9	34.0	32.9	32.9	33.0	35.0	30.0	29.4	32.9	32.9	200.4	32.2	33.0	32.3
7	18.9	22.01	28.5	31.5	28.6	28.6	28.7	23.4	29.9	32.2	28.5	31.3	41.2	25.7	25.4	29.1
8	14.0	13.65	31.3	29.5	28.6	28.6	28.7	31.3	30.0	28.6	31.4	28.5	26.2	31.8	31.8	28.3
9	-	-	22.4	29.5	28.6	28.6	28.7	22.4	29.9	129.4	22.5	22.5	22.4	22.6	22.6	28.3
10	-	-	14.0	29.5	28.6	28.6	28.7	13.8	30.0	129.1	14.0	20.2	13.8	14.1	14.0	29.1
11	-	-	-	29.5	28.6	28.6	28.7	-	29.9	27.5	-	-	-	-	-	26.5
12	-	-	-	29.5	28.6	28.6	28.7	-	30.0	30.8	-	-	-	-	-	129.9
13	-	-	-	29.5	28.6	28.6	28.7	-	37.0	29.6	-	-	-	-	-	129.9
14	-	-	-	29.5	28.6	28.6	28.7	-	34.8	29.4	-	-	-	-	-	27.1
15	-	-	-	29.5	29.6	28.6	28.7	-	27.5	29.2	-	-	-	-	-	26.5
16	-	-	-	31.5	31.9	28.6	28.7	-	11.8	28.6	-	-	-	-	-	28.3
17	-	-	-	23.0	22.7	29.6	29.8	-	-	32.6	-	-	-	-	-	22.3
18	-	-	-	14.0	14.1	31.9	32.0	-	-	22.6	-	-	-	-	-	14.1
19	-	-	-	-	-	22.7	22.4	-	-	14.1	-	-	-	-	-	-
20	-	-	-	-	-	14.1	14.0	-	-	-	-	-	-	-	-	-
1'	47.0	46.9	47.0	41.5	46.9	46.9	47.0	47.9	46.0*	46.6	46.5	46.8	47.1	47.1	47.1	46.3
2'	28.6	28.6	28.6	25.1	28.8	28.8	28.8	27.9	24.8*	26.3	26.1	26.7	26.8	26.6	26.5	29.1
3'	20.2	20.1	20.2	22.6	20.1	20.1	20.2	20.3*	26.6*	24.6	24.3	24.6	24.6	24.5	24.5	28.3
4'	20.2	20.1	20.2	22.6	20.1	20.1	20.2	20.5*	47.0*	46.0	45.9	25.6	25.6	25.6	25.5	28.1
5'	-	-	-	-	-	-	-	-	-	-	-	43.2	43.4	43.2	43.2	19.5
6'	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	19.5

<sup>a</sup>CDCl<sub>3</sub>

\*\* may be interchangeable within the same column

**Table 1S.** <sup>13</sup>C NMR data on piperamides found in the genus *Piper* [ $\delta$  (ppm)]

<sup>13</sup> C	192 <sup>d</sup>	194 <sup>d</sup>	195 <sup>d</sup>	196 <sup>d</sup>	197 <sup>d</sup>	199 <sup>d</sup>	200 <sup>f</sup>	205 <sup>d</sup>	206 <sup>a</sup>	209 <sup>a</sup>	210 <sup>a</sup>	211 <sup>a</sup>	212 <sup>a</sup>
1	N	122.0	114.9	114.7	121.9	118.0	123.4	105.6	105.3	124.8*	124.8*	123.0	126.4
2	156.8	110.4	109.0	107.4	108.0	114.1	110.8	139.6	152.3	113.2	112.9	108.5	118.4
3	154.0	154.7	149.9	148.2	144.7	152.4	155.5	153.1	138.2	153.4	153.2	148.2	152.8
4	146.4	150.9	148.7	150.2	147.0	149.4	152.2	154.6	152.3	154.9	154.9	151.4	154.1
4a	116.1	120.4	124.8	124.8	120.3	120.3	121.7	111.6	110.8	125.8*	124.7*	125.7	125.3
5	126.5	126.0	125.4	125.0	125.7	126.9	128.4	126.9	127.1	128.3*	128.1*	128.5*	128.1*
5a	126.4	126.4	127.2	126.3	125.7	126.4	127.8	126.6	126.9	127.2	127.2	128.3	127.2
6	125.7	127.3	127.1	127.4	127.1	126.0	126.2	126.1	125.5	127.2*	127.7*	127.0*	126.9
7	127.0	128.0	127.9	127.8	127.9	127.6	128.3	126.4	126.2	128.3*	128.4*	127.4*	128.2*
8	128.7	129.6	129.2	128.4	129.3	129.3	129.8	128.9	128.4	129.0	129.6	129.0	128.9
8a	133.4	135.3	134.6	134.2	134.7	131.9	136.5	133.1	132.9	133.5	133.3	133.1	133.6
9	104.5	105.1	104.9	105.8	106.2	102.8	105.6	105.4	104.6	113.2	114.3	114.2	112.3
10	N	135.6	135.6	134.4	134.8	134.1	137.1	134.6	136.3	131.5	132.7	132.4	131.8
11	N	123.8	116.3	115.5	122.3	117.1	125.6	125.4	125.1	119.5	119.9	121.3	118.4
12	165.7	168.9	169.4	170.9	168.9	162.1	170.3	167.1	165.9	178.0	176.0	175.0	178.3
13	-	-	-	-	-	-	-	-	-	156.9	156.5	156.7	157.0
OCH <sub>2</sub> O	-	-	-	-	102.4	-	-	-	-	-	-	103.8	-
2-OCH <sub>3</sub>	63.0	-	-	-	-	-	-	61.7	62.9	-	-	-	-
3-OCH <sub>3</sub>	61.3	57.4	57.6	-	-	-	57.4	62.6	61.9	56.3	56.3	-	-
4-OCH <sub>3</sub>	60.8	60.4	-	-	-	59.6	60.7	-	-	60.3	60.3	-	59.9
N-CH <sub>3</sub>	26.4	-	-	-	-	-	-	-	26.4	-	30.2	30.1	-
N-OCH <sub>3</sub>	-	-	-	63.7	63.4	64.5	-	-	-	-	-	-	-

<sup>a</sup>CDCl<sub>3</sub>, <sup>d</sup>DMSO-d<sub>6</sub> and <sup>f</sup>C<sub>5</sub>D<sub>5</sub>N

\*\* may be interchangeable within the same column

N – not reported by the authors.

**Table 1S.**  $^{13}\text{C}$  NMR data on piperamides found in the genus *Piper* [ $\delta$  (ppm)]

$^{13}\text{C}$	219 <sup>a</sup>	220 <sup>a</sup>	221 <sup>a</sup>	222 <sup>a</sup>	223 <sup>a</sup>	224 <sup>a</sup>	225 <sup>a</sup>	226 <sup>a</sup>	227 <sup>a</sup>
1	173.7	171.1	169.8	171.1	171.1	169.8	171.1	170.8	165.2
2	51.2	38.8	42.1	125.5	125.3	42.1	38.6	43.6	122.2
3	42.2	42.6	46.1	130.3	130.3	46.1	42.6	45.7	143.5
4	136.0*	127.2	127.2	45.9	45.7	123.0	120.8	128.6	45.2
5	105.0	153.1	153.1	42.8	42.9	151.6	153.1	131.2	46.6
6	152.6*	141.1	141.1	133.6	133.5	96.7	94.7	131.4	133.5
7	136.5*	145.0	145.0	110.8	110.9	146.1	146.6	105.6	108.3
8	152.6	145.0	145.0	147.4	147.5	142.1	145.1	148.0	147.8
9	105.0	107.8	107.8	146.4	146.4	110.6	107.8	147.1	146.2
10	-	-	-	107.9	108.0	-	-	108.3	108.2
11	-	-	-	123.4	123.5	-	-	-	-
OCH <sub>2</sub> O	-	101.0	101.3	100.9	100.9	101.3	101.0	101.0	100.9
1''	173.7	171.1	169.8	172.2	172.2	169.8	171.1	170.3	165.2
2''	51.2	38.6	42.1	37.7	37.7	42.1	38.8	42.6	122.2
3''	42.2	42.9	46.1	45.4	45.3	46.1	42.9	46.5	143.5
4''	136.0*	120.8	123.0	128.0	133.4	123.0	127.2	128.8	45.2
5''	105.0	153.1	151.6	131.0	132.4	151.6	153.1	130.7	46.6
6''	152.6*	94.7	96.7	131.9	127.1	96.7	141.1	131.4	133.5
7''	136.5*	146.6	146.1	105.3	131.2	146.1	145.0	105.5	108.3
8''	152.6	145.1	142.1	147.8	131.9	142.1	145.0	148.0	147.8
9''	105.0	107.8	110.6	146.7	105.3	110.6	107.8	147.1	146.2
10''	-	-	-	108.2	148.0	-	-	108.3	108.2
11''	-	-	-	120.8	147.0	-	-	-	-
12''	-	-	-	-	108.3	-	-	-	-
13''	-	-	-	-	121.1	-	-	-	-
OCH <sub>2</sub> O	-	101.0	101.3	100.9	101.0	101.3	101.0	101.0	100.9
1'	164.3	45.9	45.8	47.1	47.1	45.8	45.9	45.9	46.9
2'	125.3	26.4	24.4	26.7	26.7	24.3	26.2	26.0	26.5
3'	145.0	23.5	22.2	24.7	24.6	24.3	26.2	24.5	24.6
4'	24.1	26.4	24.4	26.4	26.4	45.8	45.9	25.7	25.5
5'	40.8	45.9	45.8	46.9	46.9	-	-	43.2	43.0
1'''	164.3	45.9	45.8	42.9	42.9	45.8	45.9	46.6	46.9
2'''	125.3	26.2	24.3	25.6	25.7	24.4	26.4	24.3	26.5
3'''	145.0	24.2	22.2	24.5	24.6	24.4	26.4	26.8	24.6
4'''	24.1	26.2	24.3	25.8	25.8	45.8	45.9	46.7	25.5
5'''	40.8	45.9	45.8	43.3	43.3	-	-	-	43.0
6, 8 -OCH <sub>3</sub>	56.0	-	-	-	-	-	-	-	-
7, 7'' -OCH <sub>3</sub>	60.7	-	-	-	-	-	-	-	-
6'', 8'' -OCH <sub>3</sub>	56.0	-	-	-	-	-	-	-	-
5-OCH <sub>3</sub>	-	-	-	-	-	60.5	60.2	-	-
5''-OCH <sub>3</sub>	-	-	-	-	-	61.2	61.5	-	-
6''-OCH <sub>3</sub>	-	-	-	-	-	-	65.3	-	-

<sup>a</sup>CDCl<sub>3</sub>

**Table 1S.**  $^{13}\text{C}$  NMR data on piperamides found in the genus *Piper* [ $\delta$  (ppm)]

$^{13}\text{C}$	228 <sup>a</sup>	229 <sup>a</sup>	230 <sup>a</sup>	231 <sup>a</sup>	232 <sup>a</sup>	233 <sup>a</sup>	234 <sup>a</sup>	235 <sup>a</sup>
1	164.9	169.1	165.2	169.0	170.6	170.5	170.4	171.2
2	120.6	44.6	121.2	45.8	43.4	42.1	42.2	45.1
3	145.4	41.2	144.6	42.2	47.6	46.3	46.4	124.8
4	50.5	127.6	46.9	134.3	135.7	128.7	133.9	130.5
5	48.5	131.1	46.4	108.5	107.7	131.1	132.1	45.5
6	135.4	131.7	133.3	147.8	147.9	131.4	126.8	133.5
7	107.1	105.5	108.5	146.1	146.6	105.6	131.8	107.9
8	147.9	147.9	147.9	108.5	108.2	148.0	131.8	147.5
9	146.4	146.9	147.0	121.1	120.7	147.2	105.4	146.8
10	108.3	108.2	108.1	-	-	108.3	148.1	110.8
11	-	120.7	121.7	-	-	120.9	147.2	123.5
12	-	-	-	-	-	-	108.4	-
13	-	-	-	-	-	-	121.8	-
OCH <sub>2</sub> O	101.0	100.9	100.9	100.9	-	-	101.1	100.9
1''	164.9	165.2	169.5	165.3	170.5	170.5	170.4	172.5
2''	120.6	122.1	46.4	121.8	41.9	42.1	42.1	40.6
3''	145.4	142.2	41.2	143.7	47.7	46.3	46.2	45.3
4''	50.5	44.2	127.5	47.6	128.7	128.7	128.7	127.3
5''	48.5	45.4	131.6	47.4	131.1	131.1	131.0	131.4
6''	135.4	127.5	131.7	133.5	131.4	131.4	131.5	132.0
7''	107.1	130.9	105.7	108.5	105.6	105.6	105.6	105.3
8''	147.9	131.8	147.7	147.8	148.0	148.0	148.0	147.8
9''	146.4	105.5	146.7	146.7	147.2	147.2	147.2	146.5
10''	108.3	148.0	108.2	108.3	108.2	108.3	108.3	108.2
11''	-	147.0	120.8	121.7	120.9	120.9	120.9	120.7
12''	-	108.2	-	-	-	-	-	-
13''	-	120.8	-	-	-	-	-	-
OCH <sub>2</sub> O	101.0	101.0	101.0	101.0	101.1	101.1	101.1	100.9
1'	46.9	42.7	42.5	46.0	46.6	46.7	46.7	46.5
2'	25.5	25.6	25.3	25.8	26.7	26.9	26.9	24.3
3'	24.6	24.5	24.2	24.3	24.5	24.6	24.6	25.8
4'	26.6	26.3	25.5	25.3	25.7	25.7	25.7	45.7
5'	43.2	46.2	44.5	42.6	43.3	43.3	43.3	-
1'''	46.9	43.1	45.9	46.9	46.7	46.7	46.7	46.7
2'''	25.5	25.5	24.5	26.5	26.9	26.9	26.9	24.3
3'''	24.6	24.6	26.0	24.6	24.5	24.6	24.6	26.1
4'''	26.6	26.6	24.5	25.5	25.7	25.7	25.7	46.1
5'''	43.2	47.1	46.8	43.0	43.2	43.3	43.3	-

<sup>a</sup>CDCl<sub>3</sub>

**Table 1S.**  $^{13}\text{C}$  NMR data on piperamides found in the genus *Piper* [ $\delta$  (ppm)]

$^{13}\text{C}$	236 <sup>a</sup>	237 <sup>a</sup>	238 <sup>a</sup>	239 <sup>a</sup>	240 <sup>a</sup>	241 <sup>a</sup>	242 <sup>a</sup>	243 <sup>a</sup>	244 <sup>a</sup>
1	171.4	171.2	170.6	171.2	171.2	171.0	170.4	170.3	171.3
2	38.8	41.8	40.9	44.3	42.9	43.5	38.4	38.2	42.1
3	122.4	124.7	123.4	125.4	125.4	125.2	123.2	123.5	123.8
4	123.6	133.6	133.9	130.9	130.4	130.5	134.1	133.8	133.6
5	45.2	47.6	45.6	47.3	45.8	43.6	46.7	46.3	41.0
6	133.2	137.7	137.8	133.6	133.6	127.2	137.8	137.7	33.5
7	108.2	109.2	108.9	111.2	111.0	132.8	109.0	108.7	25.9
8	146.4	147.7	147.6	147.1	147.4	131.9	147.5	147.4	32.4
9	146.4	146.3	146.1	146.3	146.4	105.9	146.1	146.1	22.6
10	109.1	108.1	108.1	107.6	108.0	148.0	108.1	108.0	14.1
11	130.2	121.6	121.4	123.7	123.5	147.1	121.4	121.3	-
12	-	-	-	-	-	108.3	-	-	-
13	-	-	-	-	-	121.0	-	-	-
OCH <sub>2</sub> O	100.9	100.8	100.7	100.8	100.9	101.1	100.7	100.7	-
1''	172.4	172.4	172.4	172.3	172.3	172.3	173.2	173.5	173.6
2''	45.8	43.4	44.6	37.4	37.8	38.5	45.1	48.6	40.7
3''	40.0	46.1	44.2	47.7	45.3	45.4	39.4	39.1	46.7
4''	130.4	135.2	127.6	134.8	133.4	127.6	32.0	32.0	135.4
5''	130.9	109.1	132.0	109.5	132.4	131.7	33.6	33.6	109.4
6''	131.2	147.4	132.0	146.8	127.2	131.9	136.1	136.1	147.3
7''	107.8	146.3	105.4	145.8	131.2	105.3	108.8	108.8	146.1
8''	147.2	108.0	147.9	107.3	132.1	147.9	147.5	147.5	107.9
9''	147.5	121.6	146.9	121.8	105.4	146.9	145.6	145.6	122.0
10''	111.1	-	108.2	-	148.1	108.3	108.1	108.1	-
11''	125.1	-	120.8	-	147.1	120.8	121.0	121.0	-
12''	-	-	-	-	108.4	-	-	-	-
13''	-	-	-	-	121.1	-	-	-	-
OCH <sub>2</sub> O	100.9	100.8	101.0	100.6	101.1	101.0	100.7	100.7	100.7
1'	46.6	47.1	47.4	47.4	47.1	47.1	47.1	47.1	47.1
2'	26.0	25.9	26.9	26.9	26.8	26.7	27.2	27.2	25.9
3'	26.1	24.3	24.6	24.6	24.7	24.7	24.7	24.7	24.4
4'	46.7	25.3	25.9	25.9	25.7	25.8	25.9	25.9	25.4
5'	-	43.1	43.2	43.5	43.3	43.4	43.0	43.0	43.1
1'''	46.7	46.6	46.8	47.2	47.0	47.1	47.0	46.7	47.1
2'''	24.4	25.7	26.3	26.2	26.5	26.5	26.1	25.8	26.4
3'''	24.4	24.4	24.6	24.5	24.6	24.6	24.7	24.3	24.6
4'''	46.8	25.5	25.8	25.6	25.8	25.7	25.9	45.2	25.7
5'''	-	42.4	42.8	42.7	42.9	42.9	42.9	-	42.6

<sup>a</sup>CDCl<sub>3</sub>



**Table 1S.**  $^{13}\text{C}$  NMR data on piperamides found in the genus *Piper* [ $\delta$  (ppm)]

$^{13}\text{C}$	245 <sup>a</sup>	246 <sup>a</sup>	247 <sup>a</sup>	248 <sup>a</sup>	249 <sup>a</sup>	250 <sup>a</sup>	251 <sup>a</sup>	252 <sup>a</sup>	253 <sup>a</sup>
1	170.7	171.2	172.8	170.6	171.8	171.0	173.9	170.4	170.5
2	41.4	44.6	50.2	38.1	43.9	40.8	47.7	134.0	133.9
3	122.2	124.1	124.4	123.7	125.5	123.6	123.5	123.2	123.4
4	134.3	133.5	133.7	133.4	131.1	133.6	133.9	38.3	37.9
5	38.9	40.2	40.1	48.4	47.0	45.1	40.5	46.6	46.6
6	33.8	31.8	31.8	138.1	132.0	137.8	34.0	137.8	137.9
7	25.9	27.3	27.4	109.3	111.6	108.8	26.9	108.1	108.2
8	32.3	32.1	32.1	147.3	147.4	147.6	31.9	147.5	147.5
9	22.6	22.7	22.6	145.8	146.5	146.1	22.6	146.0	146.0
10	14.1	14.0	14.0	107.7	107.9	108.1	14.0	108.9	108.9
11	-	-	-	122.0	123.9	121.4	-	121.4	121.4
OCH <sub>2</sub> O	-	-	-	100.7	100.8	100.7	-	100.7	100.7
1''	173.6	173.0	172.9	165.3	164.4	173.5	166.3	173.2	173.5
2''	41.9	38.1	38.3	122.7	122.8	52.2	125.1	45.0	45.1
3''	45.0	46.9	46.8	146.9	147.4	43.1	144.6	39.3	39.6
4''	128.2	136.1	135.9	47.4	46.2	128.9	43.3	31.9	29.8
5''	131.8	109.3	109.3	40.6	33.0	133.9	35.7	33.5	29.4
6''	132.0	147.2	147.3	31.1	32.7	32.6	32.0	136.0	27.0
7''	105.5	145.8	145.9	27.3	24.7	28.9	26.2	108.7	32.9
8''	147.9	107.7	107.8	31.9	32.4	31.4	31.9	147.5	129.2
9''	146.8	121.5	121.4	22.7	22.6	22.6	22.6	145.5	129.5
10''	108.2	-	-	14.0	14.0	14.0	14.0	108.1	132.4
11''	120.7	-	-	-	-	-	-	120.9	105.3
12''	-	-	-	-	-	-	-	-	147.9
13''	-	-	-	-	-	-	-	-	146.5
14''	-	-	-	-	-	-	-	-	108.0
15''	-	-	-	-	-	-	-	-	120.2
OCH <sub>2</sub> O	101.0	100.8	100.8	-	-	-	-	100.7	100.9
1'	47.3	47.2	47.1	47.2	47.0	47.6	47.1	42.9	42.8
2'	26.9	26.8	28.5	26.6	27.0	26.9	28.4	25.9	25.8
3'	24.6	24.6	20.1	24.7	24.7	24.7	20.1	24.6	24.6
4'	25.8	25.9	20.2	25.5	25.7	25.9	20.1	27.1	25.9
5'	43.1	43.4	-	42.9	43.4	43.2	-	47.1	47.0
1'''	47.0	47.3	47.3	46.8	46.6	46.6	46.9	42.9	42.8
2'''	26.8	26.2	26.3	27.1	26.2	28.2	28.6	26.0	26.1
3'''	24.8	24.6	24.6	24.7	24.3	19.8	20.2	24.0	24.6
4'''	25.9	25.7	25.6	25.8	45.7	19.9	20.2	27.1	26.8
5'''	42.9	42.8	42.9	42.9	-	-	-	47.0	47.0

<sup>a</sup>CDCl<sub>3</sub>

**Table 1S.**  $^{13}\text{C}$  NMR data on piperamides found in the genus *Piper* [ $\delta$  (ppm)]

$^{13}\text{C}$	254 <sup>d</sup>	255 <sup>d</sup>	256 <sup>a</sup>	258 <sup>a</sup>	262 <sup>f</sup>	263 <sup>f</sup>	264 <sup>a</sup>	265 <sup>a</sup>
1	138.7	135.1	-	165.8	62.9	62.2	167.0	166.5
2	108.4	110.0	49.5	123.5	53.9	53.2	121.1	121.3
3	147.7	147.3	40.9	144.2	77.7	77.0	141.8	141.6
4	146.3	146.5	198.3	31.8	73.3	73.1	128.1	128.1
5	108.1	107.7	163.9	27.7	35.0	34.0	143.8	143.6
6	133.4	133.3	126.1	28.9	27.5	29.7–30.8	32.9	32.9
7	47.2	49.9	N	32.6	30.5-31.2	33.5	28.4	28.4
8	128.5	127.5	128.6	128.6		131.0	31.3	31.3
9	121.0	122.4	135.6	129.4		130.9	22.4	22.4
10	36.6	36.6	67.3	132.1		33.1	14.0	14.0
11	30.6	42.2	23.4	105.2		29.7–30.8	-	-
12	28.8	33.3	19.0	147.7			-	-
13	26.4	26.9	22.7	146.3			-	-
14	26.0	26.4	23.8	108			-	-
15	35.6	30.7	-	120.0			-	-
16	46.8	42.6	-	-			-	-
17	173.6	170.2	-	-			-	-
18	-	-	-	-		32.3	-	-
19	-	-	-	-		23.1	-	-
20	-	-	-	-		14.4	-	-
21-26	-	-	-	-		-	-	-
27	-	-	-	-	33.0	-	-	-
28	-	-	-	-	23.8	-	-	-
29	-	-	-	-	15.1	-	-	-
OCH <sub>2</sub> O	101.0	100.9	-	100.8	-	-	-	-
SMe	-	-	-	-	-	-	38.5	-
4'-OMe	-	-	-	-	-	-	55.9	-
1'	45.4	45.5	-	45.0	176.1	175.4	34.2	130.6
2'	22.1	24.3	49.5	34.9	73.9	72.6	53.2	111.2
3'	24.3	26.4	40.9	27.0	36.6	35.9	-	146.6
4'	46.4	46.4	163.9	17.2	26.7	26.0	-	144.2
5'	-	-	126.1	11.3	30.5-31.2	29.7-30.8	-	114.4
6'	-	-	N	-			-	121.3
7'	-	-	128.6	-			-	35.2
8'	-	-	135.6	-			-	40.9
9'	-	-	67.3	-			-	-
10'	-	-	23.4	-			-	-
11'	-	-	19.0	-			-	-
12'	-	-	22.7	-			-	-
13'	-	-	23.8	-			-	-
14'-21'	-	-	-	-			-	-
22'	-	-	-	-		32.3	-	-
23'	-	-	-	-	33.0	23.1	-	-
24'	-	-	-	-	23.8	14.4	-	-
25'	-	-	-	-	15.1	-	-	-

<sup>a</sup>CDCl<sub>3</sub>, <sup>d</sup>DMSO-d<sub>6</sub> and <sup>f</sup>C<sub>5</sub>D<sub>5</sub>N;

N – not reported by the authors.

**Table 1S.**  $^{13}\text{C}$  NMR data on piperamides found in the genus *Piper* [ $\delta$  (ppm)]

$^{13}\text{C}$	266 <sup>a</sup>	267 <sup>a</sup>	268 <sup>a</sup>	269 <sup>a</sup>	270 <sup>a</sup>	271 <sup>a</sup>	272 <sup>a</sup>
1	169.6	169.7	165.1	165.1	165.2	171.3	166.3
2	36.3	36.6	120.8	122.2	119.7	34.8	120.2
3	30.3	30.8	141.9	136.5	142.3	28.0	139.8
4	-	-	128.3	127.3	128.8	128.9	126.7
5	-	-	139.9	138.8	143.0	131.2	141.0
6	-	-	129.9	27.9	32.8	32.4	27.1
7	-	-	139.6	32.7	28.2	28.9	27.9-29.1
8	-	-	32.9	127.7	28.9	29.0	
9	-	-	28.7	130.2	32.8	32.7	
10	-	-	31.4	-	128.9	129.3	
11	-	-	22.5	-	129.5	129.3	
12	-	-	14.0	-	-	-	
13 – 18	-	-	-	-	-	-	
19	-	-	-	-	-	-	22.8
20	-	-	-	-	-	-	14.4
1'	130.9	136.0	45.9	132.1	132.3	132.6	46.8
2'	104.7	105.3	24.3	105.4	105.3	105.3	27.9-29.1
3'	146.7	153.3	26.1	147.8	147.9	147.9	
4'	132.9	136.0	46.4	146.6	145.5	146.5	19.8
5'	146.7	153.3	-	108.2	108.2	108.2	19.8
6'	104.7	105.3	-	120.4	120.2	120.2	-
1''	118.6	118.9	-	46.5	46.2	46.6	-
2''	112.8	113.2	-	26.1	24.5	26.1	-
3''	112.8	113.2	-	24.3	24.3	24.4	-
4''	118.6	118.9	-	45.9	46.2	45.7	-
3'-OMe	55.9	55.1	-	-	-	-	-
4'-OMe	-	60.8	-	-	-	-	-
5'-OMe	55.9	55.1	-	-	-	-	-
OCH <sub>2</sub> O	-	-	-	100.9	100.9	100.8	-

<sup>a</sup>CDCl<sub>3</sub>

**Table 1S.**  $^{13}\text{C}$  NMR data on piperamides found in the genus *Piper* [ $\delta$  (ppm)]

$^{13}\text{C}$	274 <sup>a</sup>	275 <sup>a</sup>	276 <sup>a</sup>	277 <sup>a</sup>
1	170.8	170.8	174.4	171.7
2	41.5	44.4	49.1	45.3
3	124.4	123.9	122.8	124.7
4	133.4	131.8	134.1	133.6
5	46.7	47.1	37.9	40.5
6	137.6	132.0	33.7	33.6
7	109.1	110.1	29.7	26.7
8	147.7	147.0	31.9	31.9
9	146.3	146.9	28.3	22.7
10	108.2	107.5	14.10	14.1
11	121.7	123.8	-	-
OCH <sub>2</sub> O	100.8	100.7	-	-
1''	173.2	173.5	172.3	162.4
2''	51.3	45.5	48.6	125.3
3''	45.2	42.9	43.0	147.2
4''	135.6	135.0	128.8	44.4
5''	108.8	109.1	133.9	40.1
6''	147.6	146.2	32.5	32.9
7''	146.3	145.7	29.0	27.5
8''	108.3	107.4	31.4	31.4
9''	121.4	121.4	22.7	22.5
10''	-	-	14.0	14.0
OCH <sub>2</sub> O	100.8	100.5	-	-
1'	47.0	46.9	47.0	46.9
2'	25.7	26.8	28.5	28.6
3'	24.3	24.5	20.2	20.11
4'	25.2	25.7	-	-
5'	43.0	43.4	-	-
1'''	46.4	46.5	46.9	46.8
2'''	28.1	28.4	28.4	28.4
3'''	19.7	19.9	20.1	20.1
4'''	19.6	19.8	20.1	20.1

<sup>a</sup>CDCl<sub>3</sub>