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# Pentameric ellagitannin oligomers in melastomataceous plants—chemotaxonomic significance

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**Abstract**

The pantropical plant family Melastomataceae produces characteristic hydrolyzable tannin oligomers. The latter in this family are distinguished from those in other plant families by the fact that the oligomers from dimers to tetramers are composed of two different alternating monomeric units: casuarictin and pterocaryanin C. These oligomers are metabolites that are produced by intermolecular C–O oxidative coupling between the monomers (or their desgalloyl-or des-hexahydroxydiphenoyl derivatives) forming a valoneoyl group as the link between monomers. The chemotaxonomically significant oligomerization pattern of melastomataceous plants provided helpful suggestions for determining the structures of new oligomers (nobotanins Q–T and melastoflorins A–D) isolated from *Monochaetum multiflorum*, which belongs to this family. Melastoflorins A–D were characterized as pentamers, which are the largest hydrolyzable tannins composed of different monomeric units.


*Keywords:* *Monochaetum multiflorum*; Melastomataceae; Ellagitannin; Oligomer; Oligomerization pattern; Chemotaxonomical marker; Ellagitannin pentamer; Melastoflorin A

## 1. Introduction

Remarkable progress in phytochemical studies of tannin constituents in medicinal plants during the last two decades has led to the characterization of numerous hydrolyzable tannins. Ellagitannins, a large subgroup of hydrolyzable tannins, show great structural diversity based on the formation of dimeric and oligomeric metabolites via intermolecular C–O or C–C oxidative coupling between various monomeric species (Okuda et al., 1995; Haslam, 1998; Yoshida et al., 2000). More than 200 oligomeric ellagitannins from a variety of plant species have been reported. Recently, the biogenetic intermolecular coupling of monomers (Fig. 1) to form oligomers via the enzymatic production of a dimer, cornusiin E (**3**), through a monomeric ellagitannin, tellimagrandin II (**2**) from pentagalloylglucose (**1**), using cell free extract prepared from the leaves of *Tellima grandiflora* was proven (Niemetz and Gross, 2003). Unlike the monomeric hydrolyzable tannins, the structures of the oligomers are often characteristic of a plant family or genus (Okuda et al., 1995; Yoshida et al., 2000), suggesting that oligomerization modes of monomers are most likely regulated enzymatically in a similar way within each plant group. Therefore, understanding the oligomerization patterns characteristic of a plant family or genus would provide a basis for the facile structural determination of new complex oligomers. The family Melastomataceae, which produces oligomers that are distinct from those of any other plant family, is one such chemotaxonomically significant family (Yoshida et al., 2000).

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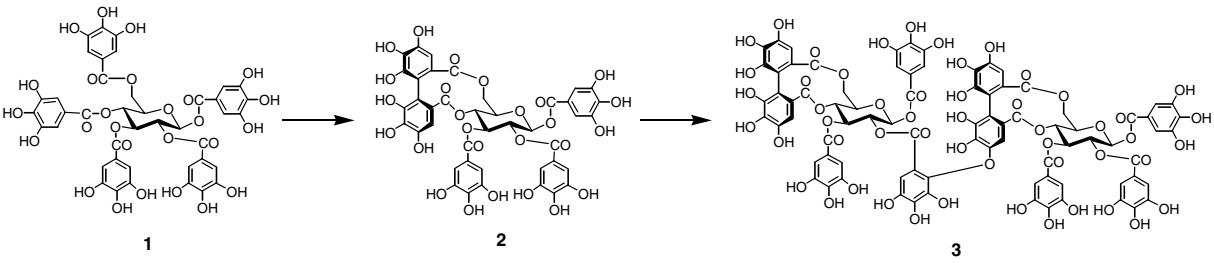



Fig. 1. Enzymatic production of cornusiin E.

This paper first gives an overview of the structural features of the oligomeric ellagitannins that are characteristic of melastomataceous plants. Then, we elucidated the structure of newly isolated pentameric ellagitannins (melastoflorins A–D) from *Monochaetum multiflorum.*

## 2. Results and discussion

### 2.1. Structural characteristics of melastomataceous plants

The Melastomataceae is a pantropical family that comprises over 166 genera, and about 4300 species (Renner, 1993). In tropical and subtropical Asia, many *Melastoma*, *Medinilla*, *Osbeckia*, and other species are traditionally used as remedies for upset stomachs, wounds, hemorrhoids, diarrhea, and dysentery, based on their astringent properties (Perry, 1980). In our continuing studies of tannins and related polyphenols in the Melastomataceae, we have investigated polyphenolics in nine plant species in six genera used medicinally: *Medinilla* (Yoshida et al., 1986), *Heterocentron* (Yoshida et al., 1986, 1995), *Tibouchina* (Yoshida et al., 1991a, 1999 ), *Melastoma* (Yoshida et al., 1992a,b), *Bredia* (Yoshida et al., 1994), and *Monochaetum* (Isaza et al., 2004). The major polyphenolics of these plants are monomeric and oligomeric hydrolyzable tannins (nobotanins A–C, E–T, etc.), as summarized in Table 1. These tannins are responsible for the astringent properties of these plants. All of these oligomeric ellagitannins are *m*-DOG type oligomers (Okuda et al., 1995), which are characterized by the presence of a valoneoyl group linking the monomers. The structures of reported melastomataceous oligomers share common features. First, they are composed of two different alternating monomeric units: casuarictin (C) (**4**) and pterocaryanin C (PC) (**5**). Moreover, of the three galloyl groups in **5**,

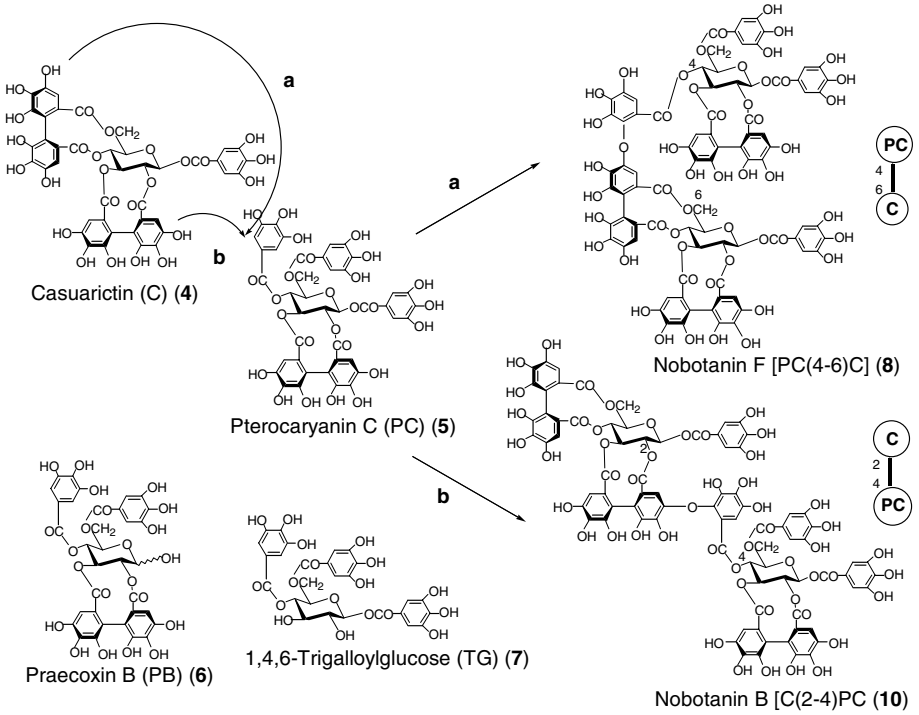
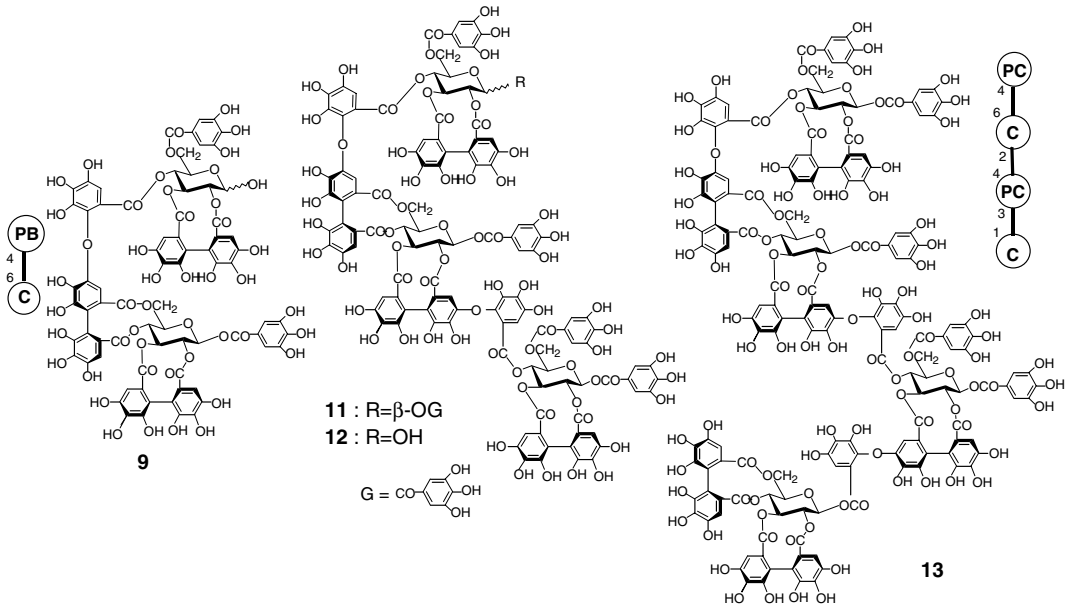
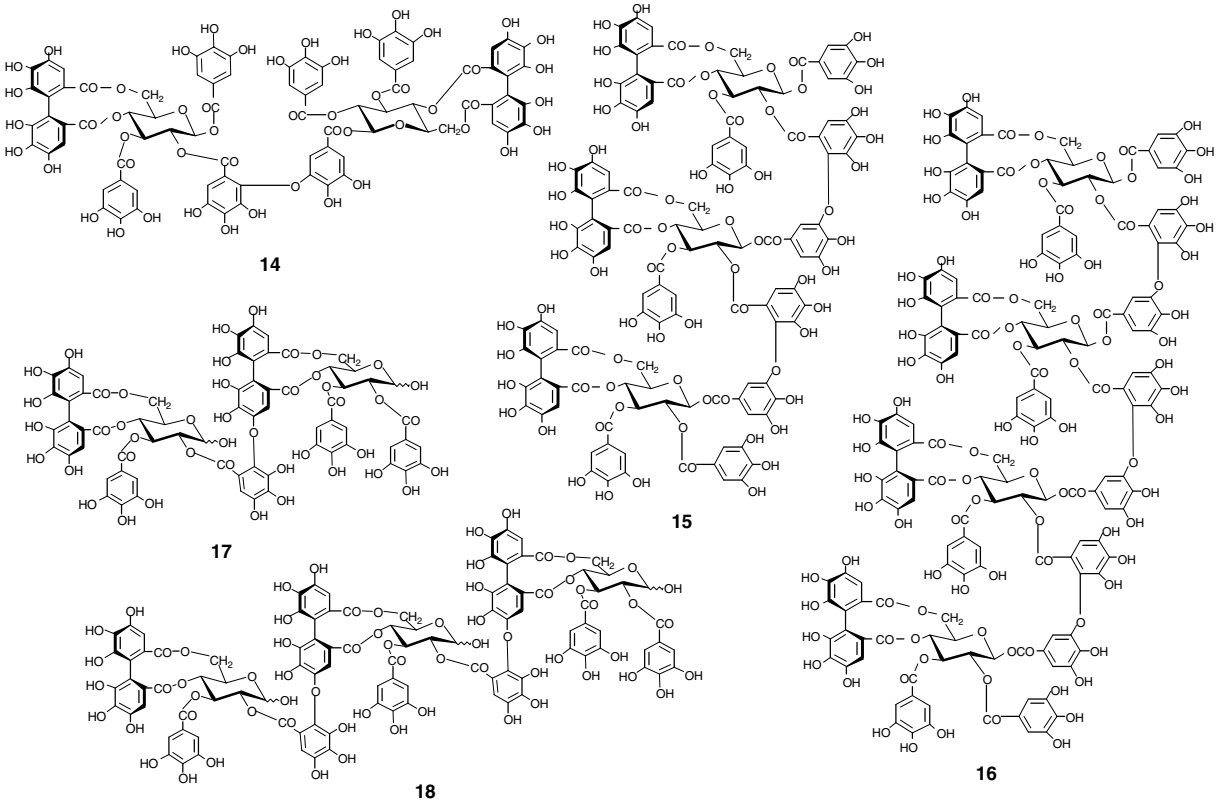


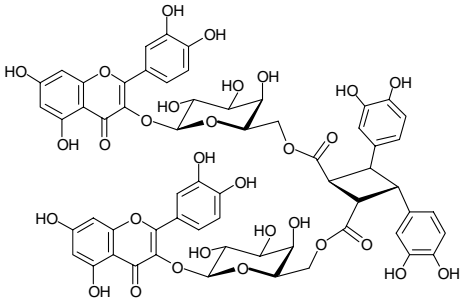

Fig. 2. Schematic patterns of coupling modes. Structures of **9**, **11**–**13** and **14**–**18**.



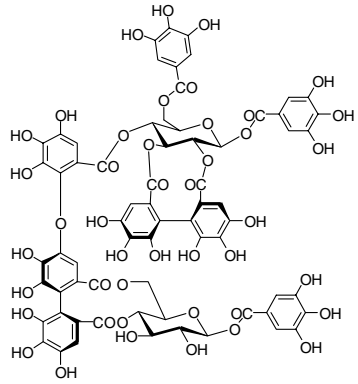




only the O-4 galloyl unit participates in intermolecular coupling with the hexahydroxydiphenoyl (HHDP) unit at O-4/O-6 or O-2/O-3 in **4** to form the valoneoyl group (Fig. 2). Nobotanins F [PC(4-6)C] (**8**), B [C(2–4)PC] (**10**) (dimers), E [PC(4-6)C(2-4)PC] (**11**) (trimer), and K [PC(4-6)C(2-4)PC(3-1)C] (**13**) (tetramer) are representative oligomers. Instead of **5**, desgalloyl or des-HHDP derivatives, such as praecoxin B (PB) (**6**) or 1,4,6-trigalloylglucose (TG) (**7**), can be monomeric component(s) of the oligomers, leading to very diverse structures, e.g., nobotanin A [PB(4-6)C] (**9**) and nobotanin C[PB(4-6)C(2-4)PC] (**12**).

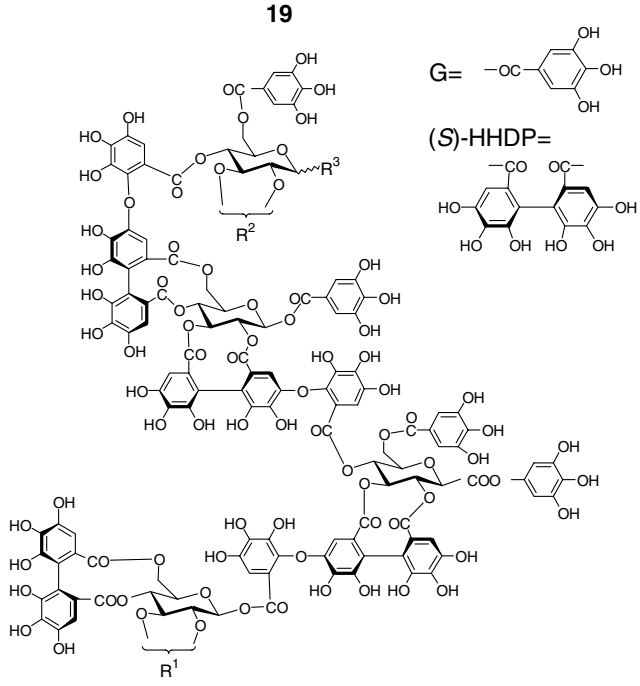
These structural features are unique compared with the *m*-DOG-type oligomers in other plant families,



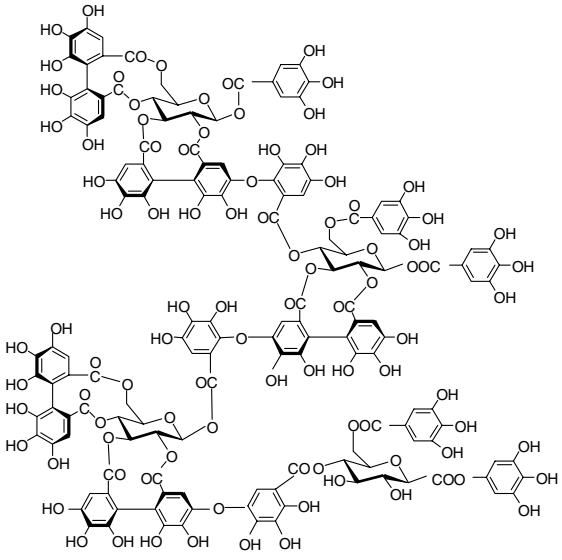
**19**



**20**




**21** : $R^1$ =(*S*)-HHDP, $R^2$ = H, H, $R^3$ =β-*O*-Gall
**23** : $R^1$ =H, H, $R^2$ = (*S*)-HHDP, $R^3$ =OH



**22**

which are mostly constructed from a single monomeric unit, as exemplified by hirtellins A (**14**), $T_1$ (**15**), and $Q_1$ (**16**) (oligomers of tellimagrandin II (**2**)) in the tamaricaceous plants (Yoshida et al., 1991b; Ahmed et al., 1994) and cornusiins A (**17**) and C (**18**) in the cornaceous plants (oligomers of tellimagrandin I) (Hatano et al., 1989).

Nobotanin B (**10**) is a major component in most of the melastomataceous plants investigated and is likely a key dimer from which trimers and tetramers are produced by further coupling with **4** or **5**. Although there are insufficient data to generalize their chemotaxonomic relationships, these biogenetic features should be helpful for determining the structures of new oligomeric ellagitannins in this plant family.

Of note, nobotanins B (**10**) and K (**13**) are specific inhibitors of poly-(ADP-ribose) glycohydrolase purified from human placenta (Aoki et al., 1993) and also exhibit anti-HIV activity (Nakashima et al., 1992). Although the metabolism of poly-(ADP-ribose) on specific chromosomal proteins in eukaryotic cells is associated with gene activation, i.e., DNA repair, replication, and transcription, its detailed physiological significance is not fully understood. Therefore, potent specific inhibitors, such as **10**, should be useful in determining the physiological role of de-poly(ADP-ribosyl)ation on chromosomal proteins. Several monomeric hydrolyzable tannins from *Osbeckia* species have been characterized as antioxidant components of plants (Su et al., 1988).

### 2.2. Polyphenolics of *Monochaetum multiflorum*

*Monochaetum multiflorum* (Bompl.) Naudin is a shrub endemic to Colombia, where it is used locally as a remedy for infections and skin injuries. We isolated

Table 1
Hydrolyzable tannins in melastomataceous plants

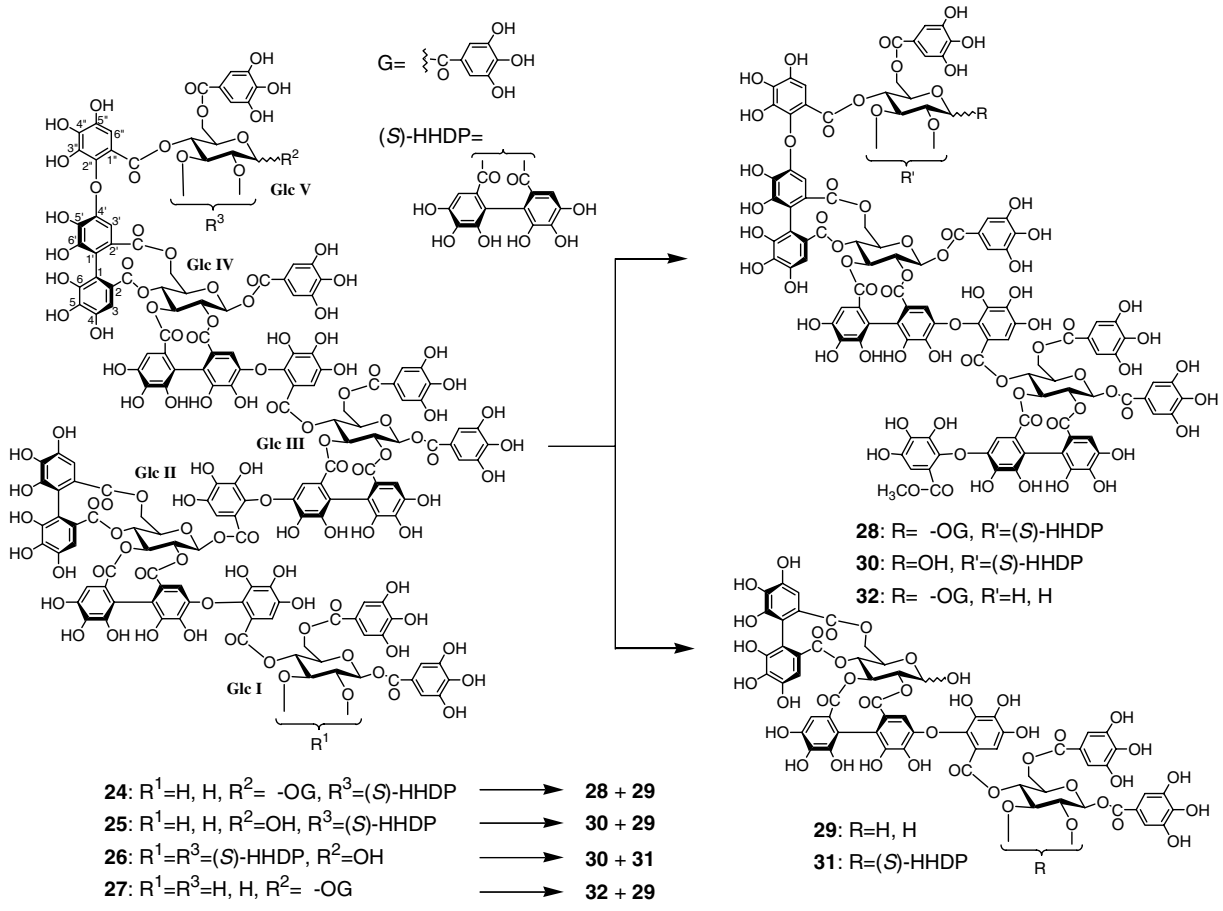
| Compounds | Structure type | *Monochaetum multiflorum* | *Melastoma malabathricum* | *M. normale* | *Tibouchina semidecandra* | *T. multiflora* | *Heterocentron roseum* | *Medinilla magnifica* | *Bredia tuberuculata* |
|---|---|---|---|---|---|---|---|---|---|
| *Monomers* | | | | | | | | | |
| Pedunculagin (PE) | | + | + | + | + | + | | | + |
| Casuarictin (C) (**4**) | | + | + | + | + | + | + | | + |
| Pterocaryanin C (PC) (**5**) | | + | + | + | | | | | |
| Praecoxin B (PB) (**6**) | | | | | + | | | | |
| Strictinin (S) | | | + | + | | | + | | |
| 1,4,6-Trigalloylglucose (TG) (**7**) | | + | + | + | + | | | | |
| *Dimers* | | | | | | | | | |
| Nobotanin F (**8**) | PC (4-6) C | + | | | + | + | + | | + |
| Nobotanin A (**9**) | PB (4-6) C, | + | | | + | + | | | + |
| Nobotanin R (**20**) | PC (4-6) S | + | | | | | | | |
| Brediatin B | TG (4-6) C | + | | | | | | | + |
| Nobotanin B (**10**) | C (2-4) PC | + | + | + | + | + | | | + |
| Nobotanin G | C (2-4) TG | | + | + | | + | + | | + |
| Nobotanin H | C (2-4) PC[a] | | + | + | | | | | |
| Nobotanin I | C (2-4) PC[b] | | | | | + | | + | |
| Nobotanin O | C (2-4) PC | + | | | | + | | | |
| Medillinin B | PB (4-6) PE | | | | | + | | + | |
| *Trimers* | | | | | | | | | |
| Nobotanin E (**11**) | PC (4-6) C (2-4) PC | + | | | + | | | | + |
| Nobotanin C (**12**) | PB (4-6) C (2-4) PC | | | | + | + | | | |
| Nobotanin L | PB (4-6) C (2-4) PB | | | | + | | | | |
| Nobotanin M | PB (4-6) C (2-4) TG | | | | + | + | | | |
| Nobotanin N | PB (4-6) C (2-4) DG[c] | | | | + | | | | |
| Nobotanin U | PB (4-6) C (2-4) PC[a] | + | | | | | | | |
| Nobotanin J | C (2-4) PC (3-1) C | + | + | | | + | + | | |
| *Tetramers* | | | | | | | | | |
| B Nobotanin K (**13**) | PC(4-6) C (2-4) PC (3-1) C | + | | | | | + | | |
| Nobotanin P | PB (4-6) C (2-4) PC (3-1) C | | | | | + | | | |
| Nobotanin Q (**21**) | DG (4-6) C (2-4) PC (3-1) C | + | | | | | | | |
| Nobotanin S (**22**) | C (2-4) PC (3-1) C (2-4) TG | + | | | | | | | |
| Nobotanin T (**23**) | PB (4-6) C (2-4) PC (3-1) S | + | | | | | | | |

S, strictinin (1-*O*-galloyl-4,6-HHDP-β-D-glucose).

[a] 2,3-Valoneyl group instead of 2,3-HHDP group.

[b] 2,3-Lactonized valoneoyl instead of 2,3-HHDP.

[c] DG, -di-*O*-galloylglucose.




and characterized several new acylated glycosides from *M. multiflorum*, including a novel diester (monochaetin **19**) (Isaza et al., 2001) of tetrahydroxy-μ-truxinic acid with two molecules of quercetin-3-*O*-galactoside. We also reported the characterization of new ellagitannin oligomers, nobotanins Q (**21**), R (**20**), S (**22**), and T (**23**), along with 16 known tannins (Isaza et al., 2004). Further investigation of the polar constituents of the plant led to the isolation of additional new polyphenols that were characterized as oligomeric hydrolyzable tannins and named melastoflorins A–D (**24**–**27**).

### 2.2.1. Structure of melastoflorins A–D (24–27)

The new tannins (**24**–**27**) were shown to be oligomers larger than tetramers by their retention volumes larger than those of **22** and **23** in normal phase HPLC (Okuda et al., 1989). They were characterized as ellagitannins composed of galloyl, HHDP, and valoneoyl groups and glucose, based on acid hydrolysis yielding gallic acid, ellagic acid, valoneic acid, dilactone, and glucose, as found for known nobotanins. Furthermore, these new ellagitannins were suggested to be structurally related, based on similarities in their $^{1}H$ and $^{13}C$ NMR spectra, as discussed below.

Melastoflorin A (**24**) was obtained as an off-white amorphous powder and its molecular formula $C_{191}H_{132}O_{122}$ was deduced from a doubly charged molecular ion species at *m/z* 2206 $(M + 2NH_4)^{2+}$ in ESI-MS and NMR data. The pentameric nature of **24** was indicated by five anomeric signals at $\delta_H$ 5.67–6.11 and $\delta_C$ 91.7–95.4 in the $^{1}H$ and $^{13}C$ NMR spectra. The remaining glucose proton signals in the $^{1}H$ NMR spectrum were assigned using $^{1}H$–$^{1}H$ COSY, TOCSY, and $^{1}H$ *J*-resolved spectra that indicated the presence of five $^{1}C_4$ glucopyranose residues (Table 2). The spectrum of **24** indicated the presence of seven galloyl, two HHDP, and four valoneoyl groups, as revealed by seven 2H-singlets [$\delta_H$ 7.26, 7.18, 7.13, 7.12, 7.11, 7.08, 6.92 (galloyl H-2,6)], and sixteen 1H-singlets [$\delta_H$ 7.07, 7.05, 7.03, 6.99 (Val H-6″), 6.58, 6.48, 6.43, 6.42 (HHDP H-3,3′), 6.51, 6.42, 6.41, 6.34 (Val H-3), 6.18, 6.14, 6.09, 5.96 (Val H-3′)] in the aromatic region. Comparing the $^{13}C$ glucose signals of **24** with those of known nobotanin oligomers, those due to four glucose cores (Glc I–IV) in **24** could almost be superimposed on the corresponding resonances of nobotanin S (**22**), while the signals of the remaining glucose (Glc V) were in agreement with those of the monomer pterocaryanin C (**5**) (Yoshida et al.,

Table 2
$^{1}H$[a] and $^{13}C$[b] NMR spectroscopic data for the glucose moiety of melastoflorin A (**24**) in acetone-$d_6$ + $D_2O$

| | | $\delta_H$ | $\delta_C$ | HMBC | |
|---|---|---|---|---|---|
| | | | | –COO– ($\delta_C$) | Aromatic-H |
| Glc I | 1 | 5.67 *d* (8) | 95.4 | 165.86 | 7.12 |
| | 2 | 3.64 *dd* (8,10) | 73.6 | | |
| | 3 | 3.70 *t* (10) | 74.8 | | |
| | 4 | 5.36 *t* (10) | 70.8 | 165.3 | 7.07 |
| | 5 | 3.53 *br d* (10) | 72.8 | | |
| | 6 | 4.65 *d* (12.5) | 63.3 | | |
| | | 3.88 *br d* (12.5) | | 167.19 | 7.18 |
| Glc II | 1 | 5.89 *d* (8.5) | 91.7 | 162.0 | 6.99 |
| | 2 | 5.09[d] | 76.3 | 169.0 | 6.14 |
| | 3 | 5.54 *br t* (10) | 76.9 | | |
| | 4 | 4.97 *t* (10) | 69.2 | 168.1 | 6.48 |
| | 5 | 4.38 *dd* (6.5,10) | 72.7 | | |
| | 6 | 5.08[d] | 63.0 | 168.3 | 6.58 |
| | | 3.67 *br d* (12.5) | | | |
| Glc III | 1 | 5.99 *d* (8.5) | 91.9 | 164.8 | 6.92 |
| | 2 | 5.17 *dd* (8.5,10) | 75.1 | 168.9 | 6.42 |
| | 3 | 5.32 *t* (10) | 77.6 | 169.2 | 5.96 |
| | 4 | 5.73 *t* (10) | 66.6 | 164.6 | 7.03 |
| | 5 | 3.38[c] | 73.7 | | |
| | 6 | 4.89 *d* (12.5) | 63.1 | | |
| | | 3.69 *dd* (4,12.5) | | | |
| Glc IV | 1 | 6.10 *d* (8.5) | 92.0[e] | 164.882 | 7.08 |
| | 2 | 5.07 *dd* (8.5,10) | 76.7 | 168.6 | 6.09 |
| | 3 | 5.79 *t* (10) | 76.4 | | |
| | 4 | 5.09 *t* (19) | 69.4 | 168.2 | 6.51 |
| | 5 | 4.54 *dd* (6,10) | 72.9 | | |
| | 6 | 5.06 *dd* (6,12.5) | 63.2 | 167.8 | 6.18 |
| | | 3.66 *br d* (12.5) | | | |
| Glc V | 1 | 6.11 *d* (8.5) | 92.0[e] | 165.34 | 7.11 |
| | 2 | 5.11 *dd* (8.5,10) | 75.0 | 168.8 | 6.43 |
| | 3 | 5.30 *t* (10) | 77.4 | 169.5 | 6.42 |
| | 4 | 5.51 *t* (10) | 67.7 | 165.1 | 7.05 |
| | 5 | 4.04 *br d* (10) | 73.1 | | |
| | 6 | 4.47 *d* (12.5) | 62.5 | 167.19 | 7.26 |
| | | 4.24 *dd* (4,12.5) | | | |

[a] 500 MHz (*J* in Hz).
[b] 126 MHz.
[c] Overlapped with HDO.
[d] Overlapped.
[e] Overlapped.

1995). Therefore, melastoflorin A (**24**) was deduced to be a pentamer produced biogenetically via oxidative coupling forming a valoneoyl group between **22** and **5**. The binding mode between the tetramer and monomer (i.e., the location and orientation of the newly formed valoneoyl group) was clearly established by HMBC, which showed the three-bond correlations of $\delta_H$ 6.18 (Val H-3′)–$\delta_C$ 168.94–8$_H$ 5.06 (Glc IV H-6); $\delta_H$ 6.51 (Val H-3)–$\delta_C$ l68.17–$\delta_C$ 5.09 (Glc IV H-4); $\delta_H$ 7.05(Val H-6″)–$\delta_C$ l65.1–$\delta_H$ 5.51(Glc V H-4). Other correlations confirming the connectivity of each acyl unit to the glucose residues (Glc I–IV) were also observed, as shown in Table 2. Therefore, the structure of melastoflorin A was deduced to be **24**, which is consistent with that of melastomataceous oligomers composed of alternating monomers of **4** and **5** or their derivatives. Mild methanolysis of **24** afforded a trimeric methyl ester (**28**) and a dimer (**29**), which were identified as products previously prepared from nobotanin K (**13**) (Yoshida et al., 1995) and nobotanin S (**22**), respectively. Based on these spectral and chemical evidence, structure **24** was assigned to melastoflorin A.

The presence of two peaks in the reversed-phase HPLC suggested that melastoflorins B (**25**) and C (**26**) exist as an equilibrium mixture of α- and β-anomers at a glucose core (Okuda et al., 1989). ESI-MS of **25** showed a doubly charged quasi-molecular ion peak at *m*/*z* 2130 $(M + 2NH_4)^{2+}$, which is 152 m.u. (galloyl) less than **24**, corresponding to the molecular formula $C_{184}H_{128}O_{118}$. The $^{1}H$ NMR spectrum of **25**, in which almost all of the signals are paired, was similar to that of **24**, except for the absence of signals due to one galloyl resonance (Table 3). Considering its existence as an anomeric mixture, melastoflorin B is a degalloylated analog of **24** in which one of the glucose cores has a free anomeric hydroxyl group. Normal phase HPLC of the reaction mixture on mild methanolysis of **25** showed peaks due to dimeric and trimeric products identical to the peaks of **29** and **30**, respectively. The latter was identified in a product previously prepared from nobotanin P (Yoshida et al., 1999). This indicated that the galloyl group at O-1 of glucose-V in **24** is lost in **25**. The $^{13}C$ NMR spectroscopic data (Table 4) and HMBC correlations of **25** were consistent with the proposed structure.

Melastoflorin C (**26**) showed a doubly charged quasi-molecular ion peak at *m*/*z* 2281 $(M + 2NH_4)^{2+}$ in ESI-MS, corresponding to the molecular formula $C_{198}H_{134}O_{126}$, making it the largest reported hydrolyzable tannin. The $^{1}H$ NMR spectrum showed paired signals in the aromatic proton region due to three HHDP, four valoneoyl, and six galloyl groups, indicating that **26** has one more HHDP group than **24** and **25**. Comparing the glucose proton signals with those of **25**, distinguishing features were observed in the glucose-I (Glc I) signals; there were remarkable downfield shifts of the Glc I-H-2 [$\delta$ 3.64 *dd* ($J$ = 8, 10 Hz) in **25** → 5.18 *m* in 26] and I-H-3 [$\delta$ 3.74 *t* ($J$ = 10 Hz) → 5.43 *t* ($J$ = 10 Hz)] and Glc I-H-1 [$\delta$ 5.70 *d* ($J$ = 8 Hz) → 6.05 *d* ($J$ = 8.5 Hz)] (Table 3). As the other glucose carbon signals resembled those of **25** (Table 4), melastoflorin C was assumed to have structure **26**. On mild methanolysis, **26** produced the trimeric methyl ester **30**, which was identical with that derived from **25**, and a dimer identified as malabathrin C (**31**) (Yoshida et al., 1992b). Consequently, structure **26** was confirmed chemically for melastoflorin C.

Similarly, structure **27** was deduced for melastoflorin D based on ESI-MS [*m*/*z* 2055 $(M + 2NH_4)^{2+}$], $^{1}H$, and $^{13}C$ NMR comparisons with those of **24**.

Table 3
$^1$H NMR spectroscopic data for the sugar moiety of **25**–**27** in acetone-$d_6$ + $D_2O$ at 500 MHz

| | | **25** | | **26** | | **27** |
|---|---|---|---|---|---|---|
| | | α-Anomer | β-Anomer | α-Anomer | β-Anomer | |
| Glc I | H-l | 5.70 *d* (8) | | 6.05 *d* (8.5) | | 5.70 *d* (8) |
| | H-2 | 3.64 *dd* (8,10) | | 5.18[c] | | 3.65 *dd* (8,9.5) |
| | H-3 | 3.74 *t* (10) | | 5.43 *t* (10) | | 3.73 *t* (9.5) |
| | H-4 | 5.38 *t* (10) | | 5.79 *t* (10) | | 5.38 *t* (9.5) |
| | H-5 | 3.52 [a] | | 3.56 *br d* (10) | | 3.52[b] |
| | H-6 | 4.65 *d* (12) | | 4.79 *d* (12) | | 4.65 *d* (12.5) |
| | | 3.88 *br d* (12) | | 3.84 *d* (12) | | 3.88 *br d* (12.5)[c] |
| Glc II | H-l | 5.87 *d* (8.5) | | 5.93 *d* (8) | | 5.90 *d* (8.5) |
| | H-2 | 5.05 *dd* (8.5,9) | | 5.06 *dd* (8,9.5) | | 5.05 *dd* (8.5,9) |
| | H-3 | 5.52 *dd* (9,10) | | 5.66 *t* (9.5) | | 5.52 *br t* (9,10) |
| | H-4 | 4.97 *t* (10) | | 4.97 *t* (9.5) | | 5.00 *t* (10) |
| | H-5 | 4.35 *dd* (10,6.5) | | 4.38 *m* | | 4.36 *dd* (10,5.5) |
| | H-6 | 5.10 *d* (12,6) | | 5.10[b] | | 5.11 *dd* (6.5,13.5) |
| | | 3.66[c] | | 3.69 *d* (14) | | 3.68 *d* (13.5) |
| Glc III | H-l | 5.99 *d* (8.5) | 6.00 *d* (8.5) | 6.00 *d* (8.5) | 6.01 *d* (8.5) | 6.01 *d* (8) |
| | H-2 | 5.15 *dd* (8.5,9.5) | | 5.17[c] | | 5.17 *dd* (8,10) |
| | H-3 | 5.32 *t* (9.5) | | 5.35 *t* (10) | 5.33 *t* (10) | 5.34 *t* (10) |
| | H-4 | 5.72 *t* (9.5) | | 5.75 *t* (10) | | 5.74 *t* (10) |
| | H-5 | 3.39[a] | | 3.39[a] | | 3.40 *br d* (10) |
| | H-6 | 3.73[c] | | 4.89 *d* (13) | | 4.90 *d* (13.5) |
| | | 4.89 *d* (12.5) | | 3.73 *d* (12) | | 3.70 *dd* (13.5) |
| Glc IV | H-l | 6.11 *d* (8.5) | 6.10 *d* (8.5) | 6.11 *d* (8.5) | 6.10 *d* (8.5) | 6.10 *d* (8.5) |
| | H-2 | 5.24 *t* (8.5) | 5.18 | 5.26 *t* (8.5) | 5.18 *dd* (8.5,10) | 5.08 *dd* (8.5,10)[c] |
| | H-3 | 5.83 *t* (10) | 5.79 *t* (10) | 5.82 *dd* (8. 5,10) | 5.79 *t* (10) | 5.81 *t* (9) |
| | H-4 | 5.13 *t* (10) | 5.09 *t* (10) | 5.13 *t* (10) | 5.09 *t* (10) | 5.09[c] |
| | H-5 | 4.55 *m* | 4.52 *m* | 4.55 *m* | 4.52 *m* overlapped | 4.57 *dd* (10,6) |
| | H-6 | 5.10 *dd* (12,4) | | 5.11[b] | | 5.12 *dd* (13,6)[c] |
| | | 3.76 *br d* (12) | | 3.74 *d* (12) | | 3.81 *d* (13)[c] |
| Glc V | H-l | 5.42 *d* (3.5) | 5.07 *d* (8) | 5.44 *d* (3.5) | 5.08 *d* (8) | 5.72 *d* (8) |
| | H-2 | 5.01 *dd* (3.5,10) | 4.81 *dd* (8,10) | 5.01 *dd* (3.5,9.5) | 4.81 *dd* (8,9.5) | 3.56 *dd* (8,9.5) |
| | H-3 | 5.54 *t* (10) | 5.14 *t* (10) | 5.58 *t* (9.5) | 5.15[c] | 3.42 [b] |
| | H-4 | 5.48 *t* (10) | 5.46 *t* (10) | 5.49 *t* (9.5) | 5.47 *t* (10) | 5.20 *t* (10) |
| | H-5 | 4.43 *br d* (10) | 3.78 *m* | 4.35 *m* | 3.76 *brd* (10) | 3.89 *m*[c] |
| | H-6 | 4.40 *d* (12) | 4.57 *d* (12) | 4.42 *d* (12.5) | 4.56 *d* (12) | 4.49 *br d* (12.5) |
| | | 4.13 *dd* (12,3.5) | 4.22 *dd* (12,2) | 4.12 *dd* (12.5,4) | 4.20 *dd* (12.5,4) | 4.20 *dd* (12.5,4) |

[a] Overlapped with solvent.
[b] Overlapped with each other.
[c] Overlapped with other signals.

The $^1$H NMR spectrum exhibited five anomeric proton signals (each *d*, $J$ = 8–8.5 Hz), indicating its pentameric nature. The spectrum also showed seven 2H-singlets and fourteen 1H-singlets in the aromatic proton region, which suggested the presence of seven galloyl, four valoneoyl, and one HHDP group. Therefore, one of the two HHDP groups in **24** is eliminated in **27**. The combination of $^1$H–$^1$H COSY, TOCSY, and *J*-resolved NMR spectra allowed us to assign most of the glucose proton signals (Table 3). As a result, the four sets of glucose proton signals in **27** were in agreement with those of glucoses I–IV in melastoflorin A (**24**). The H-1 to H-4 signals of the remaining glucose core were found to resonate at a higher field than the corresponding signals of Glc-V in **24** (Table 3), indicating that the hydroxyl groups at C-2 and C-3 on glucose-V in **27** are not acylated. In fact, one HHDP group in **27** was located at the O-4/O-6 of Glc-II due to the production of **29** on mild methanolysis of **27**. The $^{13}$C NMR data (Table 4) were also consistent with the proposed structure (**27**).

The CD spectra clearly showed that the atropisomers of the chiral HHDP and valoneoyl groups in the melastoflorin molecules (**24**–**27**) were all in the *S*-series, since the spectra all showed a strong positive Cotton effect around 230 nm (Okuda et al., 1982), although the amplitude of the Cotton effect was dependent on the number of chiral biphenyl units in the molecule (see Section 3).

Although many oligomeric ellagitannins have been found in nature, most are dimers (ca. 80%), while the numbers of trimers and tetramers are limited. Only

Table 4
$^{13}C$ NMR spectroscopic data for the sugar moiety of **25**–**27** in acetone-$d_6$ + $D_2O$ at 126 MHz

| | | **25** | | **26** | | **27** |
|---|---|---|---|---|---|---|
| | | α-Anomer | β-Anomer | α-Anomer | β-Anomer | |
| Glc I | C-1 | 95.54 | | 92.1 | | 95.5 |
| | C-2 | 73.79 | | 75.5 | | 73.8 |
| | C-3 | 74.96 | | 77.712 | | 75.0 |
| | C-4 | 70.93 | | 67.07 | | 71.0 |
| | C-5 | 73.09 | | 73.702 | | 72.9 |
| | C-6 | 63.35 | | 63.3 | | 63.4 |
| Glc II | C-1 | 91.79 | | 91.89 | | 91.8 |
| | C-2 | 76.52 | 76.49 | 76.89 | | 76.3 |
| | C-3 | 77.03 | | 76.95 | | 77.0 |
| | C-4 | 69.23 | | 69.35 | | 69.2 |
| | C-5 | 72.89 | | 72.9 | | 73.7 |
| | C-6 | 63.34 | | 63.2 | | 63.1 |
| Glc III | C-1 | 92.13 | | 92.127 | | 92.1 |
| | C-2 | 76.4 | | 76.4 | | 75.2 |
| | C-3 | 77.71 | | 77.96 | | 77.7 |
| | C-4 | 66.70 | | 66.70 | | 66.7 |
| | C-5 | 73.70 | | 73.762 | | 73.9 |
| | C-6 | 63.35 | | 63.35 | | 63.1 |
| Glc IV | C-1 | 92.13 | | 92.127 | | 92.1 |
| | C-2 | 75.15 | | 75.5 | | 76.7 |
| | C-3 | 77.03 | | 76.95 | | 76.6 |
| | C-4 | 69.53 | 69.56 | 66.69 | | 69.7 |
| | C-5 | 72.89 | | 72.907 | | 73.1 |
| | C-6 | 63.35 | | 63.11 | | 63.3 |
| Glc V | C-1 | 91.21 | 94.73 | 91.20 | 94.72 | 95.3 |
| | C-2 | 75.07 | 77.23 | 75.05 | 77.25 | 74.7 |
| | C-3 | 75.3 | 77.71 | 75.34 | 76.50 | 75.2 |
| | C-4 | 68.53 | 68.18 | 68.56 | 68.21 | 71.1 |
| | C-5 | 68.10 | 72.67 | 68.20 | 72.67 | 73.4 |
| | C-6 | 62.9 | 63.0 | 63.10 | | 63.8 |

one pentamer, castaneanin D from the heartwood of the Japanese chestnut tree, is known (Tanaka et al., 1996); it is a condensate resulting from C–C bond formation involving five molecules of a *C*-glucosidic tannin, castalagin. Therefore, melastoflorins A–D (**24**–**27**) are the first examples of pentameric hydrolyzable tannins that are composed of different monomeric units, each with a $^4C_1$ glucopyranose residue. Our findings should prompt further searches for this class of higher oligomers in nature.

## 3. Experimental

### 3.1. General

Optical rotations were measured using a JASCO DIP-1000 polarimeter, whereas UV spectra were obtained using a Hitachi U-2000 spectrophotometer. CD spectra were acquired on a JASCO J-720 spectrometer. The $^1H$ and $^{13}C$ NMR spectra were recorded on a Varian VXR-500 instrument (500 MHz for $^1H$, and 126 MHz for $^{13}C$), and the chemical shifts are given in $\delta$ (ppm) values relative to that of the solvent [$(CD_3)_2CO$ ($\delta_H$ 2.04; $\delta_H$ 29.8)] and tetramethylsilane. The standard pulse sequences that were programmed into the instrument (VXR-500) were used for each two-dimensional measurement. The $J_{CH}$ value was set at 6 Hz in the HMBC spectra. ESI-MS, including high-resolution mass spectra, were recorded on a Micromass Auto Spec OA-TOF mass spectrometer (solvent: 50% aqueous MeOH containing 0.1% $AcONH_4$; flow rate: 0.02 ml/min). Normal-phase HPLC was conducted on a YMC-Pack SIL A-003 column (4.6 i.d. × 250 mm; YMC Co., Ltd.) and was developed at room temperature with a solution of *n*-hexane/MeOH/tetrahydrofuran/formic acid (solvent A, 55:33:11:1; solvent B, 42.5:42.5:10:5) containing 450 mg/l oxalic acid (flow rate: 1.5 ml/min; detection: UV 280 nm). Reverse phase HPLC analysis and preparative HPLC were performed with a YMC-Pack ODS-A A-302 column (4.6 mm i.d. × 150 mm) and developed at 40 °C with MeOH/$H_2O$ (4:1). Column chromatography was carried out on Silica gel 60 (Merck), whereas preparative TLC was performed on Silica gel 60 $F_{254}$ (Merck).

### 3.2. Plant material

*Monochaetum multiflorum* (Bompl.) Naudin was collected near Manizales City, Caldas, Colombia, on August 12, 1997. Dr. Gustavo Lozano C. of University Nacional de Colombia identified the plant and a voucher specimen was deposited at Herbario Nacional de Colombia (COL) No. 361696.

### 3.3. Isolation and purification

Dried leaves (400 g) of *M. multiflorum* were homogenized with acetone–$H_2O$ (7:3), filtered, and concentrated in vacuo. The concentrated solution was subjected to liquid–liquid partition to give four extracts: $Et_2O$ (4.6 g), EtOAc (13.4 g), *n*-BuOH (33.8 g), and water-soluble (54.3 g) portions. The water-soluble portion (54 g) was separated using CC over Diaion HP-20 (8 × 70 cm) in a step-wise gradient of aqueous MeOH. The MeOH–$H_2O$ (60:40) (Fraction 1 of the three fractions) eluate (777 mg) was purified using a YMC ODS AQ 120 S-50 (1.1 × 45 cm) column with 5–50% aqueous MeOH to afford melastoflorins B (**25**) (21 mg) and D (**27**) (26 mg). Fractions 2 and 3 of the MeOH–$H_2O$ (60:40) eluate (481 mg) were subjected to repeated chromatography over YMC ODS AQ120 S-50 (1.1 × 45 cm) with aqueous MeOH to give melastoflorins A (**24**) (35 mg), B (**25**) (27 mg), C (**26**) (5.5 mg), and D (**27**) (29 mg).

### 3.4. Melastoflorin A (**24**)

Off-white amorphous powder; $[\alpha]_D^{27}$ +65.2° (MeOH; *c* 1.0); UV (MeOH) $\lambda_{max}$ nm (log ε): 217 (5.62), 271 (5.28); CD (MeOH) [θ] (nm) $+9.1\times10^5$ (226), $+4.7\times10^5$ (238), $-2.8\times10^5$ (262), $+1.2\times10^5$ (282), $-4.8\times10^4$ (310); positive ESI-MS *m/z*: 2206 $[M + 2NH_4]^{2+}$; $^1$H NMR δ: 7.26, 7.18, 7.13, 7.12, 7.11, 7.08, 6.92 (each 2H, galloyl-H), 7.07, 7.05, 7.03, 6.99 (each 1H, valoneoyl H-6″), 6.58, 6.48, 6.43, 6.42 (each 1H, HHDP H-3,3′), 6.51, 6.42, 6.41, 6.34 (each 1H, valoneoyl H-3), 6.18, 6.14, 6.09, 5.96 (each 1H, valoneoyl H-3′), sugar protons, see Table 2, $^{13}$C NMR δ: 120.7 (2C), 119.3, 120.0, 120.9, 119.2 (2C) (Gall C-1), 110.2 (3C), 110.1 (2C), 110.0 (2C) (Gall C-2), 139.2, 139.0, 138.9, 139.8 (2C), 139.9, 140.0 (Gall C-3), 145.8 (3C), 146.0 (2C), 145.7 (2C) (Gall C-4), 139.2, 139.0, 138.9, 139.8 (2C), 139.9, 140.0 (Gall C-5), 110.2 (3C), 110.1 (2C), 110.0 (2C) (Gall C-6), 167.19 (2C), 166.78, 165.86, 165.34, 164.882, 164.8 (Gall C-7), 114.1 (2C), 113.6, 111.7, 116.1, 114.6, 114.5, 114.3, 117.0, 116.7, 116.5, 115.9 (Val C-1), 135.6 (2C), 135.8, 138.1, 126.0, 125.6 (2C), 125.4 (2C), 124.8, 125.3, 125.2 (Val C-2), 140.5, 140.6, 140.7, 139.5, 107.5, 107.4, 107.3, 106.7, 104.6, 104.2, 103.1, 102.4 (Val C-3), 140.1, 140.2, 140.3, 142.7, 145.2, 145.0 (2C), 145.1, 146.9, 147.0, 146.6, 146.7 (Val C-4), 142.9, 143.2, 143.4, 141.4, 136.4, 136.2 (2C), 136.0 (2C), 136.9, 136.7, 136.5 (Val C-5), 110.2 (3C), 110.8, 144.7 (2C), 144.6, 144.4 (2C), 144.2 (3C) (Val C-6), 165.3, 165.1, 164.6, 162.0, 168.2, 168.9, 169.7, 169.5, 167.8, 169.0, 168.6, 169.2 (Val C-7), 114.9, 115.6, 115.4, 114.3 (HHDP C-1), 125.6 (2C), 125.9, 125.7 (HHDP C-2), 107.3, 107.8, 107.4, 106.8 (HHDP C-3), 145.2, 145.3, 145.0 (2C) (HHDP C-4), 136.4 (2C), 136.3, 136.1 (HHDP C-5), 144.9 (2C), 144.8, 144.7 (HHDP C-6), 168.1, 168.3, 169.5, 168.8 (HHDP C-7), sugar and ester carbonyl carbons, see Table 2.

### 3.5. Melastoflorin B (**25**)

Off-white amorphous powder; $[\alpha]_D^{27}$ +62.9° (MeOH; *c* 1.0); UV (MeOH) $\lambda_{max}$ nm (log ε): 217 (5.66), 271 (5.32); CD (MeOH) [θ] (nm) $+1.0\times10^6$ (226), $+5.7\times10^5$ (238), $-3.1\times10^5$ (262), $+1.2\times10^5$ (282), $-7.2\times10^4$ (310); positive ESI-MS *m/z*: 2130 $[M + 2NH_4]^{2+}$; $^1$H NMR δ: 7.24, 7.18, 7.13, 7.12, 7.09, 6.94 (each 2H, galloyl-H), 7.05, 7.001, 6.998, 6.98 (each 1H, valoneoyl H-6″), 6.58, 6.51, 6.51, 6.434, 6.432, 6.35, 6.17, 6.11,6.11, 6.09, 5.96 (each 1H, HHDP H-3,3′, valoneoyl H-3,3′), sugar protons, see Table 3, $^{13}$C NMR δ: 102.6, 103.1, 104.4, 104.5/104.6 (Val C-3′), 106.47/106.7, 106.65, 106.7, 107.4, 107.5, 107.6, 107.8, 107.9 (Val C-3, HHDP C-3,3′), 110.0, 110.06, 110.13 (2C), 110.17 (4C), 110.2 (6C), 110.25/110.3, 110.4/110.7 (Galloyl C-2,6, Val C-6″), 111.9, 113.87/113.90, 114.1/114.4, 114.3 (Val C-1″), 114.68/114.9, 114.8 (3C), 115.3/115.9, 115.6 (2C), 115.96 (Val C-1, HHDP C-1,1′), 116.15, 116.6/116.7, 116.8, 117.0/117.3 (Val C-1′), 119.4, 119.6, 120.3, 120.92/120.94, 121.19, 121.25/121.28 (Galloyl C-1), 124.87/124.92, 125.36, 125.39, 125.5, 125.53, 125.7/125.8, 125.85, 125.97/126.0, 126.1/126.3, 126.16, 126.2 (2C) (Val C-2,2′, HHDP C-2,2′), 135.6, 135.7, 135.97/136.0, 138.1 (Val C-2″), 136.2 (4C), 136.28/136.36, 136.4, 136.5, 136.53 (4C), 136.6/136.9 (Val C-5,5′, HHDP C-5,5′), 139.0/139.2, 139.7, 139.88, 139.90, 140.16 (2C each, Galloyl C-3,5), 139.5 (Val C-3″), 140.25, 140.66, 140.7 (2C each, Val C-3″,4″), 142.7 (Val C-4″), 141.4, 143.0, 143.3, 143.4/143.5 (Val C-5′), 144.1, 144.18/144.23, 144.3, 144.4/144.6, 144.75, 144.8 (Val C-6,6′), 144.9, 144.97, 145.0 (3C), 145.07/145.1, 145.2 (2C) (HHDP C-4,4″,6,6′), 145.65/145.8, 145.75, 145.87, 145.90, 145.94, 146.1 (Galloyl C-4), 146.6, 146.7, 146.84/146.87, 147.1 (Val C-4″), 161.9, 164.5, 164.7/164.8, 165.07/165.3 (Vail C-7″), 164.8, 165.2, 165.7, 166.7/166.8, 167.18, 167.23 (Galloyl C-7″), 167.8, 168.91, 169.0/169.1, 169.2 (Val C-7′), 168.0, 168.2, (HHDP C-7), 168.87, 169.5 (HHDP C-7′), 168.17/168.31, 168.6/168.8, 169.61/169.64, 169.7/170.0 (Val C-7), sugar carbons, see Table 4.

### 3.6. Melastoflorin C (**26**)

Off-white amorphous powder; $[\alpha]_D^{27}$ +60.0° (MeOH; *c* 1.0); UV (MeOH) $\lambda_{max}$ nm (log ε): 217 (5.63), 271 (5.29); CD (MeOH) [θ] (nm) $+1.5\times10^6$ (226), $+8.1\times10^5$ (238), $-4.7\times10^5$ (262), $+1.9\times10^5$ (282), $-1.1\times10^4$ (310); positive ESI-MS *m/z*: 2281 $[M + 2NH_4]^{2+}$; $^1$H NMR δ: 6.94–7.26 (2H × 6, galloyl-H), 5.97–7.14 (1H × 18, valoneoyl H-3,3′,6″, HHDP H-3,3′), sugar protons, see Table 3, $^{13}$C NMR δ: 102.6 (2C), 104.4, 104.6/104.9 (Val C-3′), 106.7, 107.0, 107.01/107.05, 107.2, 107.4 (2C), 107.45/107.49, 107.52/107.55, 107.6/107.63, 107.8 (Val C-3, HHDPC-3,3′), 110.1 (14C Galloyl C-2,6), 110.46, 110.7 (Val C-6″), 111.9, 113.85/113.90, 113.94, 114.2 (Val C-1″), 114.22, 114.3/114.31, 114.37, 114.41, 114.52, 114.65, 114.8/115.26, 114.88, 115.62, 115.88/115.91 (Val C-1, HHDP C-1,1′), 116.2, 116.6/116.7, 116,8, 117.0/117.4 (Val C-1′), 119.4 (2C), 119.6, 120.8, 120.9, 121.23/121.26 (Galloyl C-1), 124.86/124.92, 125.33, 125.36, 125.5, 125.7, 125.75, 125.76, 125.84, 125.9, 126.05/126.08, 126.14, 126.16, 126.21, 126.26 (Val C-2,2′, HHDP C-2,2′), 135.7, 135.85, 136.0/136.1, 138.1 (Val C-2″), 136.2 (2C), 136.4, 136.45 (6C), 136.5 (3C), 136.8 (Val C-5,5′, HHDP C-5,5′), 138.89, 139.0, 139.2, 139.3, 139.85, 139.94 (2C each, Galloyl C-3,5), 139.70/139.75 (Val C-3″), 140.62, 140.7, 140.78 (2C each, Val C-3″,4″), 142.71 (Val C-4″), 141.4, 142.99, 143.5 (Val C-5′), 144.1, 144.3, 144.44, 144.48 (2C), 144.7/144.75 (Val C-6,6′), 144.88 (2C), 144.7/144.75 (Val C-6,6′), 144.88 (2C), 144.88 (2C), 144.95 (2C), 145.0 (2C),

145.1 (2C), 145.17 (4C) (HHDP C-4,4″, 6,6′), 145.65/145.70, 145.76/145.80, 145.89, 145.94, 146.1 (2C) (Galloyl C-4), 146.6, 146.7, 146.8, 146.84/146.86 (Val C-4″), 161.9, 164.55/154.66, 164.74/164.8, 165.07/165.27 Val (Val C-7″), 164.85, 164.88, 164.9, 166.7/166.8, 167.2 (2C) (Galloyl C-7), 167.86, 168.91, 168.59/168.8, 169.24 (Val C-7′), 168.0, 168.27, 168.69 (HHDP C-7), 169.3, 169.59, 169.68, (HHDP C-7′), 168.18/168.3, 168.6/168.66, 169.08/168.99, 169.75/170. 1, sugar carbons, see Table 4.

### 3.7. Melastoflorin D (**27**)

Off-white amorphous powder; $[\alpha]_D^{27}$ +37.0° (MeOH; *c* 1.0); UV (MeOH) $\lambda_{max}$ nm (log $\varepsilon$): 216 (5.53), 273 (5.16); CD (MeOH) [$\theta$] (nm) $+6.3\times10^5$ (226), $+3.6\times10^5$ (238), $-1.9\times10^5$ (262), $+4.3\times10^5$ (282), $-4.2\times10^4$ (310); positive ESI-MS *m/z*: 2055 $[M + 2NH_4]^{2+}$; $^1$H NMR $\delta$: 7.24, 7.18, 7.14, 7.12, 7.11, 7.08, 6.93 (each 2H, galloyl-H), 7.07, 7.07, 7.05, 6.99 (each 1H, valoneoyl H-6″), 6.58, 6.55, 6.51, 6.45, 6.42, 6.35 (each 1H, HHDP H-3,3′ arid valonepyl H-3), 6.17, 6.12, 6.09, 5.97 (each 1H, valoneoyl H-3′), sugar protons, see Table 3,$^{13}$C NMR $\delta$: 102.4, 103.3, 104.5 (2C) (Val C3′), 107.0, 107.4, 107.5, 106.7 (Val C-3), 107.6 (2C) (HHDP C-3,3′), 109.9 (2C), 110.0 (2C) (Val C-6″), 110.2 (14C) (Galloyl C-2,6), 111.9, 113.8, 114.3, 114.4 (Val C-1″), 114.8, 114.9 (HHDP C-1,1′), 115.7, 116.0, 116.2, 116.2 (Val C-1), 117.4, 116.8, 116.5, 116.2 (Val C-1′), 119.4, 119.5, 120.2 (2C), 120.9, 121.1 (2C) (Galloyl C-1), 125.6, 125.65 (HHDP C-3,3′), 125.7, 125.8, 125.9, 126.1 (Val C-2), 125.0, 125.3, 125.4, 125.5 (Val C-2′), 135.6, 135.7, 135.8, 138.2 (Val C-2″), 136.0 (2C) (HHDP C-5,5′), 136.2 (2C), 136.3 (2C) (Val C-5), 136.5, 136.6 (2C), 136.9 (Val C-5′), 138.9, 139.3, 139.6, 139.8, 139.9, 140.0, 140.2, (2C each, Galloyl C-3,5), 140.1, 140.4, 140.7, 140.8 (Val C-3″), 139.9, 141.4, 140.2 (2C) (Val C-4″), 142.7, 143.0, 143.3, 143.4 (Val C-5′), 144.7 (2C), 144.3, 144.4 (Val C-6′), 144.8, 145.0, 144.9 (2C) (Val C-6), 145.0 (3C), 145.1 (Val C-4), 145.3 (2C), 145.2 (2C) (HHDP C-4,4″,6,6′), 145.84, 145.87, 145.91, 145.95, 146.0, 146.1 (2C) (Galloyl C-4), 147.2, 147.5, 146.8, 146.7 (Val C-4″), 162.0, 165.3, 165.4, 164.6 (Val C-7″), 164.7, 164.9, 165.8, 166.0, 166.8, 167.2, 167.3 (Galloyl C-7), 168.3, 168.89 (HHDP C-7,7′), 168.2, 168.91, 169.5, 169.7 (Val C-7), 168.1, 168.6,169.0, 169.2 (Val C-7′), sugar carbons, see Table 4.

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