European Journal of Medicinal Chemistry 58 (2012) 418–430

Contents lists available at SciVerse ScienceDirect

European Journal of Medicinal Chemistry

journal homepage: http://www.elsevier.com/locate/ejmech

Original article

# Synthesis and antiproliferative activity of helonioside A, 3′,4′,6′-tri-*O*-feruloylsucrose, lapathoside C and their analogs

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ARTICLE INFO

*Article history:*
Received 5 August 2012
Received in revised form
17 October 2012
Accepted 18 October 2012
Available online 27 October 2012

*Keywords:*
Helonioside A, 3′,4′,6′-tri-*O*-feruloylsucrose
Lapathoside C
Phenylpropanoid sucrose esters
Antiproliferative activity
Isopropylidene acetal
Regioselective acylation
Sucrose esters
HeLa cells

ABSTRACT

The first total synthesis of natural phenylpropanoid sucrose esters (PSEs) helonioside A **1**, 3′,4′,6′-tri-*O*-feruloylsucrose **2** and lapathoside C **3** along with 17 unnatural PSE analogs has been successfully accomplished in a short and simple synthetic route. A selected set of 17 synthesized PSEs were evaluated for the antiproliferative activity against human cervical epithelioid carcinoma (HeLa) cell lines using MTS assay method. Eleven (11) compounds showed significant antiproliferative activity with their $IC_{50}$values ranging from 0.16 to 6.01 μM. The structure–activity-relationship studies revealed that the antiproliferative activity is influenced by the lipophilicity and number of feruloyl substituents on these compounds. The preliminary screening indicated that these compounds are potentially very valuable source for new lead chemotherapeutics.



## 1. Introduction

*O*-feruloylsucroses belong to an important class of phenylpropanoid sucrose esters (PSEs) and are found in various medicinal plants with promising biological activities [1]. For example, helonioside A **1** (i.e. 3′,6′-di-*O*-feruloylsucrose) (Fig. 1) was isolated from the extracts of various liliaceous plants of *Heloniopsis orientalis* [2], *Smilax glabra* [3], *Smilax china* [4], *Trillium kamtschaticum* [5], *Paris polyphylla var. yunnanensis* [6,7], Smilacaceous plants of *Smilax bracteata* [8] and Polygonaceous plants of *Polygonum perfoliatum* [9], *Bistorta manshuriensis* [10] and *Rumex dentatus* [11]. The whole plant *P. polyphylla* var. *yunnanensis* (Liliaceae) has been used in traditional Chinese medicine to treat lung, liver and laryngeal carcinoma [6,12]. The extracts of *H. orientalis* displayed potent cytotoxicity against lung carcinoma cell lines (A549) with $IC_{50}$ value of 4.6 μg/mL and colon carcinoma cell lines (Col2) with $IC_{50}$ of 4.5 μg/mL [13]. The *S. china* crude extracts were found to have antimutagenic activities while its tuber showed significant cytotoxicity against various tumor cell lines [4,14]. Yan et al. reported that helonioside A **1** exhibited cytotoxic effects in a dose-dependent manner against mice lung adenocarcinoma cell line (LA 795) [6,7]. Helonioside A **1** also displayed potent antioxidant activity against stable DPPH-free radical at a concentration of 0.02 mM [5]. 3′,4′,6′-tri-*O*-feruloylsucrose **2** (Fig. 1) was isolated from the ethanol extracts of the rhizomes and roots of *Smilax riparia* [15]. Lapathoside C **3** (i.e. 6-mono-*O*-feruloyl-3′,6′-di-*O*-coumaroylsucrose) (Fig. 1) was isolated from the various Polygonaceous plant species such as *Polygonum lapathifolium* [16], *Polygonum sachalinensis* [17] and *Polygonum cuspidatum* [18]. The *Smilax* genus of Liliaceous Plants and *Polygonum* genus of the Polygonaceous plants and their extracts are widely used in traditional and folk medicines for the treatment of various disorders and diseases such as cancer, tumors, jaundice, coughs, carbuncles, dysentery ... etc. [1].

The entire published research in the area of PSEs focusses on the extraction, characterization and biological screening of these compounds [1,19–22]. With the exception of two reports [23,24], the synthesis of this large class of compounds (about 150 natural PSEs have been reported to date) has not been reported. In one of these reports, our group has successfully demonstrated the synthesis of lapathoside D and its analogs and reported their

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http://dx.doi.org/10.1016/j.ejmech.2012.10.034

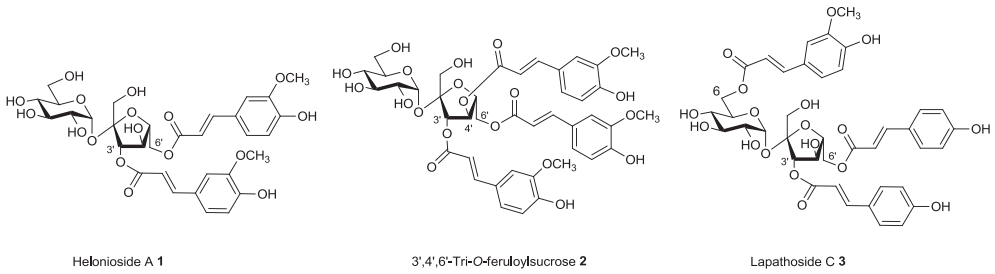



**Fig. 1.** Structure of helonioside A **1**, 3′,4′,6′-tri-*O*-feruloylsucrose **2** and lapathoside C **3**.

antiproliferative activities [24]. In continuation to our on-going research efforts for developing practical and viable synthetic routes and exploring the potential of various PSEs as anticancer drug lead compounds [24], we became interested in the synthesis of helonioside A **1**, 3′,4′,6′-tri-*O*-feruloylsucrose **2**, lapathoside C **3** and their analogs.

Herein, we report the first total syntheses of helonioside A **1**, 3′,4′,6′-tri-*O*-feruloylsucrose **2**, lapathoside C **3** and their unnatural analogs. We also report on their antiproliferative activities against human cervical epithelioid carcinoma (HeLa) cell lines and examine the structural features that contribute to better activities.

## 2. Results and discussion

### 2.1. Chemistry

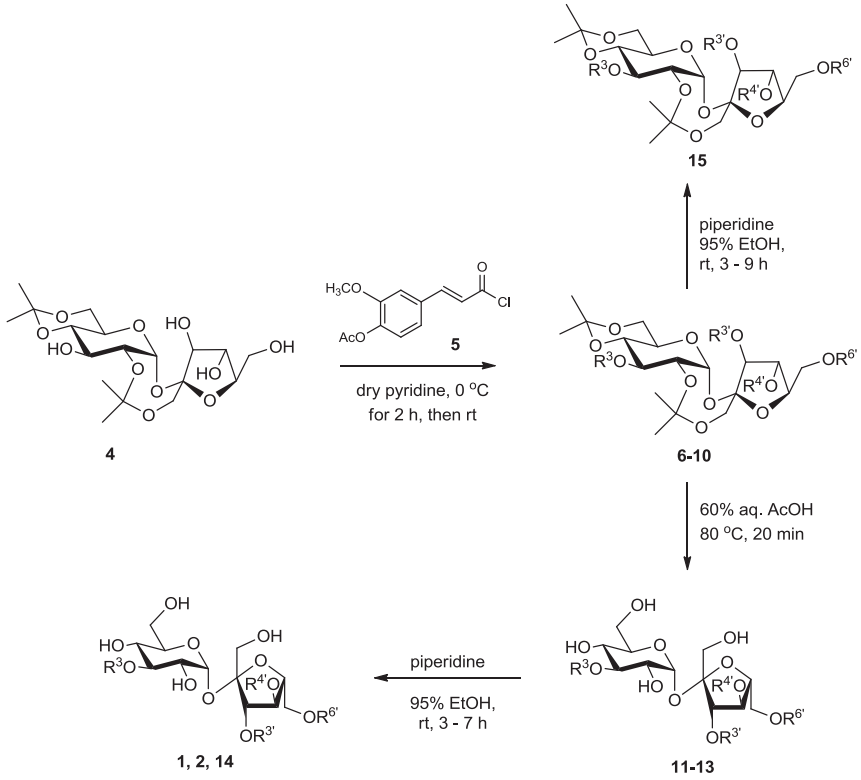
The synthesis of the target compounds, helonioside A **1**, 3′,4′,6′-tri-*O*-feruloylsucrose **2**, lapathoside C **3** and their analogs was attempted by regio- and chemoselective acylation of the versatile substrate 2,1′:4,6-di-*O*-isopropylidene sucrose **4** [24,25].

#### 2.1.1. Preparation of helonioside A *1*, 3′,4′,6′-tri-O-feruloylsucrose *2* and their analogs

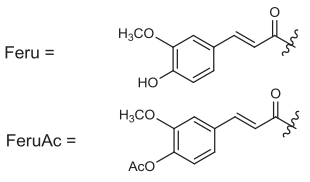
At the outset, when di-*O*-isopropylidene sucrose **4** [24,25] was reacted with 1.1 equiv of *p*-acetoxyferuloyl chloride **5** [26] at r.t. for 3 days (Scheme 1), compound **6** was obtained as the major product in 31% yield along with compounds **8** (11% yield) and **9** (12% yield) as white solids.

Reaction of di-*O*-isopropylidene sucrose **4** with 2.2 mol equiv of *p*-acetoxyferuloyl chloride **5** at r.t. (Scheme 1) afforded compound **8** as the major product (30% yield) along with compound **6** in 3% yield. Clearly this result indicated that the use of 2.2 mol instead of 1.1 mol selectively gave the di-acylated product **8** over the mono-acylated product **6**. Attempts to increase the yield by varying the reaction conditions (time, higher temperature) were not successful.

In order to prepare the tri-acylated compounds, di-*O*-isopropylidene sucrose **4** was reacted with 3.3 mol equiv of *p*-acetoxyferuloyl chloride **5** (Scheme 1). Interestingly, the di-acylated product **8** was found to be the major reaction product (44% yield) while the tri-acylated product **9** was obtained in 26% yield, both as white solids. Likewise, reaction between 4.4 mol equiv of




| Compound | $R^3$ | $R^{3'}$ | $R^{4'}$ | $R^{6'}$ |
|---|---|---|---|---|
| 6 | H | H | H | FeruAc |
| 7 | H | FeruAc | H | H |
| 8 | H | FeruAc | H | FeruAc |
| 9 | H | FeruAc | FeruAc | FeruAc |
| 10 | FeruAc | FeruAc | FeruAc | FeruAc |
| 11 | H | FeruAc | H | FeruAc |
| 12 | H | FeruAc | FeruAc | FeruAc |
| 13 | FeruAc | FeruAc | FeruAc | FeruAc |
| 1 | H | Feru | H | Feru |
| 2 | H | Feru | Feru | Feru |
| 14 | Feru | Feru | Feru | Feru |
| 15 | H | Feru | Feru | Feru |




**Scheme 1.** Regio- and chemoselective acylation of di-*O*-isopropylidene **4** with *p*-acetoxyferuloyl chloride **5**.

*p*-acetoxyferuloyl chloride **5** and di-*O*-isopropylidene sucrose **4** (Scheme 1), gave the expected tetra-acylated derivative **10** in 44% yield along with the tri-acylated product **9** (35% yield). These results indicated: (1) the reactivity of the OH groups are in the order of 6′-OH > 3′-OH > 4′-OH > 3-OH; (2) with the correct number of mole equiv of *p*-acetoxyferuloyl chloride **5**, we can have the choice to prepare the mono-, di-, tri- and tetra-acylated compounds; and (3) analogs (or unnatural *O*-feruloylsucroses) can easily be prepared by controlling the number and position of *p*-acetoxyferuloyl chloride **5**.

Next, compounds **8**–**10** were subjected separately to acetal deprotection using 60% aq. AcOH [24]. The crude products were purified by recrystallization from EtOAc or column chromatography ($CH_2Cl_2$/EtOAc) to afford compounds **11**–**13**, respectively, as white solids in good yields ranging from 67% to 89% (Scheme 1). In comparison to the NMR spectra of compounds **8**–**10**, compounds **11**–**13** revealed the absence of the characteristic signals for the two isopropylidene moieties usually observed in the $^1$H NMR spectra at $\delta$ 1.20–1.53 ppm (4× s, 12H, 2 ($CH_3$)$_2$C) and in the $^{13}$C NMR spectra at $\delta$ 19.0–29.1 ppm (4 × 2 ($CH_3$)$_2$C) and 99.6–101.8 ppm (2× ($CH_3$)$_2$*C*). The typical value of the chemical shift of the anomeric (H-1) protons for compounds **11**–**13** shifted downfield at $\delta$ 5.50 ppm compared to the same for compounds **8**–**10** at $\delta$ 6.16 ppm.

Successful deacetylation of the phenyl rings of compounds **11**–**13** would afford the final compounds helonioside A **1**, 3′,4′,6′-tri-*O*-feruloylsucrose **2** and the analog **14**. Hatfield et al. [26] demonstrated the successful deacetylation of a similar sugar, the methyl-5-*O*-acetylferuloyl-α-*L*-arabinofuranoside, using piperidine-95% ethanol in good yield. Gladly, when compounds **11**–**13** were subjected separately to the Hatfield et al. [26] deacetylation conditions, helonioside A **1**, 3′,4′,6′-tri-*O*-feruloylsucrose **2** and 3,3′,4′,6′-tetra-*O*-feruloylsucrose **14** were successfully obtained as white solids in 68%, 65% and 76% yield, respectively (Scheme 1). The success of removal of the acetyl protecting group from the feruloyl moiety selectively is due to the fact that the ferulic ester bond is stronger than an acetate ester bond, allowing the differentiation between the two acyl groups [27]. The $^1$H and $^{13}$C NMR spectra of compounds **1**, **2** and **14** indicated the loss of the characteristic signals for the acetyl moieties on the phenyl ring, represented by the characteristic proton signals at $\delta$ 2.26–2.32 ppm (s, 3H, H-11″ for the COC*H*$_3$) and acetyl ester carbon signals at $\delta$ 20.5–20.9 ppm (C-11″ for $COCH_3$) and also carbonyl carbons at $\delta$ 168.4–170.5 ppm (C-10″ for *C*OCH$_3$). Furthermore, the IR peaks corresponding to the acetyl ester carbonyl group at ca. 1764 cm$^{-1}$ for compounds **11**–**13** were missing in the spectra of compounds **1**, **2** and **14**. The HR-MS of helonioside A **1** showed *m*/*z* 717.1984 [*M* + Na]$^+$ (calcd 717.2001 for $C_{32}H_{38}O_{17}Na$). Furthermore, the structure of helonioside A **1** (Fig. 2) was confirmed by comparison to the data reported for the isolated natural product [2,6,7] (See Supporting information).

The HR-MS of the 3′,4′,6′-tri-*O*-feruloylsucrose **2** suggested the molecular formula $C_{42}H_{46}O_{20}$ based on the molecular ion peak at *m*/*z* 893.2478 [*M* + Na]$^+$ (calcd 893.2475 for $C_{42}H_{46}O_{20}Na$). The analysis data for 3′,4′,6′-tri-*O*-feruloylsucrose **2** (Figs. 3 and 4) did not completely match with literature data especially in the sucrose unit [15]. At this point, we presume that the structure of the isolated natural product needs further confirmation (See Supporting information).

In the same fashion, deacetylation of compound **9** gave the conformationally restricted PSE **15** in 71% yield as white solid (Scheme 1). The $^1$H and $^{13}$C NMR spectra of compound **15** revealed that the disappearance of the characteristic signals for the acetyl moieties at $\delta$ 2.34 ppm (s, 9H, H-11″ for the COC*H*$_3$), $\delta$ 20.7 ppm (C-11″ for $COCH_3$) and at $\delta$ 168.6, 168.7 and 168.8 ppm (C-10″ for *C*OCH$_3$).

The IR spectrum of compound **15** further indicated the successful deprotection where peaks corresponding to the acetyl ester carbonyl group of compound **9** at 1766 cm$^{-1}$ have disappeared. Furthermore, the HR-MS spectrum of compound **15** displayed *m*/*z* 973.3078 [*M* + Na]$^+$ (calcd 973.3101 for $C_{48}H_{54}O_{20}Na$). This compound was intentionally synthesized to investigate the effect of free phenolic hydroxyl groups and the presence of additional feruloyl substituents on the antiprofilative activities.

### 2.1.2. Preparation of lapathoside C and its analogs

We have previously reported the successful synthesis of 3′,6′-di-*O*-acetoxycinnamoyl sucrose **16** [24] and envisioned it to be an ideal starting substrate for the planned synthesis of lapathoside C **3** considering that the primary hydroxyl group (6-OH) of compound **16** is more reactive than the rest of the hydroxyl groups [28,29]. Consequently, reaction between compound **16** and *p*-acetoxyferuloyl chloride **5** (1.1 equiv) gave compound **18** (36% yield) along with compound **19** (7% yield) both as white solid (Scheme 2).

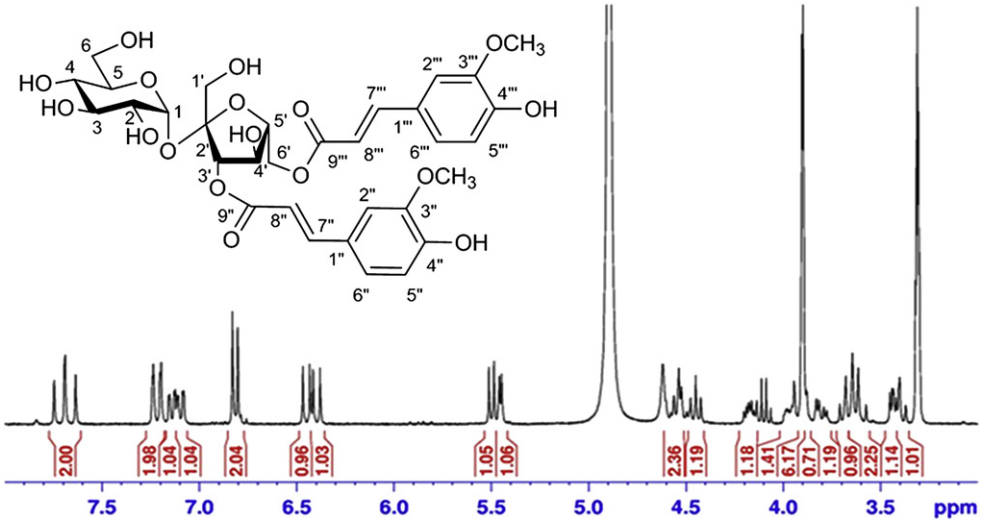



**Fig. 2.** $^1$H NMR spectrum of helonioside A **1** (300 MHz, $CD_3OD$).

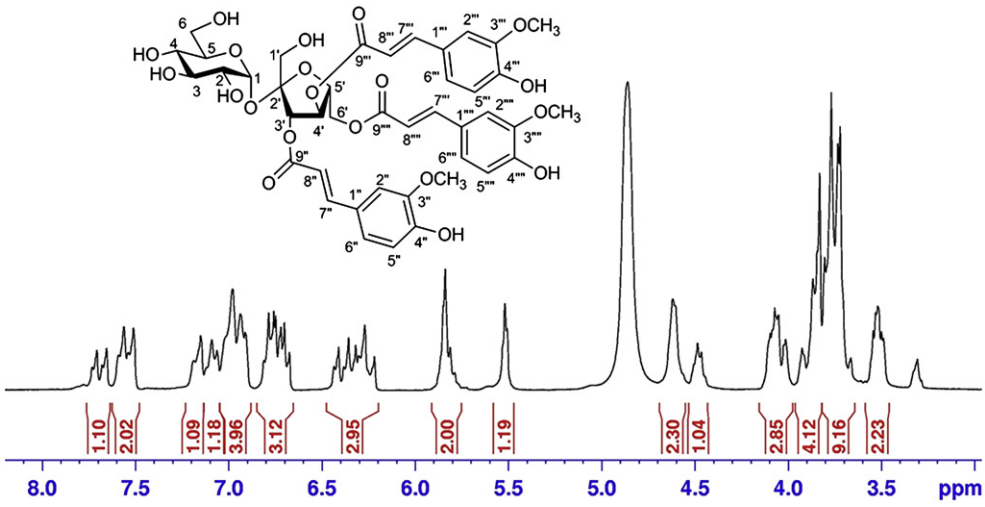



**Fig. 3.** $^{1}$H NMR spectrum of 3′,4′,6′-tri-*O*-feruloylsucrose **2** (300 MHz, $CD_3OD$).

Compound **18** would be used to prepare lapathoside C **3** at a later stage. Various analogs can be prepared in a similar fashion. Thus, reaction between sucrose **16** and *p*-acetoxycinnamoyl chloride **17** [24,27] (1.3 equiv) afforded compound **20** in just 12% yield (Scheme 2). Likewise, reaction between compound **18** and *p*-acetoxycinnamoyl chloride **17** gave compound **23** as white solid in 27% yield (Scheme 2).

Unfortunately, the Hatfield deacetylation method [26] did not work on compounds **18**–**20** and **23** since the starting materials were recovered unchanged. Therefore, the deacetylation was performed using pyrrolidine [27] (Scheme 2) which successfully gave compounds **3**, **21**, **22** and **24** in 75%, 47%, 71% and 35% yield, respectively, as white solids. The $^{1}$H and $^{13}$C NMR spectra of compounds **3**, **21**, **22** and **24** indicated the absence of the characteristic signals for the acetyl moieties at $\delta$ 2.23–2.30 ppm (s, 3H, H-11″ for the COC*H*$_3$), $\delta$ 20.6–21.1 ppm (C-11″ for CO*C*H$_3$) and $\delta$ 168.8–169.5 ppm (C-10″ for *C*OCH$_3$). The IR spectra of these compounds were devoid of peaks corresponding to the acetyl ester carbonyl groups at ca. 1765–1768 cm$^{-1}$ observed in the starting compounds **18**–**20** and **23**. The HR-MS of compound **3** showed *m*/*z* 833.2283 $[M + Na]^+$ (calcd 833.2263 for $C_{40}H_{42}O_{18}Na$). Based on the spectroscopic data and also by comparison to the reported literature data for the isolated natural lapathoside C [16] (See Supporting information), the structure of compound **3** was assigned to be lapathoside C **3** (i.e. 6-mono-*O*-feruloyl-3′,6′-di-*O*-coumaroylsucrose).

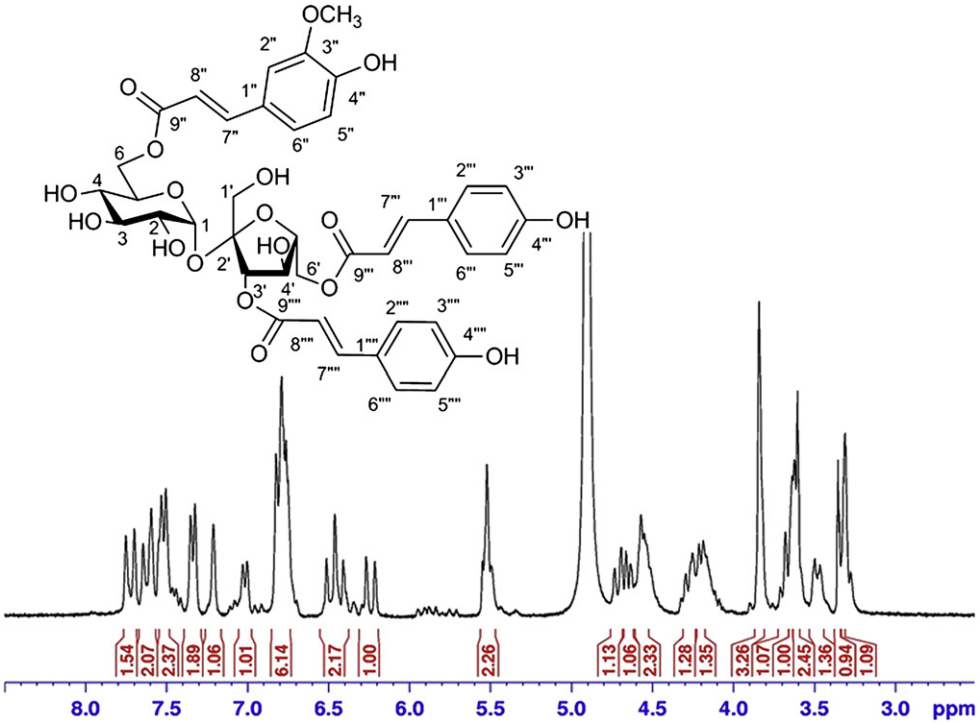
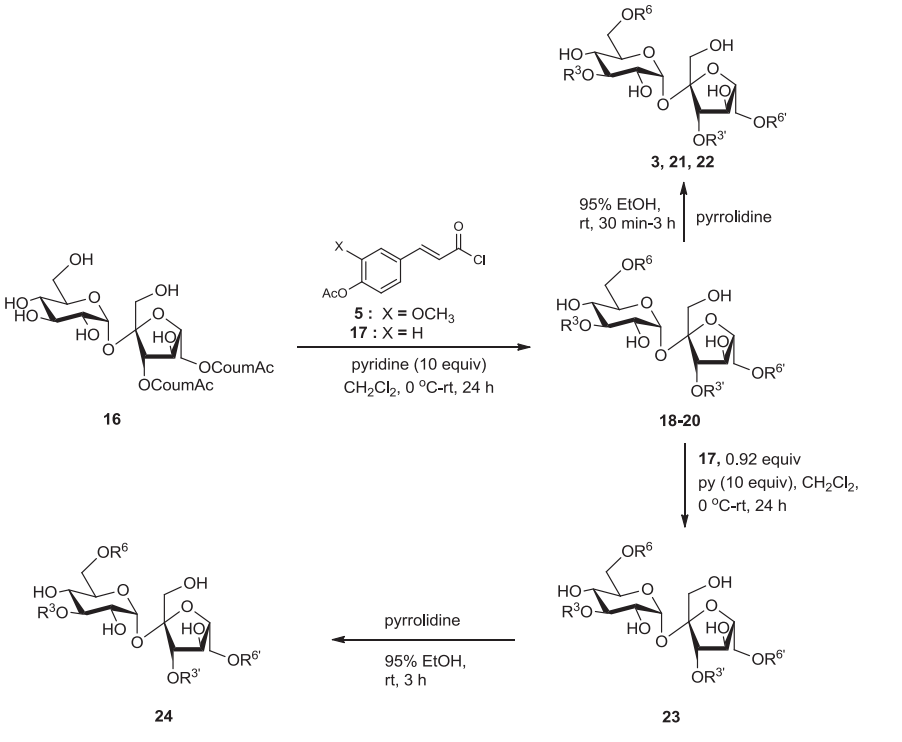
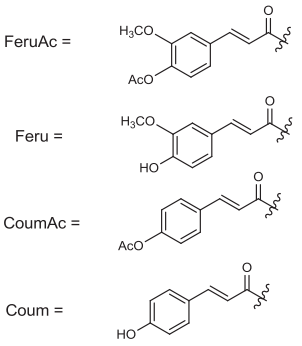



**Fig. 4.** $^{1}$H NMR spectrum of lapathoside C **3** (300 MHz, $CD_3OD$).




| Compound | $R^3$ | $R^6$ | $R^{3'}$ | $R^{6'}$ |
|---|---|---|---|---|
| 18 | H | FeruAc | CoumAc | CoumAc |
| 19 | FeruAc | FeruAc | CoumAc | CoumAc |
| 20 | CoumAc | CoumAc | CoumAc | CoumAc |
| 3 | H | Feru | Coum | Coum |
| 21 | Feru | Feru | Coum | Coum |
| 22 | Coum | Coum | Coum | Coum |
| 23 | CoumAc | FeruAc | CoumAc | CoumAc |
| 24 | Coum | Feru | Coum | Coum |




**Scheme 2.** Preparation of lapathoside C **3** and its analogs.

### 2.2. Antiproliferative activities

The antiproliferative activities of natural PSEs helonioside A **1**, 3′,4′,6′-tri-*O*-feruloylsucrose **2**, lapathoside C **3** as well as selected analogs **6**, **8**–**12**, **14**, **15**, **18**–**22** and **24** were evaluated against HeLa cells using our previously reported method [24].

The $IC_{50}$ values of these compounds along with the standard drug camptothecin (CPT) are shown in Tables 1 and 2. Helonioside A **1** (Table 2, entry 1) and its analog compound **11** in which the phenolic groups are acetylated (Table 2, entry 7) did not show any appreciable antiproliferative activity upto 100 μM concentration. Hence, acetylation of the phenolic groups seems to be ineffective in enhancing the antiprolifrative activity. Compound **2**, a tri-*O*-feruloyl sucrose, showed improved antiprolifrative activity with an $IC_{50}$ value of 22.35 μM (entry 2, Table 2) whereas tetra-*O*-feruloyl sucrose **14** exhibited greater antiprolifrative activity with an $IC_{50}$ value of 1.62 μM (entry 9, Table 2). Therefore, introduction of more feruloyl groups seems to have positive effect on the activity. Rigid compounds having di-*O*-isopropylidene groups with their phenolic OH protected with an acetyl group **8**, **9** and **10** showed significant antiproliferative activities with their $IC_{50}$ values of 6.01, 0.16 and 3.22 μM, respectively, compared to their flexible deprotected OH counterparts **1**, **2** and **14** (entries 4 vs 1, 5 vs 2 and 6 vs 9, Table 2). The trend of the antiproliferative activity of 3′,4′,6′-tri-*O*-feruloylsucrose analogs are: **9** ($IC_{50}$ = 0.16 μM) > **12** ($IC_{50}$ = 1.70 μM) > **15** ($IC_{50}$ = 4.20 μM) > **2** ($IC_{50}$ = 22.35 μM). From the above results, it is clear that the completely acetylated di-*O*-isopropylidene variants like compound **9** have superior activity while deacetonide (di-*O*-isopropylidene-free) **12** or deacetylated product **15** showed lower activities. Additionally, after cleavage of the acetyl and di-*O*-isopropylidene groups of compound **9** to give compound **2**, the activity of the obtained product was dramatically reduced due to probable differences in the lipophilicity of these compounds (entries 2 & 5, Table 2). Increased lipophilicity of molecules was reported to be responsible for enhanced cytotoxicity [30]. The presence of free feruloyl derivatives is: **14** ($IC_{50}$ = 1.62 μM) > **10** ($IC_{50}$ = 3.22 μM) (entries 9 & 6, Table 2). It was anticipated that compound **6** with a mono phenylpropanoid group would show weak activity. Instead, this compound did not show any antiproliferative activity up to 100 μM concentration (entry 3, Table 2). In this case, the positional effect of the feruloyl group on the sucrose core seems to have a great effect. We suspect that substituents at the C6′ position play no major role in the antiproliferative activity.

Tetra-phenylpropanoid sucrose esters analogs **18**–**22** and **24** (entries 3–7, Table 3) showed better antiproliferative activities compared to the tri-phenylpropanoid sucrose esters analogs **3** and **18** (entries 1 and 2, Table 3). Acetylation of **3** to give compound **18** did not improve the $IC_{50}$ value (entry 1 vs 2, Table 3). The tetra-coumaroyl PSE **22**, tetra-feruloyl PSE **14** and "mixed" PSEs **21** having a combination of coumaroyl and feruloyl units exhibited almost similar antiproliferative activity with their $IC_{50}$ values of 1.70, 1.62 and 1.67 μM, respectively (entries 5 & 6, Table 3 and entry 9, Table 2). Replacing one of the coumaroyl substituents at C3 of **24** with a feruloyl group as in **21** improved the $IC_{50}$ value from 3.12 to 1.67 μM (entry 7 vs 5, Table 3). Compound **21** (entry 5, Table 3) showed superior activity compared to its acetylated product **19** (entry 3, Table 3).

**Table 1**
Regio- and chemoselective acylation of di-*O*-isopropylidene sucrose **4** with *p*-acetoxyferuloyl chloride **5**.

| Entry | Equiv. of acid chloride **5** | Time (d) | Product | Yield (%) | Total yield (%) |
|---|---|---|---|---|---|
| 1 | 1.1 | 3 | **6** | 31 | 54 |
| | | | **7** | 11 | |
| | | | **8** | 12 | |
| 2 | 2.2 | 5 | **6** | 3 | 33 |
| | | | **8** | 30 | |
| 3 | 3.3 | 2 | **8** | 44 | 70 |
| | | | **9** | 26 | |
| 4 | 4.4 | 4 | **9** | 35 | 79 |
| | | | **10** | 44 | |

**Table 2**
In vitro cytotoxicity ($IC_{50}$ (μM)) of selected feruloyl PSEs against HeLa cells at 48 h of exposure.

| Entry | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 15 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Cpd | **1** | **2** | **6** | **8** | **9** | **10** | **11** | **12** | **14** | **15** | **CPT** |
| $IC_{50}$[a] | >100 | 22.35 | >100 | 6.01 | 0.16 | 3.22 | >100 | 1.70 | 1.62 | 4.20 | 0.40 |

[a] $IC_{50}$ (μM): the concentration that induces 50% growth inhibition compared with untreated control cells and were calculated from three independent experiments.

Additionally, compounds **2**, **8** and **14** were selected for evaluation of the cytotoxicity at two different time intervals of drug exposure by MTS assay (Table 4) in order to examine time-dependent cytotoxicity. The $IC_{50}$ values of compounds **2**, **8** and **14** were enhanced as the time of exposure increased from 24 h to 48 h. These compounds revealed time-dependent antiproliferative activities.

In summary, we can conclude that: (1) di-*O*-isopropylidene group proved to be essential for enhancing the cytotoxicity while acetyl and methoxy groups had much lower effects; (2) Substituents at the C6′ position are not essential for antiproliferative activity; (3) Lipophilicity of the examined PSEs seems to influence the cytotoxicity in MTS model [30]. Herein, the position and nature of phenylpropanoid unit had a little effect on the antiproliferative activity of PSEs; and (4) The PSEs examined also revealed time-dependent antiproliferative activities.

## 3. Conclusions

We successfully synthesized, for the first time, the natural PSEs helonioside A **1**, 3′,4′,6′-tri-*O*-feruloylsucrose **2** and lapathoside C **3** along with 17 unnatural PSEs analogs using regio- and chemoselective acylation of di-*O*-isopropylidene sucrose **4**. The reactivities of the free OH groups of di-*O*-isopropylidene sucrose **4** towards acylation using *p*-acetoxyferuloyl chloride **5** were found to be in the order of 6′-OH > 3′-OH > 4′-OH > 3-OH. The synthetic methodology used is wide in scope and applicable to wide range of PSEs. The MTS results revealed that 11 out of the 17 examined PSEs displayed significant antiproliferative activity against HeLa cells at 48 h drug exposure with their $IC_{50}$values ranging from 0.16 to 6.01 μM compared with CPT ($IC_{50}$ = 0.40 μM). The results also indicated time-dependent antiproliferative activities. Lipophilicity which is influenced by the presence/absence of di-*O*-isopropylidene group and the number of the phenylpropanoid units on the sucrose core directly influence the antiproliferative activities. Our present results provide great motivation for the synthesis of other natural and unnatural PSEs and explore their applications and mechanism of action against various human cancer cell lines such as colon cancer, lung carcinoma, breast cancer, skin cancer etc in search for new lead anticancer drug candidates.

## 4. Experimental

### 4.1. Chemistry

2,1′:4,6-di-*O*-isopropylidene sucrose **4**, 3′,6′-di-*O*-acetoxycinnamoyl sucrose **16** and *p*-acetoxycinnamoyl chloride **17** were synthesized according to the reported procedures [24]. *p*-Acetoxyferuloyl chloride **5** was synthesized according to the reported literature [26] (see Supporting information).

#### 4.1.1. Acylation of di-*O*-isopropylidene **4** with *p*-acetoxyferuloyl chloride **5**

*4.1.1.1. General procedure.* Di-*O*-isopropylidene **4** was dissolved in dry pyridine under a nitrogen atmosphere. The solution was then cooled to 0 °C in an ice bath. *p*-Acetoxyferuloyl chloride **5** was then added slowly at the same temperature and the reaction was left to stir while warming to r.t. Stirring was continued at r.t. until the reaction was completed (TLC analysis (EtOAc/hexanes 3:1)). The resulting reaction mixture was poured into vigorously stirred ice-water (100 mL) and the precipitated white solid was obtained by vacuum filtration. The precipitates were redissolved in EtOAc (25 mL) and washed once with 1 N HCl (50 mL). The combined organic layers were then successively washed with 5% $NaHCO_3$ (50 mL), brine (25 mL) and then dried over anhyd. $MgSO_4$. The EtOAc solution was evaporated under reduced pressure to give yellow syrup that was subjected to column chromatography using a gradient of $CH_2Cl_2$/EtOAc as eluent to afford compounds **6**–**10**.

*4.1.1.2. 6′-mono-O-acetoxyferuloyl-2,1′:4,6-di-O-isopropylidene sucrose **6** and 3′-mono-O-acetoxyferuloyl-2,1′:4,6-di-O-isopropylidene sucrose **7**.* Following the general procedure, the reaction between di-*O*-isopropylidene **4** (1.0 g, 2.4 mmol) and *p*-acetoxyferuloyl chloride **5** (0.7 g, 2.6 mmol) in dry pyridine (10 mL) for 3 days afforded compound **6** as a white solid (0.47 g, 31% yield) along with compounds **7** and **8** in 11% (0.16 g) and 12% (0.25 g) yield, respectively. Analytical data for **6**: $R_f$ = 0.12 (EtOAc/$CH_2Cl_2$ 3:2); mp: 147–150 °C; FT-IR (KBr) $\nu_{max}$: 3452, 2993, 2941, 1766, 1712, 1636, 1601, 1511, 1417, 1372, 1260, 1199, 1157, 1127, 1069, 1013, 943, 858, 718, 651 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ (ppm): 1.45, 1.51 (2× s, 12H, $(CH_3)_2C$), 3.50 (m, 1H, H-1′a), 3.60 (m, 1H, H-4), 3.73 (m, 2H, H-2, H-6a), 3.93 (m, 3H, H-3′, H-5, H-6b), 4.05 (m, 1H, H-3), 4.23 (m, 2H, H-4′, H-5′), 4.30 (m, 2H, H-1′b, H-6′a), 4.51 (m, 1H, H-6′b), 6.19 (br d, 1H, $J$ = 1.8 Hz, H-1); *trans-p*-feruloyl units: 2.32 (1s, 3H, H-11″), 3.85 (s, 3H, $-OCH_3$), 6.41 (d, 1H, $J$ = 15.9 Hz, H-8″), 7.00–7.19 (m, 3H, H-2″, H-5″, H-6″), 7.64 (d, 1H, $J$ = 15.9 Hz, H-7″); $^{13}C$ NMR (75.48 MHz, $CDCl_3$) δ (ppm): 19.2, 24.2, 25.3, 29.1 (4× $(CH_3)_2C$), 62.3 (C-6), 63.8 (C-5), 65.9 (C-6′), 66.5 (C-1′), 69.3 (C-3), 73.4 (C-4), 73.9 (C-2), 77.5 (C-4′), 79.0 (C-3′), 79.7 (C-5′), 91.0 (C-1), 100.1, 102.2 (2× $(CH_3)_2C$), 103.7 (C-2′); *trans-p*-feruloyl units: 20.7 (C-11″), 55.9 ($-OCH_3$), 111.3 (C-2″), 117.9 (C-8″), 121.4 (C-5″), 123.2 (C-6″), 133.2 (C-1″), 141.5 (C-3″), 144.7 (C-7″), 151.4 (C-4″), 167.0 (C-9″), 168.8 (C-10″); LC-MS (ESI): $m/z$ 663.22 $[M + Na]^+$; HR-MS: $m/z$ $[M + Na]^+$ calcd for $C_{30}H_{40}O_{15}Na$: 663.2259, found: 663.2268. Analytical data for **7**:

**Table 3**
In vitro cytotoxicity ($IC_{50}$ (μM)) of selected lapathoside C and its analogs PSEs against HeLa cells at 48 h of exposure.

| Entry | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|---|---|---|---|---|---|---|---|---|
| Cpd | **3** | **18** | **19** | **20** | **21** | **22** | **24** | **CPT** |
| $IC_{50}$[a] | 12.61 | >100 | 3.14 | 1.86 | 1.67 | 1.70 | 3.12 | 0.40 |

[a] $IC_{50}$ (μM): the concentration that induces 50% growth inhibition compared with untreated control cells and were calculated from three independent experiments.

**Table 4**
$IC_{50}$ values of selected synthesized PSEs **2**, **8** and **14** along with CPT at 24 h and 48 h of exposure.

| No | Compound | $IC_{50}$ (μM) | |
|---|---|---|---|
| | | 24 h | 48 h |
| 1 | **2** | 55.07 | 22.35 |
| 2 | **8** | 27.92 | 6.01 |
| 3 | **14** | 7.90 | 1.62 |
| 4 | **CPT** | 1.57 | 0.40 |

$R_f$ = 0.21 (EtOAc/$CH_2Cl_2$ 3:2); mp: 130–132 °C; FT-IR (KBr) $\nu_{max}$: 2994, 2936, 1765, 1716, 1638, 1590, 1510, 1467, 1421, 1373, 1333, 1260, 1199, 1156, 1125, 1069, 1033, 1015, 946, 855, 650 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ (ppm): 1.40, 1.44, 1.53 (3× s, 12H, $(CH_3)_2C$), 3.58 (m, 2H, H-1′a, H-4), 3.68 (m, 2H, H-6a, H-6′a), 3.77 (m, 1H, H-2), 3.87 (m, 4H, H-3, H-5, H-6b, H-6′b), 4.10 (m, 2H, H-1′b, H-5′), 4.87 (m, 1H, H-4′), 5.03 (d, 1H, $J$ = 7.8 Hz, H-3′), 6.22 (d, 1H, $J$ = 3.6 Hz, H-1); *trans-p*-feruloyl units: 2.05 (1s, 3H, H-11″), 3.91 (s, 3H, $-OCH_3$), 6.50 (d, 1H, $J$ = 15.9 Hz, H-8″), 7.09 (d, 1H, $J$ = 7.8 Hz, H-5″), 7.16–7.22 (m, 2H, H-5″, H-6″), 7.77 (d, 1H, $J$ = 15.9 Hz, H-7″); $^{13}C$ NMR (75.48 MHz, $CDCl_3$) $\delta$ (ppm): 19.0, 24.1, 25.3, 29.0 (4× $(CH_3)_2C$), 61.2 (C-6), 61.8 (C-6′), 63.9 (C-5), 66.5 (C-1′), 70.0 (C-3), 71.4 (C-4′), 72.7 (C-2), 73.4 (C-4), 80.0 (C-3′), 84.0 (C-5′), 91.0 (C-1), 99.9, 102.0 (2× $(CH_3)_2C$), 103.48 (C-2′); *trans-p*-feruloyl units: 20.6 (C-11″), 56.0 ($-OCH_3$), 111.3 (C-2″), 116.8 (C-8″), 122.0 (C-5″), 123.4 (C-6″), 132.9 (C-1″), 141.9 (C-3″), 146.3 (C-7″), 151.5 (C-4″), 167.2 (C-9″), 168.7 (C-10″); LC-MS (ESI): $m/z$ 663.24 $[M + Na]^+$; HR-MS: $m/z$ $[M + Na]^+$ calcd for $C_{30}H_{40}O_{15}Na$: 663.2259, found: 663.2255.

*4.1.1.3. 3′,6′-di-O-acetoxyferuloyl-2,1′:4,6-di-O-isopropylidene sucrose* ***8***. Following the general procedure, the reaction between di-*O*-isopropylidene **4** (1.0 g, 2.4 mmol) and *p*-acetoxyferuloyl chloride **5** (1.3 g, 5.2 mmol) in dry pyridine (10 mL) for 5 days gave compound **8** as a white solid (0.6 g, 30% yield) along with compound **6** in 3% (0.05 g) yield. Analytical data for **8**: $R_f$ = 0.61 (EtOAc/$CH_2Cl_2$ 3:2); mp: 109–110 °C; FT-IR (KBr) $\nu_{max}$: 3486, 2993, 2942, 1766, 1716, 1637, 1601, 1511, 1417, 1372, 1332, 1259, 1198, 1069, 1032, 1012, 947, 906, 858, 655 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ (ppm): 1.40, 1.41, 1.53 (3× s, 12H, $(CH_3)_2C$), 3.63 (m, 2H, H-1′a, H-4), 3.74 (m, 1H, H-6a), 3.79 (m, 1H, H-2), 3.88 (m, 2H, H-3, H-5), 3.94 (m, 1H, H-6b), 4.08 (d, 1H, $J$ = 12.3 Hz, H-1′b), 4.38 (m, 2H, H-5′, H-6′a), 4.46 (m, 1H, H-4′), 4.53 (m, 1H, H-6′b), 4.92 (d, 1H, $J$ = 6.3 Hz, H-3′), 6.13 (d, 1H, $J$ = 3.3 Hz, H-1); *trans-p*-feruloyl units: $R_1$: 2.33 (s, 3H, H-11″), 3.87 (s, 3H, $-OCH_3$), 6.43 (d, 1H, $J$ = 15.9 Hz, H-8″), 7.03–7.12, 7.20 (2× m, 3H, H-2″, H-5″, H-6″), 7.66 (d, 1H, $J$ = 15.9 Hz, H-7″), $R_2$: 2.33 (s, 3H, H-11″), 3.92 (s, 3H, $-OCH_3$), 6.48 (d, 1H, $J$ = 15.9 Hz, H-8″), 7.03–7.12, 7.20 (2× m, 3H, H-2″, H-5″, H-6″), 7.77 (d, 1H, $J$ = 15.9 Hz, H-7″); $^{13}C$ NMR (75.48 MHz, $CDCl_3$) $\delta$ (ppm): 19.1, 24.1, 25.4, 29.1 (4× $(CH_3)_2C$), 62.1 (C-6), 63.8 (C-5), 65.7 (C-6′), 65.9 (C-1′), 70.3 (C-3), 72.9 (C-4), 73.8 (C-2), 76.5 (C-4′), 81.3 (C-3′), 81.4 (C-5′), 90.9 (C-1), 99.9, 101.8 (2× $(CH_3)_2C$), 104.5 (C-2′); *trans-p*-feruloyl units: $R_1$: 20.7 (C-11″), 55.9 ($-OCH_3$), 111.2 (C-2″), 116.5 (C-8″), 121.4 (C-5″), 123.4 (C-6″), 132.8 (C-1″), 141.6 (C-3″), 144.6 (C-7″), 151.4 (C-4″), 166.6 (C-9″), 168.8 (C-10″); $R_2$: 20.7 (C-11″), 56.1 ($-OCH_3$), 111.4 (C-2″), 117.9 (C-8″), 122.1 (C-5″), 123.4 (C-6″), 133.3 (C-1″), 142.0 (C-3″), 146.6 (C-7″), 151.5 (C-4″), 167.7 (C-9″), 168.8 (C-10″); LC-MS (ESI): $m/z$ 881.35 $[M + Na]^+$; HR-MS: $m/z$ $[M + Na]^+$ calcd for $C_{42}H_{50}O_{19}Na$: 881.2839, found: 881.2860.

*4.1.1.4. 3′,4′,6′-tri-O-acetoxyferuloyl-2,1′:4,6-di-O-isopropylidene sucrose* ***9***. Following the general procedure, the reaction between di-*O*-isopropylidene **4** (1.0 g, 2.4 mmol) and *p*-acetoxyferuloyl chloride **5** (2.0 g, 7.8 mmol) in dry pyridine (10 mL) for 2 days furnished compound **9** as a white solid (0.67 g, 26% yield) along with compound **8** in 44% (0.89 g) yield. Analytical data for **9**: $R_f$ = 0.73 (EtOAc/$CH_2Cl_2$ 3:2); mp: 135–138 °C; FT-IR (KBr) $\nu_{max}$: 3507, 2993, 2942, 1766, 1721, 1638, 1601 1510, 1467, 1418, 1371, 1332, 1259, 1198, 1155, 1124, 1067, 1032, 1011, 944, 904, 858, 837, 726, 650 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ (ppm): 1.33, 1.41, 1.51, 1.53 (4× s, 12H, $(CH_3)_2C$), 3.62 (m, 2H, H-1′a, H-4), 3.70 (m, 1H, H-6a), 3.76 (m, 1H, H-2), 3.84 (m, 2H, H-3, H-5), 4.03 (m, 1H, H-6b), 4.19 (d, 1H, $J$ = 12.0 Hz, H-1′b), 4.51 (m, 2H, H-5′, H-6′a), 4.64 (m, 1H, H-6′b), 5.38 (d, 1H, $J$ = 5.4 Hz, H-4′), 5.60 (br dd, 1H, $J$ = 5.1 Hz, 3.6 Hz, H-3′), 6.15 (d, 1H, $J$ = 3.3 Hz, H-1); *trans-p*-feruloyl units: $R_1$: 2.34 (s, 3H, H-11″), 3.86 (s, 3H, $-OCH_3$), 6.40 (d, 1H, $J$ = 15.9 Hz, H-8″), 7.02–7.13 (m, 3H, H-2″, H-5″, H-6″), 7.66 (d, 1H, $J$ = 15.9 Hz, H-7″); $R_2$: 2.34 (s, 3H, H-11″), 3.88 (s, 3H, $-OCH_3$), 6.42 (d, 1H, $J$ = 15.9 Hz, H-8″), 7.02–7.13 (m, 2H, H-5″, H-6″), 7.20–7.22 (m, 1H, H-2″), 7.68 (d, 1H, $J$ = 15.9 Hz, H-7″); $R_3$: 2.34 (s, 3H, H-11″), 3.93 (s, 3H, $-OCH_3$), 6.52 (d, 1H, $J$ = 15.9 Hz, H-8″), 7.08 (d, 2H, $J$ = 8.7 Hz, H-5″, H-6″), 7.20–7.22 (m, 1H, H-2″), 7.79 (d, 1H, $J$ = 15.9 Hz, H-7″); $^{13}C$ NMR (75.48 MHz, $CDCl_3$) $\delta$ (ppm): 19.1, 24.1, 25.5, 29.0 (4× $(CH_3)_2C$), 62.0 (C-6), 63.9 (C-5), 64.9 (C-6′), 66.3 (C-1′), 70.2 (C-3), 72.8 (C-4), 73.8 (C-2), 77.3 (C-4′), 77.6 (C-3′), 80.1 (C-5′), 91.4 (C-1), 99.7, 101.8 (2× $(CH_3)_2C$), 104.8 (C-2′); *trans-p*-feruloyl units: $R_1$: 20.7 (C-11″), 55.9 ($-OCH_3$), 111.2 (C-2″), 116.5 (C-8″), 121.4 (C-5″), 123.2 (C-6″), 132.9 (C-1″), 141.4 (C-3″), 144.4 (C-7″), 151.3 (C-4″), 165.7 (C-9″), 168.6 (C-10″); $R_2$: 20.7 (C-11″), 56.0 ($-OCH_3$), 111.3 (C-2″), 116.8 (C-8″), 121.5 (C-5″), 123.3 (C-6″), 132.9 (C-1″), 141.8 (C-3″), 144.8 (C-7″), 151.4 (C-4″), 165.8 (C-9″), 168.7 (C-10″); $R_3$: 20.7 (C-11″), 56.0 ($-OCH_3$), 111.4 (C-2″), 117.9 (C-8″), 122.1 (C-5″), 123.4 (C-6″), 133.3 (C-1″), 141.9 (C-3″), 146.4 (C-7″), 151.5 (C-4″), 166.3 (C-9″), 168.8 (C-10″); LC-MS (ESI): $m/z$ 1099.35 $[M + Na]^+$; HR-MS: $m/z$ $[M + Na]^+$ calcd for $C_{54}H_{60}O_{23}Na$: 1099.3418, found: 1099.3401.

*4.1.1.5. 3,3′,4′,6′-tetra-O-acetoxyferuloyl-2,1′:4,6-di-O-isopropylidene sucrose* ***10***. Following the general procedure, the reaction between di-*O*-isopropylidene **4** (1.0 g, 2.4 mmol) and *p*-acetoxyferuloyl chloride **5** (2.7 g, 10.4 mmol) in dry pyridine (10 mL) for 4 days afforded compound **10** as a white solid (1.34 g, 44% yield) along with compound **9** in 35% (0.9 g) yield. Analytical data for **10**: $R_f$ = 0.88 (EtOAc/$CH_2Cl_2$ 3:2); mp: 133–135 °C; FT-IR (KBr) $\nu_{max}$: 3629, 2993, 2942, 1767, 1721,1637, 1601, 1467, 1419, 1371, 1327, 1259, 1198, 1153, 1123, 1070, 1033, 1010, 944, 903, 856, 832, 796, 727, 649 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ (ppm): 1.20, 1.30, 1.45, 1.49 (4× s, 12H, $(CH_3)_2C$), 3.65 (m, 1H, H-1′a), 3.70 (m, 2H, H-4, H-6a), 3.96 (m, 2H, H-2, H-5), 4.07 (m, 1H, H-6b), 4.25 (d, 1H, $J$ = 12.3 Hz, H-1′b), 4.52–4.63 (m, 3H, H-5′, H-6′a, H-6′b), 5.42 (m, 2H, H-3, H-4′), 5.61 (m, 1H, H-3′), 6.21 (d, 1H, $J$ = 3.6 Hz, H-1); *trans*-feruloyl units: $R_1$: 2.33 (s, 3H, H-11″), 3.86 (s, 3H, $-OCH_3$), 6.38 (d, 1H, $J$ = 15.9 Hz, H-8″), 7.02–7.15 and 7.28–7.33 (2× m, 3H, H-2″, H-5″, H-6″), 7.61 (d, 1H, $J$ = 15.9 Hz, H-7″), $R_2$: 2.33 (s, 3H, H-11″), 3.88 (s, 3H, $-OCH_3$), 6.42 (d, 1H, $J$ = 15.9 Hz, H-8″), 7.02–7.15 and 7.28–7.33 (2× m, 3H, H-2″, H-5″, H-6″), 7.66 (d, 1H, $J$ = 15.9 Hz, H-7″), $R_3$: 2.33 (s, 3H, H-11″), 3.89 (s, 3H, $-OCH_3$), 6.43 (d, 1H, $J$ = 15.9 Hz, H-8″), 7.02–7.15 and 7.28–7.33 (2× m, 3H, H-2″, H-5″, H-6″), 7.69 (d, 1H, $J$ = 15.9 Hz, H-7″), $R_4$: 2.33 (s, 3H, H-11″), 3.92 (s, 3H, $-OCH_3$), 6.57 (d, 1H, $J$ = 15.9 Hz, H-8″), 7.02–7.15 and 7.28–7.33 (2× m, 3H, H-2″, H-5″, H-6″), 7.93 (d, 1H, $J$ = 15.9 Hz, H-7″); $^{13}C$ NMR (75.48 MHz, $CDCl_3$) $\delta$ (ppm): 19.0, 23.9, 25.4, 28.8 (4× $(CH_3)_2C$), 62.1 (C-6), 64.3 (C-5), 65.0 (C-6′), 66.2 (C-1′), 70.9 (C-3), 71.5 (C-4), 71.9 (C-2), 77.4 (C-4′), 77.7 (C-3′), 80.3 (C-5′), 91.7 (C-1), 99.6, 101.5 (2× $(CH_3)_2C$), 105.0 (C-2′); *trans-p*-feruloyl units: $R_1$: 20.6 (C-11″), 55.9 ($-OCH_3$), 111.2 (C-2″), 116.8 (C-8″), 121.2 (C-5″), 123.0 (C-6″), 132.9 (C-1″), 141.4 (C-3″), 144.1 (C-7″), 151.3 (C-4″), 165.7 (C-9″), 168.7 (C-10″), $R_2$: 20.6 (C-11″), 55.9 ($-OCH_3$), 111.2 (C-2″), 116.9 (C-8″), 121.3 (C-5″), 123.2 (C-6″), 133.3 (C-1″), 141.4 (C-3″), 144.4 (C-7″), 151.4 (C-4″), 165.7 (C-9″), 168.8 (C-10″), $R_3$: 20.6 (C-11″), 56.0 ($-OCH_3$), 111.3 (C-2″), 117.9 (C-8″), 121.5 (C-5″), 123.2 (C-6″), 133.3 (C-1″), 141.6 (C-3″), 145.7 (C-7″), 151.4 (C-4″), 166.0 (C-9″), 168.8 (C-10″), $R_4$: 20.6 (C-11″), 56.0 ($-OCH_3$), 112.4 (C-2″), 118.2 (C-8″), 121.7 (C-5″), 123.3 (C-6″), 133.4 (C-1″), 141.8 (C-3″), 146.6 (C-7″), 151.4 (C-4″), 166.3 (C-9″), 168.8 (C-10″); LC-MS (ESI): $m/z$ 1317.35 $[M + Na]^+$; HR-MS: $m/z$ $[M + Na]^+$ calcd for $C_{66}H_{70}O_{27}Na$: 1317.3997, found: 1317.3980.

*4.1.2. Acetal deprotection of the diacetonoides* ***8–10***

*4.1.2.1. General procedure.* A solution of di-*O*-isopropylidene feruloyl derivatives **8–10** in 60% aq. AcOH was heated at 80 °C until the reaction was completed. The reaction was monitored by TLC

(EtOAc/$CH_2Cl_2$ 3:2). The reaction solution was then evaporated to dryness under reduced pressure by codistillation with toluene (3 × 100 mL). The products **11**–**13** were obtained from recrystallization in EtOAc and/or by column chromatography using a gradient of $CH_2Cl_2$/EtOAc as eluent.

*4.1.2.2. 3′,6′-di-O-acetoxyferuloylsucrose **11**.* Following the general procedure, a solution of compound **8** (1.1 g, 1.3 mmol) was treated with 60% aq. AcOH (66 mL) at 80 °C for 20 min. Recrystallization of the crude product in EtOAc gave compound **11** as a white solid (0.90 g, 89% yield). Analytical data for **11**: $R_f$ = 0.56 (EtOAc/MeOH 9:1); mp: 128–130 °C; FT-IR (KBr) $\nu_{max}$: 3411, 2930, 1762, 1706, 1635, 1601, 1508, 1420, 1371, 1330, 1261, 1220, 1194, 1159, 1125, 1060, 1031, 996, 938, 848, 792, 691, 650 $cm^{-1}$; $^1H$ NMR (300 MHz, $CD_3OD$) $\delta$ (ppm): 3.40–3.46 (m, 2H, H-2, H-4), 3.62 (m, 2H, H-1′a, H-1′b), 3.70 (m, 1H, H-3), 3.80 (m, 1H, H-6a), 3.94 (m, 2H, H-6b, H-5), 4.16–4.22 (m, 1H, H-5′), 4.47 (app t, 1H, $J$ = 7.8 Hz, H-4′), 4.53–4.61 (m, 2H, H-6′a, H-6′b), 5.45 (d, 1H, $J$ = 3.6 Hz, H-1), 5.53 (d, 1H, $J$ = 7.8 Hz, H-3′); *trans-p*-feruloyl units: $R_1$: 2.27 (s, 3H, H-11″), 3.86 (s, 3H, −OC*H*$_3$), 6.58 (d, 1H, $J$ = 16.2 Hz, H-8″), 7.07 (d, 1H, $J$ = 8.1 Hz, H-6″), 7.22 (dd, 1H, $J$ = 1.5 Hz, 8.4 Hz, H-5″), 7.35 (d, 1H, $J$ = 13.8 Hz, H-2″), 7.72 (d, 1H, $J$ = 16.2 Hz, H-7″), $R_2$: 2.27 (s, 3H, H-11″), 3.86 (s, 3H, −OC*H*$_3$), 6.61 (d, 1H, $J$ = 16.2 Hz, H-8″), 7.07 (d, 1H, $J$ = 8.1 Hz, H-6″), 7.22 (dd, 1H, $J$ = 1.5 Hz, 8.4 Hz, H-5″), 7.35 (d, 1H, $J$ = 13.8 Hz, H-2″), 7.78 (d, 1H, $J$ = 16.2 Hz, H-7″); $^{13}C$ NMR (75.48 MHz, $CD_3OD$) $\delta$ (ppm): 62.7 (C-6), 65.2 (C-1′), 66.5 (C-6′), 71.5 (C-4), 73.2 (C-2), 74.5 (C-5), 75.0 (C-4′, C-3), 79.5 (C-3′), 81.3 (C-5′), 93.2 (C-1), 105.1 (C-2′); *trans-p*-feruloyl units: $R_1$: 20.9 (C-11″), 56.6 (−O*C*H$_3$), 112.7 (C-2″), 118.7 (C-8″), 122.4 (C-5″), 124.3 (C-6″), 134.8 (C-1″), 143.1 (C-3″), 146.0 (C-7″), 153.0 (C-4″), 167.6 (C-9″), 170.5 (C-10″), $R_2$: 20.9 (C-11″), 56.6 (−O*C*H$_3$), 113.2 (C-2″), 118.9 (C-8″), 122.4 (C-5″), 124.3 (C-6″), 134.8 (C-1″), 143.1 (C-3″), 146.6 (C-7″), 153.1 (C-4″), 168.4 (C-9″), 170.5 (C-10″); LC-MS (ESI): $m/z$ 801.25 $[M + Na]^+$; HR-MS: $m/z$ $[M + Na]^+$ calcd for $C_{36}H_{42}O_{19}Na$: 801.2213, found: 801.2235.

*4.1.2.3. 3′,4′,6′-tri-O-acetoxyferuloylsucrose **12**.* Following the general procedure, a solution of compound **9** (0.8 g, 0.7 mmol) was reacted with 60% aq. AcOH (49 mL) at 80 °C for 20 min. Column chromatographic purification using a gradient of $CH_2Cl_2$/EtOAc as eluent afforded compound **12** as a white solid (0.50 g, 67% yield). Analytical data for **12**: $R_f$ = 0.49 (EtOAc/MeOH 9:1); mp: 128–130 °C; FT-IR (KBr) $\nu_{max}$: 3425, 2938, 1764, 1713, 1638, 1601, 1510, 1465, 1418, 1371, 1332, 1300, 1260, 1218, 1199, 1155, 1124, 1031, 1012, 903, 836, 650 $cm^{-1}$; $^1H$ NMR (300 MHz, $CD_3OD$) $\delta$ (ppm): 3.46–3.52 (m, 2H, H-2, H-4), 3.67 (m, 2H, H-1′a, H-3), 3.82 (m, 1H, H-1′b), 3.88 (m, 1H, H-6a), 3.99–4.08 (m, 2H, H-6b, H-5), 4.47–4.51 (m, 1H, H-5′), 4.61–4.65 (m, 2H, H-6′b, H-6′a), 5.49 (d, 1H, $J$ = 3.6 Hz, H-1), 5.82–5.87 (m, 2H, H-3′, H-4′); *trans-p*-feruloyl units: $R_1$: 2.26 (s, 3H, H-11″), 3.74 (s, 3H, −OC*H*$_3$), 6.47 (d, 1H, $J$ = 15.9 Hz, H-8″), 6.93–7.10 (m, 2H, H-5″, H-6″), 7.20–7.25 (m, 1H, H-2″), 7.63 (d, 1H, $J$ = 15.9 Hz, H-7″), $R_2$: 2.26 (s, 3H, H-11″), 3.78 (s, 3H, −OC*H*$_3$), 6.53 (d, 1H, $J$ = 15.9 Hz, H-8″), 6.93–7.10 (m, 2H, H-5″, H-6″), 7.20–7.25 (m, 1H, H-2″), 7.64 (d, 1H, $J$ = 15.9 Hz, H-7″), $R_3$: 2.26 (s, 3H, H-11″), 3.84 (s, 3H, −OC*H*$_3$), 6.57 (d, 1H, $J$ = 15.9 Hz, H-8″), 6.93–7.10, 7.20–7.25 (2× m, 2H, H-5″, H-6″), 7.34 (br s, 1H, H-2″), 7.76 (d, 1H, $J$ = 15.9 Hz, H-7″); $^{13}C$ NMR (75.48 MHz, $CD_3OD$) $\delta$ (ppm): 62.3 (C-6), 64.6 (C-1′), 65.8 (C-6′), 71.2 (C-4), 73.1 (C-2), 74.6 (C-5), 75.0 (C-3), 77.3 (C-4′), 77.4 (C-3′), 78.9 (C-5′), 93.6 (C-1), 105.8 (C-2′); *trans-p*-feruloyl units: $\delta$ = $R_1$: 20.5 (C-11″), 56.5 (−O*C*H$_3$), 112.5 (C-2″), 118.1 (C-8″), 122.5 (C-5″), 124.3 (C-6″), 134.4 (C-1″), 143.0 (C-3″), 146.2 (C-7″), 152.9 (C-4″), 167.2 (C-9″), 170.4 (C-10″), $R_2$: 20.5 (C-11″), 56.6 (−O*C*H$_3$), 112.8 (C-2″), 118.3 (C-8″), 122.5 (C-5″), 124.3 (C-6″), 134.5 (C-1″), 143.1 (C-3″), 147.0 (C-7″), 152.9 (C-4″), 167.5 (C-9″), 170.4 (C-10″), $R_3$: 20.5 (C-11″), 56.6 (−O*C*H$_3$), 113.2 (C-2″), 118.6 (C-8″), 122.6 (C-5″), 124.3 (C-6″), 134.7 (C-1″), 143.2 (C-3″), 147.0 (C-7″), 152.9 (C-4″), 168.0 (C-9″), 170.4 (C-10″); LC-MS (ESI): $m/z$ 1019.23 $[M + Na]^+$; HR-MS: $m/z$ $[M + Na]^+$ calcd for $C_{48}H_{52}O_{23}Na$: 1019.2792, found: 1019.2774.

*4.1.2.4. 3,3′,4′,6′-tetra-O-acetoxyferuloylsucrose **13**.* Following the general procedure, treatment of a solution of compound **10** (0.6 g, 0.4 mmol) with 60% aq. AcOH (32 mL) at 80 °C for 35 min followed by column chromatographic purification using a gradient of $CH_2Cl_2$/EtOAc as eluent yielded compound **13** as a white solid (0.45 g, 87% yield). Analytical data for **13**: $R_f$ = 0.87 (EtOAc/MeOH 9:1); mp: 127–129 °C; FT-IR (KBr) $\nu_{max}$: 3482, 2963, 2941, 1765, 1717, 1637, 1601, 1510, 1467, 1420, 1371, 1325, 1260, 1154, 1123, 1032, 1008, 945, 904, 832, 797, 704, 649 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ (ppm): 3.61 (dd, 1H, $J$ = 9.6 Hz, 9.3 Hz, H-4); 3.73 (m, 1H, H-2), 3.84 (m, 3H, H-1′b, H-1′a, H-6a), 4.01 (m, 1H, H-6b), 4.12 (m, 1H, H-5), 4.50 (m, 1H, H-5′), 4.56 (m, 1H, H-6′a), 4.67 (dd, 1H, $J$ = 7.2 Hz, 11.4 Hz, H-6′b), 5.13 (dd, 1H, $J$ = 9.6 Hz, 9.3 Hz, H-3), 5.56 (d, 1H, $J$ = 2.7 Hz, H-1), 5.59 (d, 1H, $J$ = 5.4 Hz, H-3′), 5.71 (app t, 1H, $J$ = 4.8 Hz, H-4′); *trans-p*-feruloyl units: $R_1$: 2.29 (s, 3H, H-11″), 3.82 (s, 3H, −OC*H*$_3$), 6.39 (d, 1H, $J$ = 15.9 Hz, H-8″), 7.00–7.09 (m, 3H, H-2″, H-5″, H-6″), 7.59 (d, 1H, $J$ = 15.9 Hz, H-7″), $R_2$: 2.30 (s, 3H, H-11″), 3.83 (s, 3H, −OC*H*$_3$), 6.39 (d, 1H, $J$ = 15.9 Hz, H-8″), 7.00–7.09 (m, 3H, H-2″, H-5″, H-6″), 7.68 (d, 1H, $J$ = 15.9 Hz, H-7″), $R_3$: 2.31 (s, 3H, H-11″), 3.83 (s, 3H, −OC*H*$_3$), 6.42 (d, 1H, $J$ = 15.9 Hz, H-8″), 7.00–7.09 (m, 3H, H-2″, H-5″, H-6″), 7.19 (d, 1H, $J$ = 8.4 Hz, H-2″), 7.69 (d, 1H, $J$ = 15.9 Hz, H-7″), $R_4$: 2.32 (s, 3H, H-11″), 3.85 (s, 3H, −OC*H*$_3$), 6.57 (d, 1H, $J$ = 15.9 Hz, H-8″), 7.00–7.09 (m, 1H, H-6″), 7.19 (d, 1H, $J$ = 8.4 Hz, H-5″), 7.24 (br s, 1H, H-2″), 7.84 (d, 1H, $J$ = 15.9 Hz, H-7″); $^{13}C$ NMR (75.48 MHz, $CDCl_3$) $\delta$ (ppm): 62.5 (C-6), 64.4 (C-1′), 64.5 (C-6′), 69.6 (C-4), 70.6 (C-2), 73.6 (C-5), 76.5 (C-4′), 77.0 (C-3), 78.1 (C-3′), 79.8 (C-5′), 92.5 (C-1), 105.5 (C-2′); *trans-p*-feruloyl units: $R_1$: 20.7 (C-11″), 55.9 (−O*C*H$_3$), 111.3 (C-2″), 116.4 (C-8″), 121.4 (C-5″), 123.2 (C-6″), 132.8 (C-1″), 141.6 (C-3″), 145.4 (C-7″), 151.3 (C-4″), 165.7 (C-9″), 168.4 (C-10″), $R_2$: 20.7 (C-11″), 55.9 (−O*C*H$_3$), 111.4 (C-2″), 116.5 (C-8″), 121.5 (C-5″), 123.2 (C-6″), 132.9 (C-1″), 141.7 (C-3″), 145.6 (C-7″), 151.4 (C-4″), 165.7 (C-9″), 168.7 (C-10″), $R_3$: 20.7 (C-11″), 55.9 (−O*C*H$_3$), 111.4 (C-2″), 117.4 (C-8″), 121.6 (C-5″), 123.3 (C-6″), 133.0 (C-1″), 141.8 (C-3″), 146.2 (C-7″), 151.4 (C-4″), 166.7 (C-9″), 168.7 (C-10″), $R_4$: 20.7 (C-11″), 56.0 (−O*C*H$_3$), 112.0 (C-2″), 117.4 (C-8″), 121.9 (C-5″), 123.3 (C-6″), 133.0 (C-1″), 141.9 (C-3″), 147.2 (C-7″), 151.5 (C-4″), 166.8 (C-9″), 168.8 (C-10″); LC-MS (ESI): $m/z$ 1237.28 $[M + Na]^+$; HR-MS: $m/z$ $[M + Na]^+$ calcd for $C_{60}H_{62}O_{27}Na$: 1237.3371, found: 1237.3373.

*4.1.3. Deacetylation of compounds **9**, **11**–**13***

*4.1.3.1. General procedure.* To a separate suspension of acetoxyferuloyl compounds **9**, **11**–**13** in 95% EtOH, piperidine was added, whereupon the solution turned yellow. After dissolving the starting material completely, the reaction was allowed to continue until the disappearance of the starting material. The reaction was monitored by TLC analysis (EtOAc/MeOH 9:1). The mixture was quenched with AcOH and was evaporated to a syrup. It was subjected to silica gel column chromatography using a gradient of $CH_2Cl_2$/EtOAc/MeOH as eluent. The solvent was evaporated under diminished pressure to furnish deacetylated products **1**, **2**, **14** and **15** as a white solid.

*4.1.3.2. 3′,6′-di-O-feruloylsucrose (helonioside A, **1**).* Following the general procedure, a suspension of compound **11** (0.7 g, 0.9 mmol) in 95% EtOH (47 mL) was treated with piperidine (335.0 μL, 0.3 g, 3.4 mmol) for 3 h to afford compound **1** as a white solid (0.40 g, 68% yield). Analytical data for **1**: $R_f$ = 0.49 (EtOAc/MeOH 9:1); mp: 154–156 °C; FT-IR (KBr) $\nu_{max}$: 3417, 2938, 1720, 1691, 1632, 1519, 1454, 1431, 1379, 1273, 1151, 1057, 1030, 995, 938, 841, 822, 788, 696 $cm^{-1}$; $^1H$ NMR (300 MHz, $CD_3OD$) $\delta$ (ppm): 3.39 (m, 1H, H-4), 3.44 (dd, 1H, $J$ = 3.6 Hz, 6.0 Hz, H-2), 3.61 (m, 2H, H-1′b, H-1′a), 3.69 (m, 1H, H-3),

3.80 (dd, 1H, $J$ = 4.2 Hz, 11.7 Hz, H-6a), 3.88 (m, 1H, H-6b), 3.96 (m, 1H, H-5), 4.16 (m, 1H, H-5′), 4.45 (dd, 1H, $J$ = 7.6 Hz, 7.8 Hz, H-4′), 4.57 (m, 2H, H-6′b, H-6′a), 5.45 (d, 1H, $J$ = 3.6 Hz, H-1), 5.50 (d, 1H, $J$ = 7.8 Hz, H-3′), *trans-p*-feruloyl units: $R_1$: 3.90 (s, 3H, −OC$H_3$), 6.41 (d, 1H, $J$ = 15.9 Hz, H-8″), 6.82 (d, 1H, $J$ = 8.1 Hz, H-5″), 7.14 (dd, 1H, $J$ = 1.5 Hz, 8.4 Hz, H-6″), 7.24 (d, 1H, $J$ = 1.5 Hz, H-2″), 7.66 (d, 1H, $J$ = 15.9 Hz, H-7″), $R_2$: 3.90 (s, 3H, −OC$H_3$), 6.44 (d, 1H, $J$ = 15.9 Hz, H-8″), 6.82 (d, 1H, $J$ = 8.1 Hz, H-5″), 7.10 (dd, 1H, $J$ = 1.5 Hz, 8.4 Hz, H-6″), 7.20 (d, 1H, $J$ = 1.5 Hz, H-2″), 7.72 (d, 1H, $J$ = 15.9 Hz, H-7″); $^{13}$C NMR (75.48 MHz, $CD_3OD$) $\delta$ (ppm): 62.7 (C-6), 65.2 (C-1′), 66.2 (C-6′), 71.4 (C-4), 73.2 (C-2), 74.4 (C-5), 75.0 (C-4′, C-3), 79.2 (C-3′), 81.3 (C-5′), 93.1 (C-1), 105.1 (C-2′); *trans-p*-feruloyl units: $R_1$: 56.5 (−OC$H_3$), 111.7 (C-2″), 114.9 (C-8″), 116.5 (C-5″), 124.3 (C-6″), 127.7 (C-1″), 147.3 (C-7″), 149.4 (C-3″), 150.7 (C-4″), 168.3 (C-9″), $R_2$: 56.5 (−OC$H_3$), 112.1 (C-2″), 115.1 (C-8″), 116.5 (C-5″), 124.3 (C-6″), 127.7 (C-1″), 147.8 (C-7″), 149.4 (C-3″), 150.7 (C-4″), 169.1 (C-9″); LC-MS (ESI): $m/z$ 717.21 $[M + Na]^+$; HR-MS: $m/z$ $[M + Na]^+$ calcd for $C_{32}H_{38}O_{17}Na$: 717.2001, found: 717.1984. Spectral data of helonioside A **1** was the same as reported for the isolated natural product [2,6].

*4.1.3.3. 3′,4′,6′-tri-O-feruloyl sucrose* ***2***. Following the general procedure, a suspension of compound **12** (0.4 g, 0.4 mmol) in 95% EtOH (28 mL) was treated with piperidine (232.0 μL, 0.2 g, 2.3 mmol) for 4 h to afford compound **2** [15] as a white solid (0.22 g, 65% yield). Analytical data for **2**: $R_f$ = 0.46 (EtOAc/MeOH 9:1); mp: 99–101 °C; FT-IR (KBr) $\nu_{max}$: 3355, 2969, 1715, 1699, 1653, 1595, 1517, 1457, 1430, 1272, 1157, 1034, 992, 845, 815 cm$^{-1}$; $^1$H NMR (300 MHz, $CD_3OD$) $\delta$ (ppm): 3.52 (m, 2H, H-2, H-4), 3.73 (m, 2H, H-1′b, H-1′a), 3.80 (m, 1H, H-3), 3.90 (m, 1H, H-6a), 4.05 (m, 2H, H-6b, H-5), 4.47 (m, 1H, H-5′), 4.62 (m, 2H, H-6′b, H-6′a), 5.51 (d, 1H, $J$ = 3.3 Hz, H-1), 5.81 (m, 2H, H-3′, H-4′), *trans-p*-feruloyl units: $R_1$: 3.72 (s, 3H, −OC$H_3$), 6.29 (m, 1H, H-8″), 6.74 (m, 1H, H-5″), 6.94 (m, 2H, H-2″, H-6″), 7.54 (d, 1H, $J$ = 15.9 Hz, H-7″), $R_2$: 3.77 (s, 3H, −OC$H_3$), 6.29 (m, 1H, H-8″), 6.74 (m, 1H, H-5″), 7.08 (br d, 1H, $J$ = 8.4 Hz, H-6″), 7.17 (br s, 1H, H-2″), 7.54 (d, 1H, $J$ = 15.9 Hz, H-7″), $R_3$: 3.83 (s, 3H, −OC$H_3$), 6.41 (d, 1H, $J$ = 15.9 Hz, H-8″), 6.74 (m, 1H, H-5″), 6.94 (m, 2H, H-2″, H-6″), 7.70 (d, 1H, $J$ = 15.9 Hz, H-7″); $^{13}$C NMR (75.48 MHz, $CD_3OD$) $\delta$ (ppm): 62.4 (C-6), 64.8 (C-1′), 65.7 (C-6′), 1.2 (C-4), 73.2 (C-2), 74.6 (C-5), 75.0 (C-3), 77.1 (C-3′, C-4′), 78.9 (C-5′), 93.6 (C-1), 105.8 (C-2′); *trans-p*-feruloyl units: $R_1$: 56.4 (−OC$H_3$), 111.6 (C-2″), 114.4 (C-8″), 116.5 (C-5″), 124.3 (C-6″), 127.4 (C-1″), 148.2 (C-7″), 149.2 (C-3″), 150.6 (C-4″), 168.2 (C-9″), $R_2$: 56.4 (−OC$H_3$), 111.8 (C-2″), 114.6 (C-8″), 116.5 (C-5″), 124.4 (C-6″), 127.5 (C-1″), 147.4 (C-7″), 149.2 (C-3″), 150.7 (C-4″), 168.7 (C-9″), $R_3$: 56.5 (−OC$H_3$), 112.1 (C-2″), 114.9 (C-8″), 116.4 (C-5″), 124.4 (C-6″), 127.6 (C-1″), 147.4 (C-7″), 149.2 (C-3″), 150.7 (C-4″), 167.9 (C-9″); LC-MS (ESI): $m/z$ 893.23 $[M + Na]^+$; HR-MS: $m/z$ $[M + Na]^+$ calcd for $C_{42}H_{46}O_{20}Na$: 893.2475, found: 893.2478.

*4.1.3.4. 3,3′,4′,6′-tetra-O-feruloyl sucrose* ***14***. Following the general procedure, a suspension of compound **13** (0.2 g, 0.2 mmol) in 95% EtOH (16 mL) was reacted with piperidine (150.0 μL, 0.1 g, 1.5 mmol) for 4 h to afford compound **14** as a white solid (0.15 g, 76% yield). Analytical data for **14**: $R_f$ = 0.73 (EtOAc/MeOH 9:1); mp: 123–125 °C; FT-IR (KBr) $\nu_{max}$: 3423, 2964, 2940, 1708, 1631, 1594, 1515, 1452, 1431, 1372, 1271, 1158, 1032, 1003, 846, 819, 703, 603 cm$^{-1}$; $^1$H NMR (300 MHz, $CD_3OD$) $\delta$ (ppm): 3.65–3.95 (m, 5H, H-1′b, H-1′a, H-2, H-4, H-6a), 4.03–4.07 (m, 1H, H-6b), 4.18–4.23 (m, 1H, H-5), 4.46–4.50 (m, 1H, H-5′), 4.58–4.64 (m, 2H, H-6′b, H-6′a), 5.45 (app t, 1H, $J$ = 9.6 Hz, H-3), 5.58 (d, 1H, $J$ = 3.3 Hz, H-1), 5.86 (m, 2H, H-3′, H-4′); *trans-p*-feruloyl units: $R_1$: 3.76 (s, 3H, −OC$H_3$), 6.29 (d, 1H, $J$ = 15.9 Hz, H-8″), 6.71 (d, 1H, $J$ = 8.1 Hz, H-5″), 6.95–7.08 (m, 2H, H-2″, H-6″), 7.57 (d, 1H, $J$ = 15.9 Hz, H-7″), $R_2$: 3.81 (s, 3H, −OC$H_3$), 6.34 (d, 1H, $J$ = 15.9 Hz, H-8″), 6.76 (d, 1H, $J$ = 8.1 Hz, H-5″), 6.95–7.08 (m, 2H, H-2″, H-6″), 7.59 (d, 1H, $J$ = 15.9 Hz, H-7″), $R_3$: 3.87 (s, 3H, −OC$H_3$), 6.42 (d, 1H, $J$ = 15.9 Hz, H-8″), 6.79 (d, 1H, $J$ = 8.1 Hz, H-5″), 7.16 (m, 2H, H-2″, H-6″), 7.60 (d, 1H, $J$ = 15.9 Hz, H-7″), $R_4$: 3.88 (s, 3H, −OC$H_3$), 6.46 (d, 1H, $J$ = 15.9 Hz, H-8″), 6.81 (d, 1H, $J$ = 8.1 Hz, H-5″), 6.95–7.08 (m, 1H, H-6″), 7.28 (br d, 1H, $J$ = 1.8 Hz, H-2″), 7.74 (d, 1H, $J$ = 15.9 Hz, H-7″); $^{13}$C NMR (75.48 MHz, $CD_3OD$) $\delta$ (ppm): 62.0 (C-6), 64.5 (C-1′), 65.7 (C-6′), 69.3 (C-4), 71.7 (C-2), 74.8 (C-5), 77.0, 77.1 (C-3, C-3′, C-4′), 78.8 (C-5′), 93.7 (C-1), 105.8 (C-2′); *trans-p*-feruloyl units: $R_1$: 56.4 (−OC$H_3$), 111.6 (C-2″), 114.4 (C-8″), 116.0 (C-5″), 124.0 (C-6″), 127.5 (C-1″), 146.9 (C-7″), 149.3 (C-3″), 150.6 (C-4″), 168.1 (C-9″), $R_2$: 56.5 (−OC$H_3$), 111.8 (C-2″), 114.8 (C-8″), 116.5 (C-5″), 124.3 (C-6″), 127.6 (C-1″), 147.5 (C-7″), 149.4 (C-3″), 150.7 (C-4″), 168.2 (C-9″), $R_3$: 56.5 (−OC$H_3$), 111.8 (C-2″), 115.0 (C-8″), 116.5 (C-5″), 124.4 (C-6″), 127.8 (C-1″), 147.5 (C-7″), 149.4 (C-3″), 150.7 (C-4″), 168.8 (C-9″), $R_4$: 56.6 (−OC$H_3$), 112.7 (C-2″), 115.0 (C-8″), 116.6 (C-5″), 124.5 (C-6″), 127.9 (C-1″), 148.3 (C-7″), 149.4 (C-3″), 150.9 (C-4″), 169.3 (C-9″); LC-MS (ESI): $m/z$ 1069.25 $[M + Na]^+$; HR-MS: $m/z$ $[M + Na]^+$ calcd for $C_{52}H_{54}O_{23}Na$: 1069.2948, found: 1069.2926.

*4.1.3.5. 3′,4′,6′-tri-O-feruloyl-2,1′:4,6-di-O-isopropylidene sucrose* ***15***. Following the general procedure, a suspension of compound **9** (0.3 g, 0.3 mmol) in 95% EtOH (23 mL) was treated with piperidine (176.0 μL, 0.2 g, 1.8 mmol) for 4 h to give compound **15** as a white solid (0.20 g, 71% yield). Analytical data for **15**: $R_f$ = 0.27 (EtOAc/hexanes 3:1); mp: 145–147 °C; FT-IR (KBr) $\nu_{max}$: 3067, 2991, 2939, 1715, 1632, 1593, 1516, 1465, 1431, 1383, 1271, 1211, 1154, 1065, 1031, 942, 856, 816, 724, 655, 603 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ (ppm): 1.31, 1.37, 1.49 (3× s, 12H, ($CH_3$)$_2$C); 3.62 (m, 3H, H-1′a, H-4, H-6a); 3.75 (m, 1H, H-2); 3.87 (m, 2H, H-3, H-5), 4.02 (m, 1H, H-6b), 4.14 (m, 1H, H-1′b), 4.49 (m, 2H, H-5′, H-6′a), 4.57 (m, 1H, H-6′b), 5.35 (br d, 1H, $J$ = 5.1 Hz, H-4′), 5.59 (br s, 1H, H-3′), 6.16 (m, 1H, H-1); *trans-p*-feruloyl units: $R_1$: 3.84 (s, 3H, −OC$H_3$), 6.24 (d, 1H, $J$ = 15.9 Hz, H-8″), 6.83–7.08 (m, 3H, H-2″, H-5″, H-6″), 7.59 (d, 1H, $J$ = 15.9 Hz, H-7″), $R_2$: 3.87 (s, 3H, −OC$H_3$), 6.26 (d, 1H, $J$ = 15.9 Hz, H-8″), 6.83–7.08 (m, 3H, H-2″, H-5″, H-6″), 7.59 (d, 1H, $J$ = 15.9 Hz, H-7″), $R_3$: 3.92 (s, 3H, −OC$H_3$), 6.37 (d, 1H, $J$ = 15.9 Hz, H-8″), 6.83–7.08 (m, 3H, H-2″, H-5″, H-6″), 7.71 (d, 1H, $J$ = 15.9 Hz, H-7″); $^{13}$C NMR (75.48 MHz, $CDCl_3$) $\delta$ (ppm): 19.1, 24.1, 25.5, 28.9 (4× ($CH_3$)$_2$C), 62.0 (C-6), 63.9 (C-5), 64.9 (C-6′), 66.3 (C-1′), 70.2 (C-3), 72.8 (C-4), 73.8 (C-2), 77.1 (C-4′), 77.3 (C-3′), 79.9 (C-5′), 91.4 (C-1), 99.8, 101.8 (2× ($CH_3$)$_2$C), 104.7 (C-2′); *trans-p*-feruloyl units: $R_1$: 55.8 (−OC$H_3$), 109.4 (C-2″), 113.6 (C-8″), 114.8 (C-5″), 123.2 (C-6″), 126.5 (C-1″), 145.2 (C-7″), 146.8 (C-3″), 148.0 (C-4″), 166.2 (C-9″), $R_2$: 55.9 (−OC$H_3$), 109.4 (C-2″), 113.9 (C-8″), 114.9 (C-5″), 123.4 (C-6″), 126.6 (C-1″), 146.5 (C-7″), 146.8 (C-3″), 148.4 (C-4″), 166.4 (C-9″), $R_3$: 56.0 (−OC$H_3$), 109.5 (C-2″), 113.9 (C-8″), 114.9 (C-5″), 124.1 (C-6″), 126.9 (C-1″), 146.9 (C-3″), 147.2 (C-7″), 148.5 (C-4″), 166.8 (C-9″); LC-MS (ESI): $m/z$ 973.27 $[M + Na]^+$; HR-MS: $m/z$ $[M + Na]^+$ calcd for $C_{48}H_{54}O_{20}Na$: 973.3101, found: 973.3078.

*4.1.4. Synthesis of lapathoside C and its analogous*

*4.1.4.1. Preparation of 6-mono-O-acetoxyferuloyl-3′,6′-di-O-acetoxycinnamoylsucrose* ***18*** *and 3,6-di-O-acetoxyferuloyl-3′,6′-di-O-acetoxycinnamoylsucrose* ***19***. 3′,6′-di-*O*-acetoxycinnamoyl sucrose **16** (1.1 g, 1.5 mmol) was dissolved in dry $CH_2Cl_2$ (21 mL) to which 4 Å molecular sieves powder and dry pyridine (1.1 g, 1.2 mL, 14.4 mmol) were added. The solution was then cooled to 0 °C in an ice bath. *p*-Acetoxyferuloyl chloride **5** (0.4 g, 1.6 mmol) was then added slowly at the same temperature and the reaction was left to stir while warming to r.t. Stirring was continued until the reaction was completed as indicated by TLC analysis (EtOAc/hexanes 3:1). After 24 h, the resulting mixture was poured into vigorously stirred ice-water (100 mL) and the white solid precipitated was obtained by filtration. The precipitate was redissolved in EtOAc (25 mL) and

washed with 1 N HCl (2 × 50 mL). The aqueous layer was extracted with EtOAc (25 mL). The combined organic layers were then successively washed with 5% $NaHCO_3$ (2 × 50 mL), brine (25 mL) and then dried over anhyd. $MgSO_4$. The EtOAc solution was concentrated to residue that was subjected to column chromatography using a gradient of $CH_2Cl_2$/EtOAc as eluent and further, purified by PTLC afforded compound **18** as a white solid (0.50 g, 36% yield) along with compound **19** in 7% (0.12 g) yield. Analytical data for **18**: $R_f = 0.06$ (EtOAc/hexanes 3:1); mp: 108–110 °C; FT-IR (KBr) $\nu_{max}$: 3457, 3423, 2925, 2852, 1767, 1710, 1636, 1602, 1508, 1457, 1419, 1371, 1323, 1282, 1261, 1206, 1165, 1056, 1015, 946, 912, 836, 794, 754, 649, 595 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ (ppm): 3.32 (m, 1H, H-4), 3.54 (m, 2H, H-2, H-1′a), 3.68 (m, 2H, H-1′b, H-3), 4.11 (m, 1H, H-5), 4.24 (m, 1H, H-5′), 4.46 (m, 1H, H-4′), 4.55 (m, 4H, H-6b, H-6a, H-6′b, H-6′a), 5.30 (d, 1H, $J = 5.7$ Hz, H-3′), 5.42 (br s, 1H, H-1); *trans-p*-feruloyl units: $R_1$: 2.28 (s, 3H, H-11″), 3.77 (s, 3H, $-OCH_3$), 6.41 (d, 1H, $J = 15.9$ Hz, H-8″), 6.94 (d, 1H, $J = 8.1$ Hz, H-5″), 7.00–7.09 (m, 2H, H-2″, H-6″), 7.65 (d, 1H, $J = 15.9$ Hz, H-7″); *trans-p*-coumaroyl units: $R_2$: 2.23 (s, 3H, H-11″), 6.39 (d, 1H, $J = 15.9$ Hz, H-8″), 7.00–7.09 (m, 2H, H-3″, H-5″), 7.40 (d, 2H, H-2″, H-6″), 7.56 (d, 1H, $J = 15.9$ Hz, H-7″), $R_3$: 2.26 (s, 3H, H-11″), 6.29 (d, 1H, $J = 15.9$ Hz, H-8″), 7.00–7.09 (m, 2H, H-3″, H-5″), 7.47–7.53 (m, 2H, H-2″, H-6″), 7.47–7.53 (m, 1H, H-7″); $^{13}C$ NMR (75.48 MHz, $CDCl_3$) $\delta$ (ppm): 64.3 (C-1′), 64.5 (C-6), 64.8 (C-6′), 70.3 (C-4), 71.0 (C-5), 71.7 (C-2), 73.9 (C-3), 74.7 (C-4′), 79.8 (C-3′), 80.9 (C-5′), 91.6 (C-1), 104.5 (C-2′); *trans-p*-feruloyl units: $R_1$: 20.6 (C-11″), 55.9 ($-OCH_3$), 111.5 (C-2″), 116.7 (C-8″), 121.6 (C-5″), 123.2 (C-6″), 133.1 (C-1″), 141.5 (C-3″), 146.1 (C-7″), 151.3 (C-4″), 167.4 (C-9″), 169.5 (C-10″); *trans-p*-coumaroyl units: $R_2$: 21.1 (C-11″), 117.4 (C-8″), 122.1 (C-3″, C-5″), 129.4 (C-2″, C-6″), 131.6 (C-1″), 144.5 (C-7″), 152.2 (C-4″), 166.9 (C-9″), 168.9 (C-10″), $R_3$: 21.1 (C-11″), 117.5 (C-8″), 122.2 (C-3″, C-5″), 129.8 (C-2″, C-6″), 131.8 (C-1″), 145.1 (C-7″), 152.4 (C-4″), 167.2 (C-9″), 169.2 (C-10″); LC-MS (ESI): $m/z$ 959.14 $[M + Na]^+$; HR-MS: $m/z$ $[M + Na]^+$ calcd for $C_{46}H_{48}O_{21}Na$: 959.2580, found: 959.2549. Analytical data for **19**: $R_f = 0.11$ (EtOAc/hexanes 3:1); mp: 114–116 °C; FT-IR (KBr) $\nu_{max}$: 3483, 2925, 2855, 2363, 2340, 1766, 1713, 1637, 1602, 1508, 1467, 1419, 1371, 1321, 1260, 1203, 1164, 1123, 1061, 1032, 1011, 909, 834, 652 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ (ppm): 3.54 (m, 1H, H-4), 3.74 (m, 3H, H-2, H-1′a, H-1′b), 4.24–4.28 (m, 2H, H-5, H-5′), 4.46–4.60 (m, 5H, H-4′, H-6b, H-6a, H-6′b, H-6′a), 5.25 (m, 1H, H-3), 5.29 (d, 1H, $J = 7.2$ Hz, H-3′), 5.57 (br s, 1H, H-1), *trans-p*-coumaroyl units: $R_1$: 2.28 (s, 3H, H-11″), 6.40 (d, 1H, $J = 16.2$ Hz, H-8″), 6.98–7.16 (m, 2H, H-3″, H-5″), 7.47 (d, 2H, H-2″, H-6″), 7.53–7.64 (m, 1H, H-7″), $R_2$: 2.28 (s, 3H, H-11″), 6.46 (d, 1H, $J = 16.2$ Hz, H-8″), 6.98–7.16 (m, 2H, H-3″, H-5″), 7.53–7.64 (m, 3H, H-2″, H-6″, H-7″); *trans-p*-feruloyl units: $R_3$: 2.30 (s, 3H, H-11″), 3.81 (s, 3H, $-OCH_3$), 6.52 (d, 1H, $J = 16.2$ Hz, H-8″), 6.98–7.16 (m, 3H, H-2″, H-5″, H-6″), 7.53–7.64 (m, 1H, H-7″), $R_4$: 2.30 (s, 3H, H-11″), 3.81 (s, 3H, $-OCH_3$), 6.51 (d, 1H, $J = 16.2$ Hz, H-8″), 6.98–7.16 (m, 3H, H-2″, H-5″, H-6″), 7.79 (d, 1H, $J = 16.2$ Hz, H-7″); $^{13}C$ NMR (75.48 MHz, $CDCl_3$) $\delta$ (ppm): 63.7 (C-6), 64.5 (C-6′), 64.6 (C-1′), 69.1 (C-4), 70.6 (C-2), 71.4 (C-5), 74.4 (C-4′), 76.6 (C-3), 80.5 (C-3′), 80.6 (C-5′), 91.9 (C-1), 104.5 (C-2′); *trans-p*-coumaroyl units: $R_1$: 21.1 (C-11″), 116.4 (C-8″), 122.1 (C-3″, C-5″), 129.4 (C-2″, C-6″), 131.6 (C-1″); 144.7 (C-7″), 152.2 (C-4″), 166.9 (C-9″), 168.8 (C-10″), $R_2$: 21.1 (C-11″), 116.4 (C-8″), 122.1 (C-3″, C-5″), 129.9 (C-2″, C-6″), 131.9 (C-1″), 145.3 (C-7″), 152.5 (C-4″), 167.3 (C-9″), 168.8 (C-10″); *trans-p*-feruloyl units: $R_3$: 20.7 (C-11″), 55.9 ($-OCH_3$), 111.4 (C-2″), 117.4 (C-8″), 121.5 (C-5″), 123.2 (C-6″), 133.1 (C-1″), 141.6 (C-3″), 145.6 (C-7″), 151.4 (C-4″), 167.8 (C-9″), 169.1 (C-10″), $R_4$: 20.7 (C-11″), 55.9 ($-OCH_3$), 111.4 (C-2″), 117.4 (C-8″), 121.5 (C-5″), 123.2 (C-6″), 133.1 (C-1″), 141.6 (C-3″), 146.5 (C-7″), 151.4 (C-4″), 168.2 (C-9″), 169.1 (C-10″); LC-MS (ESI): $m/z$ 1177.11 $[M + Na]^+$; HR-MS: $m/z$ $[M + Na]^+$ calcd for $C_{58}H_{58}O_{25}Na$: 1177.3159, found: 1177.3159.

*4.1.4.2. Preparation of 6-mono-O-feruloyl-3′,6′-di-O-coumaroylsucrose **3** and 3,6-di-O-feruloyl-3′,6′-di-O-coumaroylsucrose **21***

*4.1.4.2.1. General procedure.* Pyrrolidine were added to a suspension of compounds **18** and **19** in 95% EtOH. Consequently, it caused the solution to turn yellow. The starting material typically dissolved within 15 min and the reaction was allowed to continue until the disappearance of the starting material as indicated by TLC analysis (EtOAc). This mixture was directly added to a column of strongly acidic ion-exchange resin [Amberlite IRA-120 ($H^+$) washed and packed in 95% EtOH. The appropriate fractions were concentrated under diminished pressure to a residue that was subjected to column chromatography using a gradient of $CH_2Cl_2$/EtOAc/MeOH afforded compounds **3** and **21**.

*4.1.4.2.2. 6-mono-O-feruloyl-3′,6′-di-O-coumaroylsucrose (lapathoside C, **3**).* Following the general procedure, a suspension of compound **18** (0.2 g, 0.2 mmol) in 95% EtOH (10 mL) was treated with pyrrolidine (155.0 μL, 0.1 g, 1.9 mmol) for 90 min to furnish lapathoside C **3** as a white solid (0.13 g, 75% yield). Analytical data for **3**: $R_f = 0.55$ (EtOAc/MeOH 9:1); mp: 125–127 °C; FT-IR (KBr) $\nu_{max}$: 3447, 3421, 2956, 2926, 2362, 2340, 1700, 1636, 1559, 1540, 1517, 1457, 1445, 1374, 1328, 1266, 1170, 1059, 997, 946, 831, 668 $cm^{-1}$; $^1H$ NMR (300 MHz, $CD_3OD$) $\delta$ (ppm): 3.32 (m, 1H, H-4), 3.35 (m, 1H, H-5), 3.48 (m, 1H, H-2), 3.60 (m, 2H, H-1′b, H-1′a), 3.65 (m, 1H, H-3), 4.18 (m, 1H, H-5′), 4.29 (m, 1H, H-6a), 4.55 (m, 2H, H-6′b, H-6′a), 4.65 (m, 1H, H-4′), 4.71 (m, 1H, H-6b), 5.50 (m, 1H, H-1), 5.54 (m, 1H, H-3′); *trans-p*-feruloyl units: $R_1$: 3.84 (s, 3H, $-OCH_3$), 6.48 (d, 1H, $J = 15.9$ Hz, H-8″), 6.75–6.82 (m, 1H, H-5″), 7.02 (d, 1H, $J = 7.5$ Hz, H-6″), 7.21 (br s, 1H, H-2″), 7.62 (d, 1H, $J = 15.9$ Hz, H-7″); *trans-p*-coumaroyl units: $R_2$: 6.43 (d, 1H, $J = 15.9$ Hz, H-8″), 6.75–6.82 (m, 2H, H-3″, H-5″), 7.52 (d, 2H, $J = 8.4$ Hz, H-2″, H-6″), 7.73 (d, 1H, $J = 15.9$ Hz, H-7″), $R_3$: 6.24 (d, 1H, $J = 15.9$ Hz, H-8″), 6.75–6.82 (m, 2H, H-3″, H-5″), 7.34 (d, 2H, $J = 8.4$ Hz, H-2″, H-6″), 7.62 (d, 1H, $J = 15.9$ Hz, H-7″); $^{13}C$ NMR (75.48 MHz, $CD_3OD$) $\delta$ (ppm): 65.4 (C-1′), 65.8 (C-6, C-6′), 72.1 (C-4), 72.3 (C-5), 73.1 (C-2), 74.8 (C-3), 75.0 (C-4′), 79.0 (C-3′), 81.1 (C-5′), 92.5 (C-1), 104.8 (C-2′); *trans-p*-feruloyl units: $R_1$: 56.4 ($-OCH_3$), 111.5 (C-2″), 115.3 (C-8″), 116.3 (C-5″), 124.5 (C-6″), 127.7 (C-1″), 147.2 (C-7″), 149.3 (C-3″), 150.6 (C-4″), 169.3 (C-9″); *trans-p*-coumaroyl units: $R_2$: 114.6 (C-8″), 116.8 (C-3″, C-5″), 127.1 (C-1″), 131.5 (C-2″, C-6″), 147.6 (C-7″), 161.4 (C-4″), 168.4 (C-9″), $R_3$: 114.8 (C-8″), 116.8 (C-3″, C-5″), 127.1 (C-1″), 131.2 (C-2″, C-6″), 146.8 (C-7″), 161.3 (C-4″), 168.9 (C-9″); LC-MS (ESI): $m/z$ 833.13 $[M + Na]^+$; HR-MS: $m/z$ $[M + Na]^+$ calcd for $C_{40}H_{42}O_{18}Na$: 833.2263, found: 833.2283. Spectral data of lapathoside C **3** was the same as reported for the isolated natural product [16].

*4.1.4.2.3. 3,6-di-O-feruloyl-3′,6′-di-O-coumaroylsucrose **21**.* Following the general procedure, a suspension of compound **19** (0.1 g, 0.1 mmol) in 95% EtOH (5 mL) was reacted with pyrrolidine (130.0 μL, 0.1 g, 1.6 mmol) for 3 h to afford compound **21** as a white solid (0.04 g, 47% yield). Analytical data for **21**: $R_f = 0.74$ (EtOAc/MeOH 9:1); mp: 135–138 °C; FT-IR (KBr) $\nu_{max}$: 3363, 2924, 2852, 2363, 2340, 1698, 1635, 1604, 1517, 1457, 1455, 1337, 1277, 1169, 1128, 1087, 1031, 987, 932, 831, 666 $cm^{-1}$; $^1H$ NMR (300 MHz, $CD_3OD$) $\delta$ (ppm): 3.56 (m, 1H, H-4), 3.65–3.74 (m, 3H, H-1′a, H-1′b, H-2), 4.15–4.21 (m, 1H, H-5′), 4.24–4.33 (m, 1H, H-6′b), 4.41 (dd, 1H, $J = 8.7$ Hz, 9.0 Hz, H-5), 4.52–4.59 (m, 2H, H-6b, H-6a), 4.67–4.74 (m, 2H, H-4′, H-6′a), 5.34 (dd, 1H, $J = 9.9$ Hz, 9.0 Hz, H-3), 5.57–5.62 (m, 2H, H-1, H-3′); *trans-p*-coumaroyl units: $R_1$: 6.26 (d, 1H, $J = 16.2$ Hz, H-8″), 6.74–6.82 (m, 2H, H-3″, H-5″), 7.36 (d, 2H, $J = 8.7$ Hz, H-2″, H-6″), 7.54–7.65 (m, 1H, H-7″); $R_2$: 6.49 (d, 1H, $J = 16.2$ Hz, H-8″), 6.74–6.82 (m, 2H, H-3″, H-5″), 7.54–7.65 (m, 2H, H-2″, H-6″), 7.75 (d, 1H, $J = 16.2$ Hz, H-7″), *trans-p*-feruloyl units: $R_3$: 3.84 (s, 3H, $-OCH_3$), 6.42 (d, 1H, $J = 16.2$ Hz, H-8″), 6.74–6.82 (m, 1H, H-5″), 7.01 (dd, 1H, $J = 1.5$ Hz, 7.8 Hz, H-6″), 7.18 (dd, 1H, $J = 9.9$ Hz, 1.2 Hz, H-2″), 7.54–7.65 (m, 1H, H-7″), $R_4$: 3.88 (s,

3H, −OC*H*$_3$), 6.48 (d, 1H, *J* = 16.2 Hz, H-8″), 6.74–6.82 (d, 1H, *J* = 7.8 Hz, H-5″), 7.07 (dd, 1H, *J* = 1.5 Hz, 7.8 Hz, H-6″), 7.18 (dd, 1H, *J* = 9.9 Hz, 1.2 Hz, H-2″), 7.54–7.65 (m, 1H, H-7″); $^{13}$C NMR (75.48 MHz, $CD_3OD$) *δ* (ppm): 65.3 (C-1′), 65.6 (C-6), 65.7 (C-6′), 70.5 (C-4), 71.6 (C-2), 72.5 (C-5), 74.7 (C-4′), 77.0 (C-3), 79.0 (C-3′), 81.2 (C-5′), 92.7 (C-1), 105.4 (C-2′), *trans*-*p*-coumaroyl units: $R_1$: 114.7 (C-8″), 116.9 (C-3″, C-5″), 127.1 (C-1″), 131.3 (C-2″, C-6″), 146.9 (C-7″), 161.5 (C-4″), 168.7 (C-9″), $R_2$: 114.9 (C-8″), 116.9 (C-3″, C-5″), 127.3 (C-1″), 131.7 (C-2″, C-6″), 147.0 (C-7″), 161.5 (C-4″), 169.0 (C-9″); *trans*-*p*-feruloyl units: $R_3$: 56.5 (−$OCH_3$), 111.8 (C-2″), 115.3 (C-8″), 116.4 (C-5″), 124.1 (C-6″), 127.7 (C-1″), 147.4 (C-7″), 149.4 (C-3″), 150.7 (C-4″), 169.3 (C-9″), $R_4$: 56.5 (−$OCH_3$), 111.8 (C-2″), 115.8 (C-8″), 116.6 (C-5″), 124.6 (C-6″), 127.9 (C-1″), 147.8 (C-7″), 149.5 (C-3″), 150.8 (C-4″), 169.3 (C-9″); LC-MS (ESI): *m*/*z* 1009.12 $[M + Na]^+$; HR-MS: *m*/*z* $[M + Na]^+$ calcd for $C_{50}H_{50}O_{21}Na$: 1009.2737, found: 1009.2740.

#### 4.1.4.3. Synthesis of 3,6,3′,6′-tetra-O-coumaroylsucrose **22**

*4.1.4.3.1. Preparation of 3,6,3′,6′-tetra-O-acetoxycinnamoylsucrose **20**.* 3′,6′-di-*O*-acetoxycinnamoyl sucrose **16** (1.1 g, 1.5 mmol) was dissolved in dry $CH_2Cl_2$ (21 mL) to which 4 Å molecular sieves powder and dry pyridine (1.2 g, 1.2 mL, 15.3 mmol) were added. The solution was cooled to 0 °C in an ice bath and *p*-acetoxycinnamoyl chloride (**17**, 0.5 g, 2.0 mmol) was added slowly at the same temperature and the reaction mixture was left to stir while warming to r.t. Stirring was continued for 24 h. After this time, the starting material was completely disappeared as indicated by TLC (EtOAc/hexanes 3:1). The resulting mixture was poured into vigorously stirred ice-water (100 mL) and a white solid precipitated was obtained after decantation and filtration. The precipitate was redissolved in EtOAc (25 mL) and washed with 1 N HCl (2 × 50 mL). The aqueous layer was extracted with EtOAc (25 mL). The combined organic layers were then successively washed with 5% $NaHCO_3$ (2 × 50 mL) and brine (25 mL) and then dried over anhyd. $MgSO_4$. The EtOAc solution was concentrated to residue that was subjected to column chromatography using a gradient of $CH_2Cl_2$/EtOAc as eluent followed by PTLC afforded compound **20** as a white solid (0.20 g, 12% yield). Analytical data for **20**: $R_f$ = 0.43 (EtOAc/hexanes 3:1); mp: 113–115 °C; FT-IR (KBr) $\nu_{max}$: 3475, 2934, 2362, 2337, 1768, 1718, 1704, 1636, 1602, 1559, 1540, 1507, 1457, 1419, 1371, 1322, 1283, 1207, 1169, 1058, 1009, 946, 911, 836, 792, 649 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) *δ* (ppm): 3.60 (m, 1H, H-4), 3.68 (m, 1H, H-1′a), 3.78 (m, 2H, H-2, H-1′b), 4.26 (m, 3H, H-5, H-5′, H-6a), 4.53 (m, 4H, H-4′, H-6b, H-6′b, H-6′a), 5.27 (dd, 1H, *J* = 9.0 Hz, 9.3 Hz, H-3), 5.34 (d, 1H, *J* = 6.9 Hz, H-3′), 5.56 (br s, 1H, H-1); *trans*-*p*-coumaroyl units: $R_1$: 2.27 (s, 3H, H-11″), 6.38 (d, 1H, *J* = 15.9 Hz, H-8″), 7.05 (d, 2H, H-3″, H-5″), 7.44–7.49 (m, 2H, H-2″, H-6″), 7.61 (m, 1H, H-7″), $R_2$: 2.27 (s, 3H, H-11″), 6.40 (d, 1H, *J* = 15.9 Hz, H-8″), 7.05 (d, 2H, H-3″, H-5″), 7.44–7.49 (m, 2H, H-2″, H-6″), 7.62 (m, 1H, H-7″), $R_3$: 2.27 (s, 3H, H-11″), 6.44 (d, 1H, *J* = 15.9 Hz, H-8″), 7.05 (d, 2H, H-3″, H-5″), 7.44–7.49 (m, 2H, H-2″, H-6″), 7.64 (m, 1H, H-7″), $R_4$: 2.27 (s, 3H, H-11″), 6.51 (d, 1H, *J* = 15.9 Hz, H-8″), 7.05 (d, 2H, H-3″, H-5″), 7.57 (m, 2H, H-2″, H-6″), 7.76 (d, 1H, *J* = 15.9 Hz, H-7″); $^{13}$C NMR (75.48 MHz, $CDCl_3$) *δ* (ppm): 63.8 (C-6), 64.5 (C-6′), 64.7 (C-1′), 69.0 (C-4), 70.6 (C-2), 71.4 (C-5), 74.5 (C-4′), 76.5 (C-3), 80.2 (C-3′), 80.6 (C-5′), 92.0 (C-1), 104.5 (C-2′); *trans*-*p*-coumaroyl units: $R_1$: 21.1 (C-11″), 116.6 (C-8″), 122.1 (C-3″, C-5″), 129.4 (C-2″, C-6″), 131.7 (C-1″), 144.6 (C-7″), 152.2 (C-4″), 166.9 (C-9″), 169.2 (C-10″); $R_2$: 21.1 (C-11″), 117.3 (C-8″), 122.1 (C-3″, C-5″), 129.4 (C-2″, C-6″), 131.8 (C-1″), 144.8 (C-7″), 152.2 (C-4″), 167.4 (C-9″), 169.2 (C-10″); $R_3$: 21.1 (C-11″), 117.5 (C-8″), 122.1 (C-3″, C-5″), 129.5 (C-2″, C-6″), 131.8 (C-1″), 145.0 (C-7″), 152.2 (C-4″), 167.6 (C-9″), 169.2 (C-10″); $R_4$: 21.1 (C-11″), 117.5 (C-8″), 122.1 (C-3″, C-5″), 129.9 (C-2″, C-6″), 131.9 (C-1″), 146.3 (C-7″), 152.4 (C-4″), 168.1 (C-9″), 169.2 (C-10″); LC-MS (ESI): *m*/*z* 1117.15 $[M + Na]^+$; HR-MS: *m*/*z* $[M + Na]^+$ calcd for $C_{56}H_{54}O_{23}Na$: 1117.2948, found: 1117.2918.

*4.1.4.3.2. Preparation of 3,6,3′,6′-tetra-O-coumaroylsucrose **22**.* Compound **20** (0.05 g, 0.05 mmol) was suspended in 95% EtOH (4.0 mL) and pyrrolidine (70.0 μL, 0.1 g, 0.9 mmol) was added (which caused the solution to turn yellow). The starting material typically dissolved within 15 min and the reaction was allowed to continue for 15 min. Reaction was monitored by TLC analysis (EtOAc). The mixture was directly added to a column of strongly acidic ion-exchange resin [Amberlite IRA-120 ($H^+$) washed and packed in 95% EtOH]. The appropriate fractions were concentrated under diminished pressure to a residue that was subjected to column chromatography using a gradient of $CH_2Cl_2$/EtOAc/MeOH to furnish compound **22** as a white solid (0.03 g, 71% yield). Analytical data for **22**: $R_f$ = 0.76 (EtOAc/MeOH 9:1); mp: 149–151 °C; FT-IR (KBr) $\nu_{max}$: 3415, 2957, 2922, 2850, 2363, 2340, 1700, 1635, 1604, 1559, 1516, 1441, 1369, 1327, 1266, 1169, 1060, 1004, 864, 831 cm$^{-1}$; $^1$H NMR (300 MHz, $CD_3OD$) *δ* (ppm): 3.59 (m, 1H, H-4), 3.68 (m, 2H, H-1′a, H-1′b), 3.73 (m, 1H, H-2), 4.14–4.19 (m, 1H, H-5′), 4.30 (m, 1H, H-6b), 4.38 (m, 1H, H-5), 4.50–4.57 (m, 2H, H-6a, H-6′b), 4.62–4.70 (m, 2H, H-4′, H-6′a), 5.33 (app t, 1H, *J* = 9.6 Hz, H-3), 5.57 (d, 1H, *J* = 7.8 Hz, H-3′), 5.62 (d, 1H, *J* = 3.3 Hz, H-1), *trans*-*p*-coumaroyl units: $R_1$: 6.29 (d, 1H, *J* = 15.9 Hz, H-8″), 6.73–6.81 (m, 2H, H-3″, H-5″), 7.38–7.46 (m, 2H, H-2″, H-6″), 7.54–7.66 (m, 1H, H-7″), $R_2$: 6.38 (d, 1H, *J* = 15.9 Hz, H-8″), 6.73–6.81 (m, 2H, H-3″, H-5″), 7.38–7.46 (m, 2H, H-2″, H-6″), 7.54–7.66 (m, 1H, H-7″), $R_3$: 6.40 (d, 1H, *J* = 15.9 Hz, H-8″), 6.73–6.81 (m, 2H, H-3″, H-5″), 7.38–7.46 (m, 2H, H-2″, H-6″), 7.54–7.66 (m, 1H, H-7″), $R_4$: 6.48 (d, 1H, *J* = 15.9 Hz, H-8″), 6.73–6.81 (m, 2H, H-3″, H-5″), 7.54–7.66 (m, 2H, H-2″, H-6″), 7.76 (d, 1H, *J* = 15.9 Hz, H-7″); $^{13}$C NMR (75.48 MHz, $CD_3OD$) *δ* (ppm): 65.7 (C-6′), 65.8 (C-6), 65.9 (C-1′), 70.8 (C-4), 72.0 (C-2), 72.8 (C-5), 74.9 (C-4′), 77.3 (C-3), 79.4 (C-3′), 81.6 (C-5′), 93.2 (C-1), 105.6 (C-2′), *trans*-*p*-coumaroyl units: $R_1$: 114.8 (C-8″), 117.4 (C-3″, C-5″), 127.2 (C-1″), 131.6 (C-2″, C-6″), 147.2 (C-7″), 162.3 (C-4″), 169.2 (C-9″), $R_2$: 115.0 (C-8″), 117.4 (C-3″, C-5″), 127.3 (C-1″), 131.7 (C-2″, C-6″), 147.4 (C-7″), 162.4 (C-4″), 169.4 (C-9″), $R_3$: 115.1 (C-8″), 117.5 (C-3″, C-5″), 127.4 (C-1″), 131.9 (C-2″, C-6″), 147.4 (C-7″), 162.5 (C-4″), 169.8 (C-9″), $R_4$: 115.6 (C-8″), 117.6 (C-3″, C-5″), 127.4 (C-1″), 132.1 (C-2″, C-6″), 148.4 (C-7″), 162.6 (C-4″), 169.9 (C-9″); LC-MS (ESI): *m*/*z* 949.14 $[M + Na]^+$; HR-MS: *m*/*z* $[M + Na]^+$ calcd for $C_{48}H_{46}O_{19}Na$: 949.2526, found: 949.2494.

#### 4.1.4.4. Synthesis of 6-mono-O-feruloyl-3,3′,6′-tri-O-coumaroylsucrose **24**

*4.1.4.4.1. Preparation of 6-mono-O-acetoxyferuloyl-3,3′,6′-tri-O-acetoxycinnamoylsucrose **23**.* Compound **18** (0.4 g, 0.4 mmol) was dissolved in dry $CH_2Cl_2$ (7 mL) to which 4 Å molecular sieves powder followed by dry pyridine (0.3 g, 0.3 mL, 3.8 mmol) was added. The solution was then cooled to 0 °C in an ice bath and then *p*-acetoxycinnamoyl chloride **17** (0.08 g, 0.35 mmol) was added slowly at the same temperature and the reaction mixture was left to stir while warming to r.t. Stirring was continued until the disappearance of the starting material as indicated by TLC (EtOAc/hexanes 3:1). After 24 h, the resulting mixture was poured into vigorously stirred ice-water (100 mL) and a white solid precipitated was obtained after decantation and filtration. The precipitate was redissolved in EtOAc (25 mL) and washed with 1 N HCl (2 × 50 mL). The aqueous layer was extracted with EtOAc (25 mL). The combined organic layers were then successively washed with 5% $NaHCO_3$ (2 × 50 mL) and brine (25 mL) and then dried over anhyd. $MgSO_4$. The solvent was concentrated to residue that was subjected to column chromatography using a gradient of $CH_2Cl_2$/EtOAc as eluent followed by PTLC furnished compound **23** as a white solid (0.12 g, 27% yield). Analytical data for **23**: $R_f$ = 0.43 (EtOAc/hexanes 3:1); mp: 113–115 °C; FT-IR (KBr) $\nu_{max}$: 3428, 2923, 2362, 2340, 1765,

1718, 1636, 1602, 1559, 1540, 1507, 1457, 1419, 1374, 1320, 1281, 1260, 1205, 1165, 1054, 1009, 987, 913, 839, 792, 649 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ (ppm): 3.61 (m, 1H, H-4), 3.78 (m, 3H, H-2, H-1′a, H-1′b), 4.27 (m, 2H, H-5, H-5′), 4.55 (m, 5H, H-4′, H-6b, H-6a, H-6′b, H-6′a), 5.25 (m, 1H, H-3), 5.30 (m, 1H, H-3′), 5.57 (br s, 1H, H-1); *trans-p*-coumaroyl units: $\delta$ = $R_1$: 2.28 (s, 3H, H-11″), 6.40 (d, 1H, $J$ = 15.9 Hz, H-8″), 6.93–7.17 (m, 2H, H-3″, H-5″), 7.47 (d, 2H, H-2″, H-6″), 7.57–7.67 (m, 1H, H-7″), $R_2$: 2.29 (s, 3H, H-11″), 6.41 (d, 1H, $J$ = 15.9 Hz, H-8″), 6.93–7.17 (m, 2H, H-3″, H-5″), 7.47 (d, 2H, H-2″, H-6″), 7.57–7.67 (m, 1H, H-7″), $R_3$: 2.29 (s, 3H, H-11″), 6.46 (d, 1H, $J$ = 15.9 Hz, H-8″), 6.93–7.17 (m, 2H, H-3″, H-5″), 7.57–7.67 (m, 2H, H-2″, H-6″), 7.57–7.67 (m, 1H, H-7″); *trans-p*-feruloyl units: $R_4$: 2.30 (s, 3H, H-11″), 3.81 (s, 3H, −OC*H*$_3$), 6.52 (d, 1H, $J$ = 15.9 Hz, H-8″), 6.93–7.17 (m, 3H, H-2″, H-5″, H-6″), 7.77 (d, 1H, $J$ = 15.9 Hz, H-7″); $^{13}C$ NMR (75.48 MHz, $CDCl_3$): $\delta$ = $R_1$: 63.7 (C-6), 64.5 (C-6′), 64.7 (C-1′), 69.0 (C-4), 70.6 (C-2), 71.4 (C-5), 74.4 (C-4′), 76.6 (C-3), 80.5 (C-3′), 80.6 (C-5′), 91.9 (C-1), 104.5 (C-2′); *trans-p*-coumaroyl units: $R_1$: 21.1 (C-11″), 117.4 (C-8″), 122.1 (C-3″, C-5″), 129.4 (C-2″, C-6″), 131.6 (C-1″), 144.7 (C-7″), 152.2 (C-4″), 166.9 (C-9″), 168.8 (C-10″), $R_2$: 21.1 (C-11″), 117.4 (C-8″), 122.1 (C-3″, C-5″), 129.4 (C-2″, C-6″), 131.8 (C-1″), 145.2 (C-7″), 152.3 (C-4″), 167.3 (C-9″), 168.8 (C-10″), $R_3$: 21.1 (C-11″), 117.4 (C-8″), 122.1 (C-3″, C-5″), 129.9 (C-2″, C-6″), 131.9 (C-1″), 145.3 (C-7″), 152.5 (C-4″), 167.8 (C-9″), 169.1 (C-10″); *trans-p*-feruloyl units: $R_4$: 20.7 (C-11″), 55.9 (−OC*H*$_3$), 111.4 (C-2″), 116.5 (C-8″), 121.6 (C-5″), 123.2 (C-6″), 133.1 (C-1″), 141.6 (C-3″), 146.5 (C-7″), 151.4 (C-4″), 168.2 (C-9″), 169.1 (C-10″); LC-MS (ESI): $m/z$ 1147.17 $[M + Na]^+$; HR-MS: $m/z$ $[M + Na]^+$ calcd for $C_{57}H_{56}O_{24}Na$: 1147.3054, found: 1147.3036.

*4.1.4.4.2. Preparation of 6-mono-O-feruloyl-3,3′,6′-tri-O-coumaroylsucrose* ***24***. A suspension of compound **23** (0.1 g, 0.1 mmol) in 95% EtOH (7 mL) was stirred with pyrrolidine (143.0 μL, 0.1 g, 1.7 mmol) which caused the solution to turn yellow. The starting material typically dissolved within 15 min and the reaction was allowed to continue for 3 h. After this time, the starting material was completely disappeared as indicated by TLC analysis (EtOAc). The mixture was added directly to a column of strongly acidic ion-exchange resin [Amberlite IRA-120 ($H^+$) washed and packed in 95% EtOH]. The appropriate fractions were concentrated under diminished pressure to a residue that was subjected to column chromatography using a gradient of $CH_2Cl_2$/EtOAc/MeOH to afford compound **24** as a white solid (0.03 g, 35% yield). Analytical data for **24**: $R_f$ = 0.76 (EtOAc/MeOH 9:1); mp: 78–83 °C; FT-IR (KBr) $\nu_{max}$: 3428, 2923, 2340, 2362, 2337, 1765, 1718, 1734, 1699, 1653, 1636, 1602, 1559, 1540, 1507, 1457, 1419, 1374, 1320, 1281, 1260, 1205, 1165, 1054, 1009, 987 $cm^{-1}$; $^1H$ NMR (300 MHz, $(CD_3)_2CO$) $\delta$ (ppm): 3.69 (m, 3H, H-4, H-1′a, H-1′b), 3.80 (m, 1H, H-2), 4.27 (m, 1H, H-5′), 4.35 (m, 1H, H-6a), 4.45 (m, 1H, H-5), 4.58 (m, 2H, H-6b, H-6′a), 4.70 (m, 2H, H-4′, H-6′b), 5.43 (m, 1H, H-3), 5.57 (d, 1H, $J$ = 8.1 Hz, H-3′), 5.62 (d, 1H, $J$ = 3.0 Hz, H-1); *trans-p*-coumaroyl units: $R_1$: 6.36 (d, 1H, $J$ = 15.9 Hz, H-8″), 6.83–6.91 (m, 2H, H-3″, H-5″), 7.50–7.67 (m, 3H, H-2″, H-6″, H-7″), $R_2$: 6.37 (d, 1H, $J$ = 15.9 Hz, H-8″), 6.83–6.91 (m, 2H, H-3″, H-5″), 7.50–7.67 (m, 3H, H-2″, H-6″, H-7″), $R_3$: 6.49 (d, 1H, $J$ = 15.9 Hz, H-8″), 6.83–6.91 (m, 2H, H-3″, H-5″), 7.50–7.67 (m, 3H, H-2″, H-6″, H-7″); *trans-p*-feruloyl units: $R_4$: 3.89 (s, 3H, −OC*H*$_3$), 6.56 (d, 1H, $J$ = 15.9 Hz, H-8″), 6.83–6.91 (d, 1H, $J$ = 8.4 Hz, H-5″), 7.13 (d, 1H, $J$ = 6.9 Hz, H-6″), 7.36 (br s, 1H, H-2″), 7.77 (d, 1H, $J$ = 15.9 Hz, H-7″); $^{13}C$ NMR (75.48 MHz, $(CD_3)_2CO$) $\delta$ (ppm): 64.9 (C-6), 65.3 (C-6′), 65.6 (C-1′), 70.0 (C-4), 71.4 (C-2), 72.2 (C-5), 74.7 (C-4′), 76.8 (C-3), 79.3 (C-3′), 81.0 (C-5′), 92.4 (C-1), 104.8 (C-2′); *trans-p*-coumaroyl units: $R_1$: 115.1 (C-8″), 116.7 (C-3″, C-5″), 126.9 (C-1″), 130.9 (C-2″, C-6″), 145.5 (C-7″), 160.6 (C-4″), 167.3 (C-9″), $R_2$: 115.2 (C-8″), 116.7 (C-3″, C-5″), 127.0 (C-1″), 131.1 (C-2″, C-6″), 145.9 (C-7″), 160.7 (C-4″), 167.5 (C-9″), $R_3$: 115.8 (C-8″), 116.8 (C-3″, C-5″), 127.0 (C-1″), 131.4 (C-2″, C-6″), 146.1 (C-7″), 160.8 (C-4″), 167.7 (C-9″); *trans-p*-feruloyl units: $R_4$: 56.3 (−OC*H*$_3$), 111.3 (C-2″), 115.9 (C-8″), 116.0 (C-5″), 124.2 (C-6″), 127.5 (C-1″), 146.6 (C-7″), 148.7 (C-3″), 150.1 (C-4″), 167.8 (C-9″); LC-MS (ESI): $m/z$ 979.13 $[M + Na]^+$; HR-MS: $m/z$ $[M + Na]^+$ calcd for $C_{49}H_{48}O_{20}Na$: 979.2631, found: 979.2612.

### *4.2. Antiproliferative activity of selected PSEs against HeLa cells*

Antiproliferative activities of the selected PSEs against HeLa cell lines were evaluated using MTS assay method [24] at 24 and 48 h of drug exposure (For the details see the Supporting information).

## Acknowledgements

This research was supported by a grant from the National Medical Research Council (NMRC), Singapore (EDG10nv043).

## Appendix A. Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.ejmech.2012.10.034. These data include MOL files and InChiKeys of the most important compounds described in this article.

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