Supporting Information for

Original article

From Vietnamese plants to a biflavonoid that relieves inflammation by triggering the lipid mediator class switch to resolution

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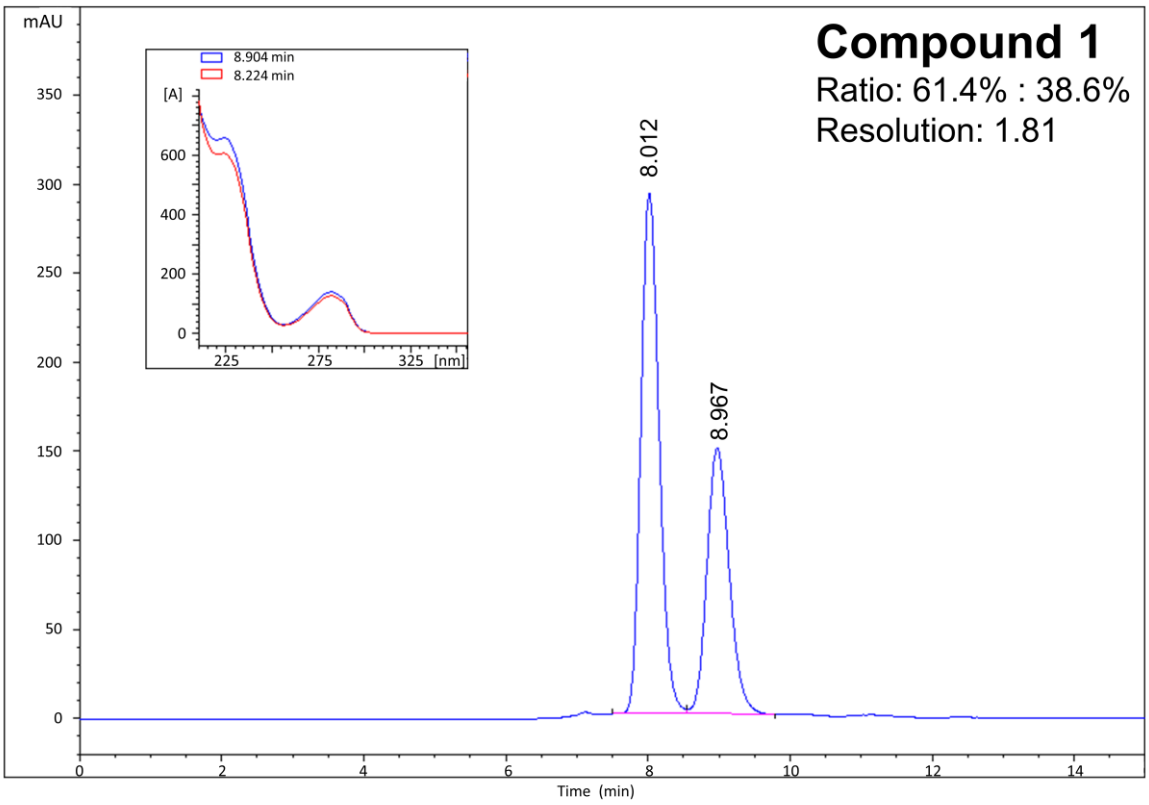
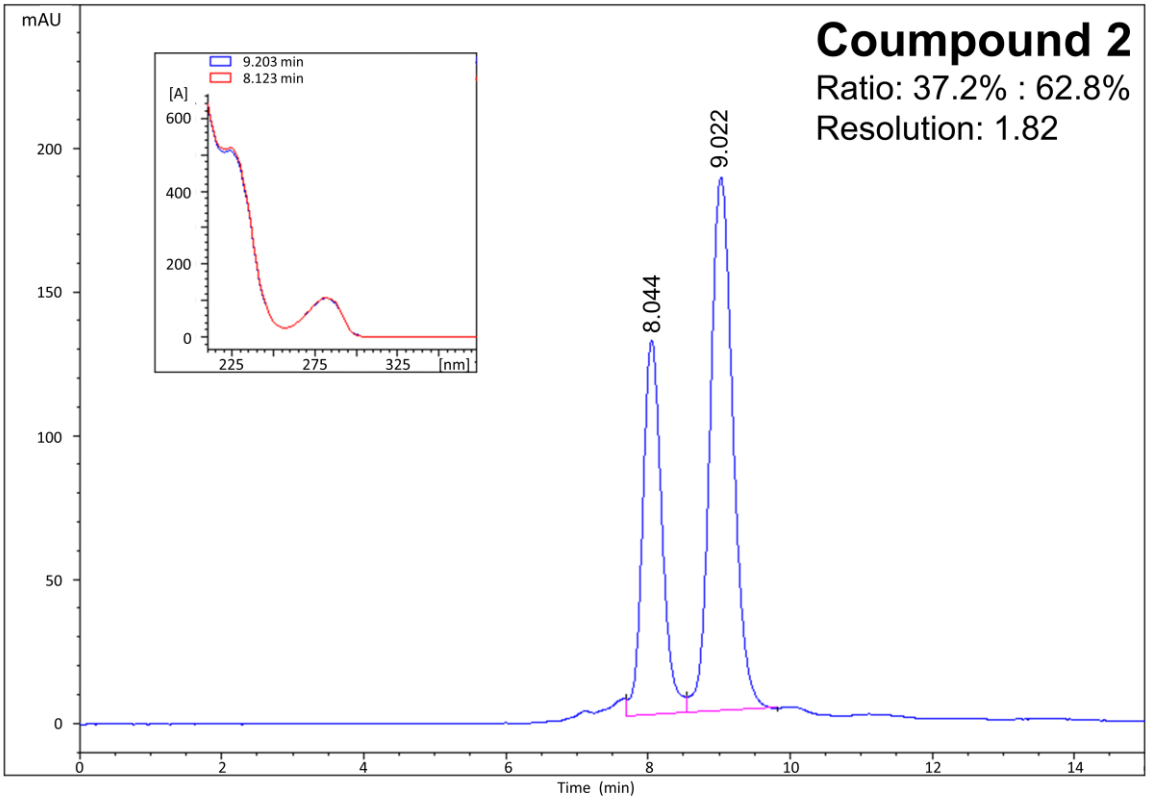
S1. Chiral HPLC-analysis of compounds 1 to 11

Chiral HPLC analysis of compound **1** ($[\alpha]_D^{20}$ +4.1 (*c* 0.2, MeOH))



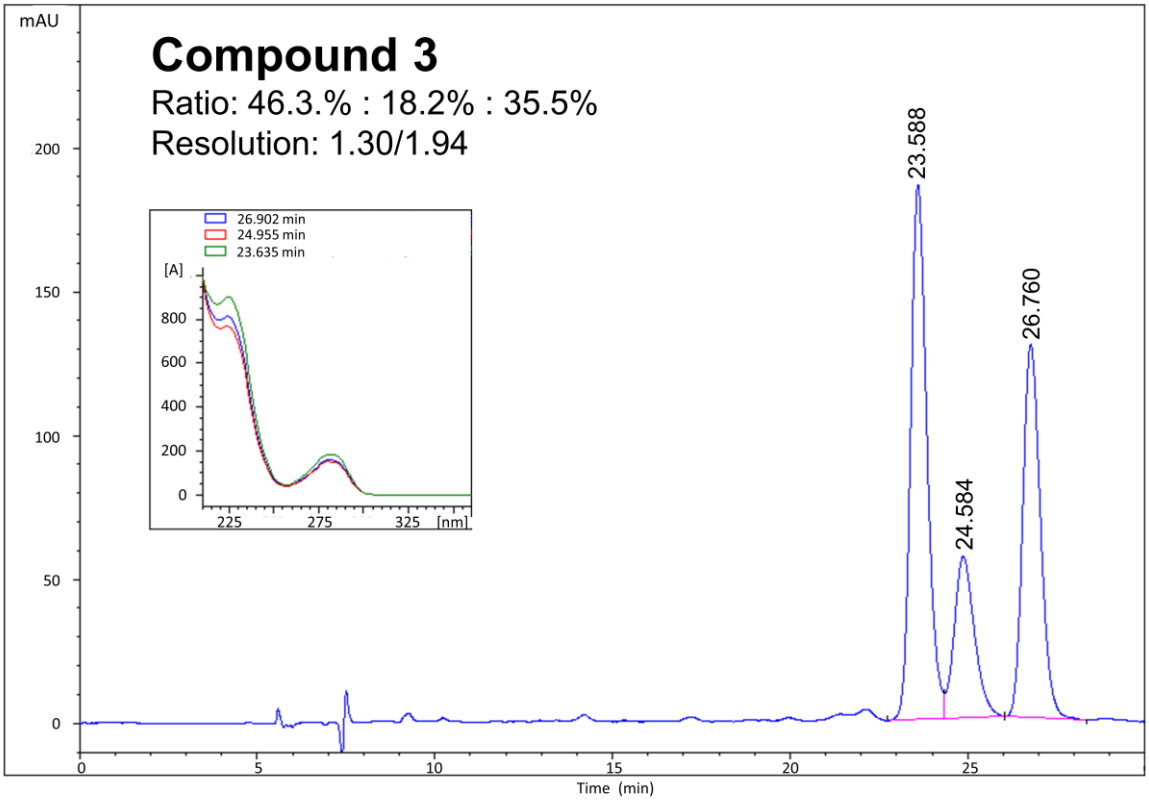
Analytical conditions: Phenomenex Lux 3 µm Cellulose-1250 mm× 4.6 mm, *n*-hexane+isopropanol with 0.1% TFA, 50+50 (*v*/*v*); 0.5 mL/min, 20 °C, injection volume: 5 µL; sample concentration: 0.95 mg/mL *n*-hexane+isopropanol (1+1); 280 nm; insert: online-UV-spectra.

Chiral HPLC analysis of compound **2** ($[\alpha]_D^{20}$ –3.0 (*c* 0.1, MeOH))



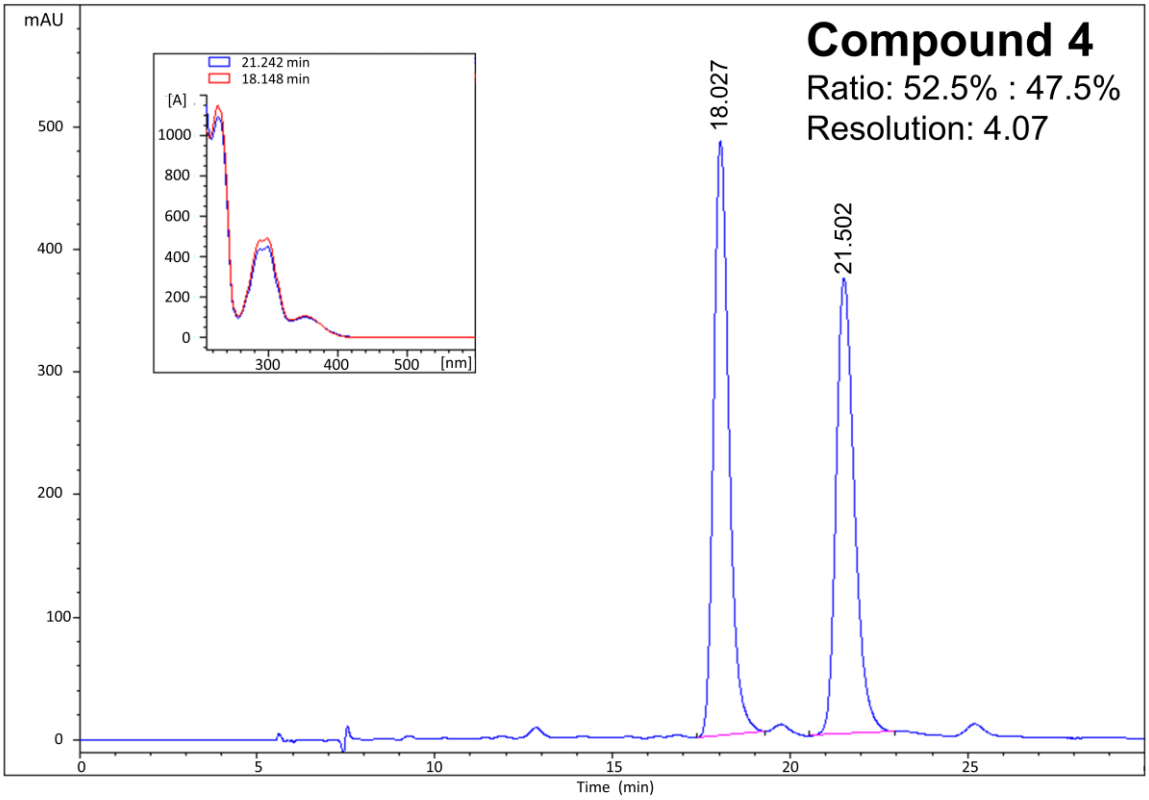
Analytical conditions: Phenomenex Lux 3 µm Cellulose-1250 mm × 4.6 mm, *n*-hexane+isopropanol with 0.1% TFA, 50+50 (*v*/*v*); 0.5 mL/min, 20 °C, injection volume: 5 µL; sample concentration: 0.90 mg/mL *n*-hexane+isopropanol (1+1); 280 nm; insert: online-UV-spectra.

Chiral HPLC analysis of compound **3** ($[\alpha]_D^{20}$ +12.7 (*c* 0.19, MeOH))



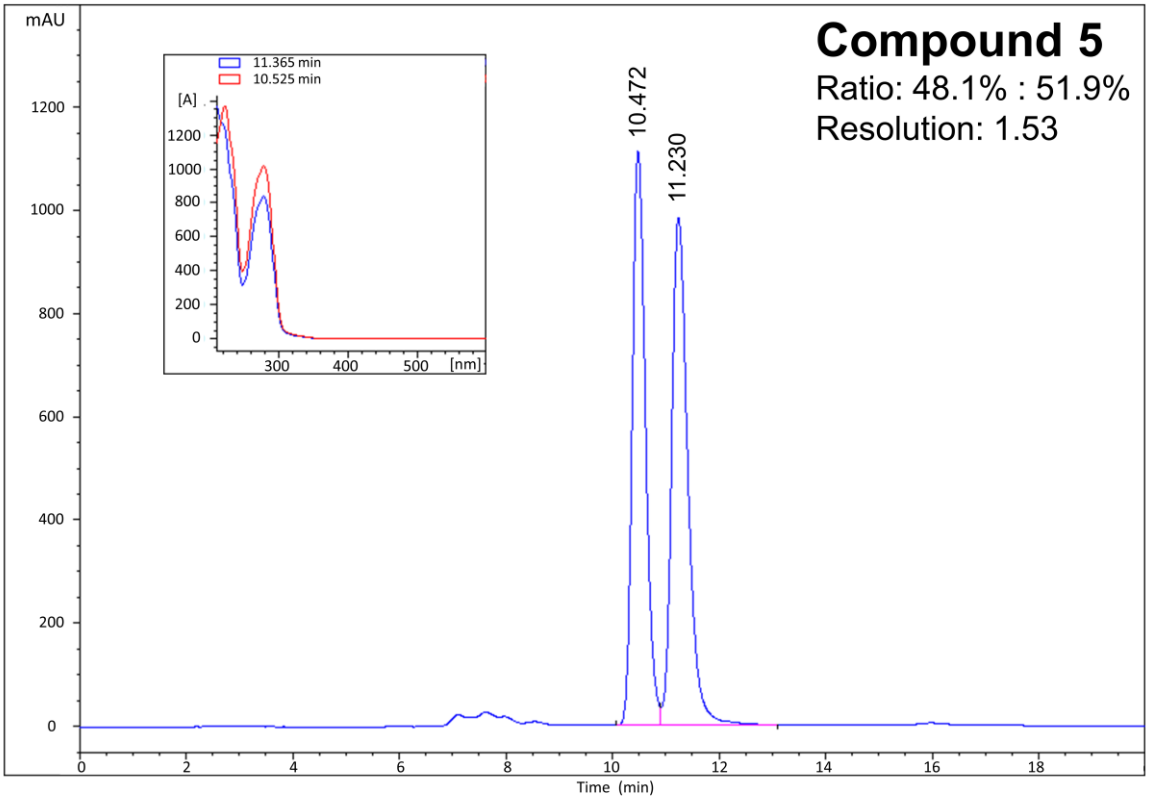
Analytical conditions: Phenomenex Lux 3 µm i-Amylose-3250 mm× 4.6 mm, *n*-hexane+ethanol with 0.1% TFA, 80+20 (*v*/*v*); 0.5 mL/min, 20 °C, injection volume: 5 µL; sample concentration: 0.85 mg/mL *n*-hexane+isopropanol (1+1); 280 nm; insert: online-UV-spectra.

Chiral HPLC analysis of compound **4** ($[\alpha]_D^{20}$ –3.4 (*c* 0.23, MeOH))



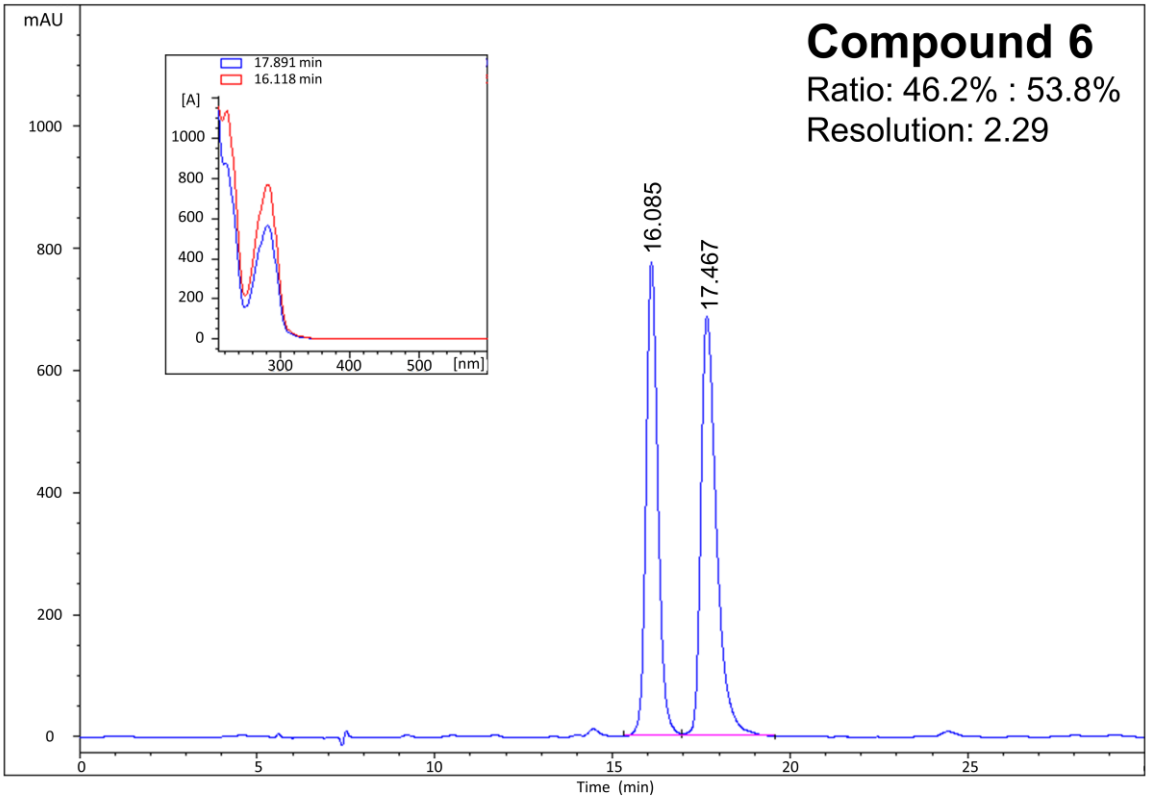
Analytical conditions: Phenomenex Lux 3 µm i-Amylose-3250 mm× 4.6 mm, *n*-hexane+ethanol with 0.1% TFA, 80+20 (*v*/*v*); 0.5 mL/min, 20 °C, injection volume: 5 µL; sample concentration: 1.27 mg/mL *n*-hexane+isopropanol (1+1); 280 nm; insert: online-UV-spectra.

Chiral HPLC analysis of compound **5** ($[\alpha]_D^{20}$ +12.4 (*c* 0.24, MeOH))



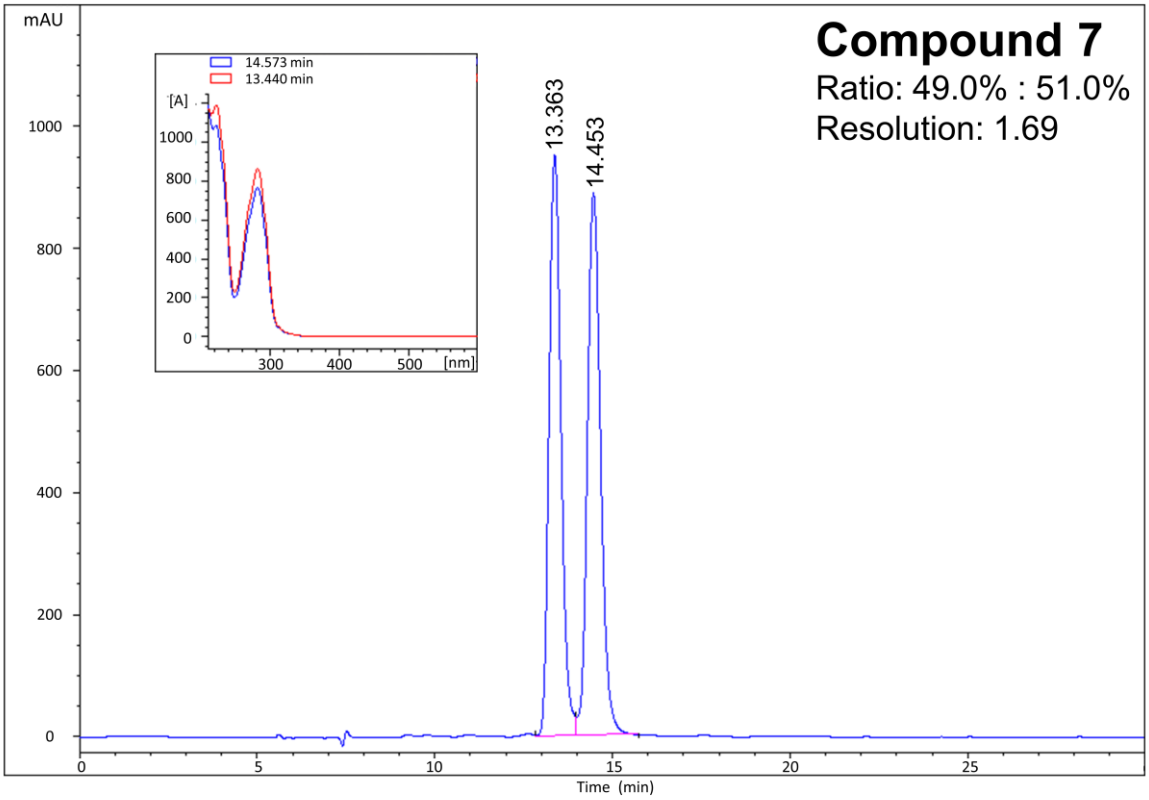
Analytical conditions: Phenomenex Lux 3 µm i-Amylose-3250 mm× 4.6 mm, *n*-hexane+isopropanol with 0.1% TFA, 60+40 (*v*/*v*); 0.5 mL/min, 20 °C, injection volume: 5 µL; sample concentration: 1.14 mg/mL *n*-hexane+isopropanol (1+1); 280 nm; insert: online-UV-spectra.

Chiral HPLC analysis of compound **6** ($[\alpha]_D^{20}$ 0 (*c* 0.25, MeOH))



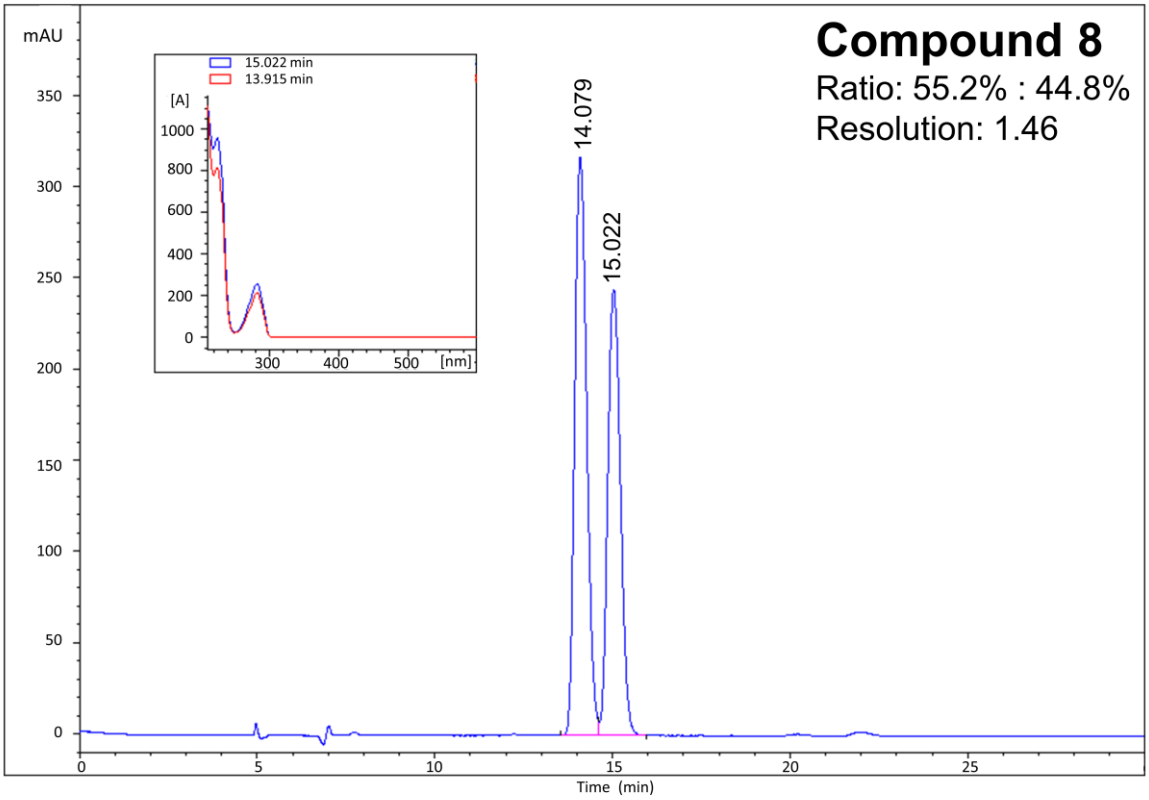
Analytical conditions: Phenomenex Lux 3 µm i-Amylose-3250 mm× 4.6 mm, *n*-hexane+ethanol with 0.1% TFA, 80+20 (*v*/*v*); 0.5 mL/min, 20 °C, injection volume: 5 µL; sample concentration: 1.17 mg/mL *n*-hexane+isopropanol (1+1); 280 nm; insert: online-UV-spectra.

Chiral HPLC analysis of compound **7** ($[\alpha]_D^{20}$ +7.7 (*c* 0.3, MeOH))



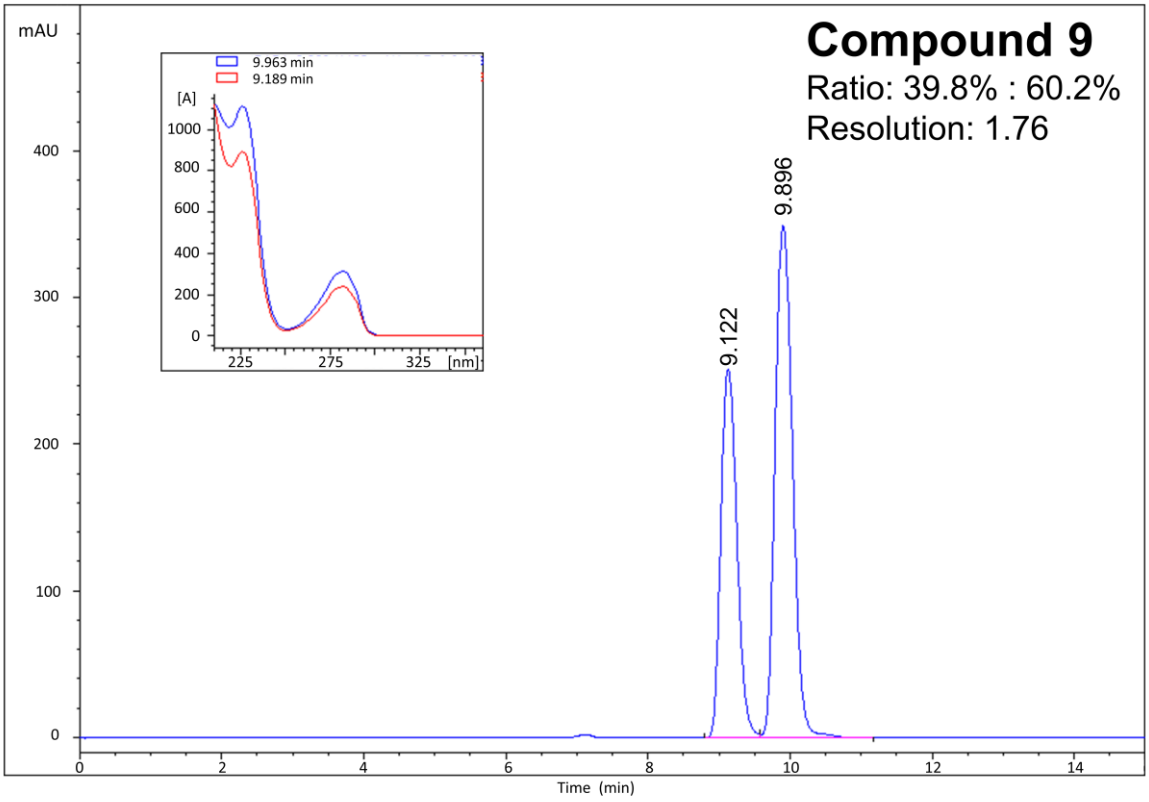
Analytical conditions: Phenomenex Lux 3 µm i-Amylose-3250 mm × 4.6 mm, *n*-hexane+ethanol with 0.1% TFA, 80+20 (*v*/*v*); 0.5 mL/min, 20 °C, injection volume: 5 µL; sample concentration: 1.27 mg/mL *n*-hexane+isopropanol (1+1); 280 nm; insert: online-UV-spectra.

Chiral HPLC analysis of compound **8** ($[\alpha]_D^{20}$ +6.8 (*c* 0.68, MeOH))



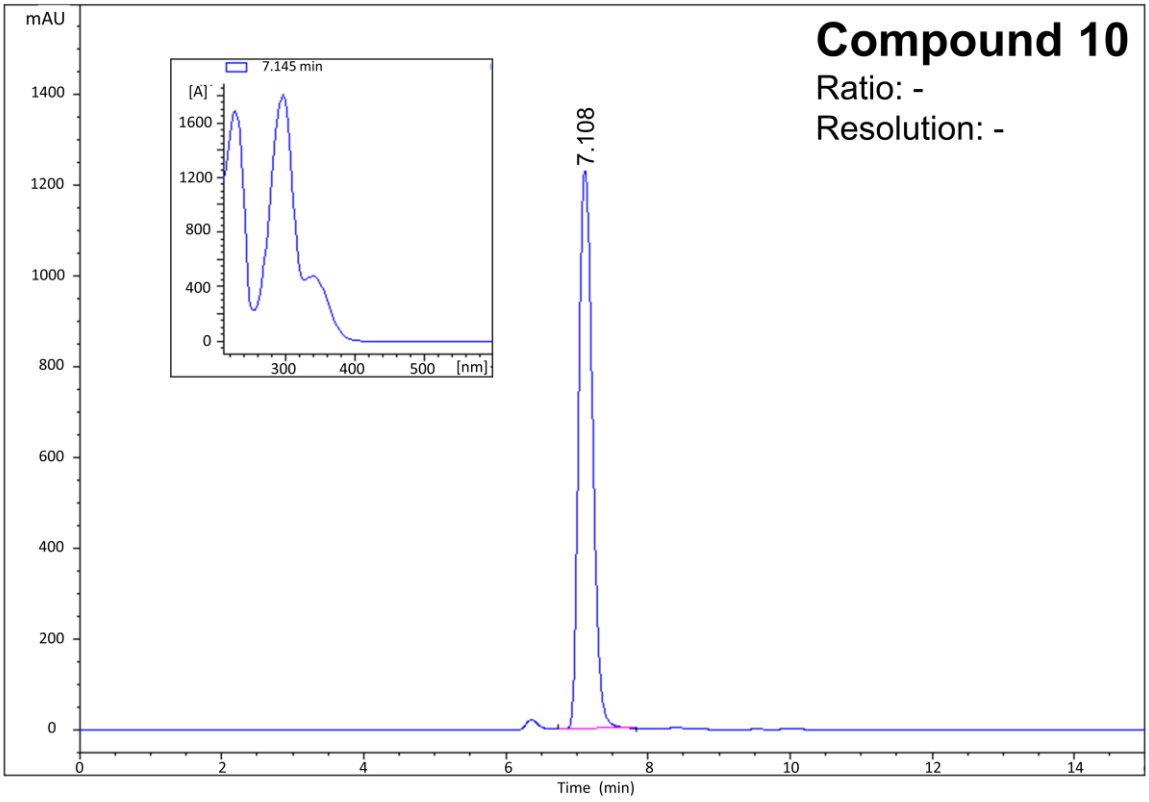
Analytical conditions: Phenomenex Lux 3 µm Cellulose-1250 mm× 4.6 mm, *n*-hexane+ethanol with 0.1% TFA, 80+20 (*v*/*v*); 0.5 mL/min, 20 °C, injection volume: 5 µL; sample concentration: 1.06 mg/mL *n*-hexane+isopropanol (1+1); 280 nm; insert: online-UV-spectra.

Chiral HPLC analysis of compound **9** ($[\alpha]_D^{20}$ –2.9 (*c* 0.35, MeOH))



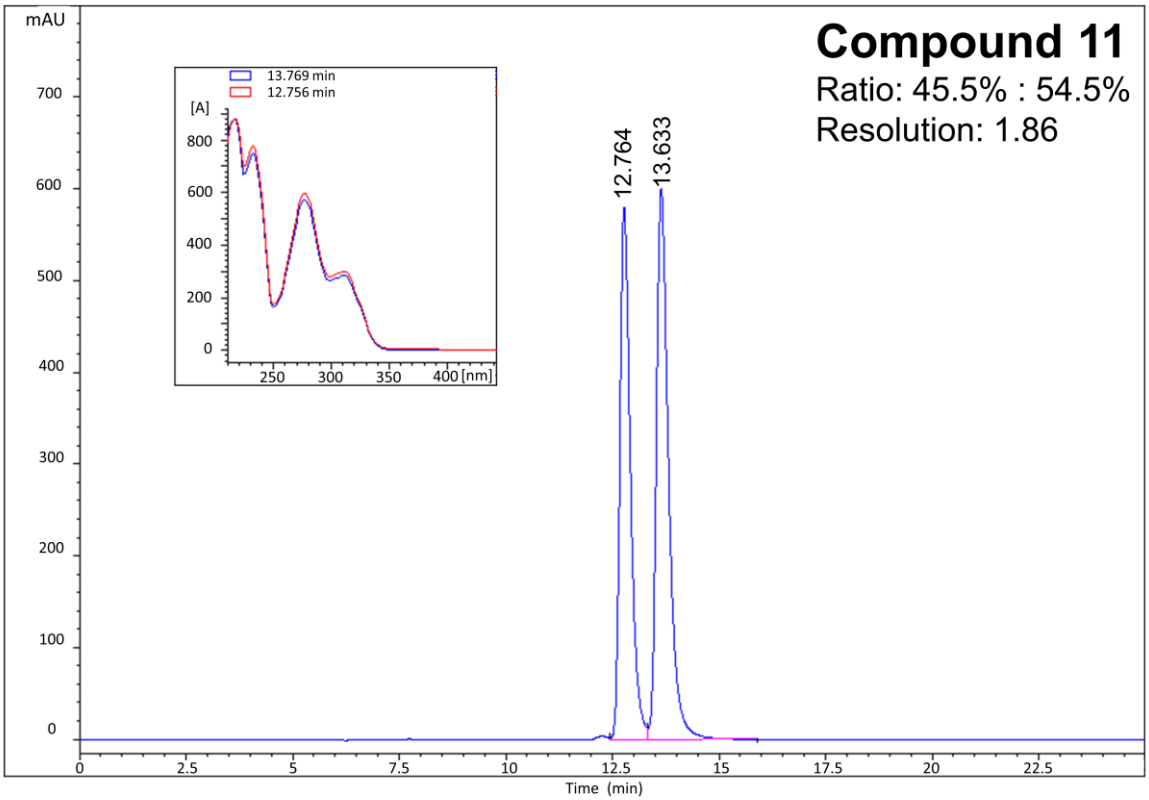
Analytical conditions: Phenomenex Lux 3 µm Cellulose-1250 mm× 4.6 mm, *n*-hexane+isopropanol with 0.1% TFA, 50+50 (*v*/*v*); 0.5 mL/min, 20 °C, injection volume: 5 µL; sample concentration: 0.84 mg/mL *n*-hexane+isopropanol (1+1); 280 nm; insert: online-UV-spectra.

Chiral HPLC analysis of compound **10** ($[\alpha]_D^{20}$ –30.3 (*c* 0.41, MeOH))



Analytical conditions: Phenomenex Lux 3 µm Cellulose-1250 mm× 4.6 mm, *n*-hexane+isopropanol with 0.1% TFA, 50+50 (*v*/*v*); 0.5 mL/min, 20 °C, injection volume: 5 µL; sample concentration: 0.87 mg/mL *n*-hexane+isopropanol (1+1); 280 nm; insert: online-UV-spectrum.

Chiral HPLC analysis of compound **11** ($[\alpha]_D^{20}$ –2.2 (*c* 0.51, MeOH)



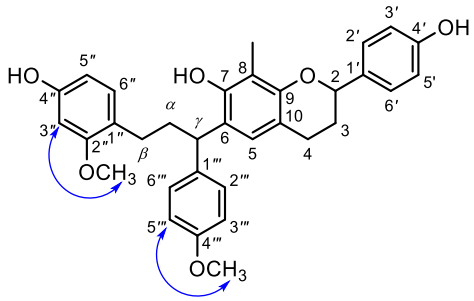
Analytical conditions: Phenomenex Lux 3 µm i-Amylose-3250 mm × 4.6 mm, *n*-hexane+isopropanol with 0.1% TFA, 80+20 (*v*/*v*); 0.5 mL/min, 20 °C, injection volume: 2 µL; sample concentration: 0.98 mg/mL *n*-hexane+isopropanol (1+1); 280 nm; insert: online-UV-spectra.

S2. Structure elucidation of the new compound 3

Compound **3** was obtained as a red amorphous powder. The HR-ESI-MS spectra showed a $[M+NH_4]^+$ ion at *m/z* 544.2690 (calculated for $C_{33}H_{38}NO_6^+$ $[M+NH_4]^+$, *m/z* 544.2694), corresponding to a molecular formula of $C_{33}H_{34}O_6$.

The ^{1}H NMR spectrum of **3** showed proton signals of two *p*-substituted phenyl rings [δ_H 7.22 and 6.76 (both 2H, d, 8.6 Hz) and δ_H 7.16 and 6.78 (both 2H, d, 8.6 Hz)], three aromatic proton signals of an ABX-system [δ_H 6.36 (1H, d, 2.3 Hz), 6.25 (1H, dd, 2.3, 8.0 Hz), 6.81 (1H, d, 8.0 Hz)], one aromatic singlet [δ 6.72 (1H, s)], signals of four methylene groups [δ_H 2.07 (1H, m) and 1.89 (1H, m); 2.84 (1H, m) and 2.62 (1H, m); 2.09 (2H, m); and 2.44 (2H, m)], one methine proton signal [δ_H 4.26 (1H, t, 7.6 Hz)], one methyl singlet [δ_H 2.03 (3H, s)], and signals of two methoxy groups [δ_H 3.72 (3H, s) and 3.74 (3H, s)], and one oxymethine proton signal [δ_H 4.87 (1H, m)].

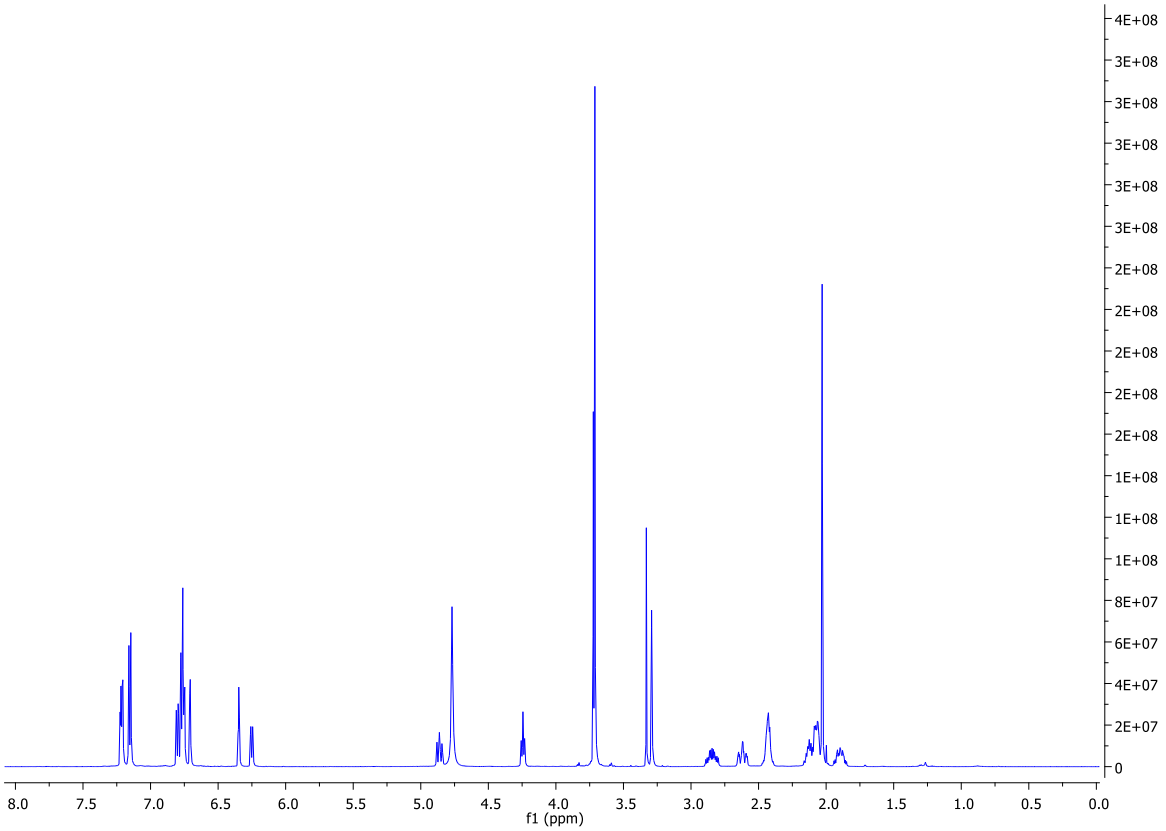
The ^{13}C-NMR spectrum and HSQC data of **3** revealed 29 signals with characteristic signals for 12 quaternary aromatic carbons with 6 carbons bearing oxygen, 14 tertiary carbons with 12 aromatic carbons, 4 methylene carbons, two identical methoxy carbons (δ_c 55.7) and one methyl carbon (δ_c 9.1). A typical oxymethine proton of the flavan skeleton at 4.87 (1H, m, H-2) and characteristic aliphatic protons at δ_H 2.07/1.89 and δ_H 2.84/2.62 indicated a biflavonoid structure consisting of a flavan and a deoxytetrahydrochalcone moiety.



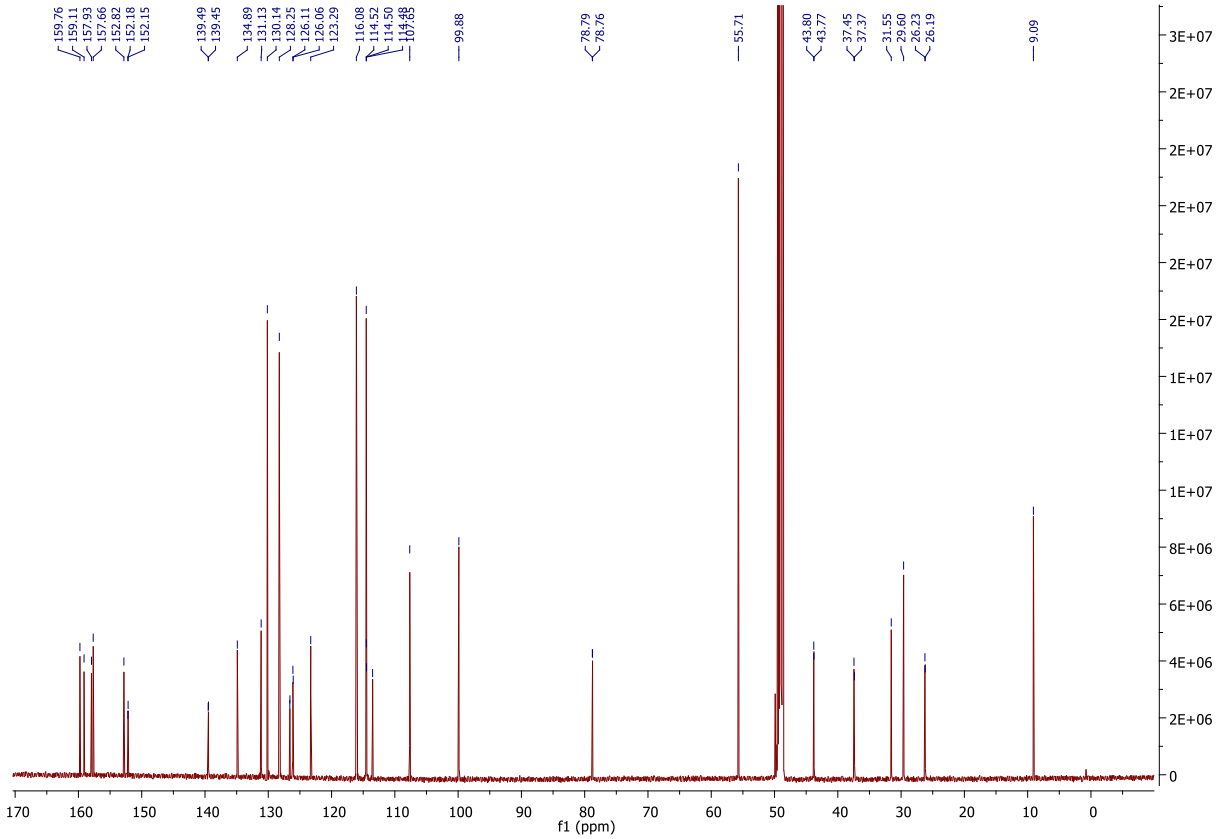
Structure of compound **3** with key NOESY-correlations

The ^{1}H and ^{13}C spectrum of **3** resembles those of compounds **1** and **2**, except for the exchange of a hydroxy group by a methoxy group in compound **3**. The HMBC correlation between the methoxy group at δ_H 3.74 and the carbon resonance at δ_c 159.1 (C-4‴) indicated the position of the additional methoxy group at C-4‴, which was further verified by the NOESY contact of the methoxy protons with H-3‴/5‴. Thus, compound **3** was identified as the new natural product 6-(3-(4-hydroxy-2-methoxyphenyl)-1-(4-methoxyphenyl)propyl)-2-(4-hydroxyphenyl)-8-methylchroman-7-ol. Interestingly, the 1D-NMR spectra of compound **3** showed for some signals a signal doubling mainly for protons/carbons (H-2, H-5, H-2′/6′, -OC*H*$_3$ at C-2″, H-5″, and H-6″; C-2, C-4, C-5, C-6, C-7, C-*α*, C-*γ*, C-1‴, and C-3‴/5‴) accompanying the stereo centers (C-2 and C-*γ*) of the compound, suggesting the presence of isomers

and/or rotamers. The chiral HPLC analysis of compound **3** revealed the presence of at least three of the four possible isomers of the compound (Section 1) and confirmed thereby this assumption.



^{1}H-NMR spectrum (600.19 MHz, methanol-d_4) of compound **3**.



^{13}C-NMR spectrum (150.91 MHz, methanol-d_4) of compound **3**

6-(3-(4-Hydroxy-2-methoxyphenyl)-1-(4-methoxyphenyl)propyl)-2-(4-hydroxyphenyl)-8-methylchroman-7-ol (3). Red amorphous powder. $[\alpha]_D^{20}$ +12.7 (*c* 0.19, MeOH). UV$_{max}$ (MeOH) λ_{max} (log ε) 203 (4.04), 224 (2.39), 282 (0.48) nm. ^{1}H-NMR (600.19 MHz, methanol-d_4; numbering according to shown figure): δ (ppm), *J* (Hz): 1.89 (m, H$_a$-3), 2.03 (s, 8-CH$_3$), 2.07 (m, H$_b$-3), 2.09 (m, H-α, 2H), 2.44 (m, H-β, 2H), 2.62 (m, H$_a$-4), 2.84 (m, H$_b$-4), 3.72 (s, 2″-OCH$_3$), 3.74 (s, 4‴-OCH$_3$), 4.26 (t, *J* = 7.6, H-γ), 4.87 (m, H-2), 6.25 (dd, *J* = 2.3, 8.0, H-5″), 6.36 (d, *J* = 2.3, H-3″), 6.72 (s, H-5), 6.76 (d, *J* = 8.6, H-3′/5′), 6.78 (d, *J* = 8.6, H-3‴/5‴), 6.81 (d, *J* = 8.0, H-6″), 7.16 (d, *J* = 8.6, H-2‴/6‴), 7.22 (d, *J* = 8.6, H-2′/6′). ^{13}C-NMR (150.91 MHz, methanol-d_4; numbering according to shown figure): δ (ppm): 9.1 (8-CH$_3$), 26.2 (C-4), 29.6 (C-β), 31.6 (C-3), 37.4 (C-α), 43.8 (C-γ), 55.7 (2″-OCH$_3$, 4‴-OCH$_3$), 78.8 (C-2), 99.9 (C-3″), 107.7 (C-5″), 113.5 (C-8), 114.5 (C-10, 3‴/5‴), 116.1 (C-3′/5′), 123.3 (C-1″), 126.1 (C-5), 126.6 (C-6), 128.3 (C-2′/6′), 130.1 (C-2‴/6‴), 131.1 (C-6″), 134.9 (C-1′), 139.5 (C-1‴), 152.2 (C-7), 152.8 (C-9), 157.7 (C-4″), 157.9 (C-4′), 159.1 (C-4‴), 159.8 (C-2″).

S3. Structure elucidation of the new compound 4

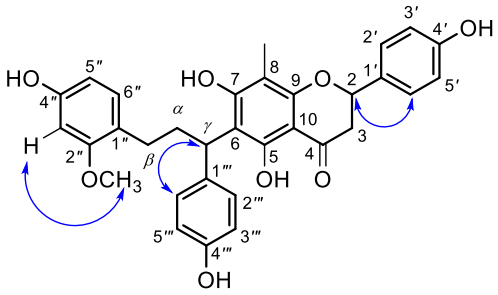
Compound **4** was obtained as red amorphous powder. The HR-ESI-MS spectra showed a $[M+H]^+$ ion at *m/z* 543.2018 (calculated for $C_{32}H_{31}O_8^+$ $[M+H]^+$, *m/z* 543.2013), corresponding to a molecular formula of $C_{32}H_{30}O_8$.

The ^{1}H-NMR spectrum of **4** showed proton signals of two 1,4-disubstituted aromatic rings [δ_H 7.33 and 6.82 (both 2H, d, 8.6 Hz) and δ_H 7.22 and 6.63 (both 2H, d, 8.6 Hz)], three aromatic proton signals of a 1,2,4-trisubstituted benzene ring [δ_H 6.33 (1H, d, 2.3 Hz), 6.23 (1H, dd, 2.3, 8.0 Hz), 6.81 (1H, d, 8.2 Hz), proton signals of three methylene groups [δ_H 2.70 (1H, dd, 2.9, 17.0 Hz) and 3.10 (1H, dd, 6.1, 13.1 Hz); 2.50 (1H, m) and 2.28 (1H, m); 2.36 (1H, m) and 2.51 (1H, m)], one oxymethine proton signal at δ_H 5.31(1H, t, 3.0 Hz), one methine proton signal [δ_H 4.47 (1H, t, 7.5 Hz)], one methyl singlet [δ_H 1.98 (3H, s)], and a signal corresponding to one methoxy group [δ_H 3.70 (3H, s)].

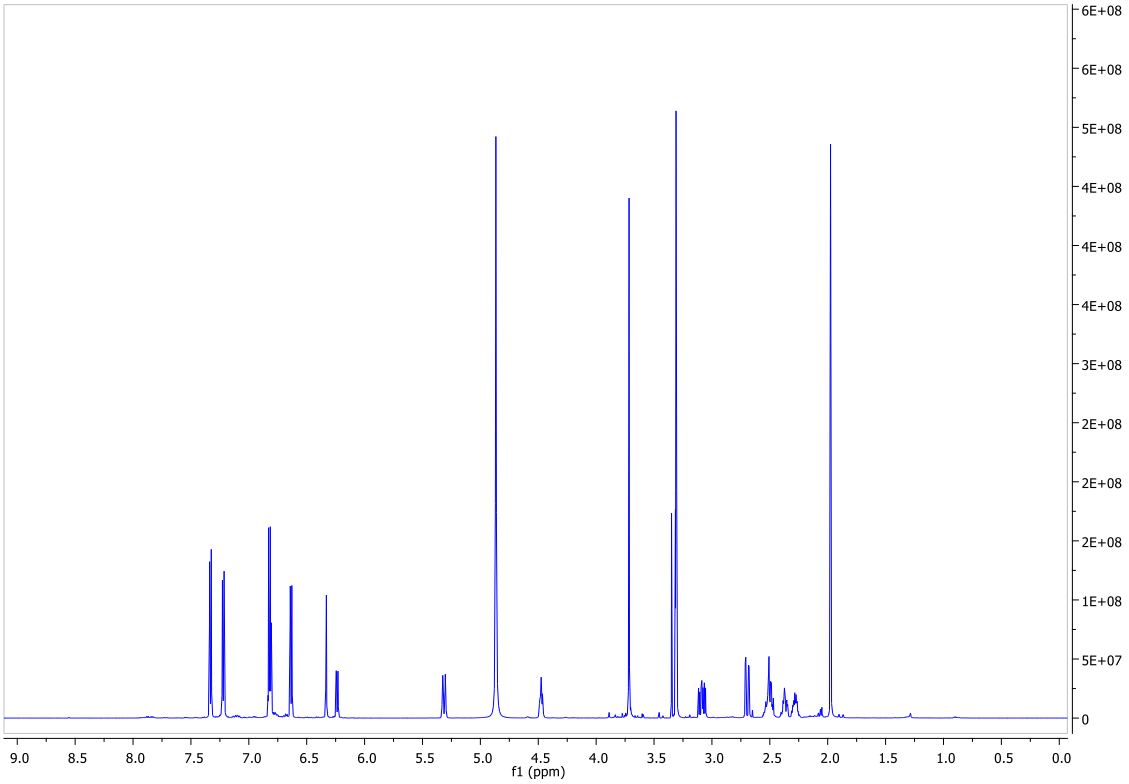
The ^{13}C-NMR spectrum and HSQC data of **4** revealed 27 signals with characteristic signals for 14 quaternary aromatic carbons with 8 carbons bearing oxygen, 13 tertiary carbons with 10 aromatic carbons, 3 aliphatic secondary carbons, one methoxy carbon (δ_c 55.6) and one methyl carbon (δ_c 8.2). The NMR data of **4** corresponded closely to those of **1** except that an aliphatic methylene carbon was replaced by a carbonyl group (δ_c 198.5) in **4**, which revealed the presence of a flavanone subunit instead of the flavan part of **1**.

Furthermore, the ^{1}H-NMR of **4** did not show the singlet signal of a proton at C-5, suggesting an additional substitution at that position, which was identified as a methyl group [δ_H 1.98 (3H, s); δ_c 8.2]. A NOESY-cross-peak between the protons of the methoxy group at δ_H 3.70 and H-3″ (δ_H 6.33 1H, d, 2.3 Hz) confirmed the location of the methoxy group at C-2″. Analysis of the complete set of NMR data identified **4** as 5,7-dihydroxy-6-(3-(4-hydroxy-2-methoxyphenyl)-1-(4-hydroxyphenyl)propyl)-2-(4-hydroxyphenyl)-8-methylchroman-4-one, representing a new natural product.

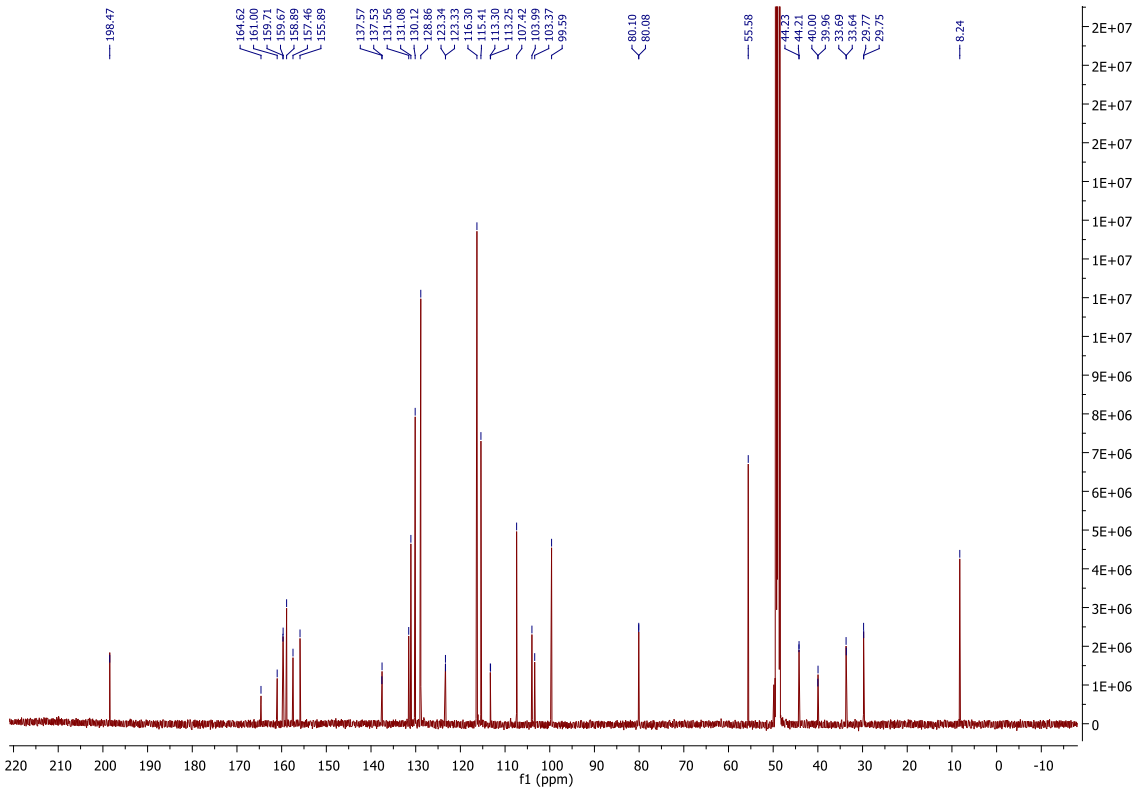
Again the 1D-NMR spectra of compound **4** showed for some signals a signal doubling mainly for protons/carbons (H-2, H_b-3, H-*γ*, -OCH_3 at C-2″, and H-5″; C-2, C-3, C-6, C-*α*, C-*β*, C-*γ*, C-1″, and C-1‴) accompanying the stereo centers (C-2 and C-*γ*) of the compound, suggesting the presence of isomers and/or rotamers. The chiral HPLC analysis of compound **4** revealed the presence of at least two of the four possible isomers of the compound (Section 1) and confirmed thereby this assumption.



Structure of compound **4** with key NOESY-correlations.



^{1}H-NMR spectrum (600.19 MHz, methanol-d_4) of compound **4.**

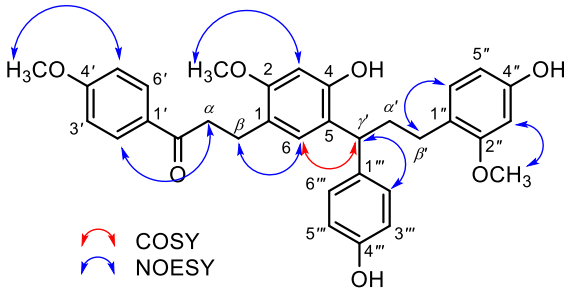


^{13}C-NMR spectrum (150.91 MHz, methanol-d_4) of compound **4.**

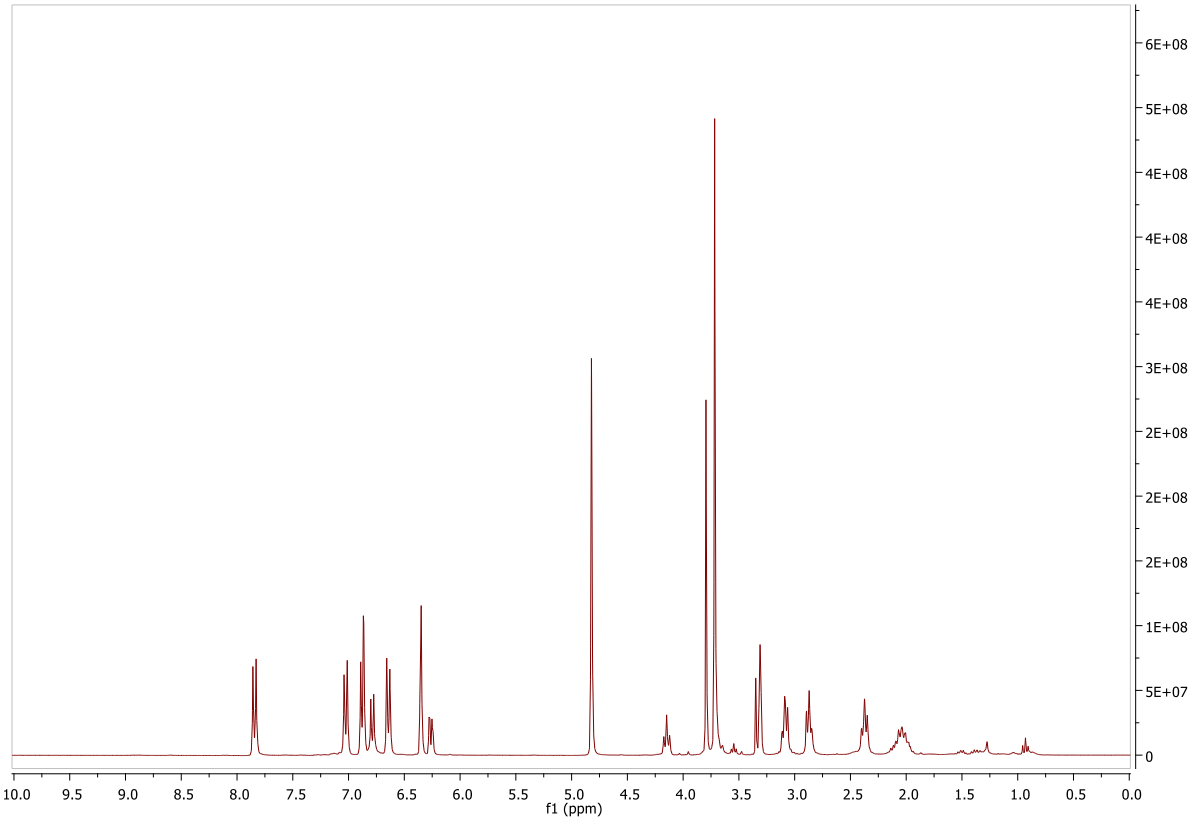
5,7-Dihydroxy-6-(3-(4-hydroxy-2-methoxyphenyl)-1-(4-hydroxyphenyl)propyl)-2-(4-hydroxyphenyl)-8-methylchroman-4-one (4). Pale red powder. $[\alpha]_D^{20}$ -3.4 (*c* 0.23, MeOH). UV_{max} (MeOH) λ_{max} (log ε) 199 (4.35), 227 (1.84), 286 (0.69), 300 (0.67) nm. ^{1}H-NMR (600.19 MHz, methanol-d_4; numbering according to shown figure): δ (ppm), *J* (Hz): 1.98 (s, 8-CH_3), 2.28 (m, H_a-α), 2.36 (m, H_a-β), 2.50 (m, H_b-α), 2.51 (m, H_b-β), 2.70 (dd, *J* = 17.0, 2.9, H_a-3), 3.10 (dd, *J* = 13.1, 6.1, H_b-3), 3.70 (s, 2″-O$\underline{C}H_3$), 4.47 (m, H-γ), 5.31 (t, *J* = 3.0, H-2), 6.24 (dd, *J* = 2.3, 8.0, H-5″), 6.33 (d, *J* = 2.3, H-3″), 6.63 (d, *J* = 8.6, H-3‴/5‴), 6.81 (d, *J* = 8.2, H-6″), 6.82 (d, *J* = 8.6, H-3′/5′), 7.22 (d, *J* = 8.6, H-2‴/6‴), 7.33 (d, *J* = 8.6, H-2′/6′). ^{13}C-NMR (150.91 MHz, methanol-d_4; numbering according to shown figure): δ (ppm): 8.2 (8-$\underline{C}H_3$), 29.8 (C-β), 33.7 (C-α), 40.0 (C-γ), 44.2 (C-3), 55.6 (2′-O$\underline{C}H_3$), 80.1 (C-2), 99.6 (C-3″), 103.4 (C-10), 104.0 (C-8), 107.4 (C-5″), 113.3 (C-6), 115.4 (C-3‴/5‴), 116.3 (C-3′/5′), 123.3 (C-1″), 128.9 (C-2′/6′), 130.1 (C-2‴/6‴), 131.1 (C-6″), 131.6 (C-1′), 137.6 (C-1‴), 155.9 (C-4‴), 157.5 (C-4″), 158.9 (C-4′), 159.7 (C-9, C-2″), 161.0 (C-5), 164.6 (C-7), 198.5 (C-4).

S4. Structure elucidation of the new compound 5

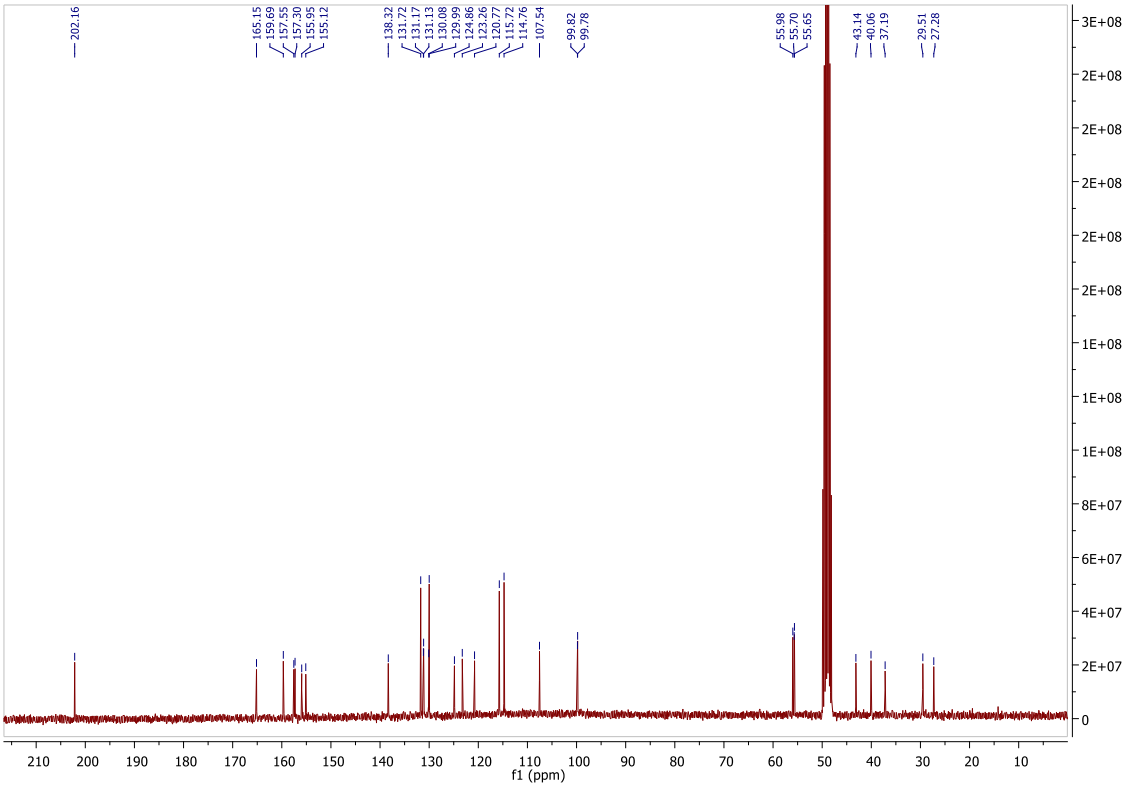
Compound **5** was obtained as pinkish amorphous powder. The HR-ESI-MS spectra of compound **5** showed a $[M+H]^+$ ion at *m/z* 543.2382 (calculated for $C_{33}H_{35}O_7^+$ $[M+H]^+$, *m/z* 543.2377), corresponding to a molecular formula of $C_{33}H_{34}O_7$. The ^{1}H-NMR spectrum of **5** showed proton signals of two AA′BB′ systems [δ_H 7.86 and 6.89 (both 2H, d, 8.6 Hz) as well as δ_H 7.04 and δ 6.66 (both 2H, d, 8.5 Hz)], three aromatic proton signals of an ABX-system [δ_H 6.35 (1H, d, 2.2 Hz), 6.26 (1H, dd, 2.2, 8.0 Hz), 6.79 (1H, d, 8.1 Hz), two singlet aromatic proton signals (δ_H 6.35 (1H, s) and 6.87 (1H, s)], proton signals corresponding to four methylene groups [δ_H 3.09 (2H, m), 2.87 (2H, m), 2.37 (2H, m), and 2.04 (2H, m)] and signals of three methoxy groups [δ_H 3.72 (6H, s) and 3.79 (3H, s)]. The ^{13}C-NMR spectrum and HSQC data of **5** revealed 29 signals with characteristic signals for a carbonyl group at δ_C 202.2, 24 aromatic carbons with 6 carbons bearing oxygen, 4 aliphatic methylene carbons, and three methoxy carbon signals [δ_c 55.7 (2C) and 56.0]. Comparison of the NMR data of **5** with those of the known biflavonoid **6** (cochinchinenene C) revealed as only difference between **5** and **6** the methoxy group location. HMBC data indicated that the methoxy groups of **5** are located at C-2, C-4′, and C-2″. This positioning could be confirmed by the observed NOESY contacts between the methoxy group at δ_H 3.79 and H-3′/5′ (δ_H 6.88) and between the methoxy group proton signals at δ_H 3.72 and H-3, H-6″, respectively. A detailed overview of the observed key correlations is given in the ^{13}C-NMR spectrum below. The structure of **5** was therefore established as the new natural product 3-(4-hydroxy-5-(3-(4-hydroxy-2-methoxyphenyl)-1-(4-hydroxyphenyl)propyl)-2-methoxyphenyl)-1-(4-methoxyphenyl)propan-1-one. The chiral HPLC analysis of compound **5** (Section 1) revealed the presence of both possible two isomers.



Structure of compound **5** with key correlations.



^{1}H-NMR spectrum (600.19 MHz, methanol-d_4) of compound **5.**



^{13}C-NMR spectrum (150.91 MHz, methanol-d_4) of compound **5.**

3-(4-Hydroxy-5-(3-(4-hydroxy-2-methoxyphenyl)-1-(4-hydroxyphenyl)propyl)-2-methoxyphenyl)-1-(4-methoxyphenyl)propan-1-one (5). Pinkish amorphous powder. $[\alpha]_D^{20}$ +12.4 (*c* 0.24, MeOH). UV_{max} (MeOH) λ_{max} (log ε) 202 (4.56), 222 (1.74), 280 (1.07) nm. ^{1}H-NMR (600.19 MHz, methanol-d_4; numbering according to shown figure): δ (ppm), *J* (Hz): 2.04 (m, H-α'), 2.37 (m, H-β'), 2.87 (m, H-β), 3.09 (m, H-α), 3.72 (s, 2-OC$\underline{H}_3$, 2″-OC$\underline{H}_3$), 3.79 (s, 4′-OC$\underline{H}_3$), 4.15 (t, *J* = 7.8, H-γ'), 6.26 (dd, *J* = 8.0, 2.2, H-5″), 6.35 (d, *J* = 2.2, H-3″), 6.35 (s, H-3), 6.64 (d, *J* = 8.4, H-3‴/5‴), 6.79 (d, *J* = 8.1, H-6″), 6.87 (s, H-6), 6.88 (d, *J* = 8.5, H-3′/5′), 7.03 (d, *J* = 8.5, H-2‴/6‴), 7.84 (d, *J* = 8.8, H-2′/6′). ^{13}C-NMR (150.91 MHz, methanol-d_4; numbering according to shown figure): δ (ppm): 27.3 (C-β), 29.5 (C-β'), 37.2 (C-α'), 40.1 (C-α), 43.1 (C-γ'), 55.7 (2-O$\underline{C}$H$_3$, 2″-O$\underline{C}$H$_3$), 56.0 (4′-O$\underline{C}$H$_3$), 99.8 (C-3, C-3″), 107.5 (C-5″), 114.8 (C-3′/5′), 115.7 (C-3‴/5‴), 120.8 (C-1), 123.3 (C-1″), 124.9 (C-5), 130.0 (C-2‴/6‴), 130.1 (C-6), 131.1 (C-6″), 131.2 (C-1′), 131.7 (C-2′/6′), 138.3 (C-1‴), 155.1 (C-4), 156.0 (C-4‴), 157.3 (C-2), 157.6 (C-4″), 159.7 (C-2″), 165.2 (C-4′), 202.2 ($\underline{C}$=O).

S5. Compounds isolated from bioactive subfractions

We isolated 18 (poly)phenolic compounds from the subfractions 5, 7 and 9-12 of the ethyl acetate subfraction that was prepared from the ethanol extract of *Dracaena cambodiana* red wood material (Table 1): the dimeric phenolic compounds 8-methylsocotrin-4′-ol (**1** and **2**)[1], 8-methylsocotrin-4′-ol-4‴-methylether (**3**), 2-(4-hydroxyphenyl)-5-hydroxy-6-[1-(4-hydroxyphenyl)-3-(4-hydroxy-2-methoxy-phenyl)propyl]-8-methylchroman-4-one-7-ol (**4**), 3-(4-hydroxy-5-(3-(4-hydroxy-2-methoxyphenyl)-1-(4-hydroxyphenyl)propyl)-2-methoxyphenyl)-1-(4-methoxyphenyl)propan-1-one (**5**), cochinchinenin C (**6**)[2], 3-[4-hydroxy-5-[3-(4-hydroxy-2-methoxyphenyl)-1-(4-hydroxyphenyl)propyl]-2-methoxyphenyl]-1-(4-hydroxyphenyl)-propanone (**7**)[3], as well as the corresponding monomers and structurally related compounds 7,4′-dihydroxyflavan (**8**)[4], 7-methoxy-4′-flavonol (**9**)[4], 8-methylnaringenin (**10**)[5], liquiritigenin (**11**)[5], 7,4′-dihydroxyflavone (**12**)[6], 2,4,4′-trihydroxydihydrochalcone (**13**)[7], loureirin C (**14**)[8], 2′-methoxyisoliquiritigenin (**15**)[9], 2,4′-dihydroxy-4-methoxychalcone (**16**)[10], resveratrol (**17**)[11], and *p*-hydroxy benzoic acid (**18**)[12].

Compounds **1** and **2**[1], **11**[13], **12**[14], **14**[13], **15**[13], and **17**[15] have previously been identified as constituents of *D. cambodiana*. The natural products **6**, **7**, **8**, **13**, and **18** are new for *D. cambodiana*, however, they have previously been isolated from other *Dracaena* species. In particular, **6** and **7** have previously been obtained from *D. cochinchinensis*[2], **8** from *D. loureiri*[16], **13** from *D. draco*[7] and *D. cochinchinensis*[2], and compound **18** from *D. angustifolia*[17]. This is the first report of compounds **9**, **10**, and **16** from a *Dracaena* species. Compounds **3-5** represent new natural products.

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Supporting figures

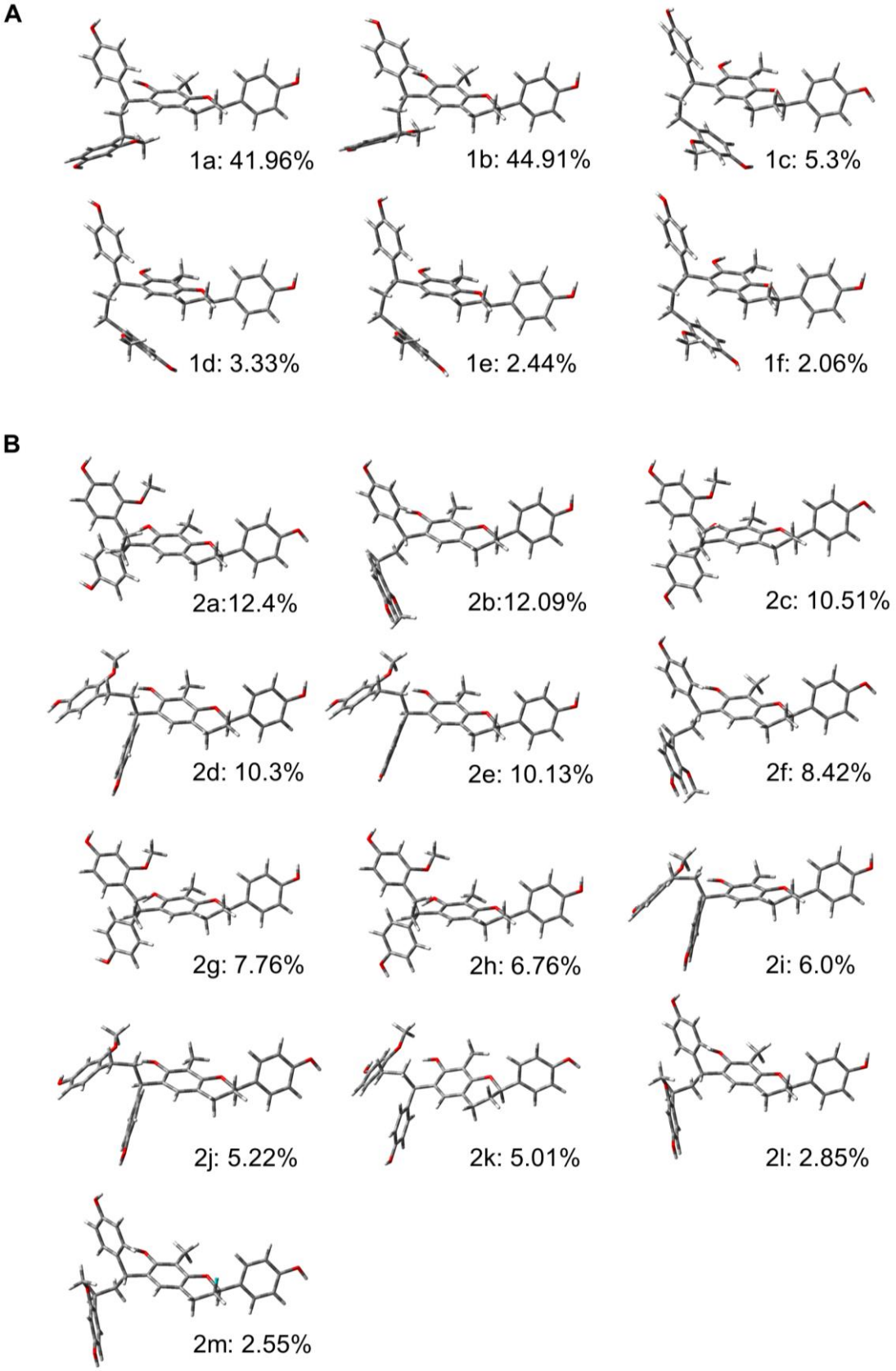

Figure S1 Low energy conformers used for ECD calculation. (A) Compound **1**. (B) Compound **2**.

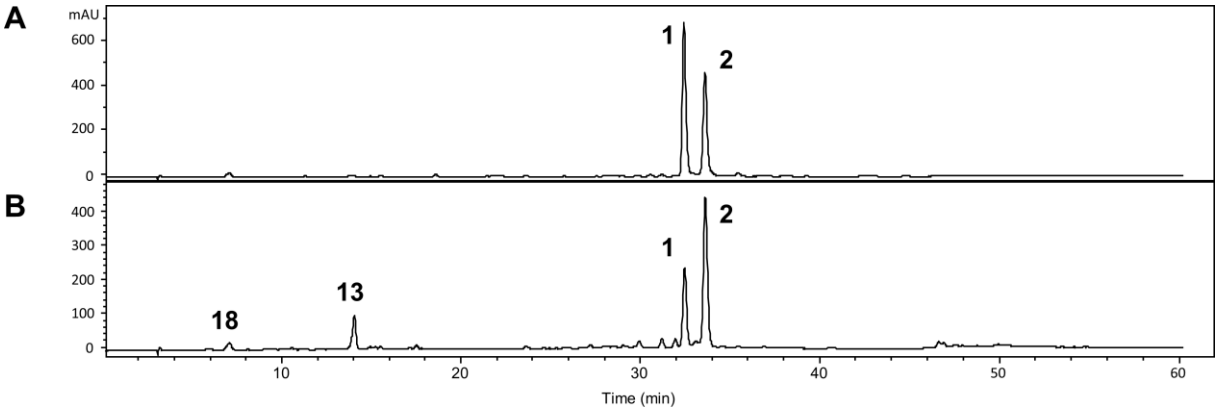

Figure S2 HLPC chromatograms of the most active subfractions. The ethanolic *D. cambodiana* extract was fractionated and the obtained EtOAc fraction was further separated. (A, B) HPLC chromatograms of the most active subfractions 11 (A) and 12 (B) at 280 nm with assigned compounds (see 2.2. for HPLC conditions).

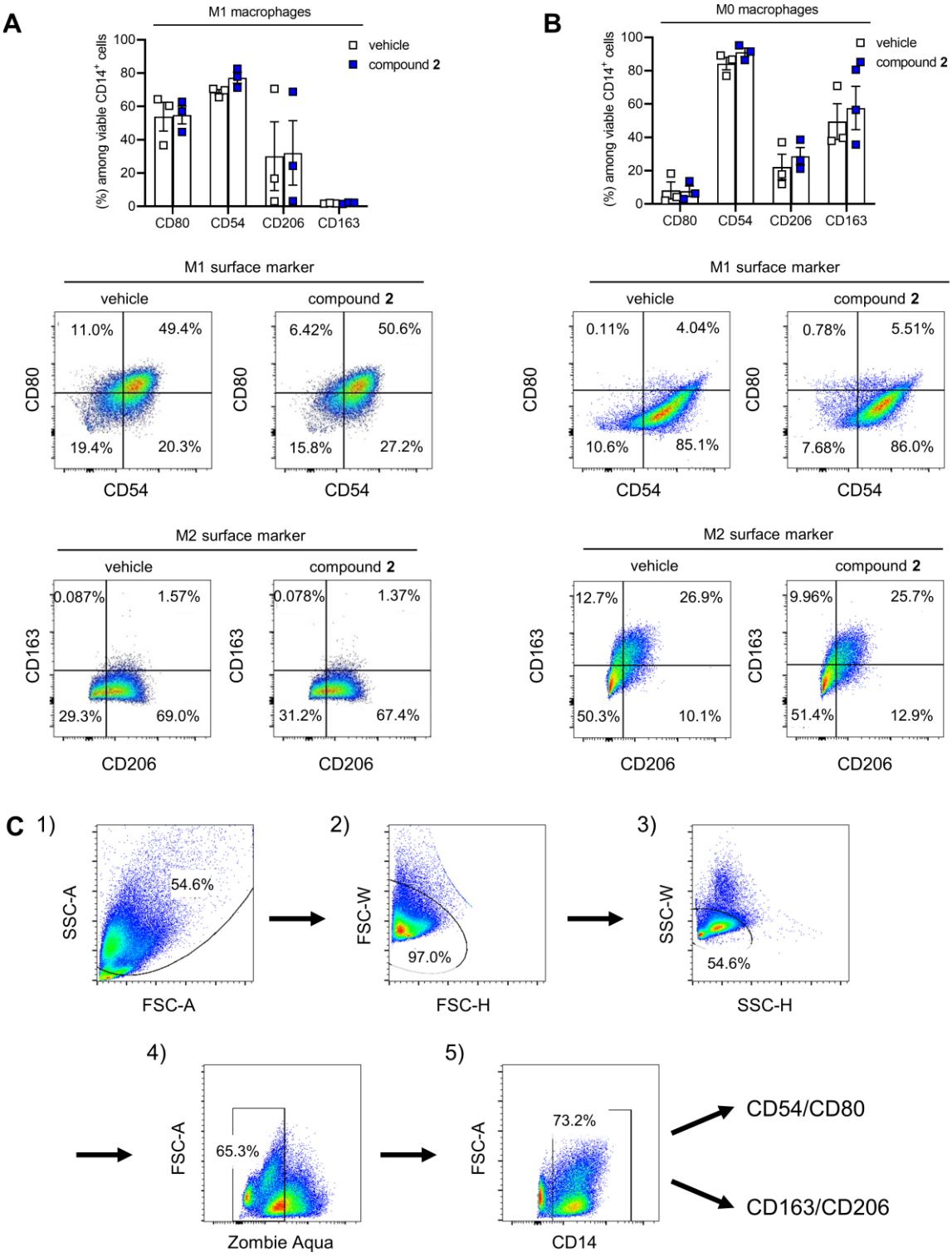

Figure S3 Macrophage polarization is not influenced by compound **2**. Human monocyte-derived macrophages (M0) were pre-treated with vehicle (DMSO) or compound **2** (3 µmol/L) for 15 min and then polarized for 48 h with LPS/IFN-γ to the M1 phenotype. (A, B) Expression of M1 (CD54 and CD80) and M2 surface markers (CD163 and CD206) among $CD14^+$ cells in M1 (A) and M0 macrophages (B) is shown in bar charts and pseudocolor dot plots. Results are given as mean ± S.E.M., percentage among viable $CD14^+$ cells, n = 3; paired t-test. (C) Gating strategy.

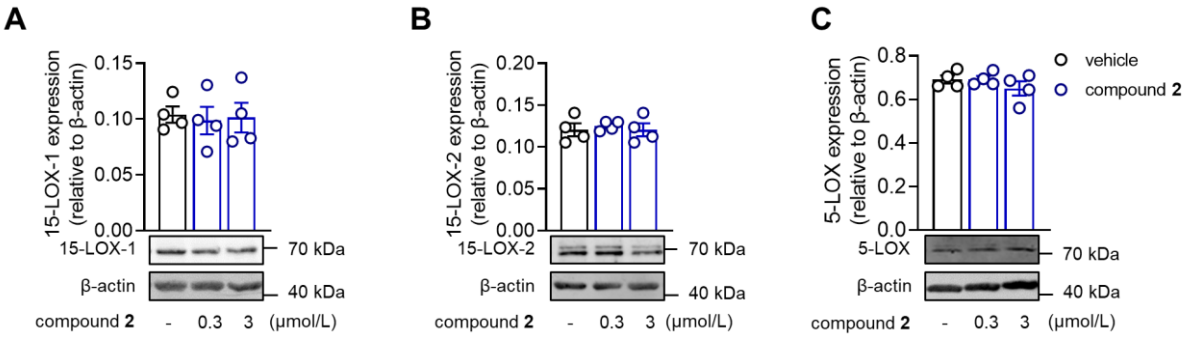

Figure S4 Compound **2** neither affects 15-LOX-1, 15-LOX-2, nor 5-LOX expression. Human monocyte-derived M2 macrophages were treated with vehicle (DMSO) or compound **2** for 24 h. (A–C) Protein expression and densitometric analysis of (A) 15-LOX-1, (B) 15-LOX-2 and (C) 5-LOX. Results are given as mean ± SEM, normalized to *β*-actin. Western blots are representative for $n = 4$ independent donors and treatments.

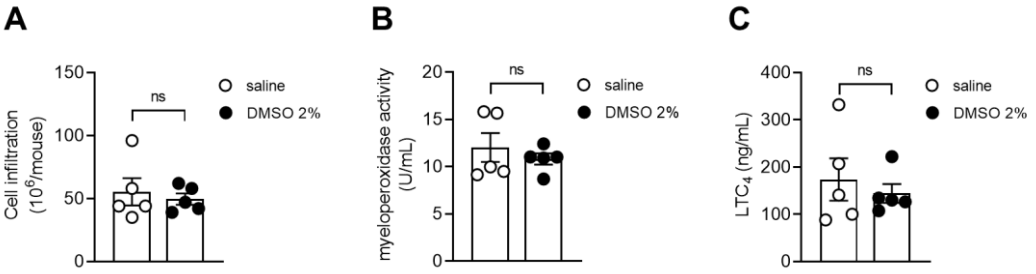

Figure S5 DMSO as vehicle does hardly influence cell infiltration and LTC_4 levels in zymosan-induced peritonitis in mice. Saline or DMSO (2%) were i.p. administrated 30 min before zymosan injection. Mice were sacrificed 4 h (A, B) or 30 min (C) after receiving zymosan. (A) Cell infiltration into the peritoneal cavity. (B) Myeloperoxidase activity of infiltrated cells as marker for neutrophils. (C) LTC_4 levels of the peritoneal exudate. Data are shown as mean ± SEM and single data points, $n = 5$ mice; ns, non-significant; unpaired *t*-test.

Supporting tables

Table S1 Inhibition of 5-LOX, 15-LOX, and 12-LOX product formation by Vietnamese plant extracts in activated PMNL.

Latin plant name	Plant family	Plant organ	Extraction solvent	5-LOX at 30 µg/mL[a]	5-LOX IC_{50}[b]	15-LOX at 30 µg/mL[a]	12-LOX at 30 µg/mL[a]
Solanum sp.	Solanaceae	Stems	Chloroform	87 ± 29	n.d.[c]	390 ± 284	108 ± 7
			Methanol	102 ± 4	n.d.	103 ± 1	101 ± 5
		Fruits	Chloroform	98 ± 8	n.d.	101 ± 1	100 ± 3
			Methanol	94 ± 10	n.d.	126 ± 19	105 ± 1
		Leaves	Chloroform	32 ± 14	21.6 ± 3.9	94 ± 2	83 ± 6
			Methanol	102 ± 11	n.d.	116 ± 9	101 ± 5
Solanum sp.	Solanaceae	Stems	Chloroform	86 ± 31	n.d.	150 ± 30	105 ± 15
			Methanol	104 ± 9	n.d.	115 ± 17	96 ± 1
		Leaves	Chloroform	41 ± 14	24.8 ± 8.2	83 ± 13	98 ± 10
			Methanol	100 ± 8	n.d.	154 ± 36	104 ± 10
Calophyllum inophyllum	Clusiaceae	Bark	Chloroform	8 ± 6	17.7 ± 1.3	158 ± 23	86 ± 14
			Methanol	59 ± 12	n.d.	138 ± 32	108 ± 8
		Seed	Chloroform	3 ± 3	14.8 ± 0.7	124 ± 94	128 ± 29
		Coat	Methanol	301 ± 9	21.3 ± 2.6	190 ± 39	109 ± 11
Brucea mollis	Simaroubaceae	Semen	Chloroform	71 ± 11	n.d.	109 ± 4	75 ± 12
			Methanol	61 ± 4	n.d.	101 ± 1	73 ± 5
Artemisia vulgaris	Asteraceae	Aerial parts	Chloroform	47 ± 7	30.0 ± 5.6	216 ± 123	335 ± 223
			Methanol	92 ± 3	n.d.	92 ± 1	92 ± 13
Piper lolot	Piperaceae	Leaves	Chloroform	70 ± 2	n.d.	124 ± 53	122 ± 40
			Methanol	95 ± 9	n.d.	141 ± 30	104 ± 6
Cibotium barometz	Dicksoniaceae	Rhizome	Chloroform	66 ± 11	n.d.	101 ± 7	114 ± 9
			Methanol	87 ± 11	n.d.	114 ± 20	99 ± 5
Drynaria fortunei	Polygonaceae	Rhizome	Chloroform	96 ± 12	n.d.	95 ± 19	94 ± 10
			Methanol	53 ± 1	n.d.	187 ± 70	79 ± 14
Momordica cochinchinensis	Cucurbitaceae	Seed	Chloroform	56 ± 12	n.d.	65 ± 22	79 ± 18
		Coat	Methanol	65 ± 2	n.d.	137 ± 49	73 ± 1
		Seedling	Chloroform	78 ± 11	n.d.	113 ± 10	136 ± 16
			Methanol	100 ± 4	n.d.	97 ± 7	115 ± 18
		Leaves	Chloroform	59 ± 1	n.d.	96 ± 6	96 ± 6
			Methanol	95 ± 1	n.d.	119 ± 7	102 ± 3
		Roots	Chloroform	98 ± 12	n.d.	66 ± 25	111 ± 10
			Methanol	53 ± 12	n.d.	153 ± 19	116 ± 28
		Bark	Chloroform	115 ± 11	n.d.	96 ± 2	90 ± 13
			Methanol	99 ± 6	n.d.	77 ± 16	97 ± 4
Dracaena cambodiana	Dracaenaceae	Wood	Chloroform	7 ± 2	2.1 ± 0.7	76 ± 9	73 ± 6
			Methanol	4 ± 2	0.4 ± 0.2	127 ± 16	38 ± 6
Siegesbeckia orientalis	Asteraceae	Aerial parts	Chloroform	73 ± 3	n.d.	80 ± 6	97 ± 8
			Methanol	108 ± 0	n.d.	127 ± 29	114 ± 1
Vitex rotundifolia	Verbernaceae	Leaves	Chloroform	13 ± 1	15.0 ± 0.8	159 ± 21	77 ± 15
			Methanol	96 ± 4	n.d.	122 ± 20	99 ± 8
		Fruits	Chloroform	12 ± 3	10.6 ± 7.1	44 ± 5	39 ± 39
			Methanol	66 ± 8	n.d.	107 ± 5	87 ± 6
Caesalpinia bonduc	Fabaceae	Seedling	Chloroform	95 ± 6	n.d.	84 ± 5	100 ± 11
			Methanol	96 ± 4	n.d.	99.3 ± 8	101 ± 2
Aleurites moluccana	Euphorbiaceae	Leaves	Chloroform	84 ± 1	n.d.	143 ± 63	132 ± 36
			Methanol	116 ± 1	n.d.	93 ± 26	92 ± 9
		Stems	Chloroform	19 ± 3	19.5 ± 1.9	157 ± 11	81 ± 3
			Methanol	105 ± 2	n.d.	127 ± 15	106 ± 6
		Roots	Chloroform	84 ± 2	n.d.	144 ± 91	130 ± 42
			Methanol	100 ± 6	n.d.	121 ± 7	97 ± 3
Nepenthes mirabilis	Nepenthaceae	Leaves	Chloroform	34 ± 8	22.4 ± 4.0	91 ± 17	94 ± 1
			Methanol	78 ± 2	n.d.	105 ± 14	71 ± 4
		Stems	Chloroform	44 ± 1	26.7 ± 0.1	118 ± 24	104 ± 5
			Methanol	78 ± 1	n.d.	94 ± 10	86 ± 2
Alstonia scholaris	Apocynaceae	Leaves	Chloroform	25 ± 8	13.0 ± 4.2	147 ± 39	130 ± 64
			Methanol	92 ± 4	n.d.	104 ± 7	88 ± 2
		Bark	Chloroform	56 ± 1	n.d.	156 ± 101	143 ± 55
			Methanol	96 ± 4	n.d.	83 ± 21	80 ± 7
Phyllanthus reticulatus	Euphorbiaceae	Leaves	Chloroform	40 ± 11	23.2 ± 7.9	111 ± 9	101 ± 6
			Methanol	102 ± 9	n.d.	88 ± 17	79 ± 8
		Bark	Chloroform	18 ± 6	19.1 ± 1.3	172 ± 23	108 ± 20
			Methanol	102 ± 14	n.d.	88 ± 18	84 ± 4
			Chloroform				

Latin plant name	Plant family	Plant organ	Extraction solvent	5-LOX at 30 µg/mL[a]	5-LOX IC_{50}[b]	15-LOX at 30 µg/mL[a]	12-LOX at 30 µg/mL[a]
Kopsia cochinchinensis	Apocynaceae	Pleaves		32 ± 11	18.0 ± 6.4	159 ± 22	125 ± 23
			Methanol	84 ± 5	n.d.	93 ± 20	82 ± 11
		Bark	Chloroform	97 ± 3	n.d.	89 ± 12	83 ± 8
			Methanol	83 ± 3	n.d.	93 ± 3	102 ± 21
Ficus benghalensis	Moraceae	Leaves	Chloroform	23 ± 11	19.3 ± 2.8	130 ± 63	94 ± 28
			Methanol	76 ± 4	n.d.	78 ± 21	64 ± 11
Symplocos annamensis	Symplocaceae	Leaves	Chloroform	31 ± 7	n.d.	102 ± 14	80 ± 6
			Methanol	86 ± 8	n.d.	96 ± 1	84 ± 0
Croton sp.	Euphorbiaceae	Leaves	Chloroform	7 ± 2	15.9 ± 2.1	88 ± 30	94 ± 26
			Methanol	10 ± 3	9.9 ± 4.6	55 ± 2	75 ± 7
Stephania venosa	Menispermaceae	Roots	Chloroform	16 ± 6	11.2 ± 5.8	126 ± 4	74 ± 9
			Methanol	86 ± 3	n.d.	85 ± 12	84 ± 12
Streptocaulon juventas	Asclepidiaceae	Roots	Chloroform	65 ± 16	n.d.	82 ± 4	84 ± 1
			Methanol	92 ± 7	n.d.	91.4 ± 5	87 ± 3
		Stems	Chloroform	36 ± 9	8.8 ± 8.8	169 ± 33	144 ± 19
		+ Leaves	Methanol	87 ± 1	n.d.	113 ± 13	97 ± 2
Plumeria rubra	Apocynaceae	Bark	Chloroform	61 ± 7	n.d.	75 ± 14	67 ± 17
			Methanol	95 ± 5	n.d.	102 ± 9	96 ± 1
Tinospora crispa	Menispermaceae	Stems	Chloroform	28 ± 5	22.5 ± 1.4	66 ± 12	58 ± 8
			Methanol	77 ± 2	n.d.	79 ± 14	74 ± 14
Stephania cambodica	Menispermaceae	Tuber	Chloroform	3 ± 3	10.6 ± 4.1	126 ± 19	81 ± 8
			Methanol	67 ± 11	n.d.	100 ± 9	81 ± 6
Stephania pierrei	Menispermaceae	Tuber	Chloroform	43 ± 6	26.2 ± 3.5	84 ± 8	71 ± 11
			Methanol	94 ± 9	n.d.	94 ± 7	88 ± 7
Adenium sp.	Apocynaceae	Bark	Chloroform	61 ± 8	n.d.	76 ± 4	74 ± 8
			Methanol	101 ± 6	n.d.	83 ± 5	87 ± 3
Aristolochia sp.	Aristolochiaceae	Stems	Chloroform	7 ± 1	19.4 ± 2.1	25 ± 1	78 ± 13
			Methanol	97 ± 2	n.d.	94 ± 24	96 ± 5
Hydnophytum formicarum	Rubiaceae	Tuber	Chloroform	66 ± 6	n.d.	80 ± 1	104 ± 11
			Methanol	79 ± 2	n.d.	71 ± 0	63 ± 1
Parameria laevigata	Apocynaceae	Stems	Chloroform	50 ± 1	n.d.	111 ± 5	119 ± 1
		+ Leaves	Methanol	98 ± 1	n.d.	79 ± 7	100 ± 8

The extract library for screening was created in the course of the project 'Drugs from nature targeting inflammation (DNTI)'[31]. Extracts were prepared according to the protocol of Thi Tran et al.[32], which we slightly modified by exchanging dichloromethane by chloroform. [a]5-LOX product formation at 30 µg/mL (% control) and [b]IC_{50} values (µg/mL) are given as mean ± SEM; n = 2–5. [c]Not determined.

Table S2 Docking results overview: ChemPLP fitness score and hydrogen bond interactions with protein residues from the binding site for the best ranked pose of each compound.

Compd.	Stereochemistry	IC_{50}(5-LOX) [µmol/L][a]	Score	R68	R101	E108	V110	H125	I126	Q129	H130	E134	E136	T137	R138	K140	Q141	D166
1a	2*R*,γ*S*	0.70	64.83				X									X		
1b	2*S*,γ*R*	0.70	72.62				X				X		X			X		
2a	2*R*,γ*R*	1.50	71.83			X		X				X						
2b	2*S*,γ*S*	0.50	70.75		X								X			X		
3a	2*R*,γ*R*		72.51			X							X					
3b	2*S*,γ*R*	0.80	71.07			X							X					
3c	2*R*,γ*S*		73.48						X							X		X
3d	2*S*,γ*S*		71.33						X							X		
4a	2*R*,γ*R*		69.23							X			X			X		
4b	2*S*,γ*R*	0.46	63.83					X				X					X	
4c	2R,γS		59.89										X					
4d	2*S*,γ*S*		66.46				X	X			X	X		X				
5a	*S*	0.51	73.76										X			X		
5b	*R*		76.62											X				
6a	*S*	0.85	74.01									X	X			X		
6b	*R*		84.61															X
7a	*S*	0.59	78.89	X		X						X						X
7b	*R*		76.71									X						
8a	*R*	>10	54.77	X			X											
8b	*S*		53.12	X										X				
9a	*R*	5.70	53.43											X				X
9b	*S*		52.84															
10	*S*	>10	58.52								X				X			X
11a	*R*	>10	56.10								X			X	X			
11b	*S*		53.42						X			X						
12		5.01	56.02								X				X			
13		>10	60.02	X								X		X				
14		8.90	55.51						X			X		X				
15		6.50	56.49	X	X										X			
16		4.39	61.18											X				
17		7.18	56.02				X					X		X				
18		n.i.	35.02															

[a]IC_{50} values inhibition of human recombinant 5-LOX
n.i. = no inhibition

Table S3 Effect of compound **2** on the lipid mediator profile of A23187-activated human blood.

	Lipid mediators	Vehicle	Compound **2** (0.3 µmol/L)	Compound **2** (1 µmol/L)	Compound **2** (3 µmol/L)	Compound **2** (10 µmol/L)	Compound **2** (30 µmol/L)
5-LOX	20-OH-LTB_4	488 ± 245	457 ± 196	429 ± 187	266 ± 79	147 ± 75	3 ± 3
	LTB_4 isomers	354 ± 166	297 ± 112	258 ± 81	197 ± 89	107 ± 67	n.d.
	LTB_4	2,494 ± 1,365	2,080 ± 1,024	2,060 ± 1,030	1,278 ± 377	675 ± 346	13 ± 13
	5S,6R-diHETE	76 ± 34	77 ± 32	70 ± 31	45 ± 13	21 ± 11	n.d.
	5-HETE	4,242 ± 2,206	3,882 ± 1,765	4,402 ± 1,859	2,516 ± 613	1,184 ± 484	294 ± 178
	5-HEPE	100 ± 39	94 ± 24	107 ± 27	63 ± 28	35 ± 17	6 ± 4
COX	PGE_2	30 ± 6	23 ± 4	26 ± 3	29 ± 8	26 ± 6	30 ± 8
	PGD_2	6 ± 4	5 ± 2	5 ± 1	3 ± 2	4 ± 2	8 ± 6
	TXB_2	789 ± 319	587 ± 159	527 ± 128	561 ± 51	767 ± 254	894 ± 330
12/15-LOX	15-HETE	268 ± 135	163 ± 51	191 ± 44	190 ± 44	397 ± 192	563 ± 335
	14-HDHA	606 ± 195	529 ± 103	583 ± 73	549 ± 118	560 ± 142	793 ± 223
	12-HETE	8,758 ± 4,186	6,513 ± 2,504	6,711 ± 1,707	4,388 ± 555	7,535 ± 2,544	9,761 ± 3,175
	12-HEPE	170 ± 56	146 ± 42	152 ± 18	110 ± 11	168 ± 48	231 ± 65
	4-HDHA	36 ± 13	26 ± 8	24 ± 6	49 ± 26	65 ± 32	93 ± 48
Fatty acids	AA	92,406 ± 13,862	87,940 ± 9,780	950,120 ± 10,076	86,695 ± 4,318	104,828 ± 16,859	110,693 ± 12,200
	EPA	76,133 ± 18,205	76,745 ± 21,976	67,997 ± 12,100	69,601 ± 18,071	74,569 ± 16,264	73,498 ± 18,021
	DHA	123,473 ± 35,237	123,537 ± 26,295	126,757 ± 31,681	120,295 ± 23,681	111,856 ± 34,923	114,093 ± 38,410

	Lipid mediators	Compound **5** (0.3 µmol/L)	Compound **5** (1 µmol/L)	Compound **5** (3 µmol/L)	Compound **5** (10 µmol/L)	Compound **5** (30 µmol/L)	Zileuton (3 µmol/L)
5-LOX	20-OH-LTB_4	488 ± 175	566 ± 227	824 ± 253	579 ± 264	455 ± 191	236 ± 96
	LTB_4 isomers	349 ± 137	337 ± 120	546 ± 164	374 ± 147	327 ± 156	115 ± 41
	LTB_4	2,251 ± 908	2,602 ± 1,028	3,807 ± 1,281	2,650 ± 1,299	2,322 ± 987	1,167 ± 577
	5S,6R-diHETE	92 ± 37	100 ± 36	141 ± 41	101 ± 49	80 ± 34	37 ± 20
	5-HETE	4,183 ± 1,884	4,879 ± 2,027	6,669 ± 2,182	4,818 ± 2,404	4,067 ± 1,848	1,995 ± 1,061
	5-HEPE	110 ± 33	131 ± 44	181 ± 50	124 ± 42	113 ± 40	36 ± 14
COX	PGE_2	35 ± 8	39 ± 8	59 ± 18	44 ± 14	38 ± 8	20 ± 7
	PGD_2	4 ± 4	9 ± 5	6 ± 6	4 ± 4	4 ± 4	7 ± 7
	TXB_2	763 ± 239	984 ± 397	1,326 ± 482	1,013 ± 349	1033 ± 383	746 ± 381
12/15-LOX	15-HETE	223 ± 52	253 ± 69	358 ± 134	277 ± 100	290 ± 104	228 ± 90
	14-HDHA	660 ± 170	715 ± 180	957 ± 256	722 ± 188	765 ± 203	564 ± 88
	12-HETE	8,612 ± 3,356	10,090 ± 4,141	12,256 ± 4,292	10,300 ± 4,315	10,136 ± 4371	8,473 ± 2,992
	12-HEPE	220 ± 77	227 ± 78	280 ± 79	215 ± 72	227 ± 62	172 ± 27
	4-HDHA	31 ± 8	29 ± 4	38 ± 10	27 ± 3	38 ± 7	34 ± 6
Fatty acids	AA	94,274 ± 10,609	100,106 ± 9,134	123,060 ± 20,518	101,992 ± 15,387	104,855 ± 14,743	97,858 ± 12,853
	EPA	62,981 ± 14,241	69,825 ± 17,109	90,022 ± 27,223	72,466 ± 14,014	74,508 ± 12,972	72,089 ± 19,021
	DHA	126,572 ± 36,366	116,962 ± 33,564	159,216 ± 79,635	129,069 ± 46,762	132,497 ± 38,354	127,202 ± 32,533

Concentrations of lipid mediators analyzed by UPLC-MS/MS are given in pg/mL blood as mean ± SEM, $n = 3$, n.d., not detectable (< 0.5 pg). 20-OH-LTB_4, 20-hydroxy-LTB_4; HEPE, hydroxy-eicosapentaenoic acid; (di)HETE, (di)hydroxy-eicosatetraenoic acid; HDHA, hydroxy-docosahexaenoic acid; AA, arachidonic acid; EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid.

Table S4 Effect of compound **2** on the lipid mediator profile of *E. coli*-stimulated human blood.

	Lipid mediators	Vehicle	Compound **2** (0.3 µmol/L)	Compound **2** (3 µmol/L)	Compound **2** (30 µmol/L)	Zileuton (3 µmol/L)
5-LOX	5-HEPE	116 ± 35	105 ± 32	91 ± 25	40 ± 8	42 ± 14
	5-HETE	2,659 ± 685	2,601 ± 584	2,217 ± 435	661 ± 190	515 ± 130
	LTB_4 isomers	546 ± 248	424 ± 95	361 ± 89	127 ± 44	54 ± 10
	LTB_4	6,313 ± 2	5,560 ± 2,084	4,499 ± 1697	560 ± 366	207 ± 164
	5S,6R-diHETE	98 ± 33	97 ± 36	79 ± 26	16 ± 6	9 ± 3
COX	PGE_2	877 ± 408	952 ± 476	887 ± 418	1 ± 472	706 ± 395
	PGD_2	120 ± 56	135 ± 64	126 ± 55	162 ± 76	134 ± 90
	$PGF_{2\alpha}$	600 ± 289	596 ± 279	602 ± 294	739 ± 363	630 ± 423
	TXB_2	27,680 ± 13,136	26,424 ± 13,955	30,649 ± 15,827	25,354 ± 13,039	24,692 ± 13,119
12/15-LOX	17-HDHA	717 ± 203	698 ± 217	768 ± 214	598 ± 167	229 ± 22
	14-HDHA	9,190 ± 3,131	8,912 ± 3,173	9,077 ± 3,105	8030 ± 2834	1,542 ± 366
	15-HEPE	172 ± 62	169 ± 71	164 ± 61	153 ± 57	65 ± 20
	12-HEPE	2,913 ± 1,180	2,799 ± 1,403	2,807 ± 1,291	2,897 ± 1,324	897 ± 388
	15-HETE	3,750 ± 790	3,694 ± 881	3,762 ± 734	3,436 ± 764	1,765 ± 353
	12-HETE	31,609 ± 3,850	29,623 ± 5,025	32,978 ± 4,717	28,654 ± 2,841	20,173 ± 4417
	7-HDHA	39 ± 15	41 ± 14	44 ± 16	33 ± 15	27 ± 10
	4-HDHA	63 ± 31	86 ± 35	79 ± 32	64 ± 35	76 ± 26
	5,15 di-HETE	69 ± 13	64 ± 10	67 ± 10	42 ± 9	20 ± 2
SPM	RvD5	6 ± 2	8 ± 2	7 ± 1	6 ± 2	2 ± 0
	RvE3	34 ± 23	38 ± 0	39 ± 1	44 ± 31	20 ± 6
Fatty acids	AA	424,337 ± 52,820	513,640 ± 51,167	340,083 ± 54,832	397,935 ± 23,643	529,704 ± 85,597
	EPA	68,231 ± 20,988	75,093 ± 16,682	53,637 ± 13,559	50,745 ± 5,157	67,085 ± 10,737
	DHA	31,698 ± 5,323	38,698 ± 3,521	23,775 ± 2,860	31,706 ± 4,176	45,337 ± 11,464

Concentrations of lipid mediators analyzed by UPLC–MS/MS are given in pg/mL blood as mean ± SEM, $n = 4$. HEPE, hydroxy-eicosapentaenoic acid; (di)HETE, (di)hydroxy-eicosatetraenoic acid; HDHA, hydroxy-docosahexaenoic acid; AA, arachidonic acid; EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid.

Table S5 Effect of compound **2** on the lipid mediator profile of *E. coli*-stimulated M1 and M2 macrophages.

	Lipid mediators	M1 vehicle	Compound **2** (0.3 µmol/L)	Compound **2** (3 µmol/L)	M2 vehicle	Compound **2** (0.3 µmol/L)	Compound **2** (3 µmol/L)
5-LOX	5-HEPE	11 ± 4	5 ± 3	2 ± 1	103 ± 65	46 ± 13	20 ± 5
	5-HETE	36 ± 16	17 ± 7	10 ± 2	658 ± 449	282 ± 124	132 ± 44
	LTB_4 isomers	8 ± 2	3 ± 1	2 ± 0	55 ± 31	25 ± 9	20 ± 10
	LTB_4	19 ± 3	16 ± 6	3 ± 0	58 ± 37	29 ± 13	21 ± 8
	5S,6R-diHETE	5 ± 1	3 ± 1	2 ± 1	41 ± 35	11 ± 7	4 ± 1
COX	PGE_2	2,334 ± 888	2,268 ± 842	1,785 ± 558	185 ± 70	219 ± 82	488 ± 172
	PGD_2	24 ± 6	20 ± 5	26 ± 5	64 ± 28	70 ± 28	128 ± 52
	$PGF_{2\alpha}$	263 ± 115	227 ± 89	191 ± 43	145 ± 58	165 ± 66	210 ± 80
	TXB_2	2,799 ± 440	2,503 ± 366	2,821 ± 503	16,293 ± 7,141	16,040 ± 6,659	11,502 ± 4,470
12/15-LOX	17-HDHA	19 ± 2	20 ± 1	30 ± 1	1,038 ± 879	2,982 ± 2,032	4,691 ± 1,694
	14-HDHA	8 ± 4	7 ± 3	16 ± 9	200 ± 164	752 ± 468	1,470 ± 374
	15-HEPE	4 ± 0	6 ± 1	10 ± 2	520 ± 450	1,463 ± 852	2,349 ± 999
	12-HEPE	4 ± 2	5 ± 3	5 ± 2	89 ± 76	249 ± 159	311 ± 142
	15-HETE	68 ± 10	87 ± 7	114 ± 9	4,459 ± 3,702	11,836 ± 6,790	22,589 ± 10,571
	12-HETE	24 ± 8	29 ± 9	31 ± 9	350 ± 299	777 ± 459	1,373 ± 670
	7-HDHA	7 ± 1	4 ± 2	6 ± 1	72 ± 45	123 ± 71	125 ± 35
	4-HDHA	7 ± 4	6 ± 3	7 ± 3	19 ± 5	20 ± 6	19 ± 5
	5,15-diHETE	31 ± 18	43 ± 7	9 ± 5	197 ± 140	388 ± 262	500 ± 344
SPM	PD1	n.d.	n.d.	n.d.	13 ± 11	42 ± 37	61 ± 40
	AT-PD1	n.d.	n.d.	n.d.	18 ± 16	55 ± 49	73 ± 46
	PDX	n.d.	n.d.	n.d.	2 ± 1	7 ± 5	14 ± 5
	RvD5	n.d.	n.d.	n.d.	159 ± 149	488 ± 414	598 ± 414
	MaR1	1 ± 0	n.d.	1 ± 0	6 ± 5	31 ± 22	58 ± 23
	RvE3	18 ± 1	16 ± 2	17 ± 1	28 ± 7	40 ± 18	74 ± 43
Fatty acids	AA	10,197 ± 3,150	32,298 ± 27,652	34,503 ± 28,783	79,482 ± 33,388	64,172 ± 23,650	67,772 ± 28,023
	EPA	1,759 ± 506	4,979 ± 4,344	5,045 ± 4,291	16,231 ± 8,294	16,134 ± 7,468	11,801 ± 5,294
	DHA	2,197 ± 625	6,497 ± 5,152	7,482 ± 6,001	19,427 ± 14,305	19,499 ± 14,221	15,678 ± 10,296

Concentrations of lipid mediators analyzed by UPLC–MS/MS are given in pg/2×10^6 cells as mean ± SEM, $n = 3$, n.d., not detectable (< 0.5 pg). HEPE, hydroxy-eicosapentaenoic acid; (di)HETE, (di)hydroxy-eicosatetraenoic acid; HDHA, hydroxy-docosahexaenoic acid; AA, arachidonic acid; EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid.

Table S6 Effect of compound **2** on the lipid mediator profile of *S. aureus*-stimulated M1 and M2 macrophages.

	Lipid mediators	M1 vehicle	Compound **2** (0.3 µmol/L)	Compound **2** (3 µmol/L)	M2 vehicle	Compound **2** (0.3 µmol/L)	Compound **2** (3 µmol/L)
5-LOX	5-HEPE	452 ± 96	193 ± 51	94 ± 8	515 ± 308	406 ± 181	179 ± 44
	5-HETE	3,835 ± 958	1,486 ± 385	333 ± 57	5707 ± 3607	3,570 ± 1,713	2,042 ± 593
	LTB_4 isomers	355 ± 105	142 ± 34	36 ± 6	664 ± 374	524 ± 136	223 ± 36
	LTB_4	1,206 ± 316	434 ± 121	37 ± 3	1,624 ± 1,011	693 ± 316	301 ± 89
	5S,6R-diHETE	189 ± 90	51 ± 27	8 ± 2	240 ± 150	100 ± 59	42 ± 17
COX	PGE_2	2,718 ± 648	3,925 ± 908	4,055 ± 944	1073 ± 501	1,234 ± 498	2,885 ± 998
	PGD_2	93 ± 13	110 ± 15	186 ± 28	276 ± 51	313 ± 48	677 ± 110
	$PGF_{2\alpha}$	1,094 ± 204	1,281 ± 194	1,299 ± 143	655 ± 261	670 ± 194	957 ± 270
	TXB_2	21,837 ± 1798	24,397 ± 1,753	19,163 ± 2,201	48,575 ± 15,755	48,792 ± 12,973	35,246 ± 9,971
12/15-LOX	17-HDHA	823 ± 102	787 ± 103	1,240 ± 72	25,340 ± 2,360	32,587 ± 7,358	34,486 ± 7,201
	14-HDHA	446 ± 234	393 ± 167	635 ± 243	5,475 ± 270	7,298 ± 1,444	8,674 ± 1,782
	15-HEPE	100 ± 19	112 ± 2	131 ± 16	7,864 ± 1,632	15,578 ± 4,754	10,315 ± 643
	12-HEPE	224 ± 159	162 ± 50	295 ± 119	1,572 ± 252	2,909 ± 581	1,687 ± 232
	15-HETE	1,310 ± 396	1,385 ± 168	1,597 ± 329	70,086 ± 10,744	117,314 ± 20,290	84,506 ± 5,519
	12-HETE	1,412 ± 1,076	2,051 ± 1,236	3,199 ± 1,547	13,557 ± 2,704	18,108 ± 1,178	16,147 ± 2,646
	7-HDHA	239 ± 59	115 ± 14	89 ± 9	513 ± 80	570 ± 95	590 ± 101
	4-HDHA	93 ± 14	92 ± 16	94 ± 13	97 ± 13	80 ± 19	91 ± 19
	5,15-diHETE	246 ± 150	63 ± 20	54 ± 29	6,380 ± 1,635	7,714 ± 1,478	6,847 ± 1,698
SPM	PD1	14 ± 4	14 ± 1	17 ± 4	71 ± 20	114 ± 66	106 ± 31
	PDX	5 ± 0	4 ± 0	4 ± 1	88 ± 20	126 ± 40	166 ± 41
	RvD2	n.d.	n.d.	n.d.	49 ± 19	92 ± 67	75 ± 39
	RvD5	16 ± 3	9 ± 2	6 ± 0	2 ± 790	2 ± 1	2 ± 967
	MaR1	4 ± 1	6 ± 1	2 ± 1	319 ± 89	417 ± 118	444 ± 146
Fatty acids	AA	140,934 ± 25,617	121,829 ± 14,902	100,344 ± 15,784	163,429 ± 56,176	155,166 ± 50,390	146,874 ± 45,143
	EPA	41,220 ± 7,626	43,151 ± 3,527	37,748 ± 7,345	52,063 ± 13,088	40,876 ± 9,447	48,845 ± 10,427
	DHA	105,163 ± 17,328	125,609 ± 10,283	97,478 ± 14,163	67,446 ± 6,404	59,757 ± 2,036	62,539 ± 1,086

Concentrations of lipid mediators analyzed by UPLC-MS/MS are given in pg/2×10^6 cells as mean ± SEM, $n = 3$, n.d., not detectable (< 0.5 pg). The heatmap shows percentage changes upon administration of compound **2** relative to the vehicle control. HEPE, hydroxy-eicosapentaenoic acid; (di)HETE, (di)hydroxy-eicosatetraenoic acid; HDHA, hydroxy-docosahexaenoic acid; AA, arachidonic acid; EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid.