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ScienceDirect
Phytochemistry 69 (2008) 988–993
PHYTOCHEMISTRY
www.elsevier.com/locate/phytochem

Anti-inflammatory 5-(11′*Z*-heptadecenyl)- and 5-(8′*Z*,11′*Z*-heptadecadienyl)-resorcinols from mango (*Mangifera indica* L.) peels

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Received 29 August 2007; received in revised form 4 October 2007
Available online 21 December 2007

Abstract

Bioassay directed extraction and purification of mango peels revealed the 5-(11′*Z*-heptadecenyl)-resorcinol (**1**) and the known 5-(8′*Z*,11′*Z*-heptadecadienyl)-resorcinol (**2**) previously not described in *Mangifera indica* L. The structures of both compounds were determined by extensive 1D and 2D NMR studies and MS. Both compounds exhibited potent cyclooxygenase (COX)-1 and COX-2 inhibitory activity with IC_{50} values ranging from 1.9 (**2**) to 3.5 μM (**1**) and from 3.5 (**2**) to 4.4 (**1**) μM, respectively, coming close to the IC_{50} values of reference drugs. 5-Lipoxygenase (5-LOX) catalyzed leukotriene formation was only slightly inhibited. Structure–activity studies by referring to synthetic saturated homologues indicated that the degree of unsaturation in the alkyl chain plays a key role for COX inhibitory activity, whereas the influence of chain length was less significant.

Keywords: *Mangifera indica* L.; Anacardiaceae; 5-(11′*Z*-Heptadecenyl)-resorcinol; Cyclooxygenase; 5-Lipoxygenase; NMR; MS

1. Introduction

Fruits of *Mangifera indica* L. (Anacardiaceae) as well as other parts of the plant have widely been used in traditional medicine (Khare, 2004). The fruits are also used as a nutrient and for the industrial production of products like juice, jams and purées. The fruit peels are discarded as a waste. The members of the family Anacardiaceae are known to contain alkyl or alkenyl derivatives of phenol, catechol, and resorcinol (Kozubek and Tyman, 2005). In the case of *M. indica*, the latter compounds occur in the latex and the fruit peel, while they are absent in the edible parts of the fruit (Bandyopadhyay et al., 1985; Ross et al., 2004). A mixture of 5-(12′-heptadecenyl)- and 5-pentadecylresorcinol isolated from the peel of unripe mango fruits was considered responsible for the resistance to *Alternaria alternata*, a fungus causing black spot disease in mango fruits (Droby et al., 1986). Recently, the isolation of the $C_{15:0}$-, $C_{17:1}$- and $C_{17:2}$-resorcinol derivatives from mango peels was reported; the latter were patch tested positive on patients with mango dermatitis and cross-reacted with urushiols (Oka et al., 2004; Hershko et al., 2005). In a more recent study, the alk(en)ylresorcinol (AR) composition in mango peels was reported to consist of a complex series of C_{15}-, C_{17}- and C_{19}-substituted resorcinols showing varying degrees of unsaturation (Knödler et al., 2007).

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0031-9422/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.phytochem.2007.10.013

Furthermore AR have been reported to exhibit antioxidant and antigenotoxic properties (Paprikka et al., 2006). Numerous other biological activities of AR, often attributed to their amphiphilic nature, *inter alia* antiparasitic, anticancer and antioxidant properties, have been extensively reviewed by Kozubek and Tyman (1999, 2005).

The two isozymes of cyclooxygenases (COX-1 and -2) are the rate-limiting enzymes in arachidonic acid metabolism catalyzing the first two steps in prostaglandin synthesis. COX-1 is constitutively expressed and COX-1 derived prostanoids maintain the integrity of the gastrointestinal mucosa; it is therefore considered to possess housekeeping functions. COX-2 expression is induced by various external stimuli. Therefore, it has been believed that inhibition of COX-1-derived prostanoid production causes side effects like gastrointestinal damage and ulcers observed for non steroidal anti-inflammatory drugs, whereas inhibition of COX-2 derived prostanoids is responsible for their anti-inflammatory, analgesic and antipyretic effects. Thus, selective COX-2 inhibitors have been preferred over COX-1 inhibitors to alleviate inflammation (Calanni and Laufer, 2003). However, several selective COX-2 inhibitors have been found to cause side effects such as cardiovascular problems (Mukherjee et al., 2001) and it was found that COX-2 is expressed constitutively in some tissues (Mattia and Coluzzi, 2005). In the first step of the leukotriene pathway of the arachidonic acid cascade, 5-LOX catalyzes the oxygenation of arachidonic acid. Leukotrienes such as LTB_4 are potent mediators of inflammatory and allergic reactions. 5-LOX inhibitors are considered to possess therapeutic potential in a range of allergic and inflammatory conditions (Calanni and Laufer, 2003).

Continuing our research on the discovery of bioactive compounds from food and pharmaceutical processing by-products [SAFEWASTES (www.safewastes.info)], the anti-inflammatory activities of mango peel extracts have been examined by means of *in vitro* assays measuring the inhibition of leukotriene formation (5-LOX) and cyclooxygenase (COX-1 and COX-2) enzymes, respectively. This paper presents the bioassay guided isolation and structure elucidation of the new 5-(11′*Z*-heptadecenyl)resorcinol (**1**) and the known 5-(8′*Z*,11′*Z*-heptadecadienyl)resorcinol (**2**) (Fig. 1), as well as the COX enzymes and leukotriene formation inhibitory activities of fractions, pure compounds **1** and **2**, along with commercially available saturated AR (**3**: 5-pentyl-, **4**: 5-pentadecyl-, **5**: 5-heptadecyl-, **6**: 5-nonadecylresorcinol; Fig. 1) and clinically used anti-inflammatory drugs indomethacin, NS-398 and zileuton.

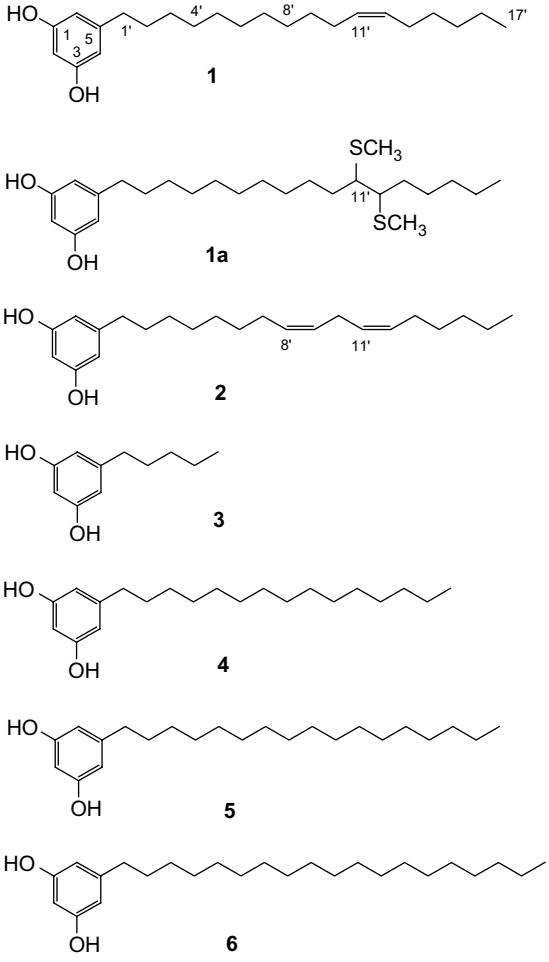

Fig. 1. Chemical structures of **1**–**6**.

2. Results and discussion

Dried mango peels were extracted with dichloromethane, ethanol (70% *v*/*v*) and water, respectively, and the resultant extracts were investigated for their COX- and leukotriene formation inhibitory activities. While the aqueous extract was inactive in all three assays, the 70% ethanolic extract showed considerable COX-1 and less pronounced COX-2 inhibitory activity at 20 μg/ml. The dichloromethane extract was highly active against COX-1 ($86.5 \pm 6.7\%$) and COX-2 ($75.4 \pm 5.7\%$) and less active against 5-LOX ($35.7 \pm 4.4\%$). Based on these results, the dichloromethane extract was subjected to solid phase extraction on polyamide followed by elution with methanol to yield the purified AR fraction which showed inhibitory activities of $95.4 \pm 0.4\%$, $92.5 \pm 1.5\%$ and $40.1 \pm 5.5\%$ against COX-1, COX-2 and 5-LOX, respectively. Semi-preparative HPLC afforded the previously not described 5-(11′*Z*-heptadecenyl)-resorcinol (**1**), obtained as a yellow coloured oil, and the known 5-(8′*Z*,11′*Z*-heptadecadienyl)-resorcinol (**2**). LC-APcI-MS/MS analysis of **1** produced a pseudo molecular ion $[M + H]^+$ at *m*/*z* 347. In the MS^2 experiment a remarkably stable product ion at *m*/*z* 123 was detected, which is due to the 1,3-dihydroxytropylium ion formed by direct β-cleavage of the aromatic ring (Knödler et al., 2007). High-resolution fourier transform ion cyclotron resonance (HR-FT-ICR+) mass spectrometry of **1** revealed a pseudo molecular ion $[M + H]^+$ at *m*/*z* 347.2945, corresponding to the molecular formula $C_{23}H_{39}O_2$ (calc. 347.2945). The ^1H and ^{13}C NMR as well

as the multiplicity-edited gHSQC NMR spectra of **1** showed the typical pattern of a 5-alkenyl substituted resorcinol with a linear 17-carbon side chain containing one double bond (δ_H 5.36 and 5.37, δ_C 131.90 and 131.20), 13 methylens between δ_C 23.68 and 36.85, and one methyl group resonating at δ_H 0.89 and δ_C 14.78 (Valcic et al., 2002; Jin and Zjawiony, 2006). Four aromatic carbons at δ 159.29 (C-1/C-3), 147.00 (C-5), 108.37 (C-4/C-6), and 101.11 (C-2) as well as a two proton signal at δ 6.15 (*d*, $J = 2.2$ Hz, H-4/H-6) *meta* coupled to proton H-2 at δ 6.08 (*t*, $J = 2.2$ Hz) indicated the resorcinol moiety in **1**. The first four positions 1′-4′ of the side chain were assigned by long-range COSY, ROESY and ^{1}H,^{13}C-long-range correlations (Fig. 2). Recently published heteronuclear pulse sequences such as adiabatic gH2BC (Nyberg et al., 2005), band-selective adiabatic gHSQC with and without ^{13}C decoupling, adiabatic and band-selective gHMBC (Crouch et al., 2004; Bradley and Krishnamurthy, 2005) were applied to determine the position of the double bond. The ^{13}C band-selection offers the possibility to record adiabatic gHSQC and gHMBC spectra of e.g. the crowded region of the methylene carbons of **1** (δ 10–40 ppm) both with a high resolution in the indirect dimension and without spectral aliasing. Thus, HMBC- and H2BC correlations between the protons of the terminal methyl group at δ 0.89 and the carbons at δ 23.68 and 32.66 established the C-16′ and C-15′ positions, respectively. A $^2J_{1H13C}$-connectivity between the latter carbon and the proton signal of H-14′ at δ 1.35 which shows another H2BC correlation to the allylic carbon C-13′ (δ 28.18) unambiguously located the double bond at the 11′-position. The above assignment was confirmed by HMBC correlations between both the olefinic resonance H-12′ (δ 5.37) and C-14′ at δ 30.61 and the methylgroup H-17′ (δ 0.89) and C-14′ ($=^4J_{1H13C}$). Homonuclear decoupling experiments of the allylic protons revealed a *Z*-configuration ($J = 10.6$ Hz) of the double bond (Table 1). To establish the position of the double bond independently, a GC–MS method involving the reaction of dimethyl disulfide with the double bond was applied (Scribe et al., 1988; Gonzales et al., 1996). Derivatization of **1** revealed **1a** with a pseudo molecular ion [M+] at *m*/*z* 440 and diagnostic key fragments at *m*/*z* 309 and 131. Both ions originate from cleavage across the C–C bond between the two adjacent methylsulfides and unambiguosly establish the 11′-position of the double bond. Further fragment ions at *m*/*z* 261 and 83 are due to the loss of methanethiol and are in in turn characteristic for the position of unsaturation. Beside **1a**, two additional GC peaks were detected

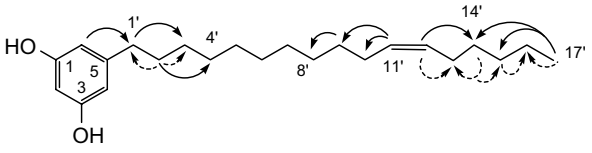

Fig. 2. Important H2BC (dashed arrows) and HMBC correlations of **1**.

Table 1
^{1}H NMR and ^{13}C NMR data of **1** and **2** in MeCN-d_3, $\vartheta = 25$ °C; (^{1}H: 500 MHz, ^{13}C: 125 MHz)

Pos	^{1}H NMR		^{13}C NMR	
	δ [ppm], *mult*, *J* [Hz][a]		δ [ppm][a]	
	1	**2**	**1**	**2**
1/3		6.80, *s* (OH)	159.29	159.29
2	6.08, *t*, 2.2	6.08, *t*, 2.2	101.11	101.09
4/6	6.15, *d*, 2.2	6.16, *d*, 2.2	108.37	108.36
5			147.00	146.99
1′	2.44, *bt*, 7.7	2.45, *bt*, 7.8	36.85	36.83
2′	1.54, *quint*, 7.4	1.55, *quint*, 7.5	32.40	32.38
3′	1.295, ov	1.30, ov	30.40	30.36
4′	1.34, ov	1.30–1.34, ov[b]	30.59	30.33[b]
5′	1.28, ov[b]	1.30–1.34, ov[b]	30.73[b]	30.42[b]
6′	1.28, ov[b]	1.34, ov[b]	30.71[b]	30.77
7′	1.29, ov[b]	2.06, *q*, 6.9	30.59[b]	28.22
8′	1.29, ov	5.38, *m*[f]	30.35	131.34[d]
9′	1.33, *quint*, 7.7	5.35, *m*[f]	30.86	129.29[b]
10′	2.03, *q*, 6.8	2.79, *t*, 6.6	28.20	26.68
11′	5.36, ov[c]	5.35, *m*[f]	131.19[d]	129.28[e]
12′	5.37, ov[c]	5.38, *m*[f]	131.20[d]	131.33[d]
13′	2.02, *q*, 6.8	2.06, *q*, 6.9	28.18	28.23
14′	1.35, *quint*, 7.0	1.36, ov	30.61	30.51
15′	1.29, *quint*, 7.6	1.30, ov	32.66	32.66
16′	1.32, ov	1.31, ov	23.68	23.66
17′	0.89, *t*, 6.7	0.89, *t*, 7.1	14.78	14.76

[a] Observed coupling constants were not averaged. Assignments based on gCOSY, ROESY, gHSQC and gHMBC spectra. ov = overlapped by other signals.

[b,d,e] Assignments may be interchanged.

[c] *Z*-Configuration determined by decoupling of H-10′ and H-13′. Coupling constant $J_{H\text{-}11'/H\text{-}12'} = 10.6$ Hz.

[f] Z-configuration determined by decoupling of aliphatic region between δ 1.70–3.00. Coupling constants between H-11′ and H-12′ as well as H-8′ H-9′ approximately 11 Hz, respectively.

displaying pseudo molecular ions [M+] at *m*/*z* 486 (**1b**) and 532 (**1c**) in the EIMS spectra, respectively. These ions indicate additional aromatic substitutions at the resorcinol moiety. A literature survey along with our finding revealed some ambiguity on the 11′- or 12′-position of the double bond in a 5-heptadecenyl-resorcinol from rice root. Cojocaru et al. (1986) reported the isolation of an AR containing mixture from mango peels whose major AR was identified as 5-(12′*Z*-heptadecenyl)-resorcinol. In the ^{13}C NMR spectrum, the authors observed a splitting of each of the last three carbons in the side chain into two or three peaks that was attributed to heterogeneity due to double bond positional isomers and/or homologues. However, the structure of the major AR in the mixture was assigned to 5-(12′*Z*-heptadecenyl)-resorcinol based on MS experiments after chemical derivatization. Some years later Bouillant et al. (1994) reported the isolation of 5-(12′*Z*-heptadecenyl)-resorcinol from rice root exudates. Since the position of unsaturation could not be directly determined from the ^{1}H and ^{13}C NMR data, they isolated the major heptadecenylresorcinol from mango peels, showing the same TLC, HPLC, MS and MS/MS fragmentation patterns as the compound they isolated from rice. Based on these data they deduced the 12′-position of the double

bond. In our studies, however, unambiguous localization of the double bond at the 11′- or 12′-position of 5-heptadecenyl-resorcinol solely based on TLC, HPLC as well as MS fragmentation without both chemical derivatization of the double bond to prevent double bond migration and intensive NMR studies was not possible. Therefore, the compound isolated from rice root exudates may also be assigned to 5-(11′*Z*-heptadecenyl)-resorcinol (**1**).

Compound **2** was obtained as yellow oil, and LC-APcI-MS/MS analysis showed a pseudo molecular ion $[M + H]^+$ at *m/z* 345. Collision induced dissociation of *m/z* 345 yielded product ions at *m/z* 123, indicating again β-fission, and at *m/z* 137, resulting from γ-cleavage. Further product ions at *m/z* 149, 163, 177 and 191 are spaced by increments of 12 and 14 amu, respectively, but were not found to be diagnostic for the determination of the position of unsaturation in the alkenyl chain. The positions of the two double bonds were derived by 1D and 2D NMR in a similar manner as described for **1** (Table 1). Although **2** is a known compound, its presence in *M. indica* L. is reported for the first time.

Both isolated ARs **1** and **2**, along with the commercially available compounds **3**–**6** strongly inhibited COX-1 at the preliminary screening concentration of 50 μM. At the same concentration, compounds **1**, **2**, **4** and **6** also exhibited strong COX-2 inhibition. IC_{50} determination revealed that compound **1** and **2** showed strong COX-1 and COX-2 inhibitory activities with IC_{50} values ranging from 1.9 (**2**) to 3.5 μM (**1**) and from 3.5 (**2**) to 4.4 (**1**) μM, respectively, coming close to those of the reference drugs indomethacin (0.9 μM) and NS-398 (2.6 μM). The most potent inhibition of the COX isoenzymes was found for compound **2**, followed by compound **1** which differs from compound **2** by lacking one double bond in position 8′ of the side chain. Compound **5**, possessing identical chain length but lacking double bonds, was less active than the unsaturated compounds (Table 2). These results suggest that COX inhibitory activity increases with the degree of unsaturation in the AR side chain. All tested compounds were found to be more active against COX-1 than against COX-2, irrespective of their chain length and degree of unsaturation (Table 2). Comparison of the COX-inhibitory activity of saturated 5-ARs possessing side chains of different length (compounds **3**, **4**, **5** and **6**) did not show a clear structure-activity relationship (Table 2). IC_{50} values for the inhibition of leukotriene formation could only be determined for compounds **2** (57.7 μM) and **3** (39.3 μM) as the activity of the other compounds was too weak (Table 2). Wagner et al. (1989) observed similar inhibitory activities (50 μM) of cardol and cardanol type alkylphenols against 5-LOX in porcine leucocysts.

Table 2
IC_{50} values of alkylresorcinols **1**–**6** in the COX-1, COX-2 and leukotriene inhibition assay

Comp.	IC_{50} COX-1 (μM)	IC_{50} COX-2 (μM)	IC_{50} LT assay (μM)
1	3.5	4.4	>125
2	1.9	3.5	57.7
3	13.1	46.4	39.3
4	3.6	4.4	>125
5	16.6	41.5	>125
6	7.8	10.9	>125

Active compounds were tested in at least three concentrations ranging from 1 to 125 μM in the assay mixture. IC_{50} values were calculated by means of logarithmic regression after graphical representation. IC_{50} values of positive controls: indomethacin (COX-1) 0.9 μM; NS-398 (COX-2) 2.6 μM; zileuton (LT-assay) 5.0 μM.

3. Experimental

3.1. General experimental procedures

A HPLC system (Bischoff, Leonberg, Germany) consisting of a LC-CaDI 22-14 control unit, two HPLC compact pumps connected to a UV–Vis detector SPD C AV *VP* (Shimadzu, Tokyo, Japan), and a dynamic mixing chamber (Knauer, Berlin, Germany) equipped with a Bischoff McDAcq 32 software were used for the semi-preparative isolation of the 5-substituted resorcinols. LC–MS analyses were performed using an Agilent (Waldbronn, Germany) HPLC series 1100 system connected in series with a Bruker (Bremen, Germany) Esquire 3000+ ion trap mass spectrometer fitted with an APcI source. LC–DAD–MS/MS parameters have previously been reported in detail by Knödler et al. (2007). GC–MS analyses were carried out using a Hewlett–Packard HP 5890A instrument equipped with selective mass detector model MSD 5970, a control system and data work station HP 59970. The column employed was a Rtx-5 MS (25 m × 0.25 mm i.d.). Helium 5.0 was used as carrier gas with a flow rate of 4 ml min^{-1} at 200 °C. The temperature of the injector and interphase area was 300 °C. Samples were injected in the splitless mode with 2 min purge off time. The column temperature was programmed at 140 °C for 3 min and from 140 to 340 °C at a rate of 40 °C/min and maintained at 340 °C for 40 min. The mass spectrometer was operated from 50 to 600 amu with full scan detection each second. UV spectra were obtained using a model G1315B diode array detector of the HPLC system mentioned above. IR spectra were obtained using a Perkin–Elmer (Norwalk, CT, USA) FT-IR Spectrum 1000 spectrometer. NMR spectra were recorded in MeCN-d_3 on a Varian Unity Inova 500 MHz spectrometer (Darmstadt, Germany). The ^1H and ^{13}C chemical shifts were referenced to residual solvent signals at δ_H 1.95 and δ_C 118.7 relative to TMS. ^1H, $^{13}C\{^1H\}$, ROESY, LR-COSY NMR spectra were measured with standard Varian pulse sequences. Adiabatic gH2BAD, adiabatic broadband and band-selective gHSQC and gHMBC spectra were recorded using CHEMPACK 4.0 pulse sequences (implemented in Varian Vnmrj 2.1B software). HRFTICR mass spectra were recorded on a APEX II FTICR mass spectrometer (4.7 T, Bruker Daltonics, Bremen, Germany).

3.2. Plant material

Dried mango peels (cv. Kaew) from main harvest season 2005 were obtained from a local canning factory in Chiang Mai, Thailand, and sent to Hohenheim University, Stuttgart, in vacuum-sealed PE containers. A voucher specimen was deposited at the Institute of Food Technology, Section Plant Foodstuff Technology, Hohenheim University, Germany.

3.3. Extraction and isolation

Dried mango peels were ground using liquid nitrogen and a stainless steel waring blender. The powdered mango peels were extracted separately with dichloromethane, ethanol (70%, *v*/*v*) and water at ambient temperature under nitrogen atmosphere. The extracts were concentrated to dryness by freeze drying or solvent evaporation *in vacuo* at temperatures below 30 °C. The dichloromethane extract was purified by solid phase extraction on polyamide (0.05–0.16 mm) to yield the purified AR fraction (Knödler et al., 2007). Compounds **1** and **2** were isolated from the concentrated purified AR fraction by preparative HPLC using a Phenomenex C18 Aqua column (250 mm × 21.2 mm i.d., particle size 5 μm, pore size 125 Å) with 95% methanol as the mobile phase at a flow rate of 12 ml/min at ambient temperature. Monitoring was performed at 275 nm. Aliquots of 500 μl were injected and the effluents collected at 15.9–16.5 min (**2**) and 20.1–20.9 min (**1**). The solvent was evaporated and the resulting yellow coloured oils stored at −80 °C in a nitrogen atmosphere until further analysis.

3.4. Preparation of dimethyl disulfide adducts

Dimethyl disulfide (DMDS) derivatives were prepared according to a method described elsewhere (Scribe et al., 1988) with slight modification. Compound **1** (1.0 mg) was treated with 500 μl of DMDS and 100 μl of iodine solution (60 mg of I_2 in peroxide free diethyl ether) in 500 μl of hexane. The reaction was carried out in a 10 ml tube closed with a Teflon-lined cap and kept at 60 °C for 48 h. Samples were diluted with 1 ml of hexane and the excessive iodine was reduced by treatment with 1 ml of $Na_2S_2O_3$ solution (5% in water). The organic layer was removed and the aqueous phase extracted a second time with 1 ml of hexane. The combined extracts were concentrated to dryness in a pure stream of nitrogen. The residue was dissolved in hexane and used immediately for GC–MS analysis.

3.5. Assays for COX-1, COX-2 and leukotriene biosynthesis inhibition

3.5.1. Sample preparation

Samples were dissolved in ethanol. Crude extracts and fractions were tested at a concentration of 20 μg/ml assay mixture. Pure compounds were tested at a screening concentration of 50 μM, and compounds showing inhibitory activity at this concentration were subjected to IC_{50} determination. Synthetic saturated alkylresorcinols (compound **3**–**6**) were obtained from ReseaChem GmbH, Burgdorf, Switzerland.

3.5.2. COX-1 and COX-2 assays

The assays were performed in 96 well plates with purified PGHS-1 (COX-1) from ram seminal vesicles and purified PGHS-2 (COX-2) from sheep placental cotyledons (Cayman Chemical Company, Ann Arbor, MI, USA) as described earlier (Fiebich et al., 2005; Reininger and Bauer, 2006). The concentration of PGE_2, the main arachidonic acid metabolite in this reaction, was determined by a competitive PGE_2 EIA Kit (Assay Designs Inc., Ann Arbor, MI, USA). Inhibition of COX refers to reduction of PGE_2 formation in comparison to a blank run without inhibitor. Indomethacin (ICN) and NS-398 (Cayman Chemical Company) were used as positive controls.

3.5.3. Leukotriene inhibition assay

The assay for inhibition of leukotriene production was performed as described by Adams et al. (2004) with slight modifications. Briefly, human neutrophile granulocytes with 5-LOX activity were isolated from venous human blood based on sedimentation rates and lysis tolerance. The assay was performed in a 96-well plate format. The cell suspension (4500 cells/ml) was incubated with the sample, $CaCl_2$, Calcimycin A23187 and arachidonic acid in a shaking water bath at 37 °C. After 10 min incubation was stopped by addition of 10% formic acid. After centrifugation samples were diluted and the concentration of LTB_4 formed during incubation was determined by means of a competitive LTB_4 EIA Kit (Assay Designs Inc., Ann Arbor, MI, USA).

3.6. 5-(11′*Z*-Heptadecenyl)resorcinol (*1*)

Yellow coloured oil; HPLC-DAD λ_{max}nm 211, 275, 280. IR ν_{max}^{film}, cm^{-1}: 3368, 3004, 2925, 2854, 1716, 1598, 1466, 1341, 1303, 1157, 995, 838, 722. ^1H (500 MHz, MeCN-d_3) and ^{13}C (125 MHz, MeCN-d_3) NMR: see Table 1. EIMS: *m*/*z* (rel. int): 346 (M+, 22), 123 (100), 137 (37), 166 (24), 250 (12). LC–APcI–MS: *m*/*z* (rel. Int.): $[M+H]^+$: 347, MS^2 [347]: 123 (100). HR-FT-ICR-MS *m*/*z*: 347.2945 $[M+H]^+$ (Calcd. 347.2945 for $C_{23}H_{39}O_2$). EIMS of thiomethylated adducts of **1**: *m*/*z* (rel. int):**1a**: 440 (M+, 32), 309 (100), 123 (99), 131 (81), 83 (39), 261 (21). **1b**: 486 (M+, 20), 307 (100), 131 (75), 169 (69), 355 (45), 83 (36). **1c**: 532 (M+, 35), 131 (100), 353 (51), 83 (41), 401 (39), 169 (37), 305 (21).

3.7. 5-(8′*Z*,11′*Z*-Heptadecadienyl)resorcinol (*2*)

Yellow coloured oil; HPLC–DAD λ_{max} nm 214, 275, 280. ^1H (500 MHz, MeCN-d_3) and ^{13}C (125 MHz, MeCN-d_3) NMR: see Table 1. LC–APcI–MS: *m*/*z* (rel. Int.): $[M+H]^+$: 345, MS^2 [345]: 123 (100), 163 (32), 177 (18), 149 (8), 137 (7), 191 (2).

Acknowledgements

This research was funded by the Sixth Research Framework Program of the European Union (No. 513949). The authors also thank Mr. Graeme Nicholson, Institute of Chemistry, University of Tübingen, for performing HR-FT-ICR-MS analysis. Mrs. Suparat Sirisakulwat and Herbstreith & Fox KG, Neuenbürg, Germany, are gratefully acknowledged for providing mango peels.

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