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Indonesian Medicinal Plants. XXI.[1] Inhibitors of Na^+/H^+ Exchanger from the Bark of *Erythrina variegata* and the Roots of *Maclura cochinchinensis*

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Through bioassay-guided separation of the methanol extracts of Indonesian medicinal plants, three inhibitors of the Na^+/H^+ exchange system, erythrinin B (2), euchrenone b_{10} (3), and 1,3,5-trihydroxy-4-(3-methylbut-2-enyl)xanthen-9-one (4), were isolated from the bark of *Erythrina variegata* (Fabaceae) (for 2) and the roots of *Maclura cochinchinensis* (Moraceae) (for 2, 3, 4). Compounds 2, 3, and 4 significantly inhibited the Na^+/H^+ exchange system of arterial smooth muscle cells, with minimum inhibitory concentrations of 1.25, 1.25, and 10 μg/ml, respectively. Three new prenylated xanthones named isocudraniaxanthones B (5) and A (7) and isoalvaxanthone (9) were also isolated from *M. cochinchinensis* and the chemical structures were elucidated on the bases of their chemical and physicochemical properties.

Key words Indonesian medicinal plant; *Erythrina variegata*; *Maclura cochinchinensis*; erythrinin B; isocudraniaxanthone; Na^+/H^+ exchanger

An electroneutral Na^+/H^+ exchange system, which was identified in the plasma membrane of a wide variety of animal cells,[3] plays a role in trans-epithelial ion transport, regulation of intracellular pH, and control of cell volume.[4] It has been reported that the overexpression of the Na^+/H^+ exchanger can be a genetic factor that interacts with excessive salt intake and causes hypertension.[5,6] Thus, the blockade of the Na^+/H^+ exchange system is expected to reduce salt-sensitive blood pressure elevation.

In a random screening of the extracts of 52 plant specimens collected in Flores and Sumatra islands of Indonesia, during our second and third expeditions (1988, 1990), we found that the extracts of the bark of *Erythrina variegata* L. var *orientalis* (L.) MERRILL and the roots of *Maclura cochinchinensis* (LOUR.) CORNER. showed an inhibitory activity against the Na^+/H^+ exchange system of spontaneously hypertensive rat (SHR) arterial smooth muscle cells.[7,8] Therefore, as a part of our search for biologically active compounds from Indonesian medicinal plants,[9] we have investigated the chemical constituents of the bark of *Erythrina variegata* and the roots of *Maclura cochinchinensis*. Here we report the isolation of three active constituents of the plants and the chemical characterization of three new prenylated xanthones which were isolated from the ethyl acetate-soluble portion of the roots of *Maclura cochinchinensis*.

Erythrina variegata is a fabaceous tree reaching 8—10 m in height and samples were collected in the Bajawa area of Flores Island, Indonesia. In this area, the bark of this plant, locally called "dadap", is mixed with coconut oil and used externally for the treatment of beriberi. The methanol extract of the air-dried bark was partitioned into a mixture of ethyl acetate and water. The ethyl acetate-soluble portion showed an inhibitory activity towards the Na^+/H^+ exchange system at a minimum concentration of 10 μg/ml. With the guidance of inhibitory activity assay on the Na^+/H^+ exchange system, the ethyl acetate-soluble portion was subjected to silica gel column chromatography and reversed-phase HPLC to afford cristacarpin (**1**, 0.016% from the air-dried bark)[10] and two active compounds, erythrinin B (**2**, 0.003%)[11] and euchrenone b_{10} (**3**, 0.001%).[12] These compounds were found to be identical with corresponding authentic samples by comparison of their physicochemical properties (NMR, UV, IR, MS, $[\alpha]_D$).

Maclura cochinchinensis (Moraceae) is a climber called "kamukune" in the Ende area of Flores Island, Indonesia. The roots of this plant are locally used as folk medicine to cure malaria and colds. The methanol extract of the air-dried roots was partitioned into an ethyl acetate and water mixture. As in the case of *Erythrina variegata*, with the guidance of inhibitory activity assay on the Na^+/H^+ exchange system, the ethyl acetate-soluble portion was subjected to silica gel column chromatography and reversed-phase HPLC to afford two active compounds, erythrinin B (**2**, 0.016%) and 1,3,5-trihydroxy-4-(3-methylbut-2-enyl)xanthen-9-one (**4**, 0.003%)[13] and three new prenylated xanthones named isocudraniaxanthone B (**5**, 0.003%), isocudraniaxanthone A (**7**, 0.002%), and isoalvaxanthone (**9**, 0.005%), and together with 1,3,5-trihydroxyxanthone (**6**, 0.002%),[14] deprenylated rheediaxanthone (**8**, 0.003%),[15] alvaxanthone (**10**, 0.007%),[16] and (+)-aromadendrin (**11**, 0.009%).[17] The known compounds **2**, **4**, **6**, **8**, **10**, and **11** were found to be identical with corresponding authentic samples by comparison of their physicochemical properties (NMR, UV, IR, MS, $[\alpha]_D$).

Isocudraniaxanthone B (5) Isocudraniaxanthone B (**5**) was obtained as a yellow powder which colored blue with ferric chloride reagent on TLC. In its FAB-MS, **5** gave a *quasi*-molecular ion peak $(M+H)^+$ at m/z 343, and the molecular composition was defined as $C_{19}H_{18}O_6$ from the high-resolution FAB-MS analysis. The IR spectrum of **5** showed absorption bands ascribable to hydroxyl (3370 cm^{-1}) and carbonyl (1650 cm^{-1}) groups, while the UV

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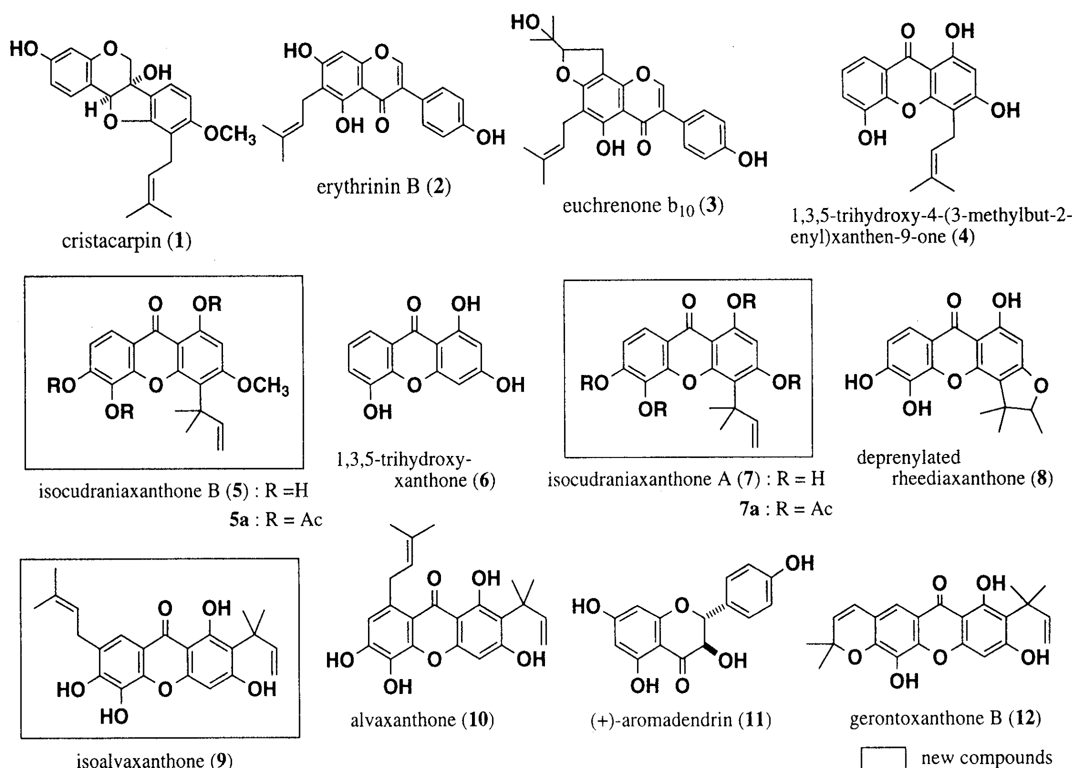

Fig. 1

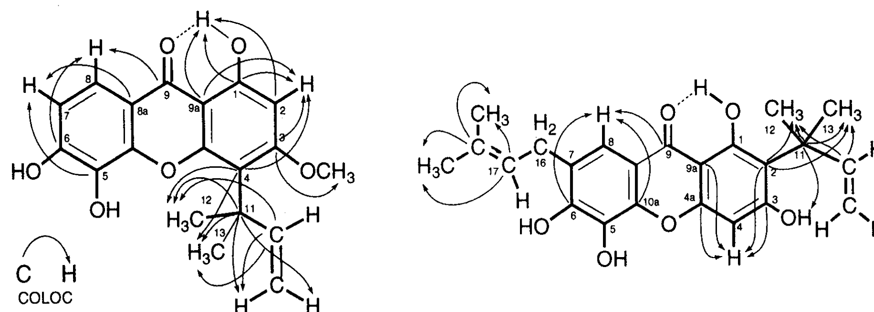

Fig. 2. COLOC Experiments on Isocudraniaxanthone B (**5**) and Isoalvaxanthone (**9**)

spectrum of **5** showed absorption maxima at 254 ($\log\varepsilon=4.26$), 285 (sh), and 328 ($\log\varepsilon=3.85$) nm, which suggested the presence of a 1,3,5,6-tetraoxygenated xanthone chromophore.[18]

The ^{1}H-NMR spectrum of **5** showed signals assignable to one hydroxyl proton [δ 13.60 (1H, s)], three aromatic protons [δ 7.61 (1H, d, $J=9$ Hz), 6.99 (1H, d, $J=9$ Hz), 6.43 (1H, s)], protons of one methoxyl group [δ 3.91 (3H, s)], and protons of a 1,1-dimethylprop-2-enyl moiety [δ 6.49 (1H, dd, $J=17.5$, 10.5 Hz), 4.98 (1H, dd, $J=17.5$, 1.5 Hz), 4.86 (1H, dd, $J=10.5$, 1.5 Hz), 1.71 (6H, s)] (Table 1). The ^{13}C-NMR spectrum of **5** showed signals assignable to one conjugated carbonyl carbon (δ_C 181.9), six oxygenated quaternary carbons (δ_C 166.3, 163.4, 155.9, 151.8, 147.0, 133.6) and one methoxyl carbon (δ_C 56.2), together with signals belong to a 1,1-dimethylprop-2-enyl moiety (Table 2). These results led us to presume that **5** is a tetraoxygenated xanthone substituted by a 1,1-dimethylprop-2-enyl moiety.

Treatment of **5** with acetic anhydride in pyridine furnished a triacetate derivative (**5a**), which had lost the hydroxyl absorption band in its IR spectrum. In the correlation spectroscopy *via* long range coupling (COLOC) NMR experiment on **5**, the following ^{1}H–^{13}C long-range correlations were observed: 1) between the hydroxyl proton at δ 13.60 (1-O$\underline{H}$, s) and the C-1, C-2, and C-9a carbon signals, 2) between the 12- and 13-methyl protons and the C-4, C-11, and C-14 carbons, 3) between the 8-aromatic proton and the C-9 and C-6 carbons, and 4) between the methoxyl protons and the C-3 carbon. In the UV spectrum of **5**, the absorption maxima immediately showed a bathochromic shift on addition of aluminum chloride, which was indicative that the 1,1-dimethylprop-2-enyl moiety is located at C-4.[18] On the bases of these results, the chemical structure of isocudraniaxanthone B (**5**) has been determined as 1,5,6-trihydroxy-3-methoxy-4-(1,1-dimethylprop-2-enyl)xanthen-9-one.

Isocudraniaxanthone A (7) Isocudraniaxanthone A (**7**) was also obtained as a yellow powder. The high-resolution FAB-MS of **7** showed a *quasi*-molecular ion peak $(M+H)^+$ at m/z 329, which corresponded to the composition $C_{18}H_{17}O_6$. The IR and UV spectra of **7** showed similar absorption patterns to those of isocudraniaxanthone B (**5**). Moreover, the ^{1}H- and ^{13}C-NMR

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Table 1. ^{1}H-NMR Data for Isocudraniaxanthones B (**5**), A (**7**), and Isoalvaxanthone (**9**)[a,b]

Proton(s)	5	7	9
2	6.43 (s)	6.30 (s)	
4			6.41 (s)
7	6.99 (d, 9)	6.99 (d, 8)	
8	7.61 (d, 9)	7.60 (d, 8)	7.53 (s)
12	1.71 (s)	1.75 (s)	1.63 (s)
13	1.71 (s)	1.75 (s)	1.63 (s)
14	6.49 (dd, 17.5, 10.5)	6.59 (dd, 17.5, 10.5)	6.38 (dd, 17.5, 10.5)
15a	4.98 (dd, 17.5, 1.5)	5.10 (br d, *ca.* 17.5)	4.96 (dd, 17.5, 1.5)
15b	4.86 (dd, 10.5, 1.5)	4.94 (br d, *ca.* 10.5)	4.85 (dd, 10.5, 1.5)
16			3.43 (br d, *ca.* 7)
17			5.40 (m)
19			1.75 (s)
20			1.75 (s)
1-OH	13.60 (s)	13.44 (s)	14.31 (s)
3-OCH$_3$	3.91 (s)		

a) The δ values in ppm and J values in Hz. *b)* Measured at 270 MHz in acetone-d_6.

Table 2. ^{13}C-NMR Data for Isocudraniaxanthones B (**5**) and A (**7**) and Isoalvaxanthone (**9**)[a,b]

Carbon	5	7	9
1	163.4	163.0	164.0
2	96.3	100.4	115.6
3	166.3	165.0	164.5
4	114.4	113.2	95.1
4a	155.9	157.2	156.3
5	133.6	134.1	133.4
6	151.8	152.0	150.5
7	113.6	114.1	126.6
8	117.2	117.6	116.7
8a	114.4	114.9	113.7
9	181.9	182.0	181.4
9a	103.7	104.0	103.2
10a	147.0	147.3	145.1
11	42.0	42.4	41.7
12	29.8	29.9	30.1
13	29.8	29.9	30.1
14	153.0	153.2	150.9
15	106.8	108.3	108.5
16			28.8
17			122.8
18			132.1
19			17.9
20			25.9
3-OCH$_3$	56.2		

a) The δ values in ppm. *b)* Measured at 67.8 MHz in acetone-d_6.

spectra of **7** also showed similar signal patterns to those of **5**, except that the former lacked the methoxyl methyl signals [δ 3.91 (s), δ_C 56.2 (q)] in **5** (Tables 1, 2). Treatment of **7** with acetic anhydride and pyridine provided a tetraacetate derivative (**7a**). Furthermore, the UV spectrum of **7** also showed an immediate bathochromic shift on addition of aluminum chloride. Consequently, the chemical structure of isocudraniaxanthone A (**7**) was concluded to be 1,3,5,6-tetrahydroxy-4-(1,1-dimethylprop-2-enyl)xanthen-9-one, the demethyl derivative of isocudraniaxanthone B (**5**).

Isoalvaxanthone (9) Isoalvaxanthone (**9**) was obtained as a yellow powder which colored blue with ferric chloride reagent on TLC. The high-resolution FAB-MS analysis of **9** revealed the molecular formula as $C_{23}H_{24}O_6$. The IR and UV spectra of isoalvaxanthone (**9**) showed similar absorption patterns to those of isocudraniaxanthones A (**7**) and B (**5**). The ^{1}H- and ^{13}C-NMR spectra of **9** were similar to those of **7** except that the signal of one aromatic proton was lacking and instead the signals due to an isoprenyl moiety [δ 5.40 (1H, m), 3.43 (2H, br d, J=*ca.* 7 Hz), 1.75 (6H, s)] were observed. These findings led us to presume that **7** also has a 1,3,5,6-tetraoxygenated xanthone skeleton. The 8-proton in **9** was observed as a singlet at δ 7.53 and the following COLOC correlations were observed: 1) between the 8-H proton and the C-6, C-9, and C-10a carbon signals, 2) between the 4-H proton and the C-2, C-3, C-4a, and C-9a carbons, and 3) between the 12- and 13-methyl protons and the C-2 carbon. In contrast with the immediate bathochromic shift shown in the UV spectra of **5** and **7** having a prenyl moiety at C-4, the UV maxima of **9** shifted slowly on addition of aluminum chloride. This phenomenon supported the idea that the 1,1-dimethylprop-2-enyl moiety in **9** is located at C-2.[17] Treatment of **9** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in benzene provided gerontoxanthone B (**12**),[19] which was identical with a corresponding authentic sample by ^{1}H-NMR, FAB-MS, and IR comparisons. On the bases of these findings, the chemical structure of isoalvaxanthone (**9**) was determined as 1,3,5,6-tetrahydroxy-2-(1,1-dimethylprop-2-enyl)-7-(3-methylbut-2-enyl)xanthen-9-one.

In conclusion, we have isolated three new prenylated xanthones named isocudraniaxanthones B (**5**) and A (**7**) and isoalvaxanthone (**9**), together with eight known compounds (**1**, **2**, **3**, **4**, **6**, **8**, **10**, **11**) from the bark of *Erythrina variegata* and the roots of *Maclura cochinchinensis*. We have tested all of these compounds for inhibitory activity against the Na^+/H^+ exchange system of SHR arterial smooth muscle cells. Among them, erythrinin B (**2**), euchrenone b_{10} (**3**) and 1,3,5-trihydroxy-4-(3-methylbut-2-enyl)xanthen-9-one (**4**) showed significant inhibitory activities at minimum concentrations of 1.25, 1.25 and 10 μg/ml, respectively (Chart 1).

Erythrinin B (**2**), one of the Na^+/H^+ exchange inhibitors, was found in the bark of *Erythrina variegata* and the roots of *Maclura cochinchinensis*. However, erythrinin B (**2**) also showed a moderate cytotoxic activity against normal cells at a concentration of 2.5 μg/ml. Therefore, we prepared some derivatives of erythrinin B (**2**) and examined their inhibitory activity. Methylation, acetylation, and DDQ treatment of **2** afforded erythrinin B dimethyl ether (**2a**), erythrinin B triacetate (**2b**), and alpinumisoflavone (**2c**),[20] respectively. Erythrinin B dimethyl ether (**2a**) did not show dose-dependent inhibitory activity and alpinumisoflavone (**2c**) showed no significant inhibitory activity towards the Na^+/H^+ exchange system. On the other hand, erythrinin B triacetate (**2b**) showed Na^+/H^+ exchange inhibitory activity almost as strong as that of erythrinin B (**2**) and weaker cytotoxicity compared to **2**. This finding led us to presume that the isoprenyl moiety in erythrinin B (**2**) is essential for inhibitory activity against the Na^+/H^+ exchange system. We are currently investigating the Na^+/H^+ exchange inhibitory activity of other prenylated flavonoids, and the

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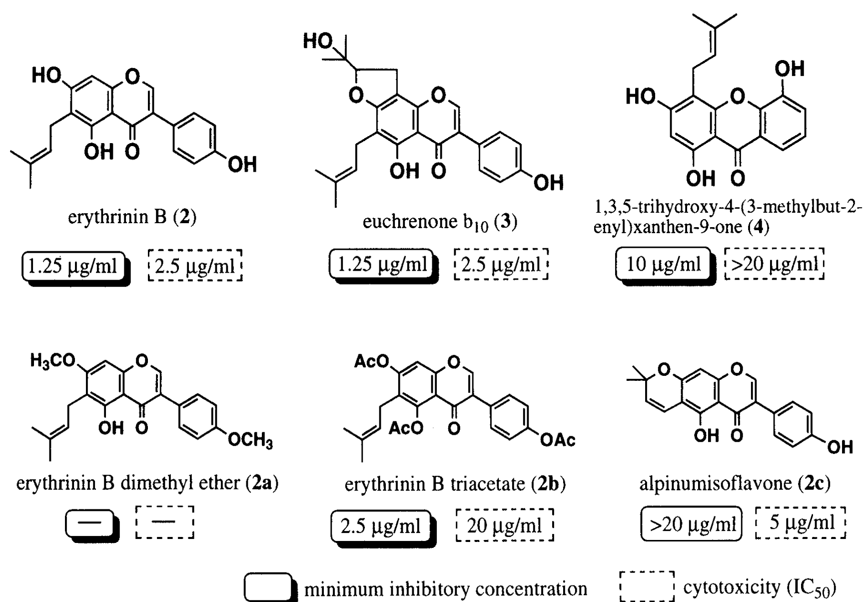

Chart 1. Na^+/H^+ Exchange Inhibitory Activity and Cytotoxicity of **2**, **2a**, **2b**, **2c**, **3** and **4**

details will be reported elsewhere.

Experimental

Melting points were determined on a Yanagimoto micro-melting point apparatus and are recorded as read. The UV spectra were obtained with a Hitachi 330 spectrophotometer, and the IR spectra were taken with a JASCO FT/IR-5300 spectrometer (by a diffusion–reflection method on KBr powder). The FAB-MS were taken on a JEOL SX-102 double-focusing high-resolution mass spectrometer with a JMA DA-6000 data system by a direct inlet method. The ^{1}H-NMR and ^{13}C-NMR spectra were measured with a JEOL JNM EX-270 spectrometer. Optical rotations were measured in a 0.5 dm length cell with a JASCO DIP-370 digital polarimeter. For HPLC, a JASCO 887-PU Intelligent Pump module was used with a JASCO 875-UV Intelligent UV/Vis detector. Column chromatography was carried out using Kieselgel 60 (70—230 mesh, Merck) or Sephadex LH-20. Thin-layer chromatography (TLC) was conducted on precoated Kieselgel 60 F_{254} plates (0.25 mm, Merck) and detection of the spots was carried out by spraying 1% $Ce(SO_4)_2$/10% H_2SO_4 on the TLC plates followed by heating or by spraying $FeCl_3$ reagent.

Isolation of Cristacarpin (1), Erythrinin B (2), and Euchrenone b_{10} (3), from the Bark of *Erythrina variegata* The air-dried bark (500 g) of *Erythrina variegata* (Fabaceae) was extracted four times with methanol (2 l each) under reflux. The combined solvent was evaporated off under reduced pressure to yield the MeOH extract (22 g, 4.4% from the dried bark). The MeOH extract was partitioned into an ethyl acetate and water (1 : 1) mixture. The ethyl acetate phase was separated and evaporated under reduced pressure to give the AcOEt extract (7 g, 1.4%) and the water extract (15 g, 3.0%). In a preliminary test of activity against the Na^+/H^+ exchange system of SHR arterial smooth muscle cells, the AcOEt extract showed inhibitory activity at a minimum concentration of 10 μg/ml. Thus, the AcOEt extract (6.3 g) was subjected to silica gel column chromatography (eluting with *n*-hexane : AcOEt = 10 : 1→1:1→AcOEt→MeOH) to give eight fractions [fr. 1 (259 mg), fr. 2 (427 mg), fr. 3 (659 mg), fr. 4 (368 mg), fr. 5 (497 mg), fr. 6 (982 mg), fr. 7 (375 mg), and fr. 8 (2810 mg)], which were then submitted to the Na^+/H^+ exchange inhibitory assay. Fraction 5 showed inhibitory activity at a minimum concentrations of 2.5 μg/ml and was further separated by HPLC (Cosmosil $5C_{18}$-AR, 10 × 250 mm, MeOH : H_2O = 85 : 15; and subsequently CAPCELL PAK C_{18} SG120, 10 × 250 mm, CH_3CN : H_2O = 50 : 50) to give cristacarpin (**1**, 0.016%), erythrinin B (**2**, 0.003%), and euchrenone B_{10} (**3**, 0.001%).

Isolation of Erythrinin B (2), 1,3,5-Trihydroxy-4-(3-methylbut-2-enyl)xanthen-9-one (4), Isocudraniaxanthone B (5), 1,3,5-Trihydroxyxanthone (6), Isocudraniaxanthone A (7), Deprenylated Rheediaxanthone B (8), Isoalvaxanthone (9), Alvaxanthone (10), and (+)-Aromadendrin (11) from the Roots of *Maclura cochinchinensis* The air-dried roots (500 g) of *Maclura cochinchinensis* (Moraceae) were extracted four times with methanol (2 l each) under reflux to give the MeOH extract (45 g, 9.0%). The MeOH extract was partitioned with an ethyl acetate and water mixture (1 : 1) to give the AcOEt extract (18 g, 3.6%) and the water extract (27 g, 5.4%). In a preliminary test of activity against the Na^+/H^+ exchange system of SHR arterial smooth muscle cells, the AcOEt extract showed inhibitory activity at a minimum concentration of 10 μg/ml. The AcOEt extract (16.7 g) was subjected to silica gel column chromatography (eluting with *n*-hexane : AcOEt = 10 : 1→1 : 1→AcOEt→MeOH) to give eight fractions [fr. 1 (1020 mg), fr. 2 (1170 mg), fr. 3 (588 mg), fr. 4 (2090 mg), fr. 5 (2710 mg), fr. 6 (829 mg), fr. 7 (938 mg), and fr. 8 (6290 mg)]. Among them, fr. 3 and fr. 4 showed inhibitory activity at minimum concentrations of 10 and 2 μg/ml, respectively. Fraction 3 was further separated by HPLC (Cosmosil 5C18-AR, 10 × 250 mm, MeOH : H_2O = 80 : 20) to give 1,3,5-trihydroxy-4-(3-methylbut-2-enyl)-xanthen-9-one (**4**, 0.003%). Fraction 4 was also separated by silica gel column chromatography (*n*-hexane:acetone = 4 : 1→AcOEt→MeOH) and HPLC (Cosmosil $5C_{18}$-AR, 10 × 250 mm, MeOH : H_2O = 80 : 20; or Capcell Pak C_{18} SG120, 10 × 250 mm, MeOH : H_2O = 75 : 25; or Capcell Pak C_{18} SG120, 10 × 250 mm, CH_3CN : H_2O = 50 : 50) to afford erythrinin B (**2**, 0.016%), isocudraniaxanthone B (**5**, 0.003%), 1,3,5-trihydroxyxanthone (**6**, 0.002%), isocudraniaxanthone A (**7**, 0.002%), deprenylated rheediaxanthone (**8**, 0.003%), isoalvaxanthone (**9**, 0.005%), alvaxanthone (**10**, 0.007%), and (+)-aromadendrin (**11**, 0.009%).

Isocudraniaxanthone B (5) A yellow powder. IR ν_{max} (KBr) cm^{-1}: 3370, 1650, 1580, 1460, 1410. UV λ_{max} (MeOH) nm (log ε): 254 (4.26), 285 (sh), 328 (3.85); λ_{max} (MeOH + $AlCl_3$) nm: 246, 275, 293 (sh), 323 (sh), 399; λ_{max} (MeOH + NaOAc): 252, 290 (sh), 361. ^{1}H-NMR (270 MHz, acetone-d_6), δ: as given in Table 1. ^{13}C-NMR (67.8 MHz, acetone-d_6, δ_C): as given in Table 2. FAB-MS *m/z*: 343 $(M+H)^+$. High-resolution FAB-MS *m/z*: Calcd for $C_{19}H_{19}O_6$: 343.1182. Found: 343.1170.

Acetylation of 5 Giving Triacetate Derivative (5a) A solution of **5** (1 mg) in pyridine (0.2 ml) was treated with acetic anhydride (0.2 ml) and stirred at 60 °C for 6 h. The reaction mixture was poured into ice water and then extracted with AcOEt. Work-up of the AcOEt-soluble portion in a usual manner gave isocudraniaxanthone B triacetate (**5a**, 1.3 mg).

5a: A yellow powder. IR ν_{max} (KBr) cm^{-1}: 1780, 1660, 1600, 1460. ^{1}H-NMR (270 MHz, $CDCl_3$), δ: 8.12 (1H, d, *J* = 9 Hz, 8-H), 7.19 (1H, d, *J* = 9 Hz, 7-H), 6.62 (1H, s, 2-H), 6.26 (1H, dd, *J* = 17.5, 10.5 Hz, 14-H), 4.85 (1H, br d, *J* = 10.5 Hz, 15-H), 4.84 (1H, br d, *J* = 17.5 Hz, 15-H), 3.85 (3H, s, 3-OCH_3), 2.48, 2.40, 2.33 (each 3H, s, OAc), 1.68 (6H, s, 12-H_3, 13-H_3). FAB-MS *m/z*: 469 $(M+H)^+$. High-resolution FAB-MS *m/z*: Calcd for $C_{25}H_{25}O_9$: 469.1499. Found: 469.1482.

Isocudraniaxanthone A (7) A yellow powder. IR ν_{max} (KBr) cm^{-1}: 3410, 1650, 1590, 1410. UV λ_{max} (MeOH) nm (log ε): 253 (4.20), 286 (sh), 328 (3.83); λ_{max} (MeOH + $AlCl_3$) nm: 244, 275, 294 (sh), 322 (sh), 394; λ_{max} (MeOH + NaOAc): 244, 290 (sh), 360. ^{1}H-NMR (270 MHz,

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acetone-d_6), δ: as given in Table 1. ^{13}C-NMR (67.8 MHz, acetone-d_6), δ_C: as given in Table 2. FAB-MS m/z: 329 $(M+H)^+$. High-resolution FAB-MS m/z: Calcd for $C_{18}H_{17}O_6$: 329.1025. Found: 329.1003.

Acetylation of 7 Giving the Tetraacetate Derivative (7a) A solution of **7** (1 mg) in pyridine (0.2 ml) was treated with acetic anhydride (0.2 ml) and stirred at 60 °C for 6 h. The reaction mixture was poured into ice water and then extracted with AcOEt. Work-up of the AcOEt extract in a usual manner gave isocudraniaxanthone A tetraacetate (**7a**, 1.5 mg).

7a: A yellow powder. IR ν_{max} (KBr) cm^{-1}: 1780, 1660, 1600, 1460. ^{1}H-NMR (270 MHz, CDCl$_3$), δ: 8.14 (1H, d, J=9 Hz, 8-H), 7.30 (1H, d, J=9 Hz, 7-H), 6.69 (1H, s, 2-H), 6.28 (1H, dd, J=17.5, 10.5 Hz, 14-H), 4.95 (1H, br d, J=17.5 Hz, 15-H), 4.93 (1H, br d, J=10.5 Hz, 15-H), 2.46, 2.42, 2.34, 2.24 (each 3H, s, OAc), 1.67 (6H, s, 12-H$_3$, 13-H$_3$). FAB-MS m/z: 497 $(M+H)^+$. High-resolution FAB-MS m/z: Calcd for $C_{26}H_{25}O_{10}$: 497.1448. Found: 497.1473.

Isoalvaxanthone (9) A yellow powder. IR ν_{max} (KBr) cm^{-1}: 3270, 1650, 1600, 1450. UV λ_{max} (MeOH) nm (log ε): 256 (4.39), 286 (sh), 332 (4.06); λ_{max} (MeOH+AlCl$_3$) nm: 220 (sh), 246, 273, 393; λ_{max} (MeOH+NaOAc): 244 (sh), 257, 356. ^{1}H-NMR (270 MHz, acetone-d_6), δ: as given in Table 1. ^{13}C-NMR (67.8 MHz, acetone-d_6, δ_C): as given in Table 2. FAB-MS m/z: 397 $(M+H)^+$. High-resolution FAB-MS m/z: Calcd for $C_{23}H_{25}O_6$: 397.1651. Found: 397.1654.

Treatment of 9 with DDQ Giving Gerontoxanthone B (12) A solution of **9** (5 mg) in dry benzene (5 ml) was treated with DDQ (5 mg) and stirred under reflux for 2 h. The reaction mixture was filtered and the filtrate was evaporated under reduced pressure to give a crude product. Purification of the crude product by silica gel column chromatography (n-hexane : acetone = 3 : 2) to give **12** (4 mg).

12: A yellow powder. IR ν_{max} (KBr) cm^{-1}: 3400, 1630, 1600, 1440. ^{1}H-NMR (270 MHz, acetone-d_6), δ: 14.21 (1H, s, 1-OH), 7.44 (1H, s, 8-H), 6.58 (1H, d, J=10 Hz, 11-H), 6.47 (1H, s, 4-H), 6.38 (1H, dd, J=17.5, 10.5 Hz, 19-H), 5.89 (1H, d, J=10 Hz, 12-H), 4.95 (1H, br d, J=17.5 Hz, 20-H), 4.85 (1H, br d, J=10.5 Hz, 20-H), 1.63 (6H, s, 17-H$_3$, 18-H$_3$), 1.49 (6H, s, 14-H$_3$, 15-H$_3$). FAB-MS m/z: 395 $(M+H)^+$. High-resolution FAB-MS m/z: Calcd for $C_{23}H_{23}O_6$: 395.1495. Found: 395.1505.

Methylation of 2 Giving Erythrinin B Dimethyl Ether (2a) A solution of **2** (15 mg) in MeOH (2 ml) was treated with diazomethane–ether and stirred at room temperature for 12 h. The reaction mixture was evaporated under reduced pressure and the residue was subjected to silica gel column chromatography (n-hexane : acetone = 4 : 1) to give erythrinin B dimethyl ether (**2a**, 6 mg).

2a: A yellow powder. IR ν_{max} (KBr) cm^{-1}: 1650, 1610, 1580, 1510. ^{1}H-NMR (270 MHz, CDCl$_3$), δ: 12.92 (1H, s, 5-OH), 7.85 (1H, s, 2-H), 7.45 (2H, d, J=9 Hz, 2'-H, 6'-H), 6.98 (2H, d, J=9 Hz, 3'-H, 5'-H), 6.40 (1H, s, 8-H), 5.22 (1H, t, J=7 Hz, 2''-H), 3.91, 3.84 (both 3H, s, OCH$_3$), 3.37 (2H, d, J=7 Hz, 1''-H), 1.79 (3H, s, 4''-H$_3$), 1.68 (3H, s, 5''-H$_3$). FAB-MS m/z: 367 $(M+H)^+$. High-resolution FAB-MS m/z: Calcd for $C_{22}H_{23}O_5$: 367.1545. Found: 367.1550.

Acetylation of 2 Giving Erythrinin B Triacetate (2b) A solution of **2** (12 mg) in pyridine (0.5 ml) was treated with acetic anhydride (0.5 ml) and stirred at 60 °C for 10 h. The reaction mixture was poured into ice water and then extracted with AcOEt. The AcOEt extract was evaporated under reduced pressure and purified over silica gel column chromatography (n-hexane : acetone = 4 : 1) to give erythrinin B triacetate (**2b**, 11 mg).

2b: A yellow powder. IR ν_{max} (KBr) cm^{-1}: 1770, 1650, 1620, 1510. ^{1}H-NMR (270 MHz, CDCl$_3$), δ: 7.87 (1H, s, 2-H), 7.48 (2H, d, J=9 Hz, 2'-H, 6'-H), 7.22 (1H, s, 8-H), 7.14 (2H, d, J=9 Hz, 3'-H, 5'-H), 5.02 (1H, t, J=7 Hz, 2''-H), 3.28 (2H, br d, J=7 Hz, 1''-H), 2.43, 2.35, 2.31 (each 3H, s, OAc), 1.75 (3H, s, 4''-H$_3$), 1.68 (3H, s, 5''-H$_3$). FAB-MS m/z: 465 $(M+H)^+$. High-resolution FAB-MS m/z: Calcd for $C_{26}H_{25}O_8$: 465.1549. Found: 465.1563.

Treatment of 2 with DDQ Giving Alpinumisoflavone (2c) A solution of **2** (15 mg) in dry benzene (15 ml) was treated with DDQ (15 mg) and stirred under reflux for 2 h. The reaction mixture was filtered and the filtrate was evaporated under reduced pressure to give a crude product. Purification of the crude product by silica gel column chromatography (n-hexane : acetone = 3 : 2) gave **2c** (8 mg).

2c: A yellow powder. IR ν_{max} (KBr) cm^{-1}: 3370, 1650, 1620, 1570, 1520. ^{1}H-NMR (270 MHz, CDCl$_3$), δ: 13.12 (1H, s, 5-OH), 7.82 (1H, s, 2-H), 7.37 (2H, d, J=9 Hz, 2'-H, 6'-H), 6.87 (2H, d, J=9 Hz, 3'-H, 5'-H), 6.73 (1H, d, J=10 Hz, 1''-H), 6.34 (1H, s, 8-H), 5.63 (1H, d, J=10 Hz, 2''-H), 1.47 (6H, s, 4''-H$_3$, 5''-H$_3$). FAB-MS m/z: 337 $(M+H)^+$. High-resolution FAB-MS m/z: Calcd for $C_{20}H_{17}O_5$: 337.1076. Found: 337.1074.

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