

桑白皮中抗人爱滋病病毒(HIV)成分研究

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摘要 从中药桑白皮(*Morus alba* L.)的根皮中分离到 6 个成分, 它们是: morusin (1), mulberrofuran D (2), kuwanon H (3), mulberrofuran K (4), kuwanon G (5), mulberrofuran G (6); 并制备了它们的乙酰化合物和葡萄糖甙; 还测定了这些化合物的体外抗人爱滋病病毒(HIV)活性和对人淋巴细胞的细胞毒活性, 发现其中黄酮 morusin, kuwanon H 和 morusin 4'-glucoside 具有一定的抗 HIV 活性。

关键词 桑白皮, 黄酮, 抗人爱滋病病毒

ANTI-HIV FLAVONOIDS FROM MORUS ALBA

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Abstract Six compounds: morusin (1), mulberrofuran D (2), kuwanon H (3), mulberrofuran K (4), kuwanon G (5), mulberrofuran G (6) were isolated from root bark of *Morus alba* and their derivatives were prepared. Anti-HIV activity of these fourteen compounds were tested. Morusin, morusin 4'-glucoside and kuwanon H show positive activity.

Key words *Morus alba*, Flavonoids, Anti-HIV

San Baipei, root bark of *Morus alba* L. (Moraceae) is a traditional Chinese medicine used as a medication for cough, asthma and other diseases^[1]. The ethanol extract of San Baipei, which displayed activity against HIV *in vitro* in root of *Morus alba* L. was studied.

Having been extracted with MeOH-CH₂Cl₂(1 : 1), the powder of San Baipei was extracted with H₂O. The biological assay results of both extracts showed that MeOH-CH₂Cl₂(1 : 1) extracts are active. CH₂Cl₂-MeOH(1 : 1) extracts was partitioned between MeOH-H₂O (9 : 1) and hexane. Anti-HIV test *in vitro* indicated that MeOH-H₂O(9 : 1) part have positive activity.

Silica gel column chromatography of MeOH-H₂O parts gave ten fractions, in which Fr. 3, Fr. 5 and Fr. 6 have anti-HIV activity. Preparative TLC on silica gel of the three active fractions provided two active flavonoids: morusin, kuwanon H and two unactive compounds: mulberrofuran D, mulberrofuran K. Another two inactive compounds: mulberrofuran G, kuwanon G were separated from another two fraction: Fr. 7 and Fr. 9 respectively with the same techniques.

Structures of the six compounds were identified according to their NMR data and other physical and chemical data. Four derivatives of morusin: morusin diacetate, morusin hydroperoxide, morusin 2'-glucoside, morusin 4'-glucoside; three derivatives of kuwanon H: kuwanon H hexacetate, kuwanon H heptoacetate, kuwanon H octoacetate were prepared. The results of anti-HIV tests of these nine compounds indicated that only morusin and morusin 4'-glucoside reserved the activity (Table 1). Taro Nomura and his coworkers reported in 1977 that in molecular of morusin, the site between 2'-free hydroxy and 3-r,r-dimethylallylic group was sensitive to photo-oxidation^[4]. Therefore we come to the conclusion that 2'-free hydroxy and 3-r,r-dimethylallylic group contributed to the anti-HIV activity of morusin.

This paper is the first report on preparing, physical data, anti-HIV activity and cytotoxicity of morusin 2'-glucoside, morusin-4'-glucoside, kuwanon H hexacetate, kuwanon H heptoacetate, kuwanon H octoacetate and mulberrofurin D triacetate.

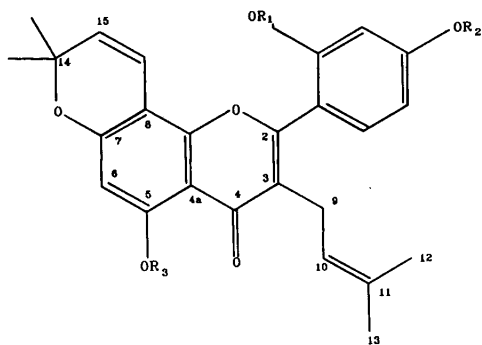
Table 1 Anti-HIV activity (EC50) and cytotoxicity (IC50) of compounds 1 to 14

| Compounds | EC50($\mu\text{g} / \text{mL}$) | IC50($\mu\text{g} / \text{mL}$) |
|---------------------------------|-----------------------------------|-----------------------------------|
| crud extract ¹ | 1.01E+01 | 4.52E+01 |
| morusin (1) | 2.91E+00 | 8.18E+00 |
| morusin diacetate (7) | | 4.43E+00 |
| morusin hydroperoxide (8) | | 2.13E+01 |
| morusin 2'-glucoside (9) | | 9.42E+01 |
| morusin 4'-glucoside (10) | 7.47E+00 | 2.29E+01 |
| kuwanon H (3) | 1.95E+00 | 1.34E+01 |
| kuwanon H hexacetate (11) | | 9.62E+00 |
| kuwanon H heptoacetate (12) | | <1.95E+00 |
| kuwanon H octoacetate (13) | | <1.95E+00 |
| mulberrofurin D (2) | | 1.04E+01 |
| mulberrofurin D triacetate (14) | | 1.65E+01 |
| mulberrofurin K (4) | | 2.79E+01 |
| mulberrofurin G (6) | | 2.75E+00 |
| Kuwanon G (5) | | 4.79E+01 |

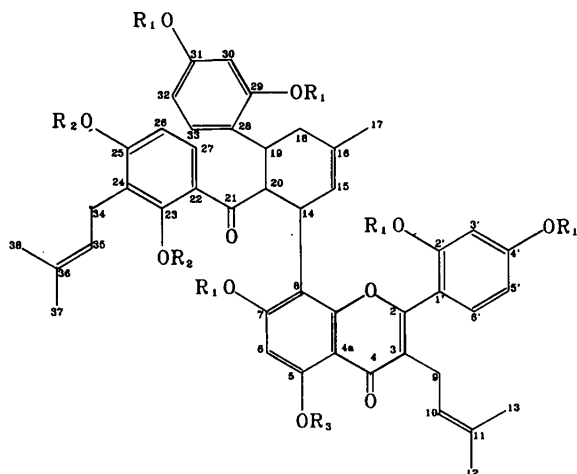
Table 2 Activity of fractions flash chromatography of residue M

| Solvents | volume (mL) | Fraction | Yield (g) | Activity | EC50($\mu\text{g} / \text{mL}$) |
|---------------------------------|-------------|----------|-----------|----------|-----------------------------------|
| CH ₂ Cl ₂ | 2000 | Fr. 1 | 3.87 | - | |
| +1% MeOH | 1000 | Fr. 2 | 0.83 | - | |
| +3% MeOH | 1000 | Fr. 3 | 2.06 | ++ | 4.88E+00 |
| +3% MeOH | 1000 | Fr. 4 | 1.03 | - | |
| +6% MeOH | 1000 | Fr. 5 | 2.47 | ++ | 1.96E+01 |
| +6% MeOH | 1000 | Fr. 6 | 1.05 | ++ | 2.23E+00 |
| +6% MeOH | 1000 | Fr. 7 | 0.43 | + | 2.24E+01 |
| +10% MeOH | 1000 | Fr. 8 | 1.50 | - | |
| +10% MeOH | 1000 | Fr. 9 | 0.58 | + | 3.90E+01 |
| +50% MeOH | 1000 | Fr. 10 | 5.72 | - | |

EXPERIMENT



Morusin (1): $R_1 = R_2 = R_3 = H$
 Morusin-diacetate (7): $R_1 = R_2 = Ac$ $R_3 = H$
 Morusin-2'-glucoside (9): $R_1 = \text{glucose}$ $R_2 = R_3 = H$
 Morusin-4'-glucoside(10): $R_1 = R_3 = H$ $R_2 = \text{glucose}$



Kuwanon H (3): $R_1 = R_2 = R_3 = H$
 Kuwanon H hex-acetate (11): $R_1 = Ac$, $R_2 = R_3 = H$
 Kuwanon H hepoacetate (12): $R_1 = R_2 = Ac$, $R_3 = H$
 Kuwanon H octo-acetate (13): $R_1 = R_2 = R_3 = Ac$

compounds: morusin and mulberrofuran D were provided.

Morusin (1): $C_{25}H_{24}O_6$ (M^+ 420, 1722) yellow crystal. mp. 168—169°C (CH_2Cl_2 -hexane). MS m/e (%): 420(55), 405(100), 387(9), 377(23), 203(35), $IR_{\nu_{max}}^{KBr} cm^{-1}$: 3400, 2950, 1650, 1560, 1480, 1345, 1150, 975, 840. 1H NMR(δ , $CDCl_3$): 6.21(1H, d, $J=0.7$, H-6), 3.13(2H, dd, $J=1.0$, 6.8, H-9), 5.14(1H, td, $J=6.9$, 1.4, H-10), 1.61(3H, q, $J=1.3$, H-12), 1.45(3H, dq, $J=1.0$, 0.4, H-13), 6.63(1H, dd, $J=10.0$, 0.7, H-14), 5.47(1H, d, $J=10.0$, H-15), 1.44(3H, s, H-17), 1.44(3H, s, H-18), 6.65(1H, d, $J=2.2$, H-3'), 6.45(1H, dd, $J=2.3$, 8.4, H-5'), 7.11(1H, d, $J=8.4$, H-6'), ^{13}C NMR (δ , DMSO): 161.3(C-2), 120.7(C-3), 182.5(C-4), 104.9(C-4a), 161.5(C-5), 99.1(C-6), 158.8(C-7), 100.8(C-8), 152.3(C-8a), 24.1(C-9), 121.5(C-10),

Mps.: uncorr.; IR spectra were obtained on a Perkin-Elmer 1430 ratio recording. NMR spectra were determined on a Varian VXR 500s soetrometer and chemical shift values are given in (δ , ppm) with TMS as internal standard. MS were obtained using BG Micrimass ZAB-2F instrument. Silica gel 60 (Merck mesh 230-400) was used for CC. and DC-plastic plates (Merck 60 F254) were employed for TLC. Detection of components was performed by spraying with 15% H_2SO_4 solution in ethanol followed by heating or by used of a UV lamp ($\lambda=254$). The plant materials was purchased from traditional pharmacy in Yunnan province, China in autumn 1989.

Milled plant materials (2kg) was soaked with CH_2Cl_2 -MeOH(1 : 1) for 24h at room temperature. The solution was evaporated in vacul under 40°C, and semi-solid residue M was supplied.

Flash chromatography of residue M (22.8 g) on a column of silica gel 6.5 × 9.2 mm(141.5 g) eluated with solvent system in Table 2 and ten fractions was obtained. The five fractions that showed positive activity were subjected on chromatography respectively.

Fraction 3: Fraction 3 was isolated on a chromatotron of silica gel plates (thin layer 4 mm and 1 mm respectively) using solvent system 1%—7% ethanol and CH_2Cl_2 , two pure

131.9(C-11), 25.5(C-12), 17.4(C-13), 115.1(C-14), 126.3(C-15), 77.6(C-16), 22.7(C-17), 27.7(C-18), 111.6(C-1'), 156.2(C-2'), 103.3(C-3'), 160.3(C-4'), 107.3(C-5'), 131.1(C-6').

Morusin Diacetate: Morusin (4 mg) was dissolved in 150 μL of Ac_2O and pyridine (1 : 1) and kepted in the room temperature for 5 minutes. The solution was evaporated in vacuo (0.1 mmHg) for 1.5 min., then 200 μL CH_2Cl_2 was added in and evaporated for two times. Product was crystallized in Hexane and CH_2Cl_2 (5 drops+200 μL), colorless crystals was obtained. $\text{C}_{29}\text{H}_{28}\text{O}_3$ (M^+ 504.1772) mp. 137.5—138.5 $^\circ\text{C}$, MS m/e (%): 504(34), 489(100), 461(10), 419(6), 405(3), 377(6), 203(40), ^1H NMR (δ , DMSO): 6.25(1H, s, H-6), 3.00(2H, br, H-9), 5.03(1H, m, H-10), 1.57(6H, s, H-12,13), 6.45(1H, d, H-14), 5.72(1H, d, H-15), 1.42(6H, s, H-17,18), 7.25(1H, s, H-3'), 7.25(1H, d, H-5'), 7.70(1H, s, H-6'), 2.11, 2.32(2 \times 3H, s, Me-CO), 12.9(1H, brs, 5-OH), ^{13}C NMR (δ , DMSO): 158.5(C-2), 119.5(C-3), 181.4(C-4), 104.3(C-4a), 160.9(C-5), 99.3(C-6), 158.4(C-7), 100.5(C-8), 151.5(C-8a), 23.3(C-9), 120.7(C-10), 131.3(C-11), 25.3(C-12), 17.3(C-13), 113.6(C-14), 128.1(C-15), 78.2(C-16), 27.6(C-17), 27.6(C-18), 122.5(C-1'), 148.7(C-2'), 120.6(C-3'), 152.5(C-4'), 117.7(C-5'), 168.6(C=O), 168.6(C=O), 20.8(Me), 20.4(Me) ^[3].

Morusin 4'-glucoside and 2'-glucoside: morusin (210 mg) was dissolved in CH_2Cl_2 (15mL), and 1-Br- β -D-pyran tetracetate glucose (1.4g) and Ag_2CO_3 (1.1g) was added in. The mixture was stirred in nitrogen for 2 h, the more Br-carbohydrate (0.5g) and Ag_2CO_3 (0.5g) was put in, stirred for another 3h. filtered, evaporated in vacuo and dissolved in the methanol (5mL), NaOCH_3 (5mL) was added and stirred for 20 min. again, put in carbondioxide gas till the pH value of the solution to 8 or 9, evaporation of solvent gave a residue. The residue is very unstability and easily reduced to morusin on silica gel or in acid it was isolated as soon as possible on chromatography using chromatotron (4 mm and 1 mm thin layer silica gel plate) and solvent system (CH_2Cl_2 -Me-OH, 5%—15%), two compounds: 10 (16.7 mg) and 9 (21.5 mg) were gained. 10 and 9 have the same molecular weight, formular and the same no-hydrogen band free hydroxy. But the chemical shift of 3',5' proton of 10 was 3 ppm downfield that of 3' proton of 9 was 0.26 ppm downfield, but 5' proton was only 0.1 ppm downfield, so the 4'-position of 10 was substituted by glucose, and 9 is 2'-glucoside.

Morusin 4'-glucoside: $\text{C}_{31}\text{H}_{34}\text{O}_{11}$, yellow powder, mp 125—131 $^\circ\text{C}$. $\text{IR}_{\text{max}}^{\text{KBr}} \text{cm}^{-1}$: 3350, 2912, 1705, 1655, 1580, 1485, 1435, 1355, 1155, 1075, 840, 770. MS m/e (%): 582(100), 567(13), 421(35), 405(25), 365(35), 309(55), 247(36), 219(20), 203(29). ^1H NMR (δ , CDCl_3): 9.15(1H, brs, OH), 7.33(1H, d, J=8.5, H-6'), 6.60(1H, d, J=10.0, H-16), 6.88(1H, s, H-3'), 6.78(1H, d, J=8.5, 2.3, H-5'), 6.19(1H, s, H-6), 5.68(1H, d, J=10.0, H-17), 5.12(1H, m, H-12), 3.10(2H, m, H-11), 1.58(3H, s, H-14), 1.45(6H, s, H-15,19), 1.30(3H, s, H-20), 5.02(1H, d, J=7.64, H-1''), 4.10, 3.92, 3.72, 3.55(4 \times H, glucoside H-2'', 3'', 4'', 5''), 3.50(2H, m, H-6'').

Morusin 2'-glucoside: $\text{C}_{31}\text{H}_{34}\text{O}_{11}$, yellow powder, mp 150—155 $^\circ\text{C}$. $\text{IR}_{\text{max}}^{\text{KBr}} \text{cm}^{-1}$: 3350, 2910, 1700, 1660, 1485, 1405, 1360, 1230, 1160, 1080, 850, 610. MS m/e (%): 582(15), 421(50), 405(10), 365(12), 309(14), 233(36), 155(97), 135(57), 119(10). ^1H NMR (δ , CDCl_3): 8.75(1H, brs, OH), 7.25(1H, d, H-6'), 6.67(1H, d, H-16), 6.82(1H, d, H-6'), 6.58(1H, s, H-6), 5.76(1H, d, H-17), 5.14(1H, m, H-12), 3.10(2H, m, H-11), 1.58(3H, s, H-14), 1.45(3H, s, H-15), 1.44(3H, s, H-19), 1.32(3H, s, H-20), 4.78(1H, d, H-1'), 4.10, 3.97, 3.79, 3.57(4 \times H, H-2'', 3'', 4'', 5''), 3.53(2H, m, H-6'').

Morusin Hydroperoxide: morusin 10 mg was dissolved in CHCl_3 and exposed to bright sunshine for 14h, one major spot on the of this solution showed the yield of this component is about 70%, preparing TLC of this solution gave 3 mg yellow needles (MeOH), mp 203—205 $^\circ\text{C}$ is accord with data in

reference^[4].

Mulberrofuran D: $C_{29}H_{34}O_4(M^+446.2457)$, mp 121—123°C, colorless crystal. $IR_{\max}^{KBr}cm^{-1}$: 3320, 2920, 1615, 1445, 1420, 1310, 1140, 820. MS m/e (%): 446(100), 377(3), 361(8), 323(11), 307(13), 279(24), 269(8), 188(20), 123(6), 69(15). 1H NMR (δ , $CDCl_3$): 6.69(1H, s, H-3), 7.28(1H, d, J=8.3, H-4), 6.78(1H, d, J=8.3, H-5), 6.42(1H, d, J=2.6, H-4'), 6.77(1H, d, J=2.6, H-6'), 3.52(2H, d, J=6.6, 1.3, H-1''), 5.29(1H, qt, J=6.6, 1.4), 1.78(3H, q, J=1.1, H-4''), 1.76(3H, q, J=1.4, H-5''), 3.68(2H, dd, J=8.7, H-1''), 5.40(1H, q, J=1.3, 7.2, H-2''), 1.65(3H, t, d, J=0.8, 1.4, H-4''), 1.76(3H, q, J=1.4, H-5''), 3.68(2H, dd, J=0.8, 7, H-1''), 5.40(1H, qt, J=1.3, 7.2, H-2''), 1.84(3H, td, J=0.8, 1.4, H-4''), 2.07(2H, m, H-5''), 2.10(2H m, H-6''), 5.05(1H, m, H-7''), 1.65(3H, qd, J=0.3, 1.3, H-9''), 1.57(3H, qd, J=0.6, 1.4, H-10''), 5.38, 5.34, 4.92(each 1H brs, OH). ^{13}C NMR (δ , $CDCl_3$): 152.3(C-2), 105.6(C-3), 110.3(C-3a), 118.6(C-4), 112.8(C-5), 154.2(C-6), 132.2(C-7), 152.3(C-7a), 122.1(C-1'), 117.7(C-2'), 156.2(C-3'), 103.7(C-4'), 154.5(C-5'), 108.3(C-6'), 26.4(C-1''), 122.4(C-2''), 134.7(C-3''), 17.9(C-4''), 25.6(C-5''), 23.1(C-1''), 120.9(C-2''), 139.1(C-3''), 16.2(C-4''), 39.6(C-5''), 26.3(C-6''), 123.7(C-7''), 132.0(C-8''), 25.7(C-9''), 17.6(C-10'')^[5].

Mulberrofuran D Triacetate: $C_{35}H_{40}O_7$, mp 97—98°C, $IR_{\max}^{KBr}cm^{-1}$: 2920, 1770, 1750, 1610, 1485, 1370, 1200, 1135, 1025, 920, 830, 685, 1H NMR(δ , $CDCl_3$): 6.84(1H, s, H-3), 7.42(1H, d, J=8.2, H-5), 7.35(1H, d, J=2.4, H-2'), 6.95(1H, d, J=2.4, H-4'), 3.47(2H, t, J=6.2, H-1''), 5.11(1H, m, H-2''), 1.68(H, bs, H-4'',5''), 3.55(2H, d, J=7.2, H-1''), 5.28(1H, t, J=7.2, H-2''), 1.79(3H, bs, H-4''), 2.00(2H, m, H-5''), 2.02(2H, m, H-6''), 5.05(1H, m, H-7''), 1.62(3H, bs, H-9''), 1.55(3H, bs, H-10''), 2.33(3H, s, Me), 2.30(3H, s, Me), 2.30(3H, s, Me). ^{13}C NMR (δ , $CDCl_3$): 153.6(C-2), 116.8(C-3), 106.3(C-3a), 119.7(C-4), 118.5(C-5), 150.0(C-6), 132.4(C-7), 154.5(C-7a), 129.6(C-1'), 126.5(C-2'), 148.6(C-3'), 118.0(C-4'), 146.0(C-5'), 118.1(C-6'), 26.8(C-1''), 122.0(C-2''), 131.4(C-3''), 18.0(C-4''), 25.5(C-5''), 23.6(C-1''), 120.8(C-2''), 136.2(C-3''), 16.2(C-4''), 39.6(C-5''), 26.6(C-6''), 124.1(C-7''), 132.3(C-8''), 25.6(C-9''), 17.6(C-10''), 21.0, 20.9, 20.8(Ac, Me), 168.9, 169.0, 167.7(Ac-C=O).

Fraction 5 and Fraction 6: The TLC of the both fractions showed two same major spots, they were subjected on chromatography (silica gel 4 mm and 1 mm plate on chromatotron) eluting with MeOH- CH_2Cl_2 (1%—5%) system. Kuwanon H and mulberrofuran K were supplied. By the same way mulberrofuran G and mulberrofuran G were isolated from fraction 7 and fraction 9 respectively.

Kuwanon H: yellow amorphous powder, $C_{45}H_{44}O_{11}$, (M^+760), mp 187—189°C (decomp). $IR_{\max}^{KBr}cm^{-1}$: 3380, 2920, 1700, 1650, 1620, 1500, 1430, 1370, 1290, 1240, 1160, 1055, 980, 845, 810, 630, MS m/e (%): 760(24), 555(10), 421(14), 355(13), 299(8), 267(11), 239(5), 205(56), 149(100), 103(19), 85(37), 59(22), 1H NMR(δ , acetone- D_6): 6.00(1H, m, H-6), 6.66(1H, m, H-3'), 6.56(1H, dd, J=2.8, H-5'), 7.30(1H, d, J=8, H-6'), 3.12(2H, d, J=7, H-9), 5.06—5.18(1H, m, H-6), 6.66(1H, m, H-3'), 1.47 and 1.62(each 3H, s, H-11), 4.43(2H, H-14, 15), 1.57(3H, br.s, H-16), 1.80, 2.05(2H, m, H-18), 3.84(1H, m, H-19), 4.62(1H, m, H-20), 6.07(1H, d, J=8, H-26), 6.82(1H, d, J=8, H-27), 6.22(1H, m, H-30), 6.00(1H, m, H-32), 7.92(2H, brs, OH), 8.82(2H, brs, OH), 9.04, 9.42(2×H, brs, OH), 12.85(1H, brs, 5-OH), 13.35(1H, brs, H-23-OH). ^{13}C NMR (δ , DMSO): 159.04(C-2), 119.53(C-3), 182.61(C-4), 103.61(C-4a), 156.26(C-5), 97.40(C-6), 161.54(C-7), 106.80(C-8), 160.17(C-8a), 23.42(C-9), 121.76(C-10), 131.12(C-11), 25.46(C-12), 17.38(C-13), 22.90(C-14), 123.15(C-15), 132.71(C-16), 22.43(C-17), C-18 and C-19 were overlapped in DMSO peaks. 45.45(C-20), 208.14(C-21), 113.69(C-22), 161.94(C-23), 113.35(C-24), 161.54(C-25), 106.71(C-26), 122.23(C-27), 121.76(C-28),

155.80(C-29), 102.61(C-30), 155.80(C-31), 106.57(C-32), 131.12(C-33), 111.29(C-1'), 156.30(C-2'), 102.50(C-3'), 160.79(C-4'), 106.39(C-5'), 129.51(C-6'), 21.13(C-34), 122.23(C-35), 130.26(C-36), 25.35(C-37), 17.59(C-38) [6].

Kuwanon H Hexacetate: kuwanon H 120 mg was reacted with Ac_2O 2 mL and pyridine (1mL) in the -26°C for 2 h and evaporated in vacuo. The residue was isolated on chromatotron (1 mm silica gel plate) eluting with 0.5% isopropanol in CH_2Cl_2 hepoacetate(34.6 mg) and octoacetate (14.8 mg) were given.

Kuwanon H Octoacetate: amorphous powder $\text{C}_{39}\text{H}_{38}\text{O}_{18}$ ($M^+1054.3621$), mp $106-108^\circ\text{C}$, MS m/e (%): 1054(12), 1012(18), 1012(8), 970(2), 765(18), 732(7), 629(4), 546(10), 489(10), 363(4), 289(21), 247(60), 205(100), 149(35), $^1\text{H NMR}$ (δ , Aceton- D_6): 8-6 no peak, 2.0-2.4(24H, 8 \times s, 8 \times AC-Me).

Kuwanon H Heptoacetate: Kuwanon H (274 mg) was reacted with Ac_2O -pyridine (4 mL+2mL) in room temperature for 2h. and evaporated in vacuo. The residue was isolated on chromatotron (1 mm silica gel plate) using solvents system 0.5% isopropanol- CH_2Cl_2 , hepoacetate (34.6mg) and octoacetate (14.8 mg) were provide.

Kuwanon H Octoacetate Kuwanon H (78.8 mg) was reacted with Ac_2O -pyridine (1mL+0.5mL) in 60°C for mins. The product was dried in vacuo and isolated on chromatotron (silica gel) using solvents 0.5% isopropanol- CH_2Cl_2 to get octoacetate(18 mg) and together heptoacetate(10.3 mg).

Kuwanon H octoacetate: amorphous powder, $\text{C}_{61}\text{H}_{60}\text{O}_{19}$, ($M^+1096.3726$), mp $110-112^\circ\text{C}$, $\text{IR}_{\text{max}}^{\text{KBr}}\text{cm}^{-1}$: 1920, 1770, 1715, 1645, 1615, 1500, 1370, 1200, 1100, 1020, 910, 830. MS m/e (%): 1096(5), 1054(10), 1012(8), 970(2), 765(18), 723(7), 629(4), 546(10), 489(10), 363(4), 289(21), 247(60), 205(100), 149(35). $^1\text{H NMR}$ (δ , Acetone- D_6): δ 8-16 no peaks, 2.0-2.4(24H, 8 \times s, 8 \times Ac-Me).

Mulberrofuran K: white amorphous powder, $\text{C}_{39}\text{H}_{32}\text{O}_8$, mp $174-179^\circ\text{C}$ (decomp). $\text{IR}_{\text{max}}^{\text{KBr}}\text{cm}^{-1}$: 3450, 2970, 1620, 1600, 1510, 1435, 1365, 1260, 1120, 1050, 975, 820, 735, 630. MS m/e (%): 628 M^+ (75), 613(14), 519(9), 453(18), 387(7), 321(100), 279(8), 255(10), 203(17), 161(30), 85(38). $^1\text{H NMR}$ (δ , Acetone- D_6): 7.05(1H, s, H-3), 7.41(1H, d, J=8.4, H-4), 6.81(1H, dd, J=8.4, 2.2, H-5), 6.98(1H, d, J=2.2, H-7), 6.95(1H, d, J=1.7, H-2'), 6.96(1H, d, J=1.7, H-6'), 6.45(1H, m, J=5.4, H-2''), 3.37(1H, m, J=5.4, H-3''), 3.39(1H, d, J=5.4, H-4''), 2.96(1H, dt, J=5.4, H-5''), 2.73, 2.04(dd, 2H, J=5.4, 17.0, H-6''), 1.78(3H, s, H-7''), 6.27(1H, d, J=8.7, H-13''), 7.07(1H, d, J=8.7, H-14''), 6.38(1H, d, J=2.5, H-17), 6.51(1H, dd, J=8.4, 2.5, H-19''), 7.15(1H, d, J=8.4, H-20''), 6.69(1H, d, J=10.0, H-21''), 5.67(1H, d, J=10.0, H-22''), 1.34(6H, s, H-24' and 25''). $^{13}\text{C NMR}$ (δ , Acetone- D_6): 154.8(C-2), 102.2(C-3), 122.5(C-3a), 121.9(C-4), 113.2(C-5), 156.7(C-6), 98.3(C-7), 156.7(C-7a), 131.1(C-1'), 105.2(C-2'), 155.0(C-3'), 113.2(C-4'), 157.0(C-5'), 104.9(C-6'), 133.8(C-1''), 122.7(C-2''), 34.8(C-3''), 37.7(C-4''), 28.4(C-5''), 36.6(C-6''), 23.8(C-7''), 101.9(C-8''), 119.0(C-9''), 154.5(C-10''), 111.1(C-11''), 152.6(C-12''), 107.6(C-13''), 129.1(C-14''), 117.6(C-15''), 153.3(C-16''), 103.8(C-17''), 157.6(C-18''), 109.7(C-19''), 127.8(C-20''), 117.9(C-21''), 129.9(C-22''), 76.6(C-23''), 27.6(C-24''), 27.5(C-25'') [6].

Kuwanon G: yellow powder. mp $214-220^\circ\text{C}$ (decomp). $\text{C}_{40}\text{H}_{36}\text{O}_{11}$, $\text{IR}_{\text{max}}^{\text{KBr}}\text{cm}^{-1}$: 3400, 2980, 1720, 1640, 1540, 1480, 1390, 1260, 1180, 1010, 875, 660. MS m/e (%): 692(M^+ 20), 555(2), 421(8), 377(5), 355(7), 279(5), 203(12), 177(10), 137(100), 119(39), 85(58), 69(48) [7].

Mulberrofuran G: white amorphous powder, mp 160°C (decomp.). $\text{C}_{34}\text{H}_{26}\text{O}_8$, $\text{IR}_{\text{max}}^{\text{KBr}}\text{cm}^{-1}$: 3400, 1690, 1625, 1600, 1510, 1445, 1370, 1260, 1150, 1045, 975, 840, 775, 630. $^1\text{H NMR}$ (Aceton- D_6): 7.04(1H, s, H-3), 7.41(1H, d, H-4), 6.81(1H, d, H-5), 6.97(1H, s, H-7), 6.98(1H, s, H-2'), 6.94(1H, s, H-6'), 6.46(1H, s, H-2''), 3.50(1H, m, H-3''), 3.35(1H, m, H-4''), 2.99(1H, m, H-5''), 2.72, 2.04(each 1H, m,

H-6"), 1.78(3H, s, H-7"), 6.42(1H, s, H-11"), 6.23(1H, d, H-13"), 7.24(1H, d, H-14"), 6.38(1H, s, H-17"), 6.51(1H, d, H-19"), 7.14(1H, d, H-20"). ^{13}C NMR (δ , Aceton- D_6): 155.0(C-2), 102.2(C-3), 122.5(C-3a), 121.9(C-4), 113.2(C-5), 156.7(C-6), 98.3(C-7), 156.7(C-7a), 131.0(C-1'), 105.1(C-2'), 154.5(C-3'), 113.4(C-4'), 157.8(C-5'), 105.4(C-6'), 133.7(C-1''), 122.8(C-2''), 35.1(C-3''), 37.2(C-4''), 28.5(C-5''), 36.2(C-6''), 23.8(C-7''), 102.6(C-3''), 116.9(C-9''), 159.8(C-10''), 104.6(C-11''), 157.4(C-12''), 107.2(C-13''), 130.3(C-14''), 117.5(C-15''), 153.3(C-16''), 103.9(C-17''), 157.7(C-18''), 109.8(C-19''), 127.8(C-20'')^[8].

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References

- [1] Jiangsu New Medical College. The Chinese Traditional Medicine Dictionary. Shanghai: Shanghai Science and Technology Press, 1985.4031.
- [2] Taro Nomura, Toshio Fukai, Sachik Yamada *et al.* Studies on the constituents of the cultivated mulberry tree I: Three new prenylflavones from the root bark of *Morus alba* L. *Chem Pharm Bull*, 1978, **26**(5): 1394—1402.
- [3] Taro Nomura, Toshio Fukai, Sachik Yamada *et al.* Studies on the constituents of the cultivated mulberry tree: Photo-oxidative cyclization of Morusin. *Chem Pharm Bull*, 1978, **26**(5): 1431—1436.
- [4] Taro Nomura, Toshio Fukai, Takako Shimada *et al.* Components of root bark of *Morus australis*. *Planta Medica*, 1983, **49**: 90—94.
- [5] Taro Nomura, Toshio Fukai. Hypotensive constituent, Kuwanon H, a new flavone derivative from the root bark of the cultivated mulberry tree (*Morus alba* L.) *Heterocycles*, 1980, **14**(12): 1943.
- [6] Yoshio Hano, Hideaki Konno, Musato Itoh *et al.* Structures of three new 2-arylbenzofuran derivatives from the Chinese Crude Drug "Sang Bai-Pi" (*Morus* root bark). *Chem Pharm Bull*, 1985, **33**(12): 5294—5300.
- [7] Taro Nomura, Toshio Fukai. Kuwanon G. A new flavone derivative from the root barks of the cultivated mulberry tree (*Morus alba* L.). *Chem Pharm Bull*, 1980, **28**(8): 2548—2552.
- [8] Toshio Fukai, Yoshio Hano, Kazuhro Hirakura. Structures of two natural hypotensive diels-alder type adducts: mulberrofuran F and G from cultivated mulberry tree. *Chem Pharm Bull*, 1985, **33**(8): 3195—3204.