

## LIGNANS AND SESQUITERPENE LACTONES FROM THE ROOT BARK OF ARTEMISIA ARGENTEA L 'HER

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### ABSTRACT

*Reinvestigation of the chemical constituents of the bark of Artemisia argentea L'Her revealed the isolation of 5 other compounds, in addition to those reported before. Spectral analysis of the isolated compounds proved the presence of  $\beta$ -sitosterol and its glucoside, the sesquiterpene lactone [1] and the two lignans kobusin [2] and yangambin (= lirioresinol- $\beta$ -dimethyl ether [3]). Yangambin [3] was tested in both P-388 and KB up to 100  $\mu$ g/ml but it was inactive.*

### INTRODUCTION

Artemisia is a large genus belonging to tribe Anthemideae (Asteraceae). Hundreds of Artemisia species have been phytochemically investigated and it was found to be rich in sesquiterpene lactones, flavonoids, coumarins <sup>1</sup> and only one report about its lignan content was traced <sup>2</sup>. Kobusin and sesamin [4] as major constituents of the bark were reported to inhibit the growth of silkworm larvae and to enhance the toxicity of wide variety of insecticides and to display the same potency as commercially used synthetic insecticide synergists.

In a previous publication <sup>3</sup> we reported the isolation of the lactones: Arborescin, argentiolide A,

deacetyl argentiolide B, argentiolide B and artemolin compounds and the lignans: Sesamin, aschantin and demethoxyexcelsin, from the root bark.

As continuation of our screening for sesquiterpene lactone and lignans we tried to seek more in the root bark of Artemisia argentea.

### EXPERIMENTAL

All mps were measured in an Electrothermal Melting Point Instrument in open capillaries and are uncorrected. MS were determined at 70 ev by direct insertion on a probe. <sup>1</sup>H-NMR spectra were obtained at 400 MHz. The <sup>13</sup>C-NMR spectra were recorded at 15 MHz with TMS as internal standard. IR spectra were run in a

Unicom SP 1025 instrument in KBr discs. Column chromatography was carried on  $\text{SiO}_2$  (60-120 mesh, E.Merck) and TLC on Si gel GF<sub>254</sub> (E.Merck).

### Plant Material, Extraction and Isolation Procedure:

As mentioned in reference <sup>3</sup>.

### $\beta$ -Sitosterol:

Crystals from MeOH or EtOAc, mp 137°C compared with authentic reference material.

### $\beta$ -Sitosterol-3-O-Glucoside:

Crystals from  $\text{CHCl}_3/\text{MeOH}$ , mp 265-267°C. IR and NMR compared with reference material.

### Sesquiterpene Lactone [1]:

Crystals from MeOH/Et<sub>2</sub>O mp 173°C. IR, NMR and  $R_f$  value compared with that compound isolated by us from the aerial parts <sup>4</sup>.

### Kobusin [2]:

Eluted with hexane/EtOAc (85:15) and crystallized from MeOH/Et<sub>2</sub>O as colourless crystals, mp 56°C, NMR (Table 1).

### Yangambin (Lirioresinol- $\beta$ -Dimethyl Ether) [3]:

Eluted with hexane/EtOAc (8:2) and crystallized from hexane/EtOAc (1:1) as fine crystalline needles, mp 120°C. <sup>1</sup>H-NMR and <sup>13</sup>C-NMR data (Table 1,2).

Table 1: Comparative <sup>1</sup>H-NMR Data for kobusin, Methyl Piperitol and Isolated Compounds Values from TMS.

Proton	Kobusin <sup>(6)</sup>	M.piperitol <sup>(7,8)</sup>	Compound 2	Compound 3
H <sub>1,5</sub>	3.10 m	3.08 m	3.15 m	3.12 m
H <sub>2,6</sub>	4.75 d	4.75 d	4.75 d	4.12 d
H <sub>4,8</sub>	3.80-4dd 4.16-4.4m	3.90 dd 4.26 dd	3.86 m 4.2-4.3m	3.94 m 4.32 m
O-CH <sub>2</sub>	5.95 s	5.95 s	5.95 s	-
OCH <sub>3</sub>	3.87 s 3.90 s	3.90 s 3.92 s	3.86 s 3.87 s	3.82 s 3.88 s
Ar-H	6.80-7m	6.94 m	6.8-6.9 m	6.58 s

m, multiplet; d, doublet; dd, doublet of doublet; s, singlet.

Table 2: <sup>13</sup>C-NMR of Yangambin (Lirioresinol- $\beta$ -Dimethyl Ether).

Carbon No.	Shift ( $\delta$ ) <sup>*</sup>
1,5	60.8
2,6	85.9
4,8	71.9
1'	137.4
2'	102.8
3'	136.8
4'	153.5
5'	136.8
6'	102.8
OCH <sub>3</sub>	56.1
OCH <sub>3</sub>	54.4

\* TMS as int. standard.

## RESULTS AND DISCUSSION

The data obtained for  $\beta$ -sitosterol,  $\beta$ -sitosterol-3-O-glucoside and the sesquiterpene lactone [1] were compared with those of the same compounds isolated by us from the aerial parts of the same plant<sup>4,5</sup> whereby the physical characters as well as the mixture mp. were matched. Compound [2] was eluted from the SiO<sub>2</sub> column with hexane/ethyl acetate (85:15) and recrystallized from methanol/ether as colourless crystals, mp 56°C. The IR spectrum of this compound suggested the presence of aromatic ring (1608, 1592 and 1515 cm<sup>-1</sup>), methoxy functions (1232-1238 cm<sup>-1</sup>) and a saturated furan system (1140, 1035 and 930 cm<sup>-1</sup>). These characters suggested the presence of a lignan compound.

The <sup>1</sup>H-NMR spectrum of this compound assured the presence of a lignan structure. The problem arising always with this type of compounds is the determination of the configuration of the phenyl groups attached to the 3,7-dioxabicyclo(3,3,0)actone system.

We determined the configuration of compound [2] on the basis suggested by Kamikado et al<sup>6</sup> and by Pelter et al<sup>7</sup> concerning the <sup>1</sup>H-NMR of the benzylic protons. In the diequatorial configuration, the two benzylic protons were observed as doublets at  $\delta$  4.75, where in the axial/equatorial system appear as two doublets at  $\delta$  4.4 & 4.8. Further, the resonance of the methylene protons lies between  $\delta$  3.75-4.7 in the diequatorial system, while it falls at  $\delta$  3.3-4.0 in the diaxial form.

The application of these rules and the comparison of data with that reported in the literature (Table 1)

suggested that compound [2] should be the diequatorial 2,6-dieq-2(piperonyl),6(dimethoxyphenyl)-3,7-dioxabicyclo-(3,3,0)octane, a compound known as Kobusin<sup>6</sup> or methyl piperitol<sup>7,8</sup>.

The spectra of all reported compounds are in agreement with those reported before. Compound [2] (mp 56°C) was isolated as an oil<sup>2,6,8</sup> and only one report<sup>7</sup> mentioned it as crystals mp 67-71°C. This is the first report on isolation of kobusin from *Artemisia argentea* L'Her root bark.

A single report<sup>6</sup> about the biological activity of this compound showed that it has an inhibitory effect on the growth of the silk worm larvae (*Bombyx mori* L).

Compound [3] was eluted with hexane-ethyl acetate (8:2) from the SiO<sub>2</sub> column and recrystallized from hexane/ethyl acetate (1:1) as fine colourless needles mp 120°C. The IR spectrum of this compound showed the presence of aromatic rings (1608, 1592 and 1515 cm<sup>-1</sup>), methoxy groups (1232-1238 cm<sup>-1</sup>) and a saturated furan system (1140, 1035 and 930 cm<sup>-1</sup>). The <sup>1</sup>H-NMR spectrum (Table 1) indicated the presence of 6 methoxy groups appearing as sharp singlets, one singlet at  $\delta$  3.82 integrated for 6 protons (2 OCH<sub>3</sub> groups) and another singlet at  $\delta$  3.88 integrated for 12 protons (4 OCH<sub>3</sub> groups), other signals are comparable to those reported for diequatorial lignans. The <sup>13</sup>C- spectrum (Table 2) assured the presence of aromatic carbons  $\delta$  100 in addition to benzylic protons at  $\delta$  60.8 and methoxyls at  $\delta$  54.4 and  $\delta$  56.1. This compound was previously isolated by us<sup>5</sup> from the aerial parts of the same plant and it was also reported<sup>2</sup> from other plants and named yangam-

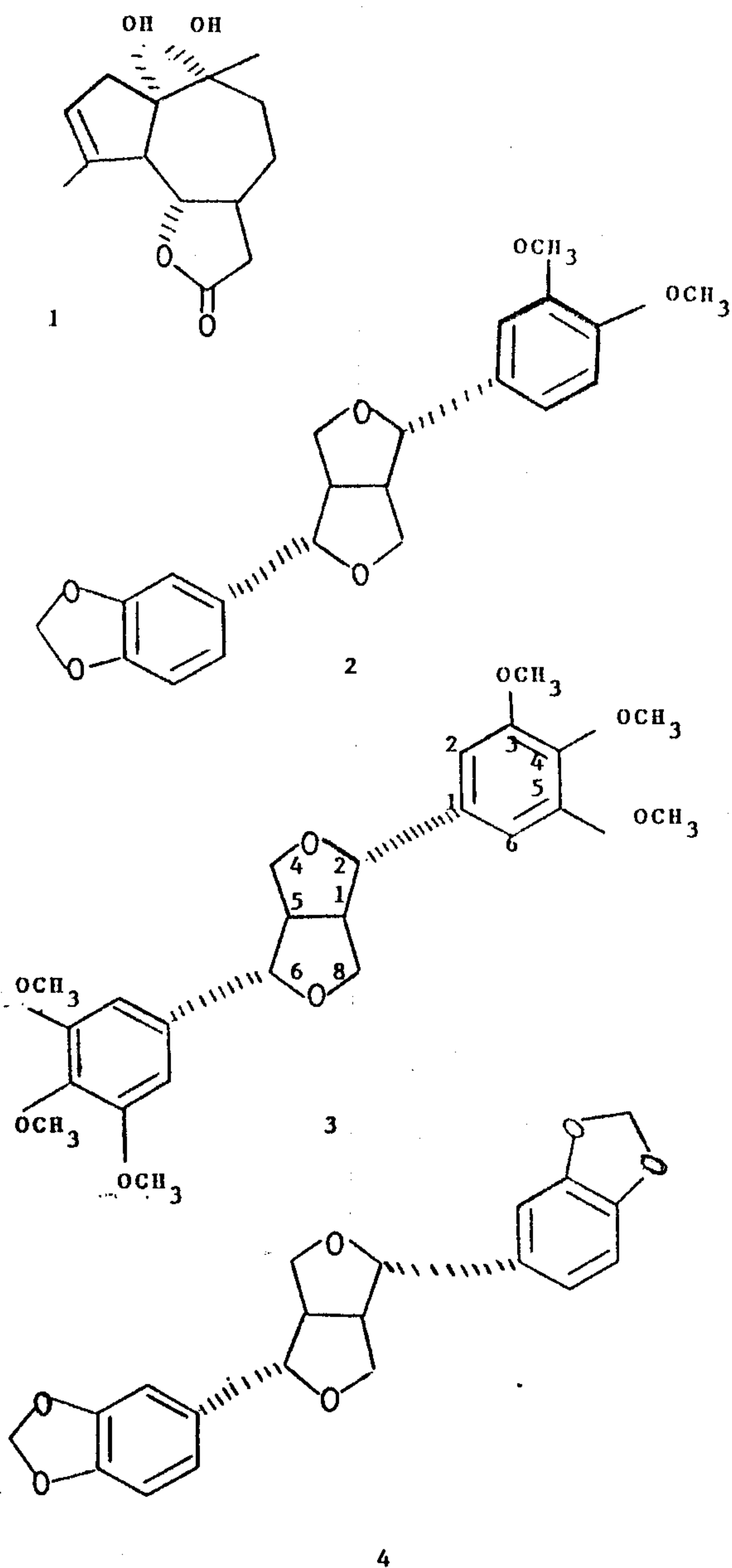
bin or Lirioresinol- $\beta$ -dimethyl ether. Mass spectrum  $M^+$  446(100%) was identical in fragmentation pattern to that reported 2. Its  $^{13}\text{C}$ -NMR spectrum has not been reported elsewhere. The use of many lignans as antitumour agents<sup>9</sup> stimulated us to test this compound against P-388 and KB, but it was found inactive up to 100  $\mu\text{g/ml}$ .

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لجنانز و سسكيتربين لاكتونز من قشر جذور

نبات الارتيميزيا ارجنتيا

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قام الباحثون باستخلاص المسحوق المجفف لقشر جذور نبات ارتيميزيا ارجنتيا بالبتروال الاثيري ثم بالكلورفورم وقد امكن فصل خمسة مركبات من خلاصة الكلورفورم وتم التعرف عليها عن طريق الصفات الطبيعية والطيافية "مثل الاشعة فوق البنفسجية - دون الحمراء - مطياف الكتلة - الرنين النووي المغناطيسي" وكانت هذه المواد هي: سسكوتربين لاكتون رقم 1 ، لجنانز "كوبوسين ويانجمبين" ، بيتا سيتوستيرول ، بيتا سيتوستيرول جليوكوزيد.