AN ARRHYTHMIC-INDUCING GLYCOSIDE FROM *ALBIZZIA JULIBRISSIN* DURAZZ. IV.[1)]

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Three pyridoxine derivatives have been isolated from the fresh stem bark of *Albizzia julibrissin* DURAZZ.. One of them, named julibrin II, was found to exhibit arrhythmic-inducing action. However, neither the others having the same aglycone nor some glycosides having the same sugar unit showed the action.

KEYWORDS *Albizzia julibrissin*; Leguminosae; pyridoxine derivative; pyridoxine glycoside; julibrine; arrhythmic-inducing action; dromotropic action

Albizziae Cortex, the dried stem bark of *Albizzia julibrissin* DURAZZ.(Leguminosae) are used in China as tonics, to ease the mind and calm the nerves. During our studies on the constituents of leguminous plants, we have obtained a number of glycosides from this plant including liriodendrin (syringaresinol diglucoside), which is responsible for the pharmacological effect as a tonic.[2)] In a further study, we have examined the methanol extract of fresh bark, which showed toxicity to frog heart. This paper describes the structural determination of compounds **1**~**3** and some pharmacological effects on frog heart of these compounds.

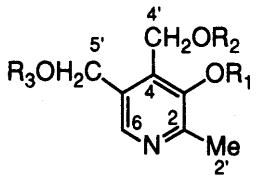
Compound **1** showed an $[M-H]^-$ ion peak at *m/z* 344 in the negative FAB-MS and UV absorption peak (λ_{max}) at 275nm. In the ^{1}H-NMR spectrum (Table I), the signals of **1** were in good agreement with those of pyridoxine (**4**) except for the signals of a methoxy group and a glycoside unit. Since signals due to the terminal β-D-glucopyranosyl group appeared in the ^{13}C-NMR spectrum (Table II), the structure of **1** was assumed to be a glucoside of pyridoxine monomethylether. On the basis of a differential NOE experiment, it was identified to be 3-hydroxy-5-hydroxymethyl-4-methoxymethyl-2-methylpyridine 3-*O*-β-D-glucopyranoside, which was isolated from the seeds of *Albizzia lucida* recently.[3)]

Julibrine I (**2**), a white amorphous powder, $[\alpha]_D$-20.0° (MeOH), showed an $[M-H]^-$ ion peak at *m/z* 520 and the fragment ion peak identical with $[M-H]^-$ ion peak of **1** at *m/z* 344 in the negative FAB-MS. Upon acid hydrolysis of **2**, the same aglycone as **1** was identified by TLC. In the ^{13}C-NMR spectrum of **2**, although signals due to the aglycone moiety resembled those of **1**, signal ascribable to C-5' was observed downfield (+7.1). Since C-4~6 appeared upfield to the contrary, the glycosyl unit was assumed to attach at C-5'. In addition, signals due to the terminal β-D-glucuronic acid and β-D-glucosyl group which shifted downfield at C-2 were appeared. Because the ^{13}C-^{1}H COSY spectrum and the differential NOE experiment supported this structure, **2** was determined to be 3-hydroxy-5-hydroxymethyl-4-methoxymethyl-2-methylpyridine 5'-*O*-β-D-glucuronopyranosyl(1→2)β-D-glucopyranoside.

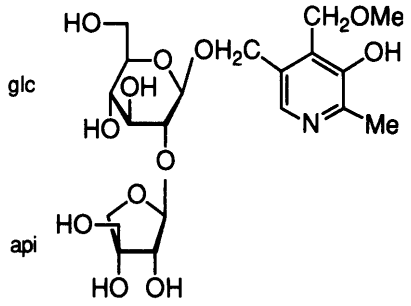
Julibrine II (**3**), a white amorphous powder, $[\alpha]_D$-65.2° (MeOH), showed an $[M-H]^-$ ion peak

at *m/z* 476 in the negative FAB-MS. The UV absorption curve (λ_{max} 333 and 285nm) was similar to that of **2**. Compound **3** gave the same aglycone for **1** and **2** by acid hydrolysis. In the ^{1}H- and ^{13}C-NMR spectrum of **3**, the signals were in accordance with those of **2** except for the signals due to sugar moiety. Since the glycosidic signals were identical to those of β-D-apiofuranosyl(1→2)β-D-glucopyranoside,[2] **3** was established to be 3-hydroxy-5-hydroxymethyl-4-methoxymethyl-2-methylpyridine 5'-*O*-β-D-apiofuranosyl(1→2)β-D-glucopyranoside.

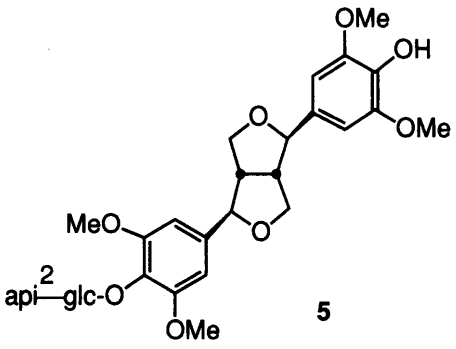
Meanwhile the methanol extract showed a negative inotropic action at 100γ (μg/ml) in Straub-Führer method using frog heart, while julibrine II (**3**) induced arrhythmia even in quite a low dose (less than 0.01γ). However, julibrine I (**2**), having the same aglycone, did not show the action even at a 10 times higher dose (1000γ). Furthermore, compound **1**, which is known as a neurotoxin, did not show any activity at 1000γ. To test further the mechanism of the action, compounds **5** and **6**, which have the same glycosidic unit, were employed. But neither compound showed a significant effect for frog heart at 100γ. These data showed that the whole structure of **3** could be essential for inducing arrythmic action. As mentioned above, the methanol extract showed a negative inotropic action, whereas julibrine II (**3**) showed arrhythmic-inducing action. The latter action might be expressed as a dromotropic action. This plant also includes liriodendrin, which was reported very recently as a Ca^{2+} channel antagonist.[4] It is well known that such antagonists cause various cardiac actions. The action of methanol extract would be complexed by these compounds. Further studies on the actions of related lignan including liriodendrin will be attempted.



	R_1	R_2	R_3
1	glc	Me	H
2 (julibrine I)	H	Me	glc(2→1)glcUA
4	H	H	H



3
(julibrine II)



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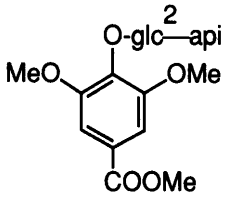

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Table I. ^{1}H-NMR Data for Compounds **1**~**4** (δ:ppm, in DMSO-d_6+D_2O)

	1	**2**	**3**	**4**
H-6	8.29(s)	7.96(s)	7.99(s)	8.12(s)
H_3-2'	2.49(s)	2.36(s)	2.38(s)	2.60(s)
H_2-4'	4.57, 4.67 (ABq, J=10.6)	4.66(s)	4.58(s)	4.78(s)
H_2-5'	4.59(s)	4.67, 4.82 (ABq, J=11.7)	4.59, 4.84 (ABq, J=12.1)	4.71(s)
4'-OMe	3.27(s)	3.26(s)	3.29(s)	
glc H-1	4.48(d, J=7.7)	4.48(d, J=7.3)	4.29(d, J=7.7)	
glc UA H-1		4.37(d, J=7.7)		
api H-1			5.22(s)	

Table II. ^{13}C-NMR Data for Compounds **1**~**3** (δ:ppm, in DMSO-d_6)

	1	**2**	**3**
C-2	151.7	147.3	146.8
3	149.2	150.0	151.7
4	135.7[a)]	130.3[a)]	129.8[a)]
5	136.2[a)]	130.9[a)]	130.2[a)]
6	143.6	140.0	140.1
2'	20.1	19.6	19.6
4'	64.4	65.1	64.0
5'	58.2	65.3	64.8
OMe	57.8	57.9	57.7
glc-1	105.4	100.1	100.1
2	73.9	80.9	76.9
3	76.4	75.0	76.0
4	69.9	69.8	70.2
5	77.0	76.8	76.8
6	61.2	61.0	60.9
glcUA-1		102.9	
2		74.3	
3		76.4	
4		72.0	
5		76.0	
6		172.8	
api-1			108.8
2			76.7
3			79.0
4			73.6
5			64.5

a) In each vertical column may be changeable.

REFERENCES AND NOTES

1) Part 32 in the series of the studies of the leguminous plants.

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