PERFORATIN : A NOVEL TETRANORTRITERPENOID FROM *HARRISONIA PERFORATA*

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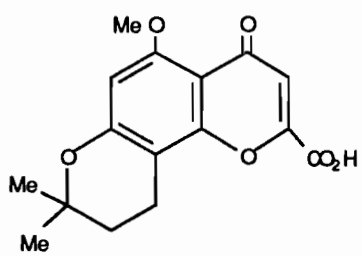
Harrisonia perforata (Blanco) Merr, a bitter shrub of the family Simaroubaceae, widely spread in South East Asia, is used as a remedy for diarrhoea, dysentery and fever.

Chinese workers have isolated an acid from the roots of *Harrisonia perforata* for which they suggest the structure :



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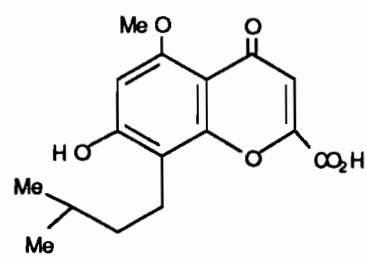

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A compound with a similar structure 2 has been isolated from the bark of this species (2) growing in Thaïland.

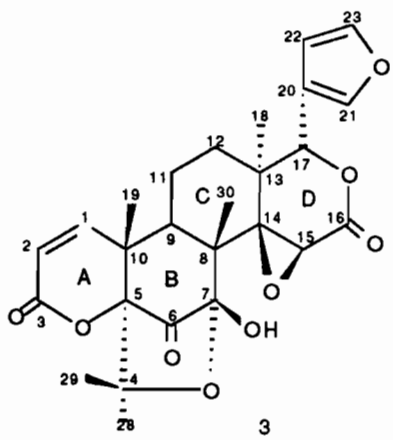
In continuation of our investigations into the chemical constituents of the plant family Simaroubaceae (3), we now report the isolation, from the leaves of *Harrisonia perforata* (Blanco) Merr, and structural determination of an unusual tetranortriterpenoid (limonoid) of the obacunol class, which we now name perforatin 3.

The leaves were collected during March 1990 In Sonla Province, Vietnam. The dried and ground leaves (600 g) were defatted with hexane and extracted several times with chloroform. The viscous product (8 g) so obtained was first fractionated over silica gel (B.D.H. 60-120 mesh) with increasing amounts of ethyl acetate in chloroform as eluent. Fractions of similar behaviour t.l.c. were combined and further purified by radial chromatography over silica gel by using a Harrison Research Chromatotron with mixtures of ethyl acetate and hexane as eluent. Perforatin (3) (20 mg) crystallized from ethyl acetate, m.p. 225-228°C, -66.6° ($CHCl_3$).

Perforatin showed a weak MH ion peak at m/z 485 in its chemical ionization mass spectrum (NH_3) and an accompanying $M+NH_4$ ion peak at m/z 502. These data, in conjunction with the elemental analysis and ^{13}C NMR spectra, indicated a molecular formula of $C_{26}H_{28}O_9$ and were consistent with perforatin being alimonoid. The ^{13}C and ^{1}H NMR data assigned through the use of DEPT and heteronuclear two - dimensional correlated (HETCOR) techniques

are given in Table 1. The ^{13}C NMR spectrum was in accord with the formulation of perforatin as a limonoid and revealed the presence of five methyl groups, 2-methylens groups, 8 CH groups, 8 quaternary carbon atoms and 3 carbonyl groups. The ^{1}H NMR spectrum revealed the presence of a ß- substituted furan and the characteristic methine proton at C-15 together with the relevant epoxide and carbonyl carbon signals for the α-ß-epoxy—lactone portion of the molecule pointed to the structure of rings C and D and the pendant furan. In fact the carbon chemical shifts for the C, D, and furan rings were closely similar to those of obacunone 4 (4, 5) harrisonin 5 (5) and acidissimin 6 (6).

The A and B rings carbon chemical shifts of perforatin 3 also showed some resemblance to those of both harrisonin 5 and acidissimin 6. The presence of an α, ß-unsaturated lactone was revealed by a signal for a carbonyl group at δ 161.11 and signals for the α - and β - carbons at δ 119.04 and 152.46 ; these latter two signals correlated with two doublets in the ^{1}H NMR spectrum at δ 5.88 and 7.36 with a coupling constant of 9.8 Hz. These carbon chemical shifts are closer to those of acidissimin rather than those of harrisonin and suggest that the A-ring lactone of perforatin is six-membered rather than seven-membered. The carbon spectrum also exhibited a signal for carbonyl group at δ 202.88 and a quaternary signal at δ 100.96 characteristic of a hemiketal carbon.



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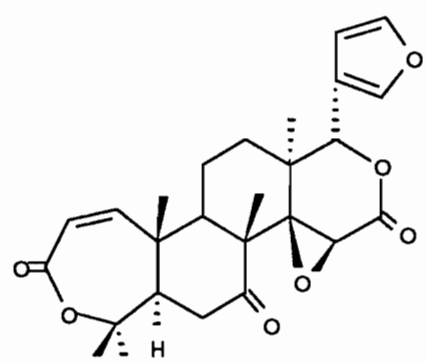
Perforatin 3



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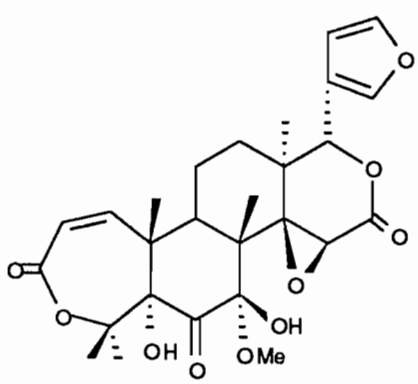
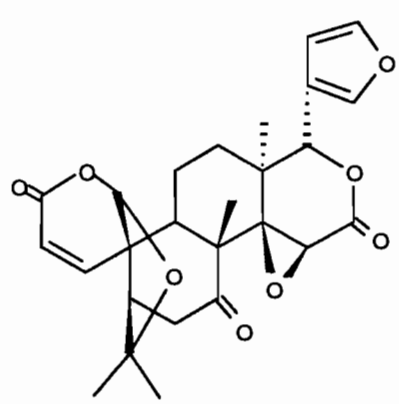
Obacunone 4



Harrisonin 5



Acidissimin 6

The electronic spectrum of perforatin showed only end absorption but the infrared spectrum (KBr) in addition to a carbonyl band at 1730cm^{-1} exhibited a sharp band at 1792cm^{-1} which must be attributed to a carbonyl group in a five membered ring. A hydroxy group was also present as revealed by a band at 3420cm^{-1} in the infrared spectrum and a sharp singlet at δ 6.48 in the ^{1}H NMR spectrum.

TABLE 1 : ^{13}C and ^{1}H NMR data $(CD_3)_2$ CO for Perforatin

Carbon	c	H^A	Carbon	c	H^A
1	152.46	7.36,d,$J_{1,2}$9.8 HZ	15	58.83	4.67,S
2	119.04	5.88,d,$J_{2,1}$9.8 HZ	16	166.22	
3	161.11		17	78.51	5.71,br S
4	89.85		20	122.08	
5	80.83		21	142.59	7.65,dt,$J_{21,23}$1.6,$J_{21,22}$
6	202.88				0.8, $J_{21,17}$ 0.8 HZ
7	100.96		22	110.96	6.53,ddd,$J_{22,23}$ 1.9
8	52.31				$J_{22,21}$ 0.8,$J_{22,17}$ 0.4 HZ
9	36.25	3.19-3.25,m	23	144.16	7.6 1,ddd, $J_{23,22}$ 1.9, $J_{23,21}$ HZ
					1.9, $J_{23,17}$ 0.4 HZ
10	44.96				
11	15.70	1.85-1.99,m,2.16-2.28,m		Me (x2)	28.01 1.44,S 1.23 B,S
12	25.98	1.52-1.62, m, 1.80-1.93,m		Me	19.86 1.20 B,S
13	40.59			Me	19.63 1.38, S
14	71.39			Me	15.43 1.21 B,S

[A] H 6.48,OH [B] May be interchanged.

If it is assumed that perforatin arises from the same ring A cleaved precursor 7 as harrisonin then the above data can be accomodated by structure 8 for the A and B rings. This proposal was vindicated by the determination of the X-ray crystal structure of perforatin which yielded the stereochemistry shown in structure 3. Perforatin thus joins the strange and much - altered limonoids of the obacunal group (4) in which both rings A and D are cleaved. It is of interest that the stereochemistry of perforatin at C-5 is opposite to that of harrisonin (8). Harrisonin is unlikely to be an artefact (7), but its circular dichroism is anomalous (5) so that the stereochemistry of harrisonin at C-5 may be incorrect or it may arise from a different stereochemical precursor to perforatin.

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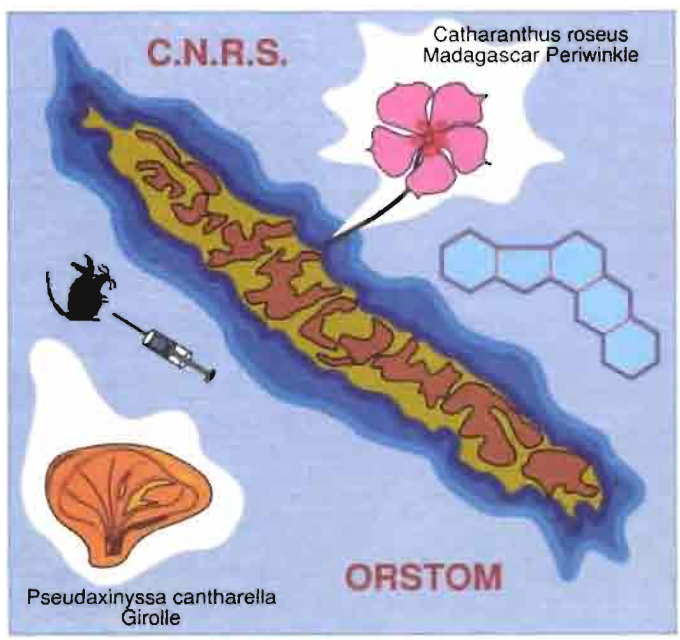

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