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Alkaloids of the leaves of *Rauwolfia vomitoria* Afz.

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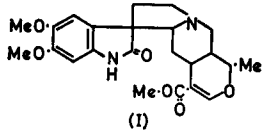
Leaves of *Rauwolfia vomitoria*, collected in Nigeria, contained at least six alkaloids, three are indole derivatives (aricine, tetrahydroalstonine, isoreserpiline) and three are isomers of α-oxindole type (carapanaubine, rauvoxine, rauvoxinine). Rauvoxine and rauvoxinine are new alkaloids. The leaves contained no reserpine.

THE tree *Rauwolfia vomitoria* Afz., family Apocynaceae, is found throughout West Africa. It is very abundant in Nigeria, especially in the southern parts, and is up to about 70 ft in height. Its root, root-bark, and, to a lesser extent, its stem bark are used as native medicines but the leaves and fruits are less frequently taken internally because of their powerful emetic properties.

Some investigations of the alkaloidal content of this species have been made but only the roots have been studied in detail and about 20 indole or indoline alkaloids have been identified (Poisson, 1958; Schlittler, 1964). Stem bark was shown to contain rauvanine (Goutarel, Gut & Parello, 1961). The fruits, rich in carotenoids, contain only traces of alkaloids and these are located in the seeds (Poisson, private communication). As yet no investigations of the alkaloidal content of the leaves have been published and hence this present work was undertaken.

The alkaloids of a leaf sample collected in Ibadan, Nigeria, from trees taxonomically identified as *Rauwolfia vomitoria* Afz., have been extracted and were fractionated by chromatography. Four crystalline alkaloids have been isolated: aricine, found in different *Rauwolfia* spp. and in *Cinchona pelletieriana* Wedd. (Goutarel, Janot, Le Hir, Corrodi & Prelog, 1954; Stoll, Hofman & Brunner, 1955), and carapanaubine, found in *Aspidosperma carapanauba* Pichon (Gilbert, Aguayo Brissolese, Finch, Taylor, Budzikiewicz, Wilson & Djerassi, 1963): the two others are new and have been named rauvoxine and rauvoxinine. In addition, small quantities of tetrahydroalstonine (Hochstein, 1955) and of isoreserpiline (Stoll, Hofmann & Brunner, 1955) have been isolated and identified. Reserpine was not found in this material.

Rauvoxine and rauvoxinine are isomers of carapanaubine or isoreserpiline-oxindole B (Finch, Gemenden, Hsiu-Chu Hsu & Taylor, 1963, Gilbert & others, 1963) and a close relationship is suggested by their similar ultra-violet and infra-red spectra. Thus, like carapanaubine, they probably possess a dimethoxyheteroyohimbane α-oxindole nucleus I.



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These three alkaloids are the first members of the oxindole group to be reported in *Rauwolfia* spp. Their structure and stereochemistry are now being studied (Poisson & Pousset, in preparation).

Experimental

Melting-points were determined by the Köffler microscopic method; unless otherwise stated, optical rotations were in chloroform containing 0·5% ethanol using a Zeiss electronic polarimeter at 578 mμ; ultra-violet spectra were obtained in ethanol solution.

Total alkaloids were extracted from 4 kg of powdered dried leaves of *Rauwolfia vomitoria* by percolation to exhaustion with ethanol containing 1% of acetic acid. Ethanol was removed from the extract by evaporation at low temperature under reduced pressure. The residue was taken up in 2·5 litres of 2% hydrochloric acid and the resins removed by filtration. The filtrate was washed several times with light petroleum (b.p. 60–80°), made alkaline with ammonium hydroxide (0·88) and extracted with chloroform. This extract was washed with a solution of sodium bicarbonate, dried and evaporated to yield 45 g of crude bases (11·2 g/kg dried leaf). When dissolved in ether 5 g of insoluble residue remained.

Separation of alkaloids. Ether-soluble bases (40 g) were dissolved in benzene (insoluble fraction 9·2 g) and were chromatographed on alumina. Elution was as follows:

(*a*) Benzene (4,900 ml) yielded 67 mg.

(*b*) Benzene : ether (99 : 1; 2,100 ml) yielded 25 mg. When run on thin-layer plates (see below), one spot had the same Rf value as an authentic specimen of tetrahydroalstonine.

(*c*) Benzene : ether (90 : 10; 3,500 ml) yielded 831 mg. Crystallisation from ether gave aricine (529 mg), m.p. 187°, giving no depression on admixture with an authentic specimen. $[\alpha]_{578}^{20}$ — 58·4° (*c*, 0·93 in ethanol). Its ultra-violet and infra-red spectra were likewise identical with those of authentic aricine.

(*d*) Ether (700 ml) yielded 2·8 g which on crystallisation from ether yielded aricine (1·57 g).

(*e*) Ether (8,400 ml) yielded 3·14 g. Chromatography on thin-layer plates showed the presence of aricine and small quantities of a second alkaloid with the same Rf value as isoreserpiline.

(*f*) Ether : methanol (99 : 1; 2,800 ml) gave 1·54 g which crystallised from methanol to yield rauvoxine, 355 mg, m.p. 210° $[\alpha]_{578}^{20}$ + 98° (*c*, 1·34). Found: C, 64·1; H, 6·7; N, 6·5. $C_{23}H_{28}O_6N_2$ requires C, 64·5; H, 6·6; N, 6·5%. Molecular weight (mass spectrometer) 428 (calc. 428·5). λ_{max} 218 mμ (ε 26,300), 280 mμ (ε 5,300), shoulders at 245 and 300 mμ; ν_{max} (in chloroform) 2,820 cm^{-1}, 1,714 cm^{-1}, 1,627 cm^{-1}.

(*g*) Ether : methanol (99 : 1; 10,500 ml) gave carapanaubine (2·67 g), m.p. 218–219°, giving no depression on admixture with an authentic specimen. $[\alpha]_{578}^{20}$ — 115° (*c*, 1·05). Found: C, 64·5; H, 6·9; N, 6·4. Calc. for $C_{23}H_{28}O_6N_2$, C, 64·5; H, 6·6; N, 6·5%. Molecular weight (mass spectrometer) 428 (calc. for $C_{23}H_{28}O_6N_2$ 428·5). λ_{max} 218 mμ (ε 28,800),

280 mμ (ε 5,000), shoulders at 245 and 300 mμ; ν_{max} (in chloroform) 2,800 cm^{-1}, 1,710 cm^{-1}, 1,635 cm^{-1}. The infra-red spectrum was identical with an authentic sample of carapanaubine.

(*h*) Ether: methanol (98:2; 4,900 ml) gave 820 mg shown by thin-layer chromatography to be a mixture of carapanaubine and rauvoxine.

(*i*) Ether: methanol (95:5; 3,500 ml) gave rauvoxinine (520 mg), m.p. 203–204° $[\alpha]_{578}^{20}$ + 64·6 (*c*, 1·17). Found: C, 64·5; H, 6·6. $C_{23}H_{28}O_6N_2$ requires, C, 64·5; H, 6·6%. Molecular weight (mass spectrometer) 428 (calc. 428·5). λ_{max} 218 mμ (ε 24,500), 280 mμ (ε 5,600), shoulders at 245 and 300 mμ; ν_{max} (in chloroform) 2,820 cm^{-1}, 1,712 cm^{-1}, 1,630 cm^{-1}.

The ultra-violet absorption spectra of carapanaubine, rauvoxine and rauvoxinine are superimposable; the infra-red spectra of the three compounds are similar.

Further elution with ether containing more methanol, then with pure methanol gave uncrystallisable residues.

Tetrahydroalstonine, aricine and isoreserpiline were detected on plates of alkaline kieselgel using dichloromethane containing 1 or 2% methanol, also on plates of alumina using benzene: acetone (3:1) and employing authentic samples as controls. Carapanaubine, rauvoxine and rauvoxinine were separated on plates of alkaline kieselgel using dichloromethane containing 3% of methanol also on plates of alumina using benzene: acetone (3:2). Separations on alumina were less sharp than on kieselgel.

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