

ALKALOIDS OF *RAUWOLFIA SELLOWII* FROM AMAZONIA

by

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SUMMARY

*Reserpiline, sarpagine, lochnerine, harman and β -yohimbine were the main alkaloids identified in the root bark of *Rauwolfia sellowii* collected in Amazonia. This chemical race could be used for the commercial preparation of reserpiline.*

*Key words: *Rauwolfia sellowii*, Apocynaceae, indole alkaloids, reserpiline, sarpagine, lochnerine, harman, β -yohimbine, chemical race.*

INTRODUCTION

The root bark of *Rauwolfia sellowii*, collected in Rio Branco (Acre), was chemically studied. To our knowledge, it is the first time *Rauwolfia sellowii* has been found in the Amazonian forest (1,2). In previous work on the root bark of *R. sellowii* collected in South-East Brazil different alkaloids were identified: reserpine (4,5,6), serpentine (3), ajmalicine (4,5), tetrahydroalstonine (4,5), ajmalinine (3), tetraphyllicine (5), ajmalidine (5), rauniticine (7) and mainly aricine (4,5,7) and ajmaline (3,5).

A preliminary screening (CoTLC with reference compounds) showed that this Amazonian sample did not contain any of these previously identified alkaloids.

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For this reason we decided to undertake a more detailed study of this sample.

EXPERIMENTAL

Plant material

Herbarium specimens and root bark of *Rauwolfia sellowii* MUELL.-ARG. were collected in 1983 at Rio Branco (Acre) where the tree is luxuriant and easy to find. Voucher specimens (No 95,767) are kept in the Herbarium of the National Research Institute of Amazonia (INPA) at Manaus (Brazil) and in the Pharmaceutical Institute of the University of Liège (Belgium).

Extraction and purification of alkaloids

Dry powder was macerated for 72 h with methanol: acetic acid: water (80:5:15) and then percolated with the same mixture. The solution was concentrated under reduced pressure and the sticky residue was dissolved in 1% aqueous HOAc. The resulting acidic solution was filtered and extracted with CHCl_3 at pH 5. The chloroform layer was dried over anhydrous sodium sulfate and evaporated to give fraction A.

The aqueous solution was basified with NaHCO_3 to pH 8 and reextracted with CHCl_3 to yield fraction B after separation and evaporation of the CHCl_3 under reduced pressure.

The fraction A was then dissolved in 5% aqueous HOAc and extracted with Et₂O to remove non-alkaloidal products. The acidic solution, after basification with Na₂CO₃, was again extracted with Et₂O to give only one crude alkaloid. This product was purified firstly by chromatography (on Sephadex LH 20[®] with MeOH) and secondly by reversed-phase liquid chromatography on a Lobar[®] column (Lichroprep RP 8 (40-63 μm) with a mixture of methanol and 0.02 M aqueous ammonium acetate (3:2). The compound so purified was finally identified as reserpiline, 1.

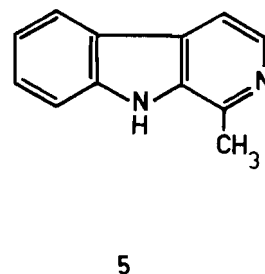
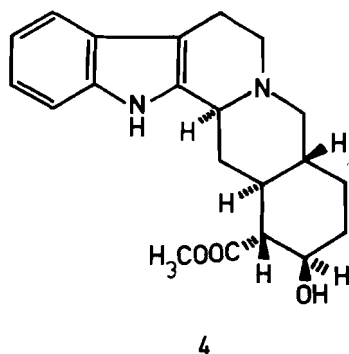
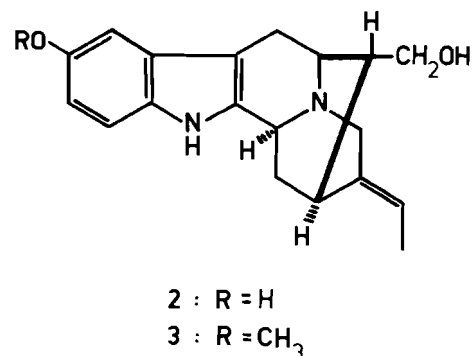
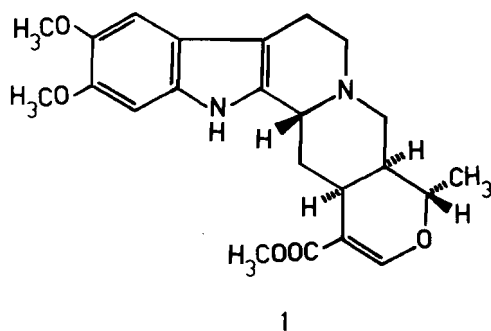
The fraction B was fractionated in a similar way (i.e. combined use of Sephadex and reversed-phase liquid chromatography with the same solvents as above).

These separations were monitored by TLC. Four alkaloids were detected and successively isolated and identified: sarpagine, 2, spontaneously crystallized from MeOH in the tubes of the fraction collector; lochnerine, 3, was finally purified by preparative TLC on silica with a mixture of solvents = EtOAc: isopropanol: NH₄OH conc. (16:3:1); β-yohimbine, 4, crystallized from methanol, cooled to 0°C; harman, 5, crystallized from hexane.

RESULTS AND DISCUSSION

Reserpiline 1, the main alkaloid, and β-yohimbine 4 were identified by their UV, IR,

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MS, ^{13}C and ^1H NMR spectra (8,9). Sarpagine 2, locherine 3 and harman 5 were compared with reference compounds and were identical in all respects (IR, UV, MS and CoTLC) (10).

It is interesting to note that the composition of this sample collected near the Equator is totally different from the alkaloidal composition of the same plant collected in a subtropical region and represents a further example of a chemical race.

Rauwolfia sellowii from Amazonia could be used for the commercial preparation of reserpiline, which is included in various pharmaceutical proprietary preparations, like REDOULINE® and SUPRESSAN® in Belgium, or GRONA® in Spain. The pharmacological properties of reserpiline, therapeutically used as antihypertensive (11), are similar to those previously found in crude extracts of *Rauwolfia sellowii* from South Eastern Brazil (12), but this batch contained reserpine instead of reserpiline.

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Résumé

Les alcaloïdes principaux des écorces de racines de *Rauwolfia sellowii*, récoltés en Amazonie, ont été isolés et identifiés à la réserpine (substance majoritaire), la sarpagine, la lochnerine, l'harmane et la β -yohimbine. Cette race chimique pourrait servir à l'extraction industrielle de la réserpine, en vue de son exploitation commerciale comme antihypertenseur.

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