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INDOLE ALKALOIDS FROM *PESCHIERA CAMPESTRIS*

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Key Word Index—*Peschiera campestris*; Apocynaceae; indole alkaloids; 12-methoxy-N_b-methylvoachalotine.

Abstract—The investigation of leaf, bark and root extracts of *Peschiera campestris*, a new species discovered in Brasilia, Brazil, afforded ten indole alkaloids. The main component from the root extract was 12-methoxy-N_b-methylvoachalotine (*ca* 0.25% of the dried roots). The structures were elucidated by spectroscopic methods and comparison with authentic samples.

INTRODUCTION

Peschiera campestris (Rizz.) Rizz., a new species which was discovered in Brasilia, Brazil, has shining leaves and scented white flowers and is considered an ornamental bush. It was initially classified as *Peschiera affinis* (Muell. Arg.) Miers var. *campestris* Rizz. by Rizzini, who some years later came to the conclusion it was a new species and not a mere variety [1]. The taxonomy of the Apocynaceae (*Tabernamontana*) has been revised by Leeuwenberg and co-workers [2] and they have pointed out that *Peschiera* and *Tabernamontana* are synonyms. Meanwhile Allorge [1] has reclassified *Peschiera campestris* (Rizz.) Rizz. as *Peschiera solanifolia* var. *fallax* (Muell. Arg.) L. Allorge.

Conscious that the taxonomy of this genus is a rather complex subject and that the identification of the alkaloid constituents can play a significant role in chemotaxonomy we have undertaken the phytochemical investigation of this species as part of our study of the Brazilian Apocynaceae.

RESULTS AND DISCUSSION

From the methanolic extracts of the leaves, bark and roots we have isolated ten known alkaloids [3–5], i.e. isovoacangine (**1**), isovoacristine (**2**), coronaridine (**3**), voacangine (**4**), voacangine-hydroxyindolenine (**5**), heyneanine (**6**), voacamine (**7**), voachalotine (**8**), vobasine (**9**) and 12-methoxy-N_b-methylvoachalotine (**10**). We believe voacangine-hydroxyindolenine (**5**) to be an artefact since it was also formed during the crystallization process of **4**. 12-Methoxy-N_b-methylvoachalotine (**10**), the main constituent of the methanolic extract of the roots (*ca* 0.25% of the dried roots), was isolated as its iodide. This compound was first isolated from *Peschiera fuchsiaefolia* A. (DC.) Miers (*Tabernamontana fuchsiifolia*) [5].

Although the alkaloids of various *Tabernamontana* (= *Peschiera*) species have been well studied, few references report the isolation of quaternary indolic alkaloids. The loss of these compounds during the isolation process (H_2O, H^+/organic solvent, partitioning) could, in part, be responsible for this fact. In our case, when the quaternary indole alkaloid **10** was present, the crude extract was fractionated on a silica gel column and the fractions eluted with methanol were first submitted to an anion exchange resin (I^-) and then once again purified on a silica gel column eluted with chloroform and methanol.

Concerning biological activity, compounds **1**, **3**, **5**, **6**, **8** and **10** were tested at a concentration of 1 mg/1ml against *Candida albicans* B311 and when compared to the standard antibiotic amphothericin B revealed no activity. Compound **10** was also submitted to a leukaemia screen test (3 PS31) showing no activity.

As the most abundant alkaloids in *Peschiera campestris* belong either to the ibogan class, corynanthean class or dimeric voacamine type the investigated species follows the general trend of the genus *Tabernamontana* (= *Peschiera*) [2]. However, compounds that have been considered by Van Beeck and *et al.* [2] to be most characteristic of *Tabernamontana* since they have been detected almost exclusively in this genus were not found in *P. campestris*.

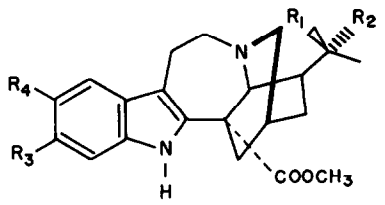
EXPERIMENTAL

All mps are uncorr. ^{1}H NMR spectra were determined using $CDCl_3$ (unless otherwise indicated) and Me_4Si as internal standard. The ^{13}C NMR spectra were recorded in $CHCl_3$. The values of the chemical shifts are in ppm from Me_4Si [$\delta(Me_4Si) = \delta(CHCl_3) + 77.2$]. Merck silica gel GF was utilized for TLC and spots were visualized by spraying Dragendorff soln followed by MeOH–H_2SO_4 and heating at 110°.

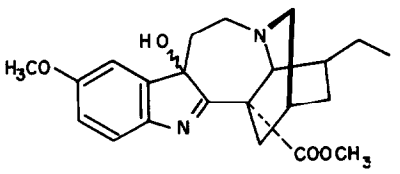
P. campestris was collected in Brasilia, Brazil in May 1983 by B.S.P.; voucher specimens (IBGE—B.A.S.P. 345 and 513) have been deposited at the herbarium of the Reserva Ecologica IBGE, Brasilia, Brazil.

After drying at 40°, the leaves (800.0 g), bark (1950.0 g) and roots (767.3 g) were extracted with MeOH yielding 206.5, 277.0 and 59.6 g of crude extract, respectively. The crude extract of the leaves was partitioned with $CHCl_3$ and 2% HCl. The aq. layer was collected and brought to pH ~ 10 with $NaHCO_3$ and extracted with $CHCl_3$. The $CHCl_3$ layer was dried (Na_2SO_4), filtered and evaporated *in vacuo* yielding 10.5 g of crude alkaloids. CC through silica gel of the crude alkaloids from the leaves and of the crude extracts of the bark and roots furnished the alkaloids, which were further purified using ion exchange resin, thick layer chromatography and crystallization.

Isovoacangine (**1**) (leaves): $[\alpha]_D^{25}$ −30.4° (*c* 4.2; $CHCl_3$); isovoacristine (**2**) (leaves): $[\alpha]_D^{25}$ −10.7°(*c* 17; $CHCl_3$); coronaridine (**3**) (roots): $[\alpha]_D^{25}$ −29.3° (*c* 1.3; $CHCl_3$); voacangine (**4**) (roots): $[\alpha]_D^{25}$ −23.8° (*c* 1.8; $CHCl_3$); voacangine-hydroxyindolenine (**5**) (roots): mp 129–132° (Et_2O); $[\alpha]_D^{25}$ −23.1° (*c* = 1.2; $CHCl_3$); heyneanine (**6**) (roots, bark): mp 108–110° (MeOH–Et_2O), $[\alpha]_D^{25}$ 18.1° (*c* = 5.2; $CHCl_3$); voacamine (**7**) (roots, bark): mp 215°



	R_1	R_2	R_3	R_4
1	H	H	OCH_3	H
2	OH	H	OCH_3	H
3	H	H	H	H
4	H	H	H	OCH_3
6	H	OH	H	H



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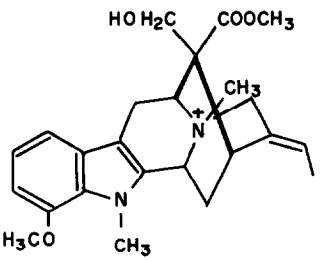

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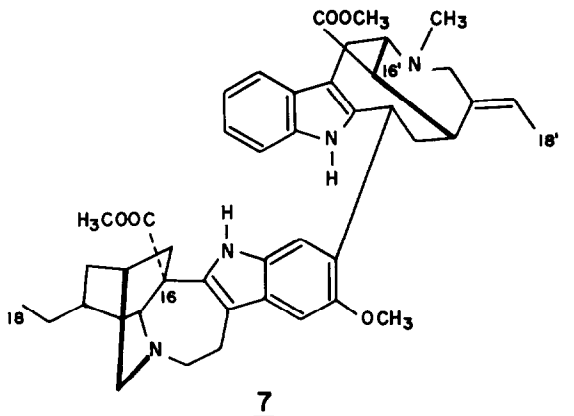

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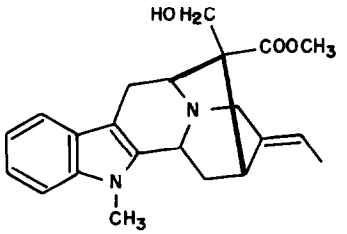

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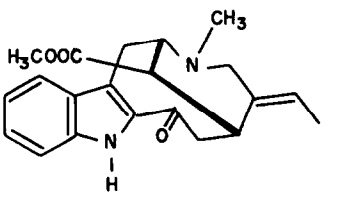

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(decomp.) (CH_2Cl_2–hexane), $[\alpha]_D^{25}$ −36.4° (*c* 7.7; $CHCl_3$); voachalotine (**8**) (roots, bark): mp 210–212° (C_6H_6), $[\alpha]_D^{25}$ 7.7° (*c* 1.0; $CHCl_3$); vobasine (**9**) (bark): $[\alpha]_D^{25}$ −141.3° (*c* 0.86; $CHCl_3$); 12-methoxy-N_b-methylvoachalotine iodide (**10**) (roots, bark): mp 256 (decomp.) (MeOH); $[\alpha]_D^{25}$ −65.6° (*c* 6.7; $CHCl_3$).

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3-DEHYDROMITRAGYNINE: AN ALKALOID FROM *MITRAGYNA SPECIOSA*

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Key Word Index—*Mitragyna speciosa*; Rubiaceae; leaves; indole alkaloids; 3-dehydromitragynine.

Abstract—An investigation of the fresh leaves of *Mitragyna speciosa* has resulted in the isolation of a new alkaloid in addition to the indole alkaloids previously reported. The new alkaloid is the 3-dehydro derivative of mitragynine and its structure was elucidated by spectral means and chemical transformations. (−)-Epicatechin was also isolated from the leaves.

INTRODUCTION

Much phytochemical work on the alkaloids of *Mitragyna* species has been carried out over the last 20 years. Interest in this genus arose primarily from the fact that the leaves of *M. speciosa* have been used as a drug of abuse in Thailand and were used as a substitute for opium. The alkaloidal content of different morphological, geographical and chronological samples of *M. speciosa* has been extensively studied [1–3]. The major alkaloid present in many samples of leaves is mitragynine together with its isomers. This compound has undergone a reasonable degree of testing of its pharmacological actions but there is little evidence to suggest that it is responsible for the sensations for which this plant is used as a drug of abuse.

Most of the work previously carried out has been done using dried plant material. This paper describes the analysis of fresh leaves and the isolation from them of (−)-epicatechin, a procyanidin, and a new type of indole alkaloid consisting of a 3-dehydro heteroyohimbine.

RESULTS AND DISCUSSION

(−)-Epicatechin was identified by comparison with published spectral data for the substance isolated and its acetate derivative. This is the first report of this type of compound from *Mitragyna* although it is well-known as the basis of the condensed tannins present in the related genus *Uncaria*.

Mitragynine, paynantheine, speciogynine, speciociliatine and mitraciliatine were all identified by comparison with their TLC behaviour and ^{1}H NMR spectra with authentic samples.

3-Dehydromitragynine (**1**) had an $[M]^+$ of *m/z* 397, one less than mitragynine. The ^{1}H NMR spectrum showed that three methoxyl groups were present and also the presence of an ethyl group. This shows that the alkaloid must have an open E ring as in corynantheidine and be 9-methoxy substituted. The UV spectrum showed that the conjugated system in the molecule was greater than that in the mitragynine-like molecules, the bathochromic shift seen in a neutral or acidic environment indicating the possible presence of a quaternary N. This would also explain the polar nature of the molecule evidenced by its low R_f values on TLC. The downfield shift of the methine and methylene protons at C-5, C-14, C-15 and C-21 (δ3.5–4.0) compared with signals given in mitragynine (δ2.4–3.4) [4] indicate the presence of an unsaturated bond in their vicinity. The lack of any signal below 4.0 for