Phytochemistry, Vol. 25, No. 11, pp. 2692–2693, 1986.
Printed in Great Britain.

0031–9422/86 $3.00 + 0.00
Pergamon Journals Ltd.

ALKALOIDS AND COUMARINS FROM *RUTA CHALEPENSIS*

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(*Revised received* 18 *March* 1986)

Key Word Index—*Ruta chalepensis*; Rutaceae; alkaloids; coumarins.

Abstract—The aerial parts of *Ruta chalepensis* yielded the alkaloids kokusaginine, skimmianine, arborinine, γ-fagarine, graveoline and the new alkaloid 3′-hydroxygraveoline, as well as the coumarins chalepensin, chalepin, rutamarin, bergapten, isopimpinellin and xanthotoxin. The structures were established by spectral methods and by TLC comparison with authentic samples where possible. Some alkaloids were tested for their effects on the prevention of early pregnancy in rats, but none was found to be active.

Ruta graveolens, the common rue, is a native of the Mediterranean region. It was introduced to Chinese medicine about two centuries ago and was soon accepted in popular use. Many therapeutic properties were subsequently ascribed to it. While the common rue is cultivated throughout European and temperate Asian regions, its close congener *R. chalepensis* is still growing wild in Turkey. Quinoline alkaloids such as γ-fagarine, kokusaginine, arborinine, skimmianine, dictamnine and graveoline were isolated from *R. graveolens* and coumarins such as chalepensin, chalepin and marmasin were isolated from *R. chalepensis* exhibiting pharmacological activities [1–3]. In Chinese medicine, *R. graveolens* is strictly contraindicated in pregnancy; a similar effect is also ascribed to *R. chalepensis* in Turkey [4, 5]. Since potent antifertility compounds have been isolated from traditional Chinese medicines, the rich ethnopharmacological background of the common rue in both Chinese and Turkish cultures deserves particular attention [6–8]. The present paper reports the alkaloids and coumarins isolated from *R. chalepensis*; by using the same bioassay given in a previous paper [7], some of them were tested in rats and found to be inactive. From the aerial parts of *R. chalepensis*, one new and five known alkaloids and six known coumarins were isolated. The predominant alkaloids were kokusaginine (300 mg) and skimmianine (150 mg). The predominant coumarin was bergapten (1 g). Other alkaloids isolated in minor quantities were arborinine (5 mg), graveoline (5 mg), γ-fagarine (10 mg) and a new alkaloid, 3′-hydroxygraveoline (10 mg). The minor coumarins isolated were chalepensin (100 mg), chalepin (10 mg), rutamarin (50 mg), isopimpinellin (50 mg) and xanthotoxin (10 mg). The structures of these compounds were determined by spectral methods (UV, IR, ^{1}H NMR and mass spectrometry) and by TLC comparison with authentic samples in all cases except chalepin, chalepensin and rutamarin.

The structure of the new alkaloid 3′-hydroxygraveolin was established mainly by ^{1}H NMR spectroscopy. All the peaks with the exception of the narrow doublets at δ6.90 and 6.87, which indicate the *meta* positions of H-2′ and H-6′ relative to one another, and the hydroxyl peak at δ6.38, were similar to those of graveoline. Although the mass peak at *m/z* 295 was very small (1%), elemental analysis gave the molecular formula $C_{17}H_{13}O_4N$. The UV spectrum was in agreement with the suggested structure.

EXPERIMENTAL

Aerial parts of *R. chalepensis* L. were collected from Sedef Adasi (Pearl Island) near Istanbul in July 1984 and identified by one of us (E.T.). A voucher (ISTE 54969) has been deposited at the Herbarium of the Faculty of Pharmacy, University of Istanbul.

3′-Hydroxygraveoline. Amorphous. UV λ_{max}^{MeOH} nm: 338 (log ε 4.5), 330 (sh), 270 (sh), 224 (log ε 4.5). IR ν_{max}^{KBr} cm^{-1}: 3450, 3050, 2920, 1625, 1600, 1490, 1450, 1250, 1120, 1080, 1030, 820, 750. ^{1}H NMR (400 MHz, $CDCl_3$): δ8.5 (1H, *dd*, *J* = 2.5 and 8 Hz, H-5), 7.74 (1H, *dt*, *J* = 1.5 and 8 Hz, H-7*), 7.56 (1H, *br d*, *J* = 9 Hz, H-8), 7.45 (1H, *br t*, *J* = 8 Hz, H-6*), 6.08 (2H, *s*, OCH_2O), 3.66 (3H, *s*, NMe), 6.92 (1H, *s*, H-3), 6.90 (1H, *d*, *J* = 1.5 Hz, H-2†), 6.87 (1H, *d*, *J* = 1.5 Hz, H-6†), 6.38 (1H, *br s*, OH). MS *m/z* (rel. int.): 295 $[M]^+$ (1), 279 $[M-16]^+$ (90), 251 $[M-CO]^+$ (70), 239 $[M-CO-Me]^+$ (64), 211 $[239-CO]^+$ (38), 199 (54). (Found: C, 69.27; H, 4.46; N, 4.78. $C_{17}H_{13}O_4N$ requires: C, 69.15; H, 4.40; N, 4.74%.)

Acknowledgements—We would like to thank Prof. Dr. F. Bohlmann (Berlin) for the 400 MHz ^{1}H NMR of the new alkaloid. Bioassay in Hong Kong was partly supported by the Special Program of Research, Development and Research Training in Human Reproduction of the World Health Organization (grant to Y.C.K.).

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Phytochemistry, Vol. 25, No. 11, pp. 2693–2695, 1986.
Printed in Great Britain.

0031–9422/86 $3.00 + 0.00
Pergamon Journals Ltd.

LUXANDRINE, A QUATERNARY BENZYLISOQUINOLINE FROM *PSEUDOXANDRA SCLEROCARPA**

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(*Received* 3 *March* 1986)

Key Word Index—*Pseudoxandra sclerocarpa*; Annonaceae; trunk bark; quaternary benzylisoquinoline alkaloid.

Abstract—A new 6,7-dihydroxytetrahydrobenzylisoquinoline has been isolated and identified from the quaternary alkaloidal fraction of the bases of *Pseudoxandra sclerocarpa*.

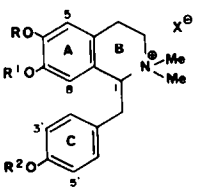
INTRODUCTION

In continuation of our investigations on the Annonaceae, we have studied the constituents of the trunk bark of *Pseudoxandra sclerocarpa* Maas, collected from the equatorial forest of Colombia. The non-quaternary alkaloidal fraction of the plant has been examined and several alkaloids have been isolated and identified [1–4]‡. The present work describes the isolation and identification of luxandrine (**1**) as the major component of the quaternary alkaloidal fraction of *P. sclerocarpa*. Luxandrine is a hitherto unknown isomer of magnocurarine (**2**) and contains a catechol unit in its structure.

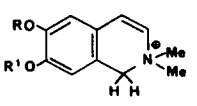
RESULTS AND DISCUSSION

The defatted trunk bark of *P. sclerocarpa* was basified with ammonia and the non-quaternary alkaloids were extracted with dichloromethane. The marc was extracted with methanol and the quaternary alkaloids were isolated as a mixture of iodomercurates. The latter were converted to chlorides by passage through Amberlite IRN-78, in the chloride form; the chlorides were separated on silica gel and the chloride of luxandrine (**1**) was isolated as the major product.

The UV spectrum of **1** clearly indicated a benzyltetrahydroisoquinoline. A pronounced bathochromic shift with alkali indicated phenolic hydroxyl groups. The mass spectrum of **1** obtained by chemical ionization indicated a simple benzyltetrahydroisoquinoline and a molecular weight of 314 for the cation of **1**. The molecular weight was consistent with the molecular formula $C_{19}H_{24}O_3N$. The mass spectruum of **1** obtained by electron impact showed a prominent fragment at *m/z* 192. This was assigned structure **7**, its formation following benzylic fission of **1** indicating the presence of two hydroxyl groups



1 R = R¹ = H; R² = Me; X = OH
2 R¹ = R² = H, R = Me; X = OH
3 R = R¹ = R² = Me, X = I
4 R = R¹ = Ac, R² = Me, X = Cl
5 R = R¹ = R² = Ac, X = OH
6 R = R¹ = R² = H; X = OH



7 R = R¹ = H
8 R = H, R¹ = Me; or R = Me, R¹ = H
9 R = H, R¹ = Ac, or R = Ac, R¹ = H

*Part 67 in the series "Alkaloids of the Annonaceae". For Part 66 see Jossang, A., Leboeuf, M., Cavé, A. and Sevenet, T. (1986) *J. Nat. Prod.* (in press).

‡*Pseudoxandra sclerocarpa* now replaces *Pseudoxandra aff. lucida*, as used in preceding publications.