A New Alkaloid from the Roots of Alstonia angustifolia

Ikram M. Said, Laily Bin Din, Nik Idris Yusoff, Colin W. Wright, Ya Cai, and J. David Phillipson

J. Nat. Prod., **1992**, 55 (9), 1323-1324• DOI: 10.1021/np50087a025 • Publication Date (Web): 01 July 2004

Journal of Natural Products
Vol. 55. No. 9. pp. 1323-1324. September 1992

A NEW ALKALOID FROM THE ROOTS OF *ALSTONIA ANGUSTIFOLIA*

IKRAM M. SAID,* LAILY BIN DIN, NIK IDRIS YUSOFF,

Department of Chemistry, Universiti Kebangsaan Malaysia, 43600 UKM Bangi, Malaysia

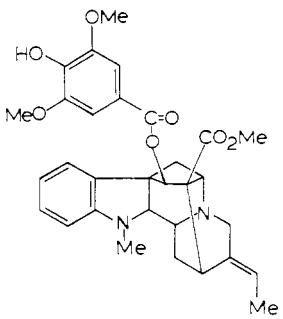
COLIN W. WRIGHT, YA CAI, and J. DAVID PHILLIPSON

Department of Pharmacognosy, School of Pharmacy, 29-39 Brunswick Square, London WC1N 1AX

ABSTRACT.—A new alkaloid, 4′-hydroxy-3′,5′-dimethoxybenzoylvincamajine [**1**], was isolated with nine known alkaloids from the roots of *Alstonia angustifolia* (Apocynaceae).

Alstonia angustifolia Wall. (Apocynaceae), known locally as "pulai," is a medium-sized tree that can grow up to 20 m high and can be found throughout the forests of Peninsula Malaysia. Most species of *Alstonia* have been generally used in traditional medicine as remedies against malaria, dysentery, and other ailments (1,2), while *A. angustifolia* has been used in Malaysia by applying the leaves to the spleen area for relapsing fever (1). Our interest in anti-malarial plants (3) led us to the investigation of *A. angustifolia*; however, previous anti-malarial tests for *Alstonia scholaris* (4) and *Alstonia congensis* (5) have not been encouraging.

Isolation of the alkaloids from the fresh bark and roots of *A. angustifolia* was carried out in the usual manner (3); the roots contained more alkaloids (0.8%) than the bark (0.2%) and also had slight differences in their distribution of components as shown on tlc. Initial screening of the two alkaloid mixtures against *Plasmodium falciparum* K1 strain (6) showed the alkaloid mixture from the roots to be more active (IC_{50} 0.35 $\mu g \cdot ml^{-1}$) than the alkaloid mixture from the bark (IC_{50} 1.21 $\mu g \cdot ml^{-1}$). Because the potential anti-malarial alkaloids from the bark and leaves have been investigated (7), the constituents of the root alkaloid mixture were determined. Extensive cc and preparative tlc resulted in the isolation of ten alkaloids, which were identified by their spectroscopic data in comparison with known compounds isolated previously (7). Nine of the alkaloids were known and identified as alstonerine (17.68% of total alkaloid mixture), alstophylline (0.69%), vincamajine (0.09%), villastonine (8.03%), macralstonine (2.71%), pleiocarpamine (0.17%), macrocarpamine (0.33%), norfluorocurarine (0.18%), and 11-methyoxyakuammicine (0.33%). Alstonerine is the major component in the roots but exists as only a minor constituent in the bark and leaves (0.07% and 0.06%, respectively) (7). Two compounds not reported to be present in the bark and leaves, but present in the roots, are macrocarpamine and norfluorocurarine.



1

A new minor (0.13%) component isolated from the roots has been identified as the ester 4′-hydroxy-3′,5′-dimethoxybenzoylvincamajine [**1**]. The uv spectrum of **1** was similar to that of vincamajine, and the presence of a phenolic group was indicated by color reactions with $FeCl_3$ and a bathochromic shift in the uv spectrum upon addition of a few drops of 0.1 N NaOH. The ^1H

nmr showed the presence of a two-proton (aromatic) singlet at δ 7.15 and a singlet at δ 3.92 for two OMe substituents. A singlet at δ 5.88 showed a downfield shift of the C-17 proton (δ 4.25 in vincamajine), while the rest of the spectrum was similar to that of vincamajine. The eims and fabms of **1** gave a mol wt of 546 while the hrms gave a mol wt of 546.2371, calcd 546.2367 for $C_{31}H_{34}N_2O_7$. Fragmentation into two main peaks at *m/z* 365 (vincamajine base, $C_{22}H_{25}N_2O_3$) and *m/z* 181 ($C_9H_9O_4$, arylacyl part) and peaks at *m/z* 349 (loss of O from vincamajine base) and *m/z* 153 (loss of CO from arylacyl part) are typical of the vincamajine esters. The presence of benzoylvincamajine (8) and 3′,4′,5′-trimethoxybenzoylvincamajine (9), has been reported before in other species of *Alstonia*.

Extensive work on the antiamebic and antiplasmodial activities of each of the alkaloids isolated above has been reported elsewhere (10).

EXPERIMENTAL

PLANT MATERIAL AND INSTRUMENTATION.—Stem bark and roots of *A. angustifolia* were collected in the southern state of Johore, and a voucher specimen was deposited in the Herbarium of the Department of Botany, Universiti Kebangsaan Malaysia. Nmr spectra were measured on a Bruker WH-400 instrument in $CDCl_3$, and resonances were referenced to TMS. Ms were obtained with a VG ZABIF spectrometer.

EXTRACTION AND ISOLATION.—Fresh stem bark (500 g) and roots (350 g) were extracted for their alkaloids according to the procedures described previously (3). Compounds were isolated by a combination of cc (Si gel 230–400 mesh, Merck) and preparative tlc using $CHCl_3$/MeOH mixtures as eluents and developing solvents. From the crude mixture (2.8 g) of root alkaloids the following were isolated: alstonerine (0.53 g), alstophylline (20.9 mg), vincamajine ester [**1**] (3.9 mg), vincamajine (3.0 mg), villastonine (241.1 mg), macralstonine (81.2 mg), pleiocarpamine (5.3 mg), macrocarpamine (10.0 mg), norfluorocurarine (5.0 mg), and 11-methoxyakuammicine (10.0 mg).

4′-Hydroxy-3′,5′-dimethoxybenzoylvincamajine [**1**].—Uv (MeOH) λ max 248, 290 nm; +0.1 N NaOH 250, 295, 335 nm; ^{1}H nmr ($CDCl_3$) δ 1.58 (d, 3H, *J* = 7 Hz, Me-18), 2.69 (s, 3H, N-Me), 3.41 (s, 3H, CO_2Me), 3.92 (s, 6H, OMe), 5.37 (br s, 1H, H-19), 5.88 (s, 1H, H-17), 6.56 (t, 1H, *J* = 7 Hz, H-11), 6.65 (d, 1H, *J* = 7 Hz, H-12), 6.85 (d, 1H, *J* = 7 Hz, H-9), 7.13 (t, 1H, *J* = 7 Hz, H-10), 7.15 (s, 2H, *J* = 7 Hz, H-2′, H-6′); ms *m/z* (%) $[M]^+$ 546.2371 (52), 365 (24), 349 (17), 338 (11), 197 (26), 181 (100), 157 (36), 153 (34), 144 (48).

ACKNOWLEDGMENTS

This study was partly funded by IRPA 4-07-03-005, IFS F/1082-1, and the British Council under its CICHE programme. IMS thanks the Association of Commonwealth Universities for funds which assisted him in carrying out a major part of this work in London.

LITERATURE CITED

1. I.H. Burkill, "A Dictionary of the Economic Products of the Malay Peninsula," Ministry of Cooperatives, Kuala Lumpur, 1966, p. 113.
2. L.M. Perry and J. Metzger, "Medicinal Plants of East and Southeast Asia," MIT Press, Cambridge, 1980, p. 22.
3. I.M. Said, A. Latiff, S.J. Partridge, and J.D. Phillipson, *Planta Med.*, **57**, 389 (1991).
4. M. Ghandi and V.K. Vinayak, *J. Ethnopharmacol.*, **29**, 51 (1990).
5. S.O. Awe and O.O. Opeke, *Fitoterapia*, **61**, 225 (1990).
6. M.J. ONeill, D.H. Bray, P. Boardman, K.L. Chan, and J.D. Phillipson, *J. Nat. Prod.*, **50**, 41 (1987).
7. K. Ghedira, M. Zeches-Hanrot, B. Richard, G. Massiot, L. Le Men-Olivier, T. Sevenet, and S.H. Goh, *Phytochemistry*, **27**, 3955 (1988).
8. G. Lewin, N. Kunesch, J. Poisson, and T. Sevenet, *J. Indian Chem. Soc.*, **55**, 1096 (1978).
9. B. Mukherjee, A.B. Ray, and A. Mukherjee, *Chem. Ind.*, 138 (1969).
10. C.W. Wright, D. Allen, Ya Cai, J.D. Phillipson, I.M. Said, G.C. Kirby, and D.C. Warhurst, *Phytother. Res.*, **6**, 121 (1992).

Received 12 February 1992