23. W. Jennings and T. Shibamoto, "Qualitative Analysis of Flavor and Fragrance Volatiles by Glass Capillary Gas Chromatography," Academic Press, London, 1980.
24. M.G. Moshonas and E.D. Lund, *Flav. Ind.*, 375 (1970).
25. A.M. Geisbrecht, N.C. Franca, and O.R. Gottlieb, *Phytochemistry*, **13**, 2285 (1974).
26. G.M. Sammy and W.W. Nawar, *Chem. Ind.*, 1279 (1968).

Received 30 January 1987

JASPAMIDE FROM THE MARINE SPONGE *JASPIS JOHNSTONI*[1]

J.C. BRAEKMAN, D. DALOZE, B. MOUSSIAUX,

Unité de Chimie Bio-organique, Faculté des Sciences, Université Libre de Bruxelles, 1050 Bruxelles, Belgim

and R. RICCIO

Dipartimento di Chimica delle Sostanze Naturali, Universita degli Studi di Napoli, Napoli, Italia

Until now, a limited number of sponges of the genus *Jaspis* (Jaspidae) have been investigated for their content in secondary metabolites. Several bright yellow triterpenes derived from the rare malabaricane skeleton have been reported from Fijian (1) and Great Barrier Reef (2) collections of *Jaspis stellifera*. Very recently, jaspamide, a cyclic depsipeptide, has been isolated by two independent groups from an unspecified *Jaspis* species collected off the Fiji and Palau Islands (3,4).

Jaspamide exhibited potent insecticidal, antifungal, anthelminthic, and in vitro cytotoxic activities (3,4). In the course of our systematic search for toxic derivatives from marine sponges (5), we have observed that the CH_2Cl_2 extract of the New Guinean marine sponge *Jaspis johnstoni* Schmidt (syn. *Zapethea digonoxea*) is toxic for the freshwater fish *Lebistes reticulatus* (LD<5 mg/liter). Fractionation of this extract monitored by toxicity testing led to the isolation of a single derivative whose spectral properties were identical to those of jaspamide.

EXPERIMENTAL

BIOLOGICAL MATERIAL.—Specimens of *J. johnstoni* (550 g dry weight) were collected off Laing Island, Madang Province, Papua, New Guinea. The sponge has been authenticated by Dr. P.A. Thomas (India) and Dr. J. Vacelet (Marseille, France). A voucher specimen has been deposited in the Laboratory of Bio-organic Chemistry of the University of Brussels (no XIV.9).

EXTRACTION AND ISOLATION.—Sun-dried, ground sponges (350 g) were exhaustively extracted at room temperature with CH_2Cl_2 to give a residue (2.08 g) that was chromatographed on a Si gel column using increasing concentrations of Me_2CO in hexane. The fractions showing toxicity against the freshwater fish *L. reticulatus* (6) were pooled and chromatographed on a second Si gel column using increasing concentrations of Et_2O in CH_2Cl_2 to give jaspamide (54 mg) as a colorless solid homogenous on tlc and hplc [$C_{36}H_{45}N_4O_6$ Br by hrfabms; uv (MeOH) λ max at 220 (42,340), 275 (9,190), 289 nm (7,015); ir (film) characteristic bands at 3300, 1710, 1670, 1635, 1620, 1510, 830, 740 cm^{-1}].

Analysis of the $^1H/^1H$ and $^1H/^{13}C$ correlated 2D-nmr spectra (COSY and COLOC) and nOe experiments as well as microhydrolysis results (HCl 6N and CH_3SO_3H 4N) led to the conclusion that the compound is a depsipeptide containing a tripeptide moiety linked to a polyketide chain. At this stage of the work two papers (3,4) appeared describing the isolation of jaspamide from an unspecified *Jaspis* species. Comparison of the spectral data of our compound with those reported for jaspamide established the identity of the two compounds.

ACKNOWLEDGMENTS

This work was supported by a NATO grant for collaborative research (Ref. D.210/86). The Belgian authors are indebted to the FNRS for financial support (Grant no. 2.4515.85). M.B. expresses her sincere thanks to the IRSIA for financial support.

[1]King Leopold III Biological Station, Laing Island, Papua New Guinea, Contribution No. 137.

LITERATURE CITED

1. B.N. Ravi, R.J. Wells, and K.D. Croft, *J. Org. Chem.*, **46**, 1998 (1981).
2. B.N. Ravi, R.J. Wells, *Aust. J. Chem.*, **35**, 39 (1982).
3. T.M. Zabriskie, J.A. Klocke, C.M. Ireland, A.H. Marcus, T.F. Molinski, D.J. Faulkner, C. Xu, and J.C. Clardy, *J. Am. Chem. Soc.*, **108**, 3123 (1986).
4. P. Crews, L.V. Manes, and M. Boehler, *Tetrahedron Lett.*, **27**, 2797 (1986).
5. J.C. Braekman and D. Daloze, *Pure Appl. Chem.*, **58**, 357 (1986).
6. J.C. Braekman, D. Daloze, M. Kaisin, and B. Moussiaux, *Tetrahedron*, **41**, 4603 (1985).

Received 2 February 1987

STUDIES ON ZOAPATLE, VII. ANGELOYLGRANDIFLORIC ACID, A SPONTANEOUS UTERINE CONTRACTION INHIBITOR (SUCI) FROM *MONTANOA TOMENTOSA* SSP. *TOMENTOSA*[1]

ZHI-ZHEN LU,[2] HUI-ZHONG XUE,[3] ZHI-BEN TU,[4] CHOHACHI KONNO,[5] DONALD P. WALLER, D.D. SOEJARTO, GEOFFREY A. CORDELL,* and HARRY H.S. FONG

Program for Collaborative Research in the Pharmaceutical Sciences, College of Pharmacy, University of Illinois at Chicago, Chicago, Illinois 60612

As part of our ongoing investigation of *Montanoa tomentosa* Cerv. ssp. *tomentosa* (Compositae), several fractions and isolates have been tested in guinea pigs for both in vitro activity [uterine stimulant (US^+), spontaneous uterine contraction inhibitory ($SUCI^+$)] and in vivo activity [uterine evacuation (UE^+)]. Kaur-9(11),16-dien-19-oic acid, isolated from the leaves of *M. tomentosa*, had previously been reported to be US^+ (1), which activity was confirmed in our laboratory (2,3). However, both this compound and its methyl ester derivative were shown to be UE^- (2,3). Zoapatanolide A and zoapatanol, on the other hand, were shown to be $SUCI^+$ and UE^+ (2,3), although a further compound, tomexanthin, was found to be $SUCI^+$ and UE^-. The present study was undertaken in an attempt to isolate further constituents which might have the desired in vivo (UE^+) activity and to determine how such activity might correlate with in vitro results; chemical modification was anticipated for isolates, as appropriate, prior to testing in vivo.

Isolated during the course of this study were the kaurene diterpenes, (−)-kaur-16-en-19-oic acid, (−)-kaur-9(11),16-dien-19-oic acid (grandiflorenic acid), monoginoic acid, grandifloric acid (grandiflorolic acid), and angeloylgrandifloric acid (angeloylgrandiflorolic acid), as well as the ubiquitous sterol stigmasterol. In addition, methyl kaur-16-en-19-oate was prepared by methylation of (−)-kaur-16-en-19-oic acid. (−)-Kaur-16-en-19-oic, kaur-9(11),16-dien-19-oic, and monoginoic acids had been found in this plant previously (4), whereas the occurrence of grandifloric and angeloylgrandifloric acids in this genus is being reported for the first time.

In vitro bioassay showed that angeloylgrandifloric acid inhibited the spontaneous contractions of guinea pig uterine strips ($SUCI^+$) at a concentration of 1.2 mg/ml, whereas (−)-kaur-16-en-19-oic and monoginoic acids were inactive ($SUCI^-$) at concentrations of 4.0 and 4.6 mg/ml. The desire to conserve material for in vivo evaluation precluded the testing of methyl kaur-16-en-19-oic acid in vitro at this time. In the in vivo, 22-day, pregnant guinea pig bioassay, methyl kaur-16-en-19-oic and angeloylgrandifloric acids were both found to be inactive (UE^-) at the dose of 100 mg/kg i.p. Previously, we had shown kaur-9(11),16-dien-19-oic acid and its methyl ester to be UE^- at doses of 100 and 200 mg/kg, respectively (2,3); we had tested only the former in vitro and had reported it to be US^+ at a concentration of 0.21 mg/ml. Paucity of material precluded in vivo testing at this time of (−)-kaur-16-en-19-oic acid and monoginoic acid and any testing of grandifloric acid.

---

[1]For the previous paper in this series see Fong *et al.* (3).

[2]Present Address: Shanghai Institute of Materia Medica, Academia Sinica, Shanghai, People's Republic of China.

[3]Present Address: Nanjing Institute of Materia Medica, Nanjing, People's Republic of China.

[4]Present Address: Wuhan Institute of Botany, Wuhan, People's Republic of China.

[5]Present Address: Faculty of Pharmaceutical Sciences, Tohoku University, Sendai, Japan.