PLANT ANTICANCER AGENTS. XI.[1] 2,6-DIMETHOXYBENZOQUINONE AS A CYTOTOXIC CONSTITUENT OF *TIBOUCHINA PULCHRA*

ELLERY JONES, OLUSEGUN EKUNDAYO and DAVID G. I. KINGSTON*

Department of Chemistry, Virginia Polytechnic Institute and State University, Blacksburg, VA 24061

As part of a systematic search for anticancer agents from natural sources, we examined the woody stems of *Tibouchina pulchra* (Cham.) Cogn. (=*Lasiandra pulchra* Cham.) (Melastomataceae) for cytotoxic constituents.

Extraction of the ground plant material with ethanol followed by liquid-liquid partition of the ethanol fraction between chloroform and water and of the chloroform fraction between 90% aqueous methanol and hexane yielded a methanol fraction which showed an ED_{50} of 37 μg/ml in KB cell culture, and an aqueous fraction had an ED_{50} of 5.5 μg/ml in KB cell culture. Attempts at purification of the aqueous fraction by a variety of mild techniques yielded only inactive mixtures, but separation of the methanol fraction by chromatography on silica gel yielded a fraction which showed an ED_{50} of 2.5 μg/ml in KB cell culture. Purification of this fraction by preparative thin-layer chromatography yielded a compound identified as 2,6-dimethoxybenzoquinone as the only identifiable cytotoxic material.

2,6-Dimethyoxybenzoquinone has previously been reported as a cytotoxic constituent of *Xylosma veluntina* (1), and the cytotoxicity of benzoquinones has been tabulated in a summary review (2).

[1]For Part X, see D. A. Cairnes, O. Ekundayo, and D. G. I. Kingston, *J. Nat. Prod.*, **43**, 495 (1980).

EXPERIMENTAL[2]

PLANT MATERIALS.—Dried stems of *T. pulchra* (family Melastomataceae: B 678547, PR 47923) were collected in Brazil and authenticated by the Economic Botany Laboratory, USDA, Beltsville, Maryland. An herbarium specimen documenting this collection is deposited in the Herbarium of the National Arboretum, Agricultural Research Service, USDA, Washington, DC. The material was ground in a hammermill.

ISOLATION AND IDENTIFICATION OF 2,6-DIMETHOXYBENZOQUINONE.—The aqueous methanol fraction described above (15 g) was subjected to chromatography on silica gel, with elution by chloroform and chloroform-methanol. The first fraction eluted with chloroform (3g) had an ED_{50} of 2.6 μg/ml in the KB cell culture. Purification of a 200 mg portion of this fraction by preparative tlc (silica gel, chloroform-methanol, 98:2) yielded crystals (11 mg, 1.1% of aqueous methanol fraction), which were sublimed *in vacuo* to give material with mp 253° (lit. (3) 254°). The material had an identical ir spectrum and identical retention time on hplc (CH_3CN-H_2O, 55:50, EM Labs RP-8 column) as an authentic sample,[3] and its nmr, uv, and mass spectral data were consistent with its formulation as 2,6-dimethoxybenzoquinone, $C_8H_8O_4$.

2,6-Dimethoxybenzoquinone (NSC-56336) has been reported as having an ED_{50} of 2.8 μg/ml in KB cell culture (1). Our sample, although having a higher melting point, had an essentially identical ED_{50} value of 3.1 μg/ml.

ACKNOWLEDGMENTS

This work was supported by grant number CA 12831 awarded by the National Cancer Institute and by a Public Health Service International Research Fellowship to O. E. (1 FO5 TWO2594-01). E. J. was supported as an undergraduate research participant

[2]General experimental details are given in part III of this series. D. G. I. Kingston, B. T. Li, and F. Ionescu, *J. Pharm. Sci.*, **66**, 1135 (1977).

[3]Kindly provided by Dr. H. H. S. Fong, University of Illinois.

on National Science Foundation Grant No. 7827277. The authors thank Dr. H. H. S. Fong, University of Illinois, for a sample of 2,6-dimethoxybenzoquinone. Receipt of plant material from the U. S. Department of Agricultural Economic Botany Laboratory *via* Dr. Monroe E. Wall is acknowledged with thanks.

Received 19 November 1980

LITERATURE CITED

1. G. A. Cordell, P. T. O. Chang, H. H. S. Fong, and N. R. Farnsworth, *Lloydia*, **40**, 340 (1977).
2. J. S. Driscoll, G. F. Hazard, Jr., H. B. Wood, Jr., and A. Coldin, *Cancer Chemother. Rep. Pt.* **2**, **4** (2), 1 (1974).
3. H. Richtzenhain, *Chem. Ber.*, **77**, 409 (1944).