Phytochemistry, Vol 27, No 5, pp 1563–1564, 1988
Printed in Great Britain

0031–9422/88 $3 00 + 0 00
Pergamon Press plc

CYTOTOXIC APORPHINOID ALKALOIDS FROM *THALICTRUM SESSILE**

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(*Received* 9 *September* 1987)

Key Word Index—*Thalictrum sessile*, Ranunculaceae, alkaloids; liriodenine, (+)-thalifarazine

Abstract—Two cytotoxic aporphinoid alkaloids, liriodenine and (+)-thalifarazine, were isolated from the *Thalictrum sessile* Hayata. Liriodenine, isolated for the first time from the family Ranunculaceae, showed potent cytotoxicity against human lung carcinoma A-549 and human colon tumour HCT-8 at 0.7 μg/ml.

Thalictrum sessile Hayata (Ranunculaceae), a 60 cm tall perennial herb, is endemic to Taiwan [1]. In a previous communication, the roots of this plant were found to contain two new C_{20}-diterpene alkaloids thalicsessine [2] and thalicsiline [3] of the spiradine and the ajaconine type, respectively As a result of our continuing searches for novel plant antitumour agents, the alcoholic extract of the aerial part of *T. sessile* was found to show significant cytotoxicity against *in vitro* tissue culture cells in human KB, A-549 lung carcinoma and HCT-8 colon tumour as well as in murine P-388 and L-1210 lymphocytic leukaemia. Bioassay—directed fractionation of the foregoing active extract led to the isolation and characterization of two cytotoxic aporphinoid alkaloids liriodenine (**1**) (i.e. oxoushinsunine) and (+)-thalifarazine (**2**). Liriodenine is the most widely distributed oxoaporphine alkaloid which has been thus far isolated from the families of Annonaceae, Araceae, Eupomatiaceae, Lauraceae, Magnoliaceae, Menispermaceae, Monimiaceae, Nymphaceae, Papaveraceae, Rhamnaceae and Rutaceae [4–9]. (+)-Thalifarazine has recently been isolated from *Thalictrum cultratum* by Hussain *et al* [10]. Liriodenine (**1**) demonstrated potent cytotoxicity against KB, A-549, HCT-8, P-388 and L-1210 with ED_{50} values of 1.00, 0 72, 0.70, 0.57 and 2.33 μg/ml, respectively (+)-Thalifarazine (**2**) showed cytotoxicity with ED_{50} (KB) = 1.50, (HCT-8) = 4 30, (A-549) = 6.53, (P-388) = 3.75 and (L-1210) = 5.69 μg/ml. Liriodenine is isolated for the first time from the family of Ranunculaceae.

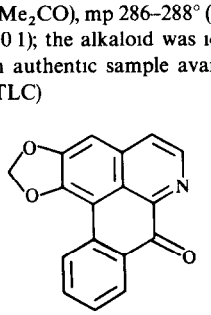
EXPERIMENTAL

Mp uncorr. Optical rotations were taken in MeOH solns ^{1}H NMR spectra were run in $CDCl_3$ at 400 MHz with chemical shifts recorded in ppm (δ).

Plant material. The plant *T sessile* Hayata used in this investigation was collected from Mt Yuh (Yuh-Shan), Taiwan in July, 1976 A voucher specimen is kept in the School of Pharmacy, Kaohsiung Medical College, Taiwan, Republic of China

Extraction and isolation The air-dried aerial part of *T sessile* (3 6 kg) was extracted with 95% EtOH Bioassay-directed fractionation of the resulting alcoholic extract led to the identification of the cytotoxic alkaloidal fractions Separation of these alkaloids by standard methods [11] gave rise to a nonphenolic fraction which showed significant cytotoxicity Subsequent repeated CC over silica gel and prep TLC using $CHCl_3$ and $CHCl_3$–MeOH–NH_4OH (10 1 : 0 1) as the eluting solvents, led to the isolation of liriodenine (**1**, R_f = 0.72) and (+)-thalifarazine (**2**, R_f = 0 63), respectively

Liriodenine (**1**) Compound **1** was isolated as yellow micro needles 12 mg (Me_2CO), mp 286–288° (lit. 282–284°) [11]; $[\alpha]_D^{24}$ ±0° (MeOH, *c* 0 1); the alkaloid was identified by direct comparison with an authentic sample available in our laboratory (mmp, IR and TLC)



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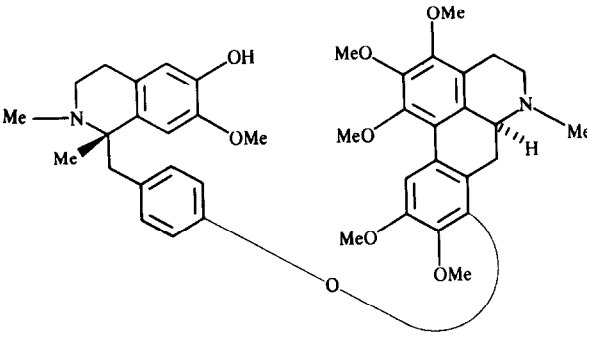

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(+)-*Thalifarazine* (**2**) This compound was obtained as yellowish white amorphous powders 8 mg, $[\alpha]_D^{24}$ +48° (MeOH, *c* 0 1) This alkaloid was characterized by spectral (UV, IR, ^{1}H NMR and MS) analyses and comparison with literature data [10]

Biological evaluation The cytotoxicity assay was carried out according to a procedure described in literature [12]

Acknowledgements—We thank Prof I S Chen, School of Pharmacy, Kaohsiung Medical College, for the identification and collection of plant material This investigation was supported by a grant from the National Cancer Institute (CA 17625) awarded to K H Lee

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Phytochemistry, Vol 27 No 5 pp 1564 1566, 1988
Printed in Great Britain

0031 9422/88 $3 00+0 00
Pergamon Press plc

PLANT GROWTH INHIBITING PROPERTIES OF PHALAENOPSINE T FROM *PHARAENOPSIS* SPP

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(*Revised received* 6 *October* 1987)

Key Word Index—*Phalaenopsis* spp, Orchidaceae, pyrrolizidine alkaloid, phalaenopsine T, growth inhibitory activity

Abstract—A pyrrolizidine alkaloid, phalaenopsine T was identified as a growth inhibitory compound contained in *Phalaenopsis* spp using the lettuce seedling and *Calanthe* seedling tests

INTRODUCTION

In continuing studies on growth inhibitors of plants, we have already reported the isolation of eucomic acid and hydroxyeucomic acid from *Cattleya trianaei* [1, 2] and *p*-coumaroyl ester of 2,3-dihydroxy-1,2-propanedicarboxylic acid and diferuloylsucrose from *Lilium longiflorum* [3. 4] In the case of *Phalaenopsis* spp, the growth of the shoot tip is occasionally inhibited during the shoot tip culture The growth inhibitor was detected by the lettuce seedling and the *Calanthe biscolor* (Orchidaceae) seedling test and localized in the alkaline fraction The following report deals with the isolation of a constituent with significant plant growth inhibiting activity which was shown to be identical with the pyrrolizidine alkaloid, phalaenopsine T[5]

RESULTS AND DISCUSSION

A methanol extract (Fr 1) of sliced fresh leaves of *Phalaenopsis* spp was extracted with ether (Fr. 2) and ethylacetate (Fr. 3) successively under acidic condition and then chloroform (Fr 4) and *n*-butanol (Fr 5) successively under alkaline conditon The inhibiting assay for individual fraction was carried out using the lettuce