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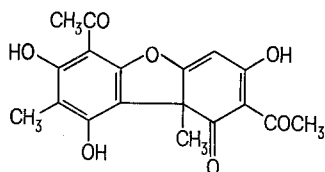
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l-Usnic Acid: Tumor Inhibitor Isolated from Lichens¹

Lichens have been used to treat cancers from the time of ABU MANSUR (circa A.D. 970), and references to their use in folk medicine have appeared in the herbal literature of many countries².

In the course of our continuing search for tumor inhibitors of plant origin, an alcohol-water (1:1) extract of the lichen *Cladonia leptoclada* des. Abb. (Cladoniaceae)³ from New Zealand showed significant inhibitory activity when tested in mice against the Lewis lung carcinoma. We report herein the fractionation of an active extract and the characterization of the principal tumor-inhibitory constituent, which is identified as *l*-usnic acid. *l*-Usnic acid shows significant inhibitory activity against the Lewis lung carcinoma, when administered as a suspension in Gum Acacia.

Evaluation of assay results on a statistical basis in sequential testing is such that a material is considered active if it causes an increase in survival of treated animals (T) over controls (C) resulting in a T/C \geq 125%. Results corresponding to T/C-values of 135–152% were found upon treatment with *l*-usnic acid in the 20–200 mg/kg dose range⁴.



Structure of *l*-usnic acid.

Alcohol extraction of the dried plant (1 kg) yielded a residue (195 g) which was partitioned between chloroform and water. The tumor-inhibitory activity was found to have been concentrated in the chloroform solubles (57 g). When the latter solids were treated with 10% aqueous methanol and Skellysolve B, the insoluble residue (20 g) was found to be most active. Crystallization of this solid from chloroform-methanol yielded *l*-usnic acid (8 g), characterized by comparison of melting point, specific rotation in chloroform, and nuclear magnetic resonance

and infrared spectra, with those described for *l*-usnic acid^{5,6}.

Several species of *Cetraria* have been used in the treatment of cancer², and *Cetraria* is known to be a rich source of *l*-usnic acid⁵. It will be of interest to determine whether the optical antipode, *d*-usnic acid, found in numerous *Usnea* species used in folk medicine^{2,7}, is also active as a tumor inhibitor⁸.

Zusammenfassung. Die systematische Fraktionierung eines Alkoholauszugs der Flechte *Cladonia leptoclada* ergab, dass *l*-Usninsäure der hauptsächliche tumorhemmende Bestandteil ist.

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Charlottesville (Virginia 22901, USA), 4 February 1975.

¹ Tumor Inhibitors. 105. For previous paper in the series, see C. H. LANTZ, J. G. KALPAXIS, J. LARNER, R. M. SCHUBERT and S. M. KUPCHAN, *Biochem. Pharmacol.*, in press.

² J. L. HARTWELL, *Lloydia* 34, 386 (1971).

³ Thalli of *Cladonia leptoclada* were collected in New Zealand in June, 1965. We thank Dr. ROBERT E. PERDUE JR., U.S. Department of Agriculture, Beltsville, Md., for supplying the plant material.

⁴ Tumor-inhibitory activity was assayed under the auspices of the National Cancer Institute as described by R. I. GERAN, N. H. GREENBERG, M. M. McDONALD, A. M. SCHUMACHER and B. J. ABBOTT, *Cancer Chemother. Rep.* part 3, 3, 1 (1972).

⁵ W. KARRER, *Konstitution und Vorkommen der organischen Pflanzenstoffe* (Birkhäuser Verlag, Basel 1958), p. 710.

⁶ S. FORSEN, M. NILSEN and C. WACHTMEISTER, *Acta chem. scand.* 16, 583 (1962).

⁷ K. ADACHI, Japanese Patent 73 16, 603; *Chem. Abstr.* 80, 30695z (1974).

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