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# ANTITUMOR AGENT FROM PENSTEMON DEUTUS DOUGL. EX LINDL. (SCROPHULARIACEAE): PENSTEMIDE, A NOVEL IRIDOID-TYPE GLUCOSIDE

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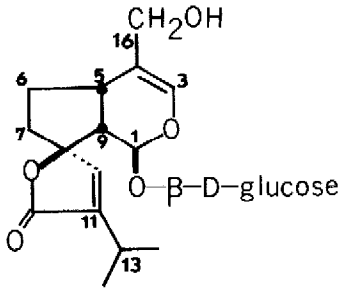
As a result of the continuing search for plants having antitumor activity, an ethanol extract of the root, stems, leaves, flowers, and fruit of Penstemon deutus Dougl. ex Lindl. (Scrophulariaceae) was found to exhibit activity against the P-388 lymphocytic leukemia test system (PS) of the Drug Evaluation Branch, Drug Research and Development, Division of Cancer Treatment, National Cancer Institute, National Institutes of Health, Department of Health, Education, and Welfare, Bethesda, MD.

Penstemide (I) was the major component isolated by solvent extraction, partition, $SiO_2$-60 column chromatography, and preparative thin-layer chromatography. Hydrolysis, catalyzed by acid or β-glucosidase, gave β-D-glucose (confirmed by thin-layer and paper chromatography comparison with an authentic sample) and a highly unstable aglycone moiety.

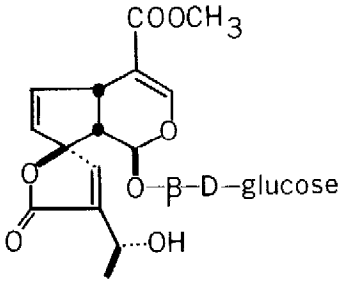
Carbon-hydrogen analysis of I indicated an empirical formula of $C_{21}H_{30}O_{10}.H_2O$ (calc: C, 54.54, H, 6.93; found: C, 54.52, H, 7.09). The presence of an α,β-unsaturated-γ-lactone ring was established by the UV spectrum ($\lambda_{max}$ 214, $\log \varepsilon = 4.33$) and IR spectrum (1750 and 1665 $cm^{-1}$). CMR spectra (22.6 MHz, broad-band decoupled and off resonance) confirmed the presence of 21 carbon atoms: δ174.9 (carbonyl), 142.0 (C11), 115.8 (C4), 140.4 and 130.4 (2 monosubstituted vinylic carbons), 102.1 (C1), 69.1 (quaternary carbon attached to oxygen), 93.1, 76.7 (2), 74.1, 70.5, and 61.6 (6 glucose carbons), 60.5 (alcoholic methylene group), 43.7 and 37.3 (2 methylene groups), 46.4, 36.8, and 26.1 (3 methinyl groups), and 22.5 (2 methyl groups)[1]. The PMR spectra (60 and 100 MHz, $D_2O$) account for 32 protons: δ6.4 (s, 1H, C3), 5.8 (s, 1H, C10), 5.7(d: J=8Hz, 1H, C1), 4.3(d: J=7.Hz, 1H, glucose C1), 4.1(d: J=4Hz, 2H, C16), 2.0 (m, 1H, C13), 0.8(d: J=6Hz, 6H, 2 methyls), 2.2-3.1 (m, 6H, C5,6,7, and 9), 3.2-3.9 (m, 6 glucose protons), and 4.7(s, HOD, 7H). Spin-spin decoupling confirmed the presence of the isopropyl group (2.0 and 0.8), that the proton

at 5.7 was coupled to a proton at 2.3, and that the glucose C1 proton at 4.3 was coupled to a proton absorbing at δ3.3. The relative configuration between C1 and C9 is consistent with the large (8 Hz) coupling constant observed between the attached protons.

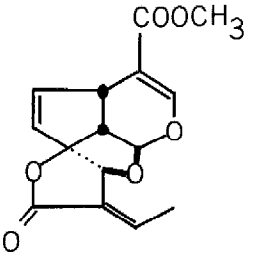
The only biogenetically reasonable structure consistent with the above data is I, closely related to plumeride[2] (II) and the antibiotic plumericin[3] (III).




I




II




III

Penstemide exhibited an activity of 184% T/C (test/control) at 50 mg/kg in the PS test system. Activity in the PS system is defined as T/C $\geq$ 125%[4].

References

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Acknowledgements

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