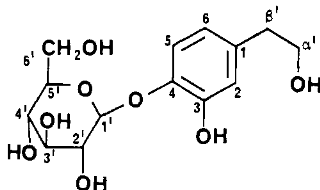
LEMAIRIN, A NEW GLUCOSIDE FROM THE MEXICAN CACTUS, *PACHYCEREUS WEBERI*

RACHEL MATA and JERRY L. MCLAUGHLIN*

Department of Medicinal Chemistry and Pharmacognosy, School of Pharmacy and Pharmacal Sciences, Purdue University, West Lafayette, Indiana 47907

ABSTRACT.—Lemairin (1), β-[4-(β-D-glucopyranosyloxy)-3-hydroxyphenyl]-ethanol, has been crystallized from the phenolic fraction of an ethanol extract of the title plant. This novel glucoside may be involved in the rapid darkening characteristic of damaged tissues in certain cactus species.

In our search for new cactus alkaloids (1) a simple glucoside, lemairin (**1**), was isolated from the giant Mexican cactus, *Pachycereus weberi* (Coult.) Backeb. [syn. *Lemaireocereus weberi* (Coult.) Br. and R.]. Lemairin crystallized directly (0.018% yield) from the phenolic fraction of condensed percolates of the field-dried and defatted plant material. The compound was homogeneous (six tlc systems); its high water solubility, a positive Molisch test, and a bathochromic shift in base in the uv spectra suggested a phenolic glucoside. After hydrolysis of **1** with a β-glycosidase, glucose was identified (tlc); the aglycone rapidly darkened in air suggesting a catechol function.



1

Acidic hydrolysis of **1** under nitrogen permitted determination of the exact mass of the aglycone (EIms *m/z* 154.066, $C_8H_{10}O_3$). Methylation of **1**, followed by acidic hydrolysis, produced the aglycone with one additional methyl group (*m/z* 168) which was located on the phenolic ms fragment (*m/z* 137). Field desorption ms (FDms) was necessary to determine the molecular formula of the entire glycoside [*m/z* 339; $(M+Na^+)$]. The ir spectrum of **1** confirmed the expected polyhydroxylation and aromaticity (C=C stretching).

^{13}C nmr spectra (coupled and decoupled) confirmed the presence of 14 carbon atoms, six of which were readily assigned to β-D-glucose (2). That the glucose was attached to position 4, rather than position 3, was determined by comparison of the ^1H nmr spectra with those reported for dopamine-3-*O*-glucoside and dopamine-4-*O*-glucoside (3). Routine assignments of the ^1H nmr and ^{13}C nmr shifts permitted the conclusion that lemairin is β-[4-(β-D-glucopyranosyloxy)-3-hydroxyphenyl]-ethanol.

Lemairin is apparently a new natural product although the aglycone, 3,4-dihydroxy-β-phenylethanol, has been reported as part of very complex glycosides in *Magnolia grandiflora* L. (Magnoliaceae) (4). The darkening of certain cacti upon injury (5) is not understood chemically but has been traditionally attributed

to an oxidation of dopa and/or dopamine. We now believe that lemairin and its aglycone may be involved in this darkening process; thus, air oxidation to colored quinones of the aglycone of lemairin, rather than of dopa and/or dopamine, may explain the darkening reaction. Nevertheless, the biosynthesis of the aglycone would seem to involve possible transamination of dopamine followed by reduction. In our previous work with the alkaloids of this species (1), we isolated eight tetrahydroisoquinolines but none of the expected precursor β-phenethylamines; perhaps this species converts its β-phenethylamines into β-phenylethanol derivatives such as lemairin. The similarity of the aglycone of lemairin to dopamine and the presence of glucose as a possible carrier might elicit some interesting pharmacologic action.

The susceptibility of lemairin and cactus glucoalkaloids, such as pterocereine (6), to acidic hydrolysis suggests that future phytochemical fractionations should avoid work ups involving strong acids; some previously isolated natural phenolic substances may in actuality be extraction artifacts of natural glycosides such as lemairin.

EXPERIMENTAL[1]

PLANT MATERIAL.—Field-dried specimens of shredded *P. weberi* were received from the Medicinal Plant Resources Laboratory, Agriculture Research Center, USDA, Beltsville, Maryland, in March, 1976. The plant material was collected by Edward H. Sallee near Puebla, Mexico, in November, 1975. Reference specimens are maintained at the Agriculture Research Center, and reference photographs are on file at Purdue University. The dried shredded material was ground through a 2 mm screen in a Wiley mill.

EXTRACTION AND ISOLATION.—A total 2 kg of the powdered plant material was defatted (Soxhlet, 3 days) with petroleum ether. The dried marc was percolated with ethanol to yield 145.3 g of residue after vacuum evaporation. A portion (140 g) of the ethanol residue was redissolved in ethanol and resolved into phenolic and nonphenolic fractions using a 9 x 178 cm glass column containing 1 kg of Amberlite IRA 401S (hydroxide form) (7). The phenolic fraction (2.5 g) was dissolved in warm ethanol and, overnight, yielded 0.5 g of brown crystals. Recrystallization from hot ethanol yielded 350 mg of **1** (0.018% yield, mp 175°, positive Molisch test, homogeneous in six tlc systems); during tlc analysis, **1** produced an orange-brown chromophore with tetrazotized benzidine (7) and a pale white color with iodoplatinate (8).

ACID HYDROLYSIS OF **1**.—Several attempts to hydrolyze **1** and isolate the aglycone failed because of the rapid decomposition of the hydrolysis product in air (darkening with alteration of the uv spectra). Finally 10 mg of **1** was refluxed under nitrogen for 1 hr with 2 ml of 2 N sulfuric acid. The acid solution was extracted with two 3 ml-portions of ethyl acetate, and the ethyl acetate extract was washed twice with 4 ml of 5% aqueous sodium bicarbonate. The extract was then concentrated under nitrogen and submitted for mass spectral analysis [EIms, *m/z* (%): 154(3), 137(13), 123(100), 124(21), and 77 (11)]. Completeness of hydrolysis was indicated by tlc (silica gel, n-butanol-benzene-methanol-water, 4:4:4:1).

ENZYMATIC HYDROLYSIS OF **1**.—Varying amounts of **1** dissolved in water were mixed with adequate amounts of emulsin (Calbiochem) and phosphate buffer (pH 4). The mixtures were incubated usually for 48 hr at 40°. The completeness of the hydrolysis was monitored by tlc. Glucose was readily identified by tlc in the hydrolysates (6).

METHYLATION OF **1**.—20 mg of **1** was dissolved in 5 ml of methanol and an ethereal solution of diazomethane was added. The solution was allowed to stand for 48 hr under refrigeration and was then concentrated to dryness leaving a glassy solid. This residue was recrystallized

[1]Melting points were determined on a Mel-Temp capillary tube apparatus and are uncorrected. Uv absorption spectra were obtained on a Perkin-Elmer double beam spectrometer. Ir spectra were determined on a Beckman IR-33 using KBr pellets. ^{1}H nmr spectra were recorded with a Jeol E-C 80 MHz or a Varian EM-360 spectrometer and ^{13}C nmr spectra were recorded with a Jeol PFT-100; D_2O was used as the solvent with DDS as the internal standard. Low resolution ms spectra were determined on a DuPont 21-492B; high resolution ms spectra were determined on a Hitachi RMU-6; and field desorption ms spectra were obtained through the courtesy of David Brent of Burroughs Wellcome Research Labs. The tlc systems, adsorbants, and spray reagents used were essentially as previously reported (6–9). The optical rotation was determined by W. C. Bogart, Jr., Department of Chemistry, Purdue University.

from ethyl acetate (mp 130°). Acid hydrolysis of the methylated product followed by EIms of the aglycone indicated monomethylation of a phenolic hydroxyl [*m/z* (%): 168(23), 137(100)].

SPECTRAL CHARACTERIZATION OF **1**.—Uv λ H_2O max (log ϵ): 278(3.2) shifted to 294(3.3) in 0.1 N NaOH; $[\alpha]^{23}D = -117°$; ir ν KBr max (cm^{-1}): 3500–3000, 1570, 1470, 1200, 1060, 1030, 1000, 895, 860, and 820; ^1H nmr (80 MHz, D_2O, δ): 7.1, d, 1H, J_o=8.1 Hz (=CH-5); 6.6, d, 1H, J_m= 2.1 Hz (=CH-2); 6.4, dd, 1H, J_o=8.1 Hz, J_m= 2.1 Hz (=CH-6); 4.8, bm, 1H, (CH-1'); 4–3.8, m; 3.8, t, J=7 Hz (CH_2-β'); 3.6–3.5, m; 2.7, t, 2H, J=7 Hz (CH_2-α'); ^{13}C nmr (table 1); CIms, *m/z*: 155 (aglycone+H)$^+$; EIms, (high resolution) *m/z*: 154.065 (aglycone, $C_8H_{10}O_3$); EIms, *m/z* (%): 154(23), 137(6.5), 123(100), 124(12), 101(6), 104(6), 105(6), 77(22); FDms, *m/z* (%): 339 (M+Na$^+$) (100), 361 (M-H+2 Na$^+$) (12.6).

TABLE 1. ^{13}C nmr spectral data of lemairin (**1**), 100 MHz, D_2O.

Assignment	ppm
C-3	156.4, s
C-4	146.6, s
C-1	135.6, s
C-6	120.4, d
C-5	117.8, d
C-2	115.0, d
C-1'	103.0, d
C-5'	76.4, d
C-3'	75.9, d
C-2'	73.3, d
C-4'	69.8, d
C-α'	63.2, t
C-6'	61.1, t
C-β'	37.9, t

ACKNOWLEDGMENTS

Grant support from NIH BRSG RRO-5586 and the Cactus and Succulent Society of America and a fellowship from the Universidad Central de Venezuela are gratefully acknowledged. Special thanks are due to R. Perdue, C.-j. Chang, B. Meyer, W. Bogart, Jr., D. Brent, J. Cassady, Y. Mohamed, R. Cooks, and J. Kozlowski.

Received 26 November 1979.

LITERATURE CITED

1. R. Mata and J. L. McLaughlin, *Phytochemistry*, **19**, 673 (1980).
2. J. B. Strother, "Carbon-13 NMR Spectroscopy," Academic Press, Inc., New York, N.Y., 1972.
3. P. G. Larsen, E. Pedersen, H. Sorensen, and P. Sorup, *Phytochemistry*, **12**, 2243 (1973).
4. V. R. Kappaka and R. J. Juneau, *Lloydia*, **38**, 339 (1975).
5. A. C. Gibson and K. E. Horak, *Ann. Missouri Bot. Gard.*, **65**, 999 (1978).
6. Y. A. H. Mohamed, C.-j. Chang, and J. L. McLaughlin, *J. Nat. Prod.* (*Lloydia*), **42**, 197 (1979).
7. J. L. McLaughlin and A. G. Paul, *Lloydia*, **29**, 315 (1966).
8. R. L. Ranieri and J. L. McLaughlin, *J. Chromatogr.*, **111**, 234 (1975).
9. R. L. Ranieri and J. L. McLaughlin, *J. Org. Chem.*, **41**, 319 (1976).