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PYRROLIZIDINE ALKALOIDS FROM *MERTENSIA* SPECIES OF COLORADO

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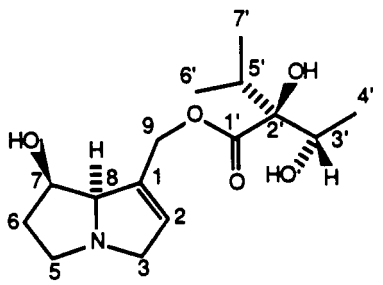
Mertensia (Boraginaceae), known in Colorado as the mountain bluebell, is reported to be a difficult genus taxonomically, with many "puzzling relationships" and is a genus that "does not lend itself to a straight-forward enumeration of characters by which entities may be differentiated" (1). Character overlap among species is still recognized, although field distinction among them is reported to seldom be a problem (2). A recent flora (3) subsumes the long-recognized species *Mertensia bakeri* and *Mertensia viridis* under *Mertensia lanceolata* because these three species seem to merge and recombine. Alpine, lowland, and various morphological races (such as the so-called "tall" and "low" taxa) occur. The greatest diversity of *Mertensia* is in western Colorado, and many of the problem species are readily available for alkaloid analysis as a possible means to aid in delimiting some of the taxa. There have been no literature reports up to now on alkaloids in *Mertensia*, but they are often encountered in the Boraginaceae. The mountain bluebell is reported to be commonly consumed as an emergency ration by hikers.[2] Our interest in the pyrrolizidine alkaloid content of consumed herbs (4,5), and pyrrolizidine structure-activity relationships related to DNA cross-linking properties (6) provided further impetus for the present work, wherein we investigated the alkaloid content of three species: *M. bakeri* (Greene), *Mertensia ciliolata* (James) G. Don, and *M. lanceolata* (Pursh) DC.

From *M. bakeri* we isolated lycopsamine [**1**] (1.7%) and from *M. ciliata* a 1:1 mixture of intermedine [**2**] and lycopsamine (0.3%). Alkaloids were detected in major amounts only after a Zn reduction, so are present in the plants mainly as *N*-oxides. With the same isolation scheme, no alkaloids could be detected (even by tlc) from one population of *M. lanceolata*, while a second population gave a faint trace of an alkaloid spot on tlc when one half of the entire crude base fraction was spotted. An NH_3 ci mass spectrum of the other half showed some pyrrolizidine fragment peaks but nothing that could be assigned to a molecular ion.



1

2 C-3′ epimer

Lycopsamine and intermedine are unsaturated monoester pyrrolizidine alkaloids and are suspect toxins, although monoesters and *N*-oxides appear to be less toxic than diesters or macrocyclic esters (7). Pancreatic tumors were found in rats given a single large dose of an intermedine-lycopsamine mixture (8). Binding to DNA and crosslinking by metabolites of unsaturated pyrrolizidines have also been studied (9).

The high alkaloid content of *M. bakeri*

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and lack or very minor trace of alkaloids in *M. lanceolata* suggest continued separation of these taxa, although study of additional populations of each as well as an investigation of *M. viridis* will be important. Further populations of *M. lanceolata* should be studied because alkaloid accumulation could vary among populations. For example, one population of *Senecio longilobus* was recently found (10) to be devoid of pyrrolizidine alkaloids, while two other populations had high alkaloid content.

EXPERIMENTAL

M. bakeri (FRS 258; CSU 46479), *M. ciliata* (TRS 7; CSU 57111), and *M. lanceolata* (FRS 232 at Red Hill and FRS 347 at Michigan Hill) were collected in the Colorado mountains and identified by Professor D.H. Wilken, Department of Biology, Colorado State University. Voucher specimens are in the Colorado State University herbarium.

From dried, ground, whole above-ground material of *M. bakeri* (85 g) was isolated 1.41 g of crude alkaloid material from extraction of the purified basic aqueous (with prior Zn reduction) according to the procedure of Hartman and Zimmer (11). The 270-MHz ^{1}H-nmr spectrum and tlc R_f values were identical to those of authentic lycopsamine (5), and no other alkaloid spots were detected in the tlc. An isolation without Zn reduction yielded no alkaloids. Similarly, 0.41 g of crude alkaloid was obtained from 136 g of dried, whole, above-ground *M. ciliata*. The ^{1}H- and ^{13}C-nmr and mass spectra and tlc R_f value were essentially identical with the 1:1 mixture of lycopsamine and intermedine previously reported (12). Traces of other alkaloid-positive spots were seen on tlc but not further investigated. An isolation without Zn reduction gave a much smaller alkaloid yield. Similar procedures were carried out on 10-g samples of *M. lanceolata* from two populations designated Red Hill and Michigan Hill. No alkaloids were detected in the former, while a trace tlc spot was seen at R_f 0.2 if one-half the entire crude base fraction (Zn reduction) was spotted. An NH_3CI mass spectrum of the other one-half showed peaks at *m/z* 156 (42), 138 (55), 136 (100), 124 (22), 122 (38), 120 (30), and 58 (38). These are typical fragmentation peaks of a pyrrolizidine alkaloid.

Full details are available from F.R. Stermitz.

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