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ALKALOIDS OF *ARGEMONE ALBIFLORA*, *A. BREVICORNUTA* AND *A. TURNERAE**

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OWNBEY has described[1] 23 species of *Argemone* in North America and one new species was recently discovered.[2] We report here the alkaloid content of two previously uninvestigated species (bringing the total to 23 of the 24 described North American species) and one species which was previously investigated, but which was restudied in order to identify a reported cytotoxic component.

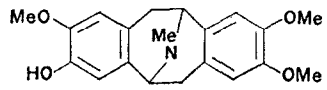
Argemone turnerae A. M. Powell. This newly discovered species[2] was found as a gypsophilic endemic in Chihuahua, Mexico, and its 'unarmed fruits, buds, stems, and leaf surfaces, cream-white latex, and leaf characters'[2] as well as its perennial character did not allow Powell to place it in any of Ownbey's groupings[1] nor could we speculate on its placement in any of our[3] alliances. It was suggested[2] upon 'distributional considerations' that it might have relationships with *A. ochroleuca*, *A. chisosensis* or other southwestern taxa. We have now found the major alkaloids to be (+)-armepavine and (−)-tetrahydropalmatine, neither of which has previously been found in *Argemone* species. Indeed, as far as we can determine, this is the first reported occurrence of tetrahydropalmatine in the entire subfamily Papaveroideae, although it occurs in both *Corydalis* and *Fumaria* of the subfamily Fumarioideae. Armepavine is also a relatively rare alkaloid with its occurrence in the subfamily Papaveroideae being restricted to only those species of *Papaver* which belong to the Section Miltantha of that genus.[4] Armepavine also occurs in *Corydalis*. We are currently attempting to obtain karyological data which may allow us to say more about this very unique species of *Argemone*. *A. turnerae* is unlikely, in our view, to have any close relationship to either *A. ochroleuca* or *A. chisosensis*.

Argemone brevicornuta G. B. Ownbey. This taxon was collected by Ownbey for the first time in 1950 and assigned species rank[1] but no report was made on any possible relationships to the other *Argemone*. On the basis of Ownbey's description of *A. brevicornuta*, we predicted[3] that it might be related to species of our alliance I (*A. hispida*, *A. munita* and *A.*

* Part XV in the series 'Alkaloids of the Papaveraceae'. For Part XIV see STERMITZ, F. R., ITO, R. J., WORKMAN, S. M. and KLEIN, W. M. (1973) *Phytochemistry* **12**, 381. This work was supported in part by NIH Grant CA 13648 from the National Cancer Institute and in part by Vipont Chemical Company.

[1] OWNBEY, G. B. (1958) *Memoirs Torr. Bot. Club*, **21**, No. 1.
[2] POWELL, A. M. (1972) *The Southwest Naturalist*, **17**, 106.
[3] STERMITZ, F. R., NICODEM, D. E., WEI, C. C. and MCMURTREY, K. D. (1969) *Phytochemistry* **8**, 615.
[4] KUHN, L., THOMAS, D. and PFEIFER, S. (1970) *Wiss. Z. Humboldt-Univ. Berlin Math.-Nat. R.* **19**, 81.

gracilenta) and therefore would be likely to contain the pavine-type alkaloids as major constituents. Indeed, we have now found that norargemonine (I) is the main alkaloid of this species along with small amounts of berberine. Thus, the predictive value of our classification[3] has received support.



(I)

Argemone albiflora Hornem. subsp *texana* G. B. Ownbey. The alkaloid content of '*A. alba* Lestib.' collected from a garden in Czechoslovakia was reported[5] previously. Ownbey[1] considered *A. alba* Lestib. to be a *nomen nudum* of no taxonomic standing and therefore returned to the first valid name *A. albiflora* Hornem. This species has been known to be cultivated in gardens in Europe since 1812, and hence, there is no reason to doubt the validity of the previous work[5] as indeed belonging to this species. However, Ownbey divided the species into two subspecies with subspecies *texana* more or less restricted to Texas and central United States while subspecies *albiflora* was common to the east coast. Thus, it seemed likely that it was subspecies *albiflora* which was introduced to Europe. More importantly, the sap of *A. albiflora* subsp. *texana* was discovered[6] to have cytotoxic properties in the National Cancer Institute *in vitro* 'KB' cell culture test. We, therefore, investigated the alkaloid content of subspecies *texana* and also monitored cytotoxicity of the various extracts, including the non-alkaloidal fractions, using the 'KB' test system. The alkaloid content was found to correspond very closely to that reported[5] for *A. alba* with sanguinarine, protopine, and allocryptopine being the major alkaloids along with smaller amounts of berberine and coptisine. Cytotoxicity was found only in those fractions containing sanguinarine. Sanguinarine has undergone extensive testing in many standard NCI *in vivo* animal tumor systems, but has shown no efficacy in any of these tests.[6]

EXPERIMENTAL

Plants of *A. turnerae* and *A. brevicornuta* were collected[7] in August 1972 in Mexico and voucher samples are deposited in the Colorado State University Herbarium under Accession Nos. 52403 and 52402, respectively. Plants of *A. albiflora* subsp. *texana* were collected[8] in April 1972 near Seguin, Texas, and a voucher sample is available under Accession No. 51358.

Dried, ground plant material was soaked overnight in 1:1 BuOH–C_6H_6 solution and, after filtration, the organic solution was extracted with 1 M H_2SO_4. The acidic solution was extracted with $CHCl_3$ and then made alkaline to about pH 9. This solution was extracted with $CHCl_3$ and a crude alkaloid mixture obtained upon evaporation of the $CHCl_3$. Pure individual alkaloids were then isolated by preparative tlc and by column chromatography on Florisil.

A. albiflora subsp. *texana* yielded 0·02% total alkaloids of the following composition: sanguinarine (33%), allocryptopine (28%), protopine (23%), berberine (9%) and coptisine (6%). The alkaloids were identified by comparison with samples available from previous work in these laboratories. Portions of the BuOH–C_6H_6 and aqueous pH 9 solutions remaining after extraction were evaporated and the residues tested for cytotoxicity,[9] but little activity was shown. The crude alkaloid mixture, however, did show cytotoxicity. Each pure alkaloid was then tested and only sanguinarine showed activity.

[5] SLAVIKOVA, L. and SLAVIK, J. (1960) *Coll. Czech. Chem. Commun* **25**, 756.

[6] HARTWELL, J. L. (National Cancer Institute), private communication.

[7] We thank T. H. ZANONI of the Department of Botany and Plant Pathology for making this collection.

[8] We thank Col. E. C. CUSHING of Stockdale, Texas, for guiding us to this location and for the original collection of cytotoxic material.

[9] 'Protocols for Screening Chemical Agents and Natural Products Against Animal Tumors and Other Biological Systems', Drug Evaluation Branch, National Cancer Institute, Bethesda, Maryland 1971.

A. brevicornuta yielded 0·03% total alkaloids with 85% of the total represented by (−)-norargemonine and 15% by berberine as shown by comparison with authentic samples.

A. turnerae yielded 0·11% total alkaloids composed of 60% (−)-armepavine [proven by diazomethane methylation to *N*-methyl-6,7-dimethoxy-1-(4′-methoxybenzyl)-1,2,3,4-tetrahydroisoquinoline which was available as a synthetic sample[10]] and 40% (−)-tetrahydropalmatine which was spectrally identical to an authentic sample.[11]

[10] We thank J. R. FALCK of the Department of Chemistry for this synthesis.
[11] We are indebted to Dr. R. H. F. MANSKE for supplying the authentic material.