

## ALKALOIDS OF *ARGEMONE SUBINTEGRIFOLIA* AND *A. MUNITA*\*

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**Key Word Index**—*Papaver subintegrifolia*; *P. munita*; Paraveraceae; alkaloids; allocryptopine; chemotaxonomy.

**Abstract**—*Argemone subintegrifolia* G. B. Ownb. (Papaveraceae) was found to contain 0.14% total alkaloids consisting of 70% allocryptopine, 20% protopine, 5% berberine and 5% trace unidentified alkaloids. *A. munita* Dur. & Hilg. subsp. *argentea* G. B. Ownb. was found to contain 0.28% total alkaloids consisting of 60% allocryptopine, 20% (–)-isonorargemonine, 5% (–)-argemonine, 5% protopine and 10% unidentified trace alkaloids. The chemotaxonomic significance of these results is discussed.

### INTRODUCTION

IN THE authoritative description<sup>1</sup> of the genus *Argemone* in North America, Ownbey proposed the new species *A. subintegrifolia* G. B. Ownb. to accomodate specimens (relatively incomplete) of an *Argemone* collected in 1921 on Angel de la Guarda Island (Gulf of California) and in 1933 at Laguna Macuata (Laguna Salada) at the western base of the Cocupah (Cocopah, Cucupah) mountains in northern Baja California. It was suggested<sup>1</sup> that *A. subintegrifolia* was distinct from all other species of *Argemone*. Since that time, Ownbey has seen a few additional specimens of *A. subintegrifolia* and has suggested<sup>2</sup> that this taxon might actually have affinities with *A. munita* Dur. & Hilg. subsp. *argentea* G. B. Ownb. The alkaloid composition of neither of these had previously been determined and we considered that chemical work might assist in the taxonomic placement of these species as well as possibly uncover further cytotoxic alkaloids.

### RESULTS

Our search of the area of the western base of the Cocupah mountains of Baja California revealed no *Argemone*. However, south of Mexicali (not far from the eastern base of the above mountains) a relatively small population of *Argemone* was found. The plants had recently come into bloom and only a few capsules had formed. Plants were collected and a voucher was later keyed<sup>1</sup> to the *A. munita* group. In our hands, the closest affinity appeared to be to *A. munita* subsp. *munita*. The voucher was then submitted to Ownbey

\* Part XXI in the series "Alkaloids of the Papaveraceae". For Part XX, see COOMES, R. M., FALCK, J. R., WILLIAMS D. K. and STERMITZ, F. R. (1973) *J. Org. Chem.* **38**, 3701. This work was supported in part by NIH grant CA 13648 from the National Cancer Institute.

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<sup>1</sup> OWNBEY, G. B. (1958) *Memoirs Torr. Bot. Club*, **21**, No. 1.

<sup>2</sup> OWNBEY, G. B. private communication.

who identified<sup>2</sup> it as his taxon *A. subintegrifolia* and noted that it has similarities to *A. munita* subsp. *argentea*. A collection of "true" *A. munita* subsp. *argentea* was then made near the holotype location<sup>1</sup> in Imperial County, California. These plants (although at a higher elevation and more arid location than the *A. subintegrifolia* collection) were at a slightly later blooming stage and numerous capsules were evident. Whereas the *A. subintegrifolia* plants exuded a bright yellow latex when cut, the *A. munita* subsp. *argentea* plants exuded a nearly white latex.

Alkaloid analysis of the two collections showed considerable differences although the major alkaloid in each case was identical. Thus, *A. subintegrifolia* yielded 0.14% total alkaloids which proved to consist of ca 70% allocryptopine, 20% protopine, 5% berberine and 5% mixture of several trace alkaloids which could not be identified. *A. munita* subsp. *argentea* yielded 0.28% total alkaloids which consisted of ca 60% allocryptopine, 20% (–)-isonorargemonine, 5% (–)-argemonine, 5% protopine and 10% a mixture of several unidentified trace alkaloids, none of which was berberine.

#### DISCUSSION

The alkaloid content of *A. subintegrifolia* is completely different from that of *A. munita* subsp. *rotundata*<sup>3</sup> and distinct, but somewhat less different from that of *A. munita* subsp. *argentea* here reported. Indeed, the allocryptopine-protopine-berberine make-up of *A. subintegrifolia* (without the presence of pavinane-type alkaloids) is exactly that of the more specialized<sup>4</sup> species of *Argemone* (Alliance IV<sup>4</sup>) rather than that of the *A. munita* group (Alliance I<sup>4</sup>) which we consider to be more primitive.

The chemical differences between *A. subintegrifolia* and *A. munita* subsp. *argentea* would be more distinct were it not for the high percentage of allocryptopine found in the latter. Thus, the typical species of our Alliance I (*A. munita* subsp. *rotundata*, *A. hispida*, and *A. gracilentia*) have the pavinane alkaloids representing 80–95% of the alkaloid content while compounds such as allocryptopine occur only in trace amounts.

Although this work has not defined the exact placement of *A. subintegrifolia*, our tentative view is that it should remain distinct from *A. munita* as represented by subsp. *rotundata*. On the basis of morphology alone, Ownbey suggested<sup>2</sup> that *A. subintegrifolia* and *A. munita* subsp. *argentea* might be mergable under the former name. The fact that both have the same compound as the major alkaloid component certainly lends credence to this possibility. However, the major differences among the other alkaloids makes the merging of these two taxa questionable at this time. It is evident that chemical analysis of the remaining *A. munita* subspecies (subsp. *munita* and subsp. *robusta*) as well as both chemical and morphological examination of additional *A. subintegrifolia* collections would be of further help in solving this taxonomic question.

#### EXPERIMENTAL

Plants of *A. subintegrifolia* were collected 19 March, 1973 at La Puerta (36 km south of Mexicali), Baja California, Mexico and a voucher sample was deposited in the Colorado State University Herbarium under Accession No. 54153. Plants of *A. munita* subsp. *argentea* were collected 20 March, 1973, 16 km E. of Niland, California (Imperial Co.) on Beal Road (Accession No. 54060).

Dried, ground plant material of *A. munita* subsp. *argentea* (2.16 kg) was wet with 162 g NaHCO<sub>3</sub> as a 10% aq. soln and 10.8 l. 1:1 BuOH-C<sub>6</sub>H<sub>6</sub> added. After standing overnight, the mixture was filtered and the organic layer extracted with 1 M H<sub>2</sub>SO<sub>4</sub>. This was washed with CHCl<sub>3</sub> and then made basic to pH 9 and again

<sup>3</sup> STERMITZ, F. R. and SEIBER, J. N. (1966) *J. Org. Chem.* **31**, 2925.

<sup>4</sup> STERMITZ, F. R., NICODEM, D. E., WEI, C. C. and McMURTREY, K. D. (1969) *Phytochemistry* **8**, 615.

extracted well with  $\text{CHCl}_3$ . The organic washings were combined, dried over  $\text{Na}_2\text{SO}_4$  and evaporated to leave 5.7 g (0.28%) of crude alkaloid mixture. The mixture was dissolved in  $\text{CHCl}_3$  and 1 M  $\text{H}_2\text{SO}_4$ , the layers were separated and the aqueous layer extracted with  $\text{CHCl}_3$  after adjusting the pH to 12.5 and then 8.6. From the pH 12 extract, allocryptopine was recovered by crystallization. The mother liquors yielded an alkaloid mixture which was separated on prep TLC to give protopine, (–)-argemonine, and a mixture of trace alkaloids. From the pH 9 extract, crystalline (–)-isonorargemonine was obtained. Based upon isolated crystalline compounds and estimation (from TLC) of unseparated mother liquor residues, the alkaloid content was estimated to be composed of 60% allocryptopine, 20% (–)-isonorargemonine, 5% (–)-argemonine, 5% protopine and 10% mixture of trace alkaloids. TLC of the latter showed no spot characteristic of standard berberine.

In a similar manner, 304 g of dried, ground *A. subintegrifolia* was extracted and yielded 415 mg (0.14%) of crude alkaloid mixture. As above, this was separated and the components isolated as 70% allocryptopine, 20% protopine, 5% berberine and 5% unknown trace alkaloids.

Structures of the isolated alkaloids were all proven by TLC and NMR and/or IR comparisons with standard samples isolated from previous work in these laboratories.