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# ALKALOIDS FROM *PAPAVER FUGAX* OF TURKISH ORIGIN

J. DAVID PHILLIPSON*

Pharmacognosy Research Laboratories, Department of Pharmacy, Chelsea College, University of London, London SW3 6LX

and

GÜNAY SARIYAR and TURHAN BAYTOP

Department of Pharmacognosy, Faculty of Pharmacy, University of Istanbul, Turkey

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**Key Word Index**—*Papaver fugax*; Papaveraceae; poppy; alkaloids; thebaine; morphinane; narcotine: phthalide isoquinoline; rhoeadine; armepavine.

**Abstract**—Thebaine, narcotine, rhoeadine and armepavine were identified in the aerial parts of *Papaver fugax* of Turkish origin.

## INTRODUCTION

THE GENUS *Papaver* is divided into nine sections, one of which, Miltantha Bernh., contains 14 species including *P. fugax* Poir.[1] There are conflicting reports about the major alkaloid of *P. fugax* since it has been reported to be armepavine,[2,3] pronuciferine,[4] palmatine[5] (later, coptisine[6]) and aporheine with armepavine.[6] 1-Benzyl-1,2,3,4-tetrahydroisoquinoline, pro-aporphine, aporphine, promorphinane, protoberberine, protopine, papaverrubine and benzophenanthridine-type alkaloids have also been reported.[7] The names *P. caucasicum* Bieb. and *P. floribundum* Desf. appear in the chemical literature and they can be considered as synonyms of *P. fugax*.[8] Exactly the same types of alkaloids have been isolated from plants stated to be *P. caucasicum*,[7] while 1-benzyl-1,2,3,4-tetrahydroisoquinoline and promorphinane-types have been found in material stated to be *P. floribundum*.[9] Two members of the section Miltantha, closely related to *P. fugax*, namely *P. armeniacum* (L.) DC. and *P. tauricola* Boiss. contain alkaloids which are identical with some of those in *P. fugax* and so far 1-benzyl-1,2,3,4-tetrahydroisoquinoline, pro-aporphine, protoberberine, protopine and papaverrubine-types have been isolated.[6,7] The current work was undertaken since there appears to be no literature reports on the alkaloidal constituents of Turkish *P. fugax*.

## RESULTS

The sample of Turkish *P. fugax* investigated yielded thebaine (morphinane-type) as the major alkaloid with narcotine, rhoeadine and armepavine as minor alkaloids.

* Present address: Department of Pharmacognosy, The School of Pharmacy, University of London 29–39, Brunswick Square, London WC1N 1AX.

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## DISCUSSION

The plant material used for the present investigation was compared with herbarium material at The Royal Botanic Gardens, Kew. The plant is a setose biennial herb with pink flowers and is readily identified as belonging to the section Miltantha. According to Cullen,[8] there are eight Turkish species in the Miltantha. Three of these species, *P. fugax* Poir., *P. armeniacum* (L.) DC, and *P. tauricola* Boiss., form a complex and while most of the herbarium samples at Kew are fairly easy to distinguish, there are a number of connecting intermediates. By comparison, our material was found to be most similar to *P. fugax*, particularly in the nature of its capsules. Fedde[1] considers that *P. fugax* Poir., *P. causasicum* Bieb. and *P. floribundum* Desf. are distinct species which are very closely related, but Cullen[8] considers that the latter two names can be used as synonyms for *P. fugax*. No distinction could be made by us between the herbarium samples which were labelled as *P. fugax*, *P. caucasicum* and *P. floribundum*. According to Fedde[1] *P. fugax* is found in East Turkey (Pontus), in Armenia and into West Iran; *P. caucasicum* is considered to be more developed since it occurs not only in the same areas as *P. fugax* but also extends into the Caucasus; *P. floribundum* is to be found in Armenia and West Persia. Cullen[8] notes that the area of distribution of *P. fugax* also extends into North Iraq and that the plant grows on dry slope screes at a height of 1700–3100 m. Our material was collected in the mountains near Bingöl, Turkey, in an area which approaches the extreme western part of the plant's distribution.

The material investigated appears to be unusual since the major alkaloid has proved to be thebaine and morphinanes have not previously been reported in the section Miltantha. However, the promorphinane alkaloid, salutaridine, has previously been found in *P. fugax* and since promorphinanes can undergo oxidative phenolic coupling to form morphinanes, it is perhaps not too surprising that these alkaloids should be found in *P. fugax*. Thebaine has previously been thought to be restricted to four sections of *Papaver*,[7] viz. Macrantha, Pilosa, Mecones and Orthorhoeades but morphinanes may well be present in other members of the Miltantha. Promorphinanes also occur in the section Scapiflora, so that morphinanes may well be produced here although none have so far been detected.

The phthalide isoquinoline alkaloid narcotine has previously been found only in the Mecones and was thought to be unique to this section.[7] The isolation of narcotine from a member of the Miltantha is therefore of considerable interest. Although rhoeadine has not previously been reported from a member of the Miltantha, it was to be expected as it is found throughout the genus and the closely related papaverrubines have previously been isolated from *P. fugax*. The presence of armepavine is in agreement with other workers although the yield in our Turkish sample appears to be very low in comparison to their findings. All the Miltantha species investigated have armepavine present and until now this section is the only one in *Papaver* containing this alkaloid although it is known to be present in other genera of other families.

The question arises as to why the Turkish *P. fugax* investigated contains some alkaloids which are different from those found in previous investigations. None of the samples of *P. fugax* previously examined have been grown in Turkey and our material was obtained from an area which is at the extreme western part of the plant's distribution. Furthermore, the material was collected in the wild state while several samples previously examined have been grown from seeds in European botanical gardens[4–6] although one sample collected in the wild state from Russian Armenia did have similar constituents to cultivated material.[2] The differences in alkaloidal content between the Turkish material and the other samples of *P. fugax* previously examined may prove to be due to the presence of different chemical

races within the species although modification of alkaloid metabolism by edaphic or climatic factors cannot yet be excluded.

The present findings illustrate the fact that despite the considerable amount of work which has so far been done on the alkaloids of *Papaver*, our knowledge is far from complete and that morphinanes and phthalide isoquinoline alkaloids may be more widespread in the genus than our present knowledge indicates.

The possibility of another source of thebaine may prove to be of commercial significance for the continued production of codeine since the Turkish Government has banned the production of opium from *P. somniferum* L.[10]

## EXPERIMENTAL

The plant material was collected at Göynük, Bingöl, Eastern Turkey, on 26 August 1970. A reference sample labelled T. Baytop18. 269, *P. fugax* Poir., is in the Herbarium at the Royal Botanic Gardens, Kew. The IR spectra were obtained from Nujol mulls using an SP 200 spectrometer, the 60 MHz NMR spectra were obtained with a Perkin–Elmer R 60 spectrometer and the MS with a MS 109 high resolution instrument at temperatures between 215° and 225°. The TLC systems used were silica gel G (Merck) with: (a) Hexane–$CHCl_3$–MeOH (5:13:2), (b) $C_6H_6$–EtOH–conc. $NH_4OH$ (80:20:0·15), (c) $C_6H_6$–$Me_2CO$–MeOH (7:2:1), (d) $C_6H_6$–EtOH (19:1).

The $hR_f$ values were as follows:

| | Narcotine | Rhoeadine | Thebaine | Armepavine |
|---|---|---|---|---|
| (a) | 0·85 | 0·50 | 0·37 | 0·22 |
| (b) | 0·81 | 0·80 | 0·45 | 0·34 |
| (c) | 0·80 | 0·65 | 0·22 | 0·14 |
| (d) | 0·45 | 0·29 | 0·00 | 0·00 |

A Becker 407 instrument was used for the GLC separations. A 1·8 m glass column containing 3% OV 17 on Gas Chromosorb Q (100/120 mesh) at a column temp. of 260° and a $N_2$ pressure of 15·5 kN/m² gave the following $R_t$ values: thebaine 6, armepavine 6·75, rhoeadine 17 and narcotine 40 min. For column chromatography silica gel 60 PF 254 (30 g) was activated at 110° for 24 hr and then mixed with 10% $H_2O$.

*Extraction and separation of alkaloids.* 3·5 kg of dried, powdered aerial parts (less capsules) were moistened with 10% $NH_4OH$ and extracted in a Soxhlet with $Et_2O$. The concentrated $Et_2O$ extract was shaken with three successive portions of 3% $H_2SO_4$ and the combined acid extracts made alkaline with 10% $NH_4OH$ and extracted with three successive portions of $Et_2O$. The combined $Et_2O$ extracts were washed, dried and concentrated to dryness yielding 14·8 g (0·42%) of crude tertiary alkaloid. 1 g of crude alkaloid was dissolved in $CHCl_3$ and shaken with three successive portions of 5% NaOH. The $CHCl_3$ solution was washed, dried and concentrated to dryness yielding 915 mg of non-phenolic alkaloid. The 5% NaOH extract was made acidic with conc. HCl, then alkaline with conc. $NH_4OH$ and extracted with three successive portions of $CHCl_3$. The combined $CHCl_3$ extracts were washed, dried and concentrated to dryness yielding 46 mg of phenolic alkaloid.

*Non-phenolic alkaloids.* 915 mg were dissolved in TLC solvent system (c), added to a silica gel column and eluted with the same solvent mixture, collecting 2 ml fractions. Each fraction was examined by TLC, like-ones combined and evaporated to dryness. Fractions 3–5 (135 mg) were separated into five bands by preparative TLC (system d). The bands were extracted with $CHCl_3$–EtOH (1:1), filtered, concentrated to dryness, the residue dissolved in $CHCl_3$, filtered and evaporated to dryness. The major band yielded 39 mg (0·016%) of narcotine which crystallized from abs EtOH, mp. 174°. Fractions 6–9 (105 mg) were separated by preparative TLC using the same method. The major band yielded 23 mg (0·01%) of rhoeadine which crystallized from abs. EtOH, m.p. 252°. Fractions 33–100 showed only one spot on several TLC systems and yielded 363 mg (0·15%) of amorphous thebaine which crystallized from abs. EtOH m.p. 205–207°.

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*Phenolic alkaloids.* 46 mg were separated by preparative TLC (silica gel G/MeOH) into 5 bands. The major band was extracted as described above yielding 7·8 mg of armepavine (0·003%).

*Capsule alkaloids.* 400 g of capsule, extracted by the same method described for the aerial parts, yielded 2·2 g (0·55%) total alkaloid. Preliminary TLC and GLC examination indicated that the major alkaloids are the same in the capsule as in the other aerial parts.

*Identification of alkaloids.* The following physical properties of the isolated alkaloids were identical with those of reference alkaloids: m.p., m. m.p.—narcotine, rhoeadine, thebaine; UV and MS[11–13], $R_t$ and $R_F$—narcotine, rhoeadine, thebaine, armepavine; NMR—thebaine;[14,15] Reference alkaloids—narcotine and thebaine from Macfarlan Smith Ltd., Edinburgh; rhoeadine from Professor F. Šantavý; armepavine from *Euonymus europaeus*.[16]

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