

Narcotic Alkaloids of Four *Papaver* Species from Iran

Peyman Salehi^{a,*}, Ali Sonboli^b, Alireza Fakhari Zavareh^c, Fatemeh Sefidkon^d, Manijeh Dayeni^a, and Bahram Cheraghi^c

^a Department of Phytochemistry, Medicinal Plants and Drugs Research Institute, Shahid Beheshti University, Evin, P. O. Box 19835-389, Tehran, Iran. Fax: (+9821) 22431783. E-mail: p-salehi@sbu.ac.ir

^b Department of Biology, Medicinal Plants and Drugs Research Institute, Shahid Beheshti University, Evin, Tehran, Iran

^c Department of Chemistry, Faculty of Science, Shahid Beheshti University, Evin, Tehran, Iran

^d Research Institute of Forests and Rangelands, Tehran, Iran

* Author for correspondence and reprint requests

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Four native *Papaver* species of Iran, i. e. *P. glaucum*, *P. tenuifolium*, *P. dubium* and *P. fugax*, were collected from their natural habitat and subjected to HPLC analysis for determination of their morphine, codeine and thebaine content. *P. dubium* and *P. glaucum* contained all of the three mentioned narcotic alkaloids, while morphine was not found in *P. fugax*, and *P. tenuifolium* was free from codeine.

Key words: Morphine, Thebaine, *Papaver*

Introduction

Morphine and codeine are among the most important natural compounds which are widely used as narcotic analgesics (Carins, 2003; Kapoor, 1995; Heinrich *et al.*, 2004). Thebaine is also considered as a precursor for the synthesis of powerful analgesics, oxycodone and buprenorphine (McNicholas and Martin, 1984; Lewis, 1973), or can serve as a substitute for morphine as starting material for the production of codeine (Theuns *et al.*, 1986). These morphinans are classified as benzyloquinoline alkaloids. More than 2500 benzyloquinoline alkaloids have been found in five plant families including the Papaveraceae (Preininger, 1985; Facchini, 2001). However, only a number of closely related *Papaver* species has the capacity to produce morphinan alkaloids (Phillipson, 1983; Wiczorek *et al.*, 1986). Therefore the screening of different *Papaver* species for the presence of morphine, codeine and thebaine is of importance.

The alkaloid contents of *Papaver* species from the section Rhoeadium and of Turkish origin have

extensively been reviewed by Preininger (1986) and Sariyar (2002). There are also two reports relating to the existence of trace amounts of thebaine in *Papaver albiflorum* subsp. *albiflorum* collected from Southwestern Slovakia (Slavik *et al.*, 1981), and the presence of it as a major alkaloid in a herbarium sample from Central Slovakia (Slavik and Slavikova, 1990).

In this paper the extraction and determination of morphine, codeine and thebaine from *P. glaucum*, *P. tenuifolium*, *P. dubium* and *P. fugax* as four native species of Iran are reported.

Material and Methods

Plant material

The immature fruits of four *Papaver* species, i. e. *P. glaucum*, *P. tenuifolium*, *P. dubium* and *P. fugax*, were collected from their natural habitats in Iran. The locality information and voucher numbers of the studied species are listed in Table I. Voucher

Table I. The locality information and voucher number of studied *Papaver* species.

Species	Locality	Voucher number
<i>P. glaucum</i>	Sanandaj: Sanandaj-Kermanshah road, km 3, 1500 m; May 29, 2002	MP-347
<i>P. tenuifolium</i>	Tehran: Tehran-Qom highway, km 60, 1300 m; May 8, 2002	MP-174
<i>P. dubium</i>	Tehran: Firuzkuh-Tehran road, 110 km to Tehran, 2200 m; May 23, 2002	MP-208
<i>P. fugax</i>	Sanandaj: Salavat Abad mountain, 2000 m; May 30, 2002	MP-333

Entry	Plant material	Morphine (ppm) ^a	Codeine (ppm) ^a	Thebaine (ppm) ^a
1	<i>P. dubium</i>	64.2 ± 0.3	30.8 ± 0.2	10.1 ± 0.1
2	<i>P. glaucum</i>	98.4 ± 0.8	27.2 ± 0.4	9.0 ± 0.1
3	<i>P. fugax</i>	–	179.6 ± 1.2	34.2 ± 0.3
4	<i>P. tenuifolium</i>	54.0 ± 0.7	–	46.7 ± 0.6

Table II. Morphine, codeine and thebaine contents of four native *Papaver* species of Iran.

^a Calculated amount of the alkaloid (μg/g) based on the weight of the ground dry capsules (mean ± standard deviation for three replications).

specimens have been deposited at the Medicinal Plants and Drugs Research Institute Herbarium, Shahid Beheshti University (Tehran, Iran).

Extraction of total alkaloids

Extraction of alkaloids was carried out according to a previously reported procedure (Williams and Ellis, 1989). Briefly, 20 g of the capsules were ground and extracted by methanol (80%, 200 ml) for 24 h. The mixture was acidified to pH 1 by 1 M HCl. Extraction by petroleum ether (3 × 50 ml) was followed by raising the pH value of the aqueous layer to 8.5 by addition of 1 M ammonium hydroxide solution. The resulting aqueous mixture was extracted by CHCl₃/*i*-PrOH (3:1 v/v, 3 × 55 ml). The organic layer was separated and concentrated at 40 °C under diminished pressure. The resulting extract was directly subjected to HPLC analysis.

HPLC analysis

HPLC analysis was carried out on a Knauer HPLC system (Berlin, Germany) equipped with a C18 column (250 mm, 4 mm i. d., RP, particle size 5 μm) and a PDA detector. For elution a gradient mixture of two different solutions, (a) 2% CH₃CN, 98% H₂O, 0.1 M NaH₂PO₄, pH 2.8, and (b) 25% CH₃CN, 75% H₂O, 0.1 M NaH₂PO₄, pH 2.5, was used at the flow rate of 1.5 ml/min (Rembery and Buchbauer, 1994). Standard pure morphine and

codeine were obtained from TEMAD Pharmaceutical Company (Tehran, Iran), and thebaine from Pasteur Institute of Iran.

Results and Discussion

Screening the total alkaloid extracts of *P. dubium*, *P. glaucum*, *P. fugax* and *P. tenuifolium* showed that these species contained few amounts of morphine, codeine and thebaine. The results are summarized in Table II where the amount of morphinans is reported in ppm (μg/g) based on the weight of the ground dry capsules. As shown, *P. dubium* and *P. glaucum* contained all of the three mentioned narcotic alkaloids. No trace amount of morphine was found in *P. fugax*. The extract of *P. tenuifolium* was free from codeine. 180 ppm of codeine was quantified in *P. fugax* and the highest amount of morphine was found in *P. glaucum* (98 ppm). An interesting finding was the presence of thebaine in all studied species where the highest amount was found in *P. tenuifolium*. Thebaine has already been found in *P. dubium* subsp. *lecoqii* var. *lecoqii* from Turkey (Unsal *et al.*, 2006).

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Carins D. (2003), Essentials of Pharmaceutical Chemistry, 2nd ed. Pharmaceutical Press, New York.
 Facchini P. J. (2001), Alkaloid biosynthesis in plants, biochemistry, cell biology, molecular regulation and metabolic engineering applications. Annu. Rev. Plant Physiol. Plant Mol. Biol. **52**, 29–66.
 Heinrich M., Barnes J., Gibbons S., and Williamson E. M. (2004), Fundamentals of Pharmacognosy and Phytotherapy, Section 2. Elsevier Health Sciences Press, New York.

Kapoor L. D. (1995), Opium Poppy: Botany, Chemistry & Pharmacology. Haworth Press, New York.
 Lewis J. W. (1973), Ring C-bridged derivatives of thebaine and oripavine. Adv. Biochem. Psychopharmacol. **8**, 123–136.
 McNicholas L. F. and Martin W. R. (1984), New and experimental therapeutic roles for naloxone and related opioid antagonists. Drugs **27**, 81–93.
 Phillipson J. D. (1983), Intraspecific variation and alkaloids of *Papaver* species. Planta Med. **48**, 187–192.

- Preininger V. (1985), Chemotaxonomy of the Papaveraceae alkaloids In: The Chemistry and Biology of Isoquinoline Alkaloids (Phillipson J. D., Roberts M. F., and Zenk M. H., eds.). Springer, New York, pp. 23–75.
- Preininger V. (1986), Chemotaxonomy of Papaveraceae and Fumariaceae. In: Alkaloids, Vol. 29 (Brossi A., ed.). Academic Press, San Diego, pp. 1–98.
- Rembery B. A. and Buchbauer G. (1994), Fifty years of development of opium characterization methods. Bull. Narcotics U. N. Dept. Social Affairs **46**, 79–108.
- Sariyar G. (2002), Biodiversity in the alkaloids of Turkish *Papaver* species. Pure Appl. Chem. **74**, 557–574.
- Slavik J. and Slavikova L. (1990), Alkaloids of the Papaveraceae. 90. Alkaloids from *Papaver albiflorum* Pacz subsp. *albiflorum* and P. C. F. *Stevenianum* Mikhchev, A. D. Collect. Czech. Chem. Commun. **55**, 1812–1816.
- Slavik J., Slavikova L., and Dolejs L. (1981), Alkaloids from *Papaver pinnatifidum* MORIS. Collect. Czech. Chem. Commun. **46**, 2587–2593.
- Theuns H. G., Theuns H. L., and Lousberg J. (1986), Search for new natural sources of morphinans. Econ. Bot. **40**, 485–497.
- Unsal C., Sariyar G., Mat A., Oktayoglu E., and Ozhatay N. (2006), Distribution of alkaloids in the samples of *Papaver dubium* subsp. *lecoqii* var. *lecoqii* from Turkey: A potential source for thebaine. Biochem. Syst. Ecol. **34**, 170–173.
- Wieczorek U., Nagakura N., Sund C., Jendrzejewski S., and Zenk M. H. (1986), Radioimmunoassay determination of six opium alkaloids and its application to plant screening. Phytochemistry **25**, 2639–2644.
- Williams R. D. and Ellis B. E. (1989), Age and tissue distribution of alkaloids in *Papaver somniferum*. Phytochemistry **28**, 2085–2088.