

RECENT DEVELOPMENTS IN OPIATES

by

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Opiates are potent substances derived from Opium, latex from the capsules of *papaver somniferum*, and these include principally Morphine, Codeine, Thebaine, Narcotine (Noscapine) and papaverine beside other minor alkaloids. The main alkaloids used medicinally are morphine, codeine, narcotine, to some extent papaverine and some derivatives of morphine like heroin, naloxone, levorphanol, levallorphan etc. Although thebaine is not used medicinally as such, it is used for the preparation of highly analgesic compounds called oripavines and also for preparing Etorphine, an analgesic used in veterinary medicine. The main source of these alkaloids is opium, but lately poppy straw is being used for this purpose. The total production of morphine from opium and poppy straw in 1957 was approximately seventy three tons of which twelve tons was obtained from straw. The production of opium increased to one hundred seventy tons in 1972 of which approximately sixty tons was obtained from straw. Poppy straw consists of dried capsule walls and stems. Table I¹ gives the composition of opium from various sources.

TABLE I

Country	Morphine	Codeine & Cryptopine	Thebaine	Papaverine	Narcotine
Turkey	12.25—16.10	1.67—3.56	1.70—4.85	2.25—2.80	5.72—6.33
Greece	19.07	1.56	1.28	3.69	7.25
Yugoslavia	16.88—20.33	1.63—1.67	1.19—1.44	3.06—3.26	5.61—6.68
Iran	11.13—12.58	2.87—4.27	3.14—5.46	2.57—3.09	8.19—9.38
India	12.94—13.67	3.45—3.87	2.52—2.66	0.64—2.81	8.05—9.16
Korea	14.29—18.53	4.76—6.12	3.19—5.41	1.48—1.67	7.79—7.85
Pakistan ²	7.16	4.25	2.43	2.36	6.87

It is evident from this table that the principal alkaloid is morphine. As the amount of codeine which is very commonly used in pharmaceutical industry is low, it is, therefore, prepared by methylation of morphine. In 1963 it was reported³ for the first time that the roots of *Papaver bracteatum* contain about 1.0% of alkaloid and of these 98% is thebaine. This report was of great significance because thebaine was a minor component of opium obtained from *P. somniferum*. Thebaine can be converted to codeine⁴ thereby giving an alternative source for the preparation of codeine, which was previously

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obtained from morphine. Thus the propagation of *Papaver bracteatum* will solve a major narcotic problem because thebaine is non-addictive. An Iranian variety of *P. bracteatum* Lindl contain 26% thebaine in the dried latex.⁵ The content of thebaine in different organs of a better strain *P. bracteatum* Lindl: ARYA II⁶ is as follows:—

Part of plant	% Thebaine
Petals	1.02 (0.85-1.15)
Stigmas	0.63 (0.55-0.75)
Bracts	1.81 (1.01-2.12)
Young leaves	0.02 (0.02-0.02)
Stems	1.03 (0.91-1.21)
Capsule	3.58 (3.35-3.75)

According to another report,⁷ the thebaine content in different parts of plant is as follows:

Capsule	1.24%
Root	0.59-0.77
Leaf	0.102-0.099
Dried latex	34.16-35.66

Yield of alkaloid. The yield of morphine from opium is about 1 kg/hectare and from poppy straw 1.5 kg/hectare. On the other hand a yield of thebaine of 34.0 kg/hectare is obtained from the roots of *P. bracteatum*. Fairbairn and Hakim⁸ obtained a yield of 15.0 kg of thebaine/hectare but it should be higher (40-70 kg) if a better strain of *P. bracteatum* (ARYA I or ARYA II) is used. Even then it compares favourably with the yield of morphine as 1 kg/hectare. The highest yield of morphine is in India⁹ which corresponds to 3.0 kg/hectare, whereas in Pakistan it is about 2.6 kg/hectare. The lowest is in Bulgaria corresponding to 0.1 kg/hectare.

Leaves.¹⁰ Thebaine content in the leaves of various varieties of *P. bracteatum* varies from 0.1 to 0.15% so it is not a commercially feasible source of thebaine.

Latex: It is the most convenient and economic source of thebaine where manual labour is cheap. Thebaine content is 28 to 53% in the dried latex and the maximum percentage occurs during 3-4 weeks after petal opening.

When samples of dried latex are prepared keeping in view the peak yield time, thebaine content is 43-55% on dry basis. In this case the bled latex is 46% of the total thebaine present, the rest remains in the capsule. Theoretical yield of thebaine from this source is 58 Kg/hectare.

Fruiting tops. Fruiting tops include capsules and stems. This is the best source and a yield of 50 kg/hectare can be obtained. Peak yield time is 3 weeks after petal opening.

Other sources of opiates. Various other species of Papaver i.e., *P. fugax* from W. Turkey., *P. armeniacum* from Iran contain thebaine as the major alkaloid. There is a need that all the species of papaver available in Pakistan should be analysed for alkaloidal content which may lead us to a better source of thebaine, codine etc.

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