DIMERIC ALKALOIDS FROM TASMANIAN-GROWN *PAPAVER SOMNIFERUM*

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Apart from wide-spread illicit cultivation, the opium poppy (*Papaver somniferum*) is grown under official control for preparing ethical drugs in various countries extending from the Balkans through to India. Disorders in much of this region have led to Tasmania being chosen to provide a stable supply, and in consequence a special poppy variety was developed which would give good yields of alkaloid under local conditions. However, while a high content of morphine has been achieved, considerable variation in the nature and content of the minor bases has ensued.

Many varieties of *P. somniferum* exist, with divergent morphological characteristics and alkaloidal constituents. Different countries have selected those varieties best adapted to local conditions, with the result that opium from different sources varies considerably in composition. The first four entries in Table 1 relate to varieties cultivated in the main countries where it is legally grown (1 ,2, 3). These are followed by figures for varieties grown illicitly in two other countries (4).

Table 1: Principal Opium Alkaloids from Poppy Varieties grown in different Countries (%) (1, 2, 3, 4)

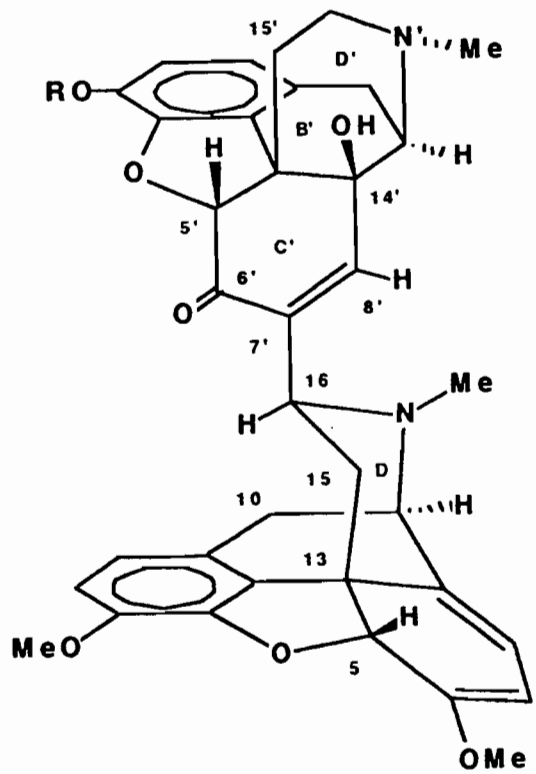
	Morphine	Narcotine	Codeine	Papaverine	Thebaine
Turkey	10-16	3-4	0.3-1.4	1-1.5	1-1.5
Yugoslavia	13-17	2-9	0.3-1.5	1-1.5	0.8-1.2
Iran	9-12	5-6	2.5-4	2-2.5	3-4
India	10-11	6-9	2.5-4	0.8	0.5-1
Thailand	7-18	3-10	2-5	0.3	2-6
Mexico	3-17	5-17	1-4	2-8	0.2-1.9

Altogether about sixty alkaloids have been isolated from different varieties of poppy (5), reflecting the large amount of work carried out on this plant. As far as Tasmanian-grown poppies are concerned, narcotine, a major constituent of Indian opium in particular, is virtually absent, but much higher amounts of thebaine are present than in other opiums. Thebaine is accompanied by appreciable quantities of its *O*-demethyl product, oripavine, which had previously been recorded in *P. orientale*, but not in any variety of *P. somniferum* (6).

Considerable amounts of minor alkaloids, hitherto unrecorded and of an unusual nature, were found; one of these, obtained as an amorphous base, was named somniferine (7). The formula $C_{36}H_{36}N_2O_7$ was deduced by HRMS and supported by the nmr data, which revealed 34 non-exchangeable protons, two tertiary *N*-methyl groups, and two methoxyls. From its ^1H and ^{13}C nmr spectra the alkaloid appeared to be a dimer of two morphinin units with resonances attributable to thebaine and 14-hydroxymorphinone (8) being discernible.

The ^{13}C data suggested a C-16 to C-7' linkage between the two halves, and this was confirmed by the ^{3}J long-range coupling observed between the ketone carbon and H-16, and an allylic coupling between H-16 and H-8'. The *N*-methyl is very strongly shielded by the conjugated carbonyl. Detailed examination of 2D correlation spectra enabled the unambiguous assignment of all proton and carbon resonances and established the complete structure of somniferine as 1.

The relative stereochemistry of somniferine was deduced as follows: The observed n.O.e's indicated that the H-5 protons must be cisoid to the ethanamine bridges in both halves and a g-gauche effect in ring D' betweeen the C-14' hydroxyl group and C-15' shows that rings B' and C' are cis-fused. The great steric bulk of the hydroxymorphinone residue requires it to be equatorially substituted, and the strong n.O.e observed between the axial H-16 and the equatorial H-10 proves that ring D adopts the chair form in somniferine, whose structure and relative stereochemistry are thus represented by 1. This also represents its absolute configuration, since the CD spectrum of 1 corresponds closely to a simple summation of the spectra of thebaine (9) and 14-hydroxycodeinone (10).



1 Somniferine R = H
2 O-methylsomniferine R = Me

An exhaustive extraction of the heads and straw of Tasmanian poppies yielded crude opium in 1.88% yield. The alkaloids isolated are shown in Table 2. A second dimeric alkaloid proved to be O-methylsomniferine (2). In addition, several other minor bases have been identified by spectroscopic means. These include codeinone, both thebaine *N*-oxides, laudanosine, laudanine and orientaline.

Table 2: Principal Alkaloids of Tasmanian Opium (%)

	Isolated Yield	by GC
Morphine	43.7	37.2
Narcotine	-	-
Codeine	4.6	5.4
Papaverine	3.4	4.0
Thebaine	8.5	8.8
Oripavine	-	0.3
O-Methylsomniferine	4.3	-
Somniferine	1.9	-

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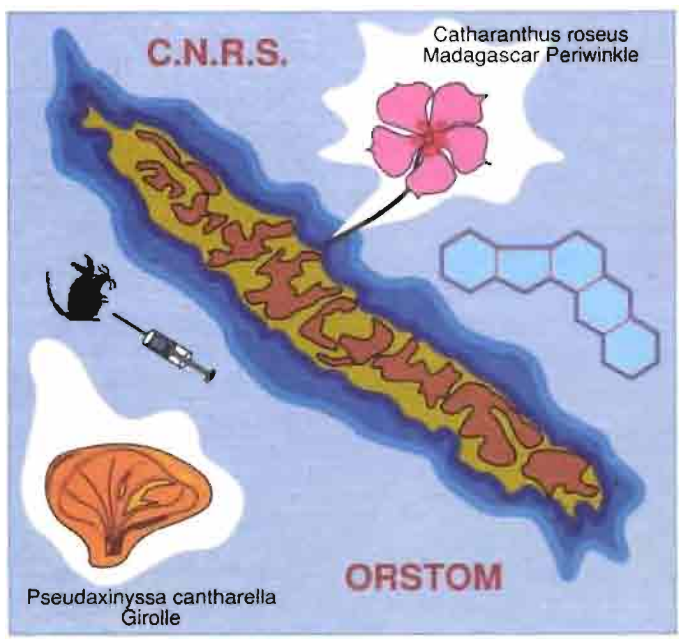

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