



THE CHEMISTRY AND PHARMACOLOGY OF SOME MALAYSIAN MEDICINAL PLANTS

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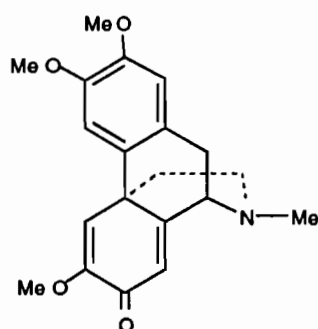
Résumé : L'étude des alcaloïdes de *Alseodaphne perakensis* a conduit à l'isolement de la sébiférine, de la sébiférine *N*-oxyde, et d'un composé non-alcaloïdique, l'hydroxy-7 triméthoxy-2, 3, 6 phénanthrène. L'alcaloïde majoritaire, la sébiférine présente des propriétés d'utéro-stimulation, hypotensive, et analgésique. Des alcaloïdes poly-pyrrolo-indoliques ont été isolés de *Psychotria rostrata*. Les alcaloïdes minoritaires ont été identifiés à la (+)-chimonanthine, la (-)-calycanthine et à la (-)-calycosidine. La pyrroloindoline majoritaire est la quadrigémine B qui s'avère être cytotoxique. *Lindera pipericarpa* contient trois alcaloïdes aporphiniques, identifiés à la thaliporphine, l'isocorydine et la norisocorydine, alors que l'alcaloïde majoritaire de *Breynia coronata* est la sécurinine. Notre étude des alcaloïdes de *Cyclea laxiflora* a conduit à l'isolement de la dicentrine.

Abstract : a study on the alkaloids of *Alseodaphne perakensis* resulted in the isolation of sebiferine, sebiferine *N*-oxide and a non-alkaloidal component, 7-hydroxy-2,3,6-trimethoxyphenanthrene. The major alkaloid, sebiferine showed uterine stimulant, hypotensive and analgesic properties. Poly-pyrroloindolinic alkaloids were isolated from *Psychotria rostrata* (+)-Chimonanthine, (-)-Calycanthine and, (-)-calycosidine were identified as the minor alkaloids. The major tetrameric pyrroloindoline was identified as quadrigemine-B, and was found to be cytotoxic. *Lindera pipericarpa* contained three aporphine alkaloid identified as thaliporphine, isocorydine and norisocorydine while *Breynia coronata* contained securinine as the major alkaloid. Our study on the alkaloids of *Cyclea taxiflora* led to the isolation of dicentrine.

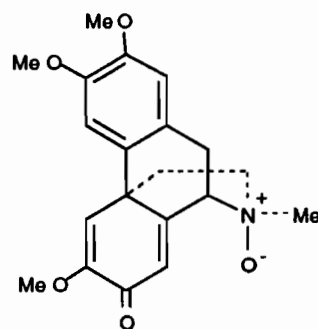
Discussion:

Alseodaphne perakensis, (Lauraceae), is a medium size tree known locally as *Medang kapas*. The wood were claimed to make durable timber for houses. Even though no medicinal use was recorded, a claim that the fruits are poisonous attracted our attention for chemical investigation (Burkill I.H., 1935). Our initial phytochemical screening indicated that all parts of the plants (leaves, bark and fruits) were rich in alkaloids.

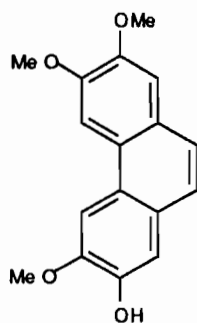
Preliminary thin layer chromatography of the basic fraction of crude extracts of the leaves and bark showed that they consisted basically of the same components. Further isolation and purification gave one major component identified as sebiferine (Lajis *et al*, 1989). Pharmacological screening of sebiferine was carried out and showed activities including uterine stimulant and hypotensive as well as having analgesic properties (Kanjanapothi, 1988). A new minor alkaloid was also isolated. A molecular ion peak (M^+) at 357 suggested the addition of an oxygen in the major alkaloid and the nuclear magnetic resonance (NMR) supported the structure to be sebiferine *N*-oxide. This structure was also confirmed by reducing the *N*-oxide (zinc/sulfuric acid) to sebiferine, as well as oxidising sebiferine to the *N*-oxide derivative using hydrogen peroxide (Lajis *et al*, 1990).



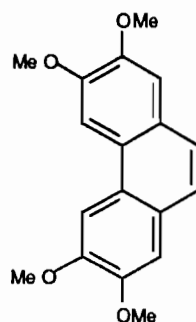
Sebiferine

Sebiferine *N*-oxide

A non alkaloidal minor component was also isolated. This compound gave a molecular ion peak (M^+) at 284 consistent with the molecular formula $C_{17}H_{16}O_4$. The NMR spectrum showed four aromatic peaks in addition to three methyl singlets which suggested the structure to be 7-hydroxy-2,3,6-trimethoxyphenanthrene. This structure was supported by comparison the NMR with the related structure of tylophorine. To support this conclusion the phenanthrene was methylated ($Me_2SO_4/NaOH$) to give 2,3,6,7-tetramethoxyphenanthrene. Eventhough this compound was reported previously, its isolation from plant has never been documented.

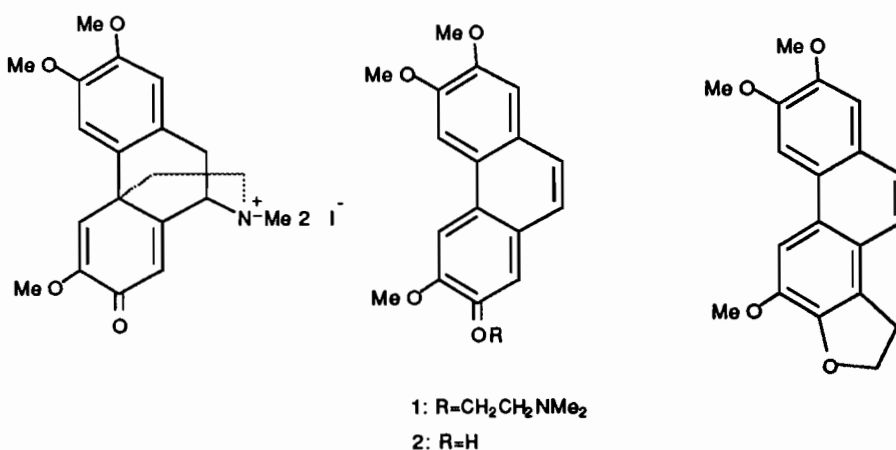


7-Hydroxy-2,3,6-trimethoxy-phenanthrene

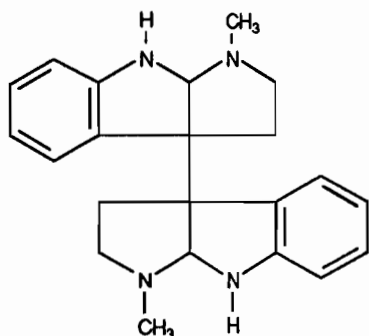


2,3,6,7-tetramethoxy-phenanthrene

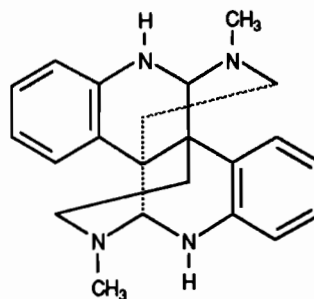
Even though this compound was co-isolated with other basic components, the presence of it in non-basic fraction during isolation was detected. Furthermore, when the major alkaloid was subjected to all isolation and purification procedures, no degradation was detected. These tests therefore excluded the possibility that the phenanthrenoid was an artifact resulting from degradation of the major alkaloid. Sebiferine methiodide was however degraded to 7-hydroxy-2,3,6-trimethoxyphenanthrene when it was heated in aqueous NaOH. Two other minor by-products were also isolated in this reaction.



Our investigation on *Psychotria rostrata* (Rubiaceae) was initiated due to its high content of alkaloids and its use in traditional medicine to relieve constipation (Burkill, 1935). *Psychotria rostrata* or locally called *Sedoman* is a shrub commonly found at the edge of the forests. The basic fraction of methanolic extracts of the leaves gave several components of polypyrroloindolinic compounds. Two pyrroloindoline dimers were isolated after purification using column and thin layer chromatography. The M.S., NMR and other spectroscopic data were consistent with chimonanthine and calycanthine.



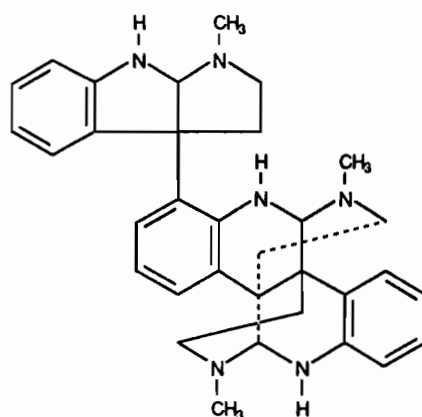
Chimonanthine



Calycanthine

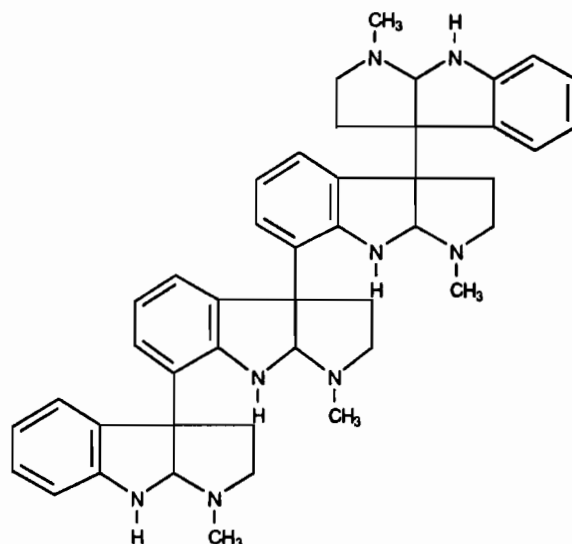
The isolation of both compounds have been reported. The optical rotation of chimonanthine was however opposite to the ones previously isolated from other plants. In fact our compounds were identical with the ones isolated from the skin of the *Columbian poisonous dart frog* (Tokuyama and Daly, 1983).

A trimeric pyrroloindoline was isolated as a minor component. Spectral arguments based on the spectra (M.S., NMR, U.V., I.R.) of chimonanthine and calycanthine led us to conclude that the structure consisted of a calycanthine with a pyrroloindoline unit attached to one of the calycanthine benzene ring. Eventhough no report on such structure has ever been documented at the time of our finding, a similar structure was reported soon after and it was named calycosidine. This compound was isolated from *Calycodendron milnei* (Libot *et al*, 1988) a native plant of New Caledonia.



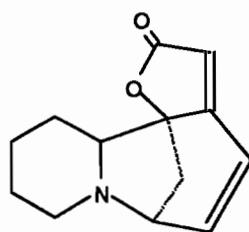
calycosidine

The major components of the basic fraction proved to be difficult to purify. Multiple development thin layer chromatography, centrifugal thin layer chromatography and even droplets counter current chromatography did not give satisfactory results eventhough partial purification was achieved. Purification was only achieved using preparative HPLC and only one of the pure components was identified as quadrigemine B. Pharmacological screening of the major component was carried out in collaboration with School of Pharmacy, USM to show that it has strong cytotoxic activity.



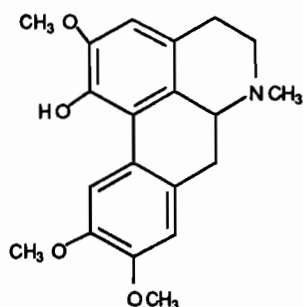
quadrigemine-B

In our investigation of *Breynia cronata* (Euphorbiaceae), a common shrub in peninsular Malaysia, one major alkaloid was isolated from the basic fraction of methanolic extracts of leaves and twigs after column chromatography. This alkaloid was identified as securinine, an alkaloid reported to be used clinically for treatment of paralysis (Cordell, 1981). Two other minor components were isolated but was not identified due to its instability. These compounds deteriorated during postage overseas.

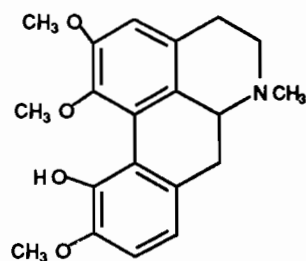


securinine

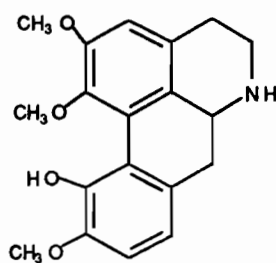
Our study of the alkaloids of *Lindera pipericarpa* (Lauraceae), a tree locally called *Medang air* and used in traditional cosmetics (Burkill, 1936) gave us one major compound in addition to two minor ones. Based on its spectral data (M.S., NMR, I.R. and U.V.) the major alkaloid was identified as thaliporphine. Two polar minor alkaloids were identified as isocorydine and norisocorydine.



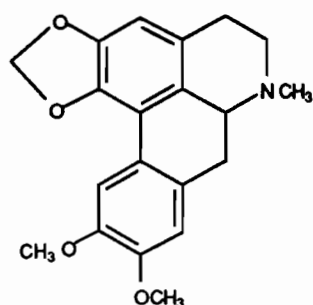
thaliporphine



isocorydine



norisocorydine



dicentrine

The tuber of *Cyclea laxiflora* (Menispermaceae), locally known as *Terung kemang* is used by the people in Northern Peninsular Malaysia for treatment of sinus (Burkill, 1935). Our investigation on the alkaloid component of this tuber has led to the isolation of dicentrine.

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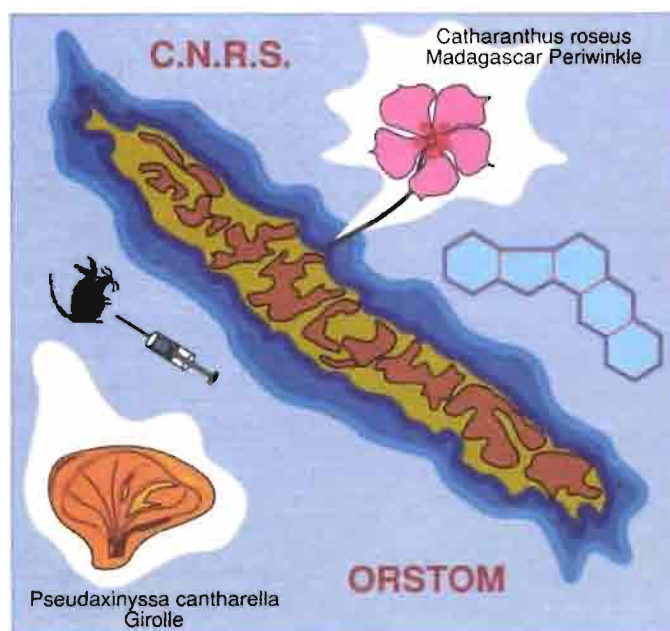
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