

A REVIEW OF BIOACTIVE ALKALOIDS FROM THE GENUS OF PSYCHOTRIA

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ABSTRACT

Psychotria (Rubiaceae) is a very large genus of plants, but according to published information available before the 1980s, it appears to be relatively unimportant medicinally, although several species have been used in poultices for sores, ulcers, skin disorders, and also in connection with parturition. However, since the 1990s, several papers have reported that alkaloids found from *Psychotria* species have cytotoxic, antibacterial, and analgesic properties. The genus *Psychotria* is well known as a source of pyrrolidinoindoline alkaloids in monomeric, dimeric, trimeric and higher polymeric forms. This genus has contributed several novel indole-type alkaloids with quite a broad spectrum of bioactivities. This paper reviewed the bioactive alkaloids from at least eight species from the plants of *psychotria* genus.

Keywords : Review, Alkaloids, Psychotria

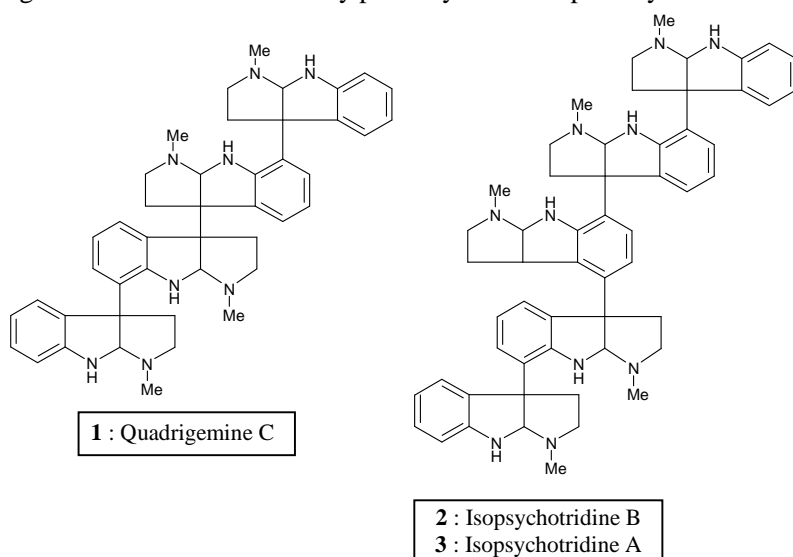
INTRODUCTION

Psychotria (Rubiaceae) is a very large genus, but according to published information available before the 1980s, it appears to be relatively unimportant medicinally, although several species have been used in poultices for sores, ulcers, skin disorders, and also in connection with parturition.¹ However, since the 1990s, several papers have reported that alkaloids found from *Psychotria* species have cytotoxic, antibacterial, and analgesic properties.²⁻⁴ The species recorded are distributed in many tropical regions, such as Indo-China, Malaysia, the Philippines, and the Solomon islands.

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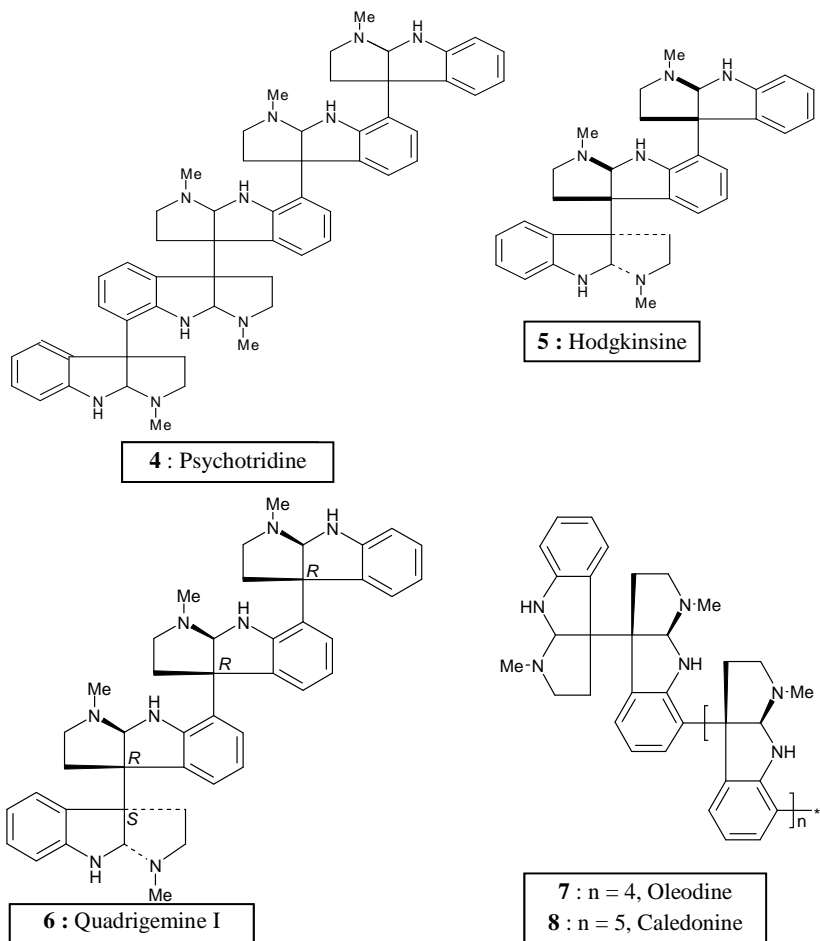
at least eight species from the genus have been reported and are reviewed below.

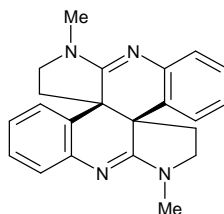
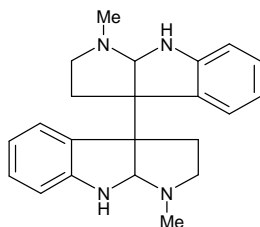
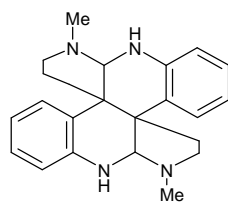
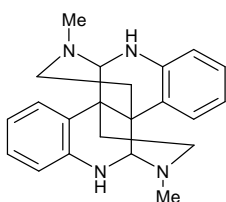
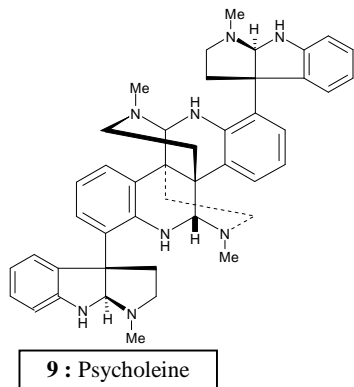
Psychotria oleoides. Libot *et al.*⁵ have reported the isolation of three new pyrrolidinoindoline alkaloids from *Psychotria oleoides*, which are named quadrigemine C **1**, isopsychotridine B **2**, and isopsychotridine A **3**. Two known alkaloids were also isolated, psychotridine **4** and hodgkinsine **5**. Jannic *et al.*⁶ have independently reported that this species produced three other new alkaloids, quadrigemine I **6**, oleidine **7**, and caledonine **8**. Moreover, following a bioactivity-guided purification of the methanol extract of this plant, a new alkaloid, psycholeine **9**, was isolated by Gueritte-Voegelein *et al.*⁷ They reported that psycholeine interacts with somatostatin receptors and exhibits a somatostatin antagonistic activity on growth hormone secretion by pituitary cells in a primary culture.



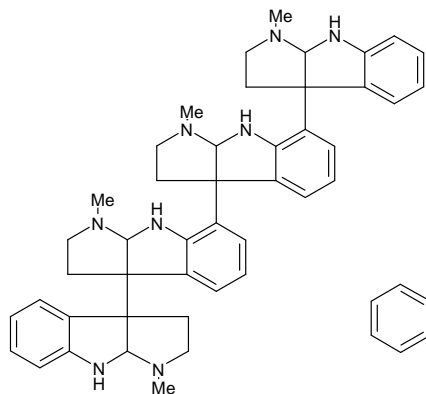
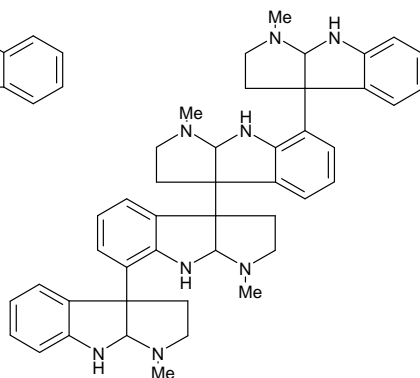
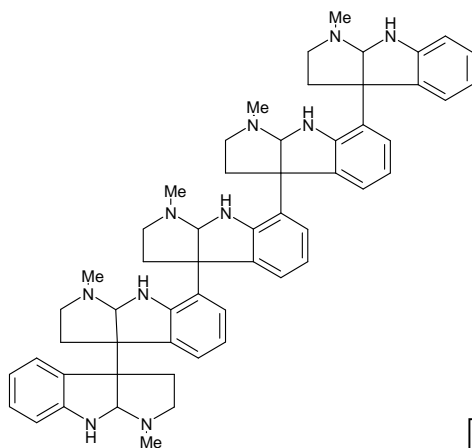
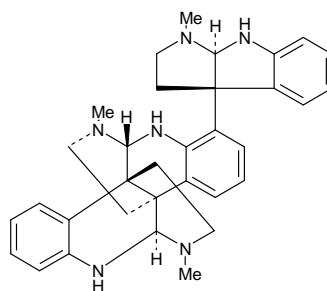
Psychotria colorata. In the plant *Psychotria colorata* dimeric pyrrolidinoindolines predominate, for example, (-)-calycanthine **10**, isocalycanthine **11**, (+)-chimonanthine **12** and (8-8a), (8'-8'a)-tetrahydroisocalycanthine **13**. Trimeric hodgkinsine **5**, tetrameric quadrigemine C **1** and pentameric psychotridine **4** have also been obtained as minor compounds from this species.⁸ Analgesic properties

have been reported for the alkaloid extract. Further studies by Amador *et al.*⁹ reported that psychotridine **4** shows a dose-dependent analgesic effect in the rat tail-flick model and does not induce motor deficits at doses effective in analgesic models. It was also suggested that NMDA receptors participate in psychotridine-induced analgesia. Similar analgesic activity, and with an analogous mechanism, was found with the trimeric alkaloid hodgkinsine.¹⁰ A further bioactivity study was reported on quadrigemine C **1**, which was shown to be cytotoxic towards HEP-2 cells and normal human lymphocytes, with the cytotoxicity being time- and dose-dependent. This compound also exhibited bactericidal activity against *Escherichia coli* and *Staphylococcus aureus*.¹¹





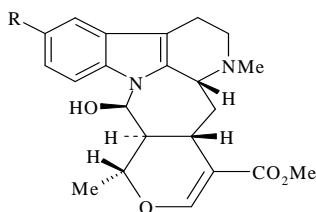
Psychotria forsteriana. From the leaves of *Psychotria forsteriana*, four optically active alkaloids have been isolated, namely quadrigemine B **14**, quadrigemine A **15**, psychotridine **4** and a new stereoisomer of psychotridine called isopsychotridine C **16**.¹² All four of these compounds were reported to be potent inhibitors of the aggregation of washed human platelets induced by ADP, collagen, or thrombin and appeared to act at a later stage in platelet activation, possibly through an interaction with cytoskeletal proteins.¹³

**14** : Quadrigemine B**15** : Quadrigemine A**16**: Isopsychotridine**16a** : Calycosidine

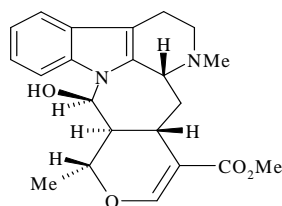
Psychotria rostata. The plant, *Psychotria rostata*, found in Malaysia, and studied by the Zurinah group,² was reported to yield quadrigemine B **14** as the main alkaloid component, together with hodgkinsine **5**, (-)-calycanthine **10**, (+)-chimonanthine **12**, and calycosidine **16a** as minor components.

Psychotria correae. From *Psychotria correae*, six new alkaloids have been obtained, namely correantoside **17**, 10-hydroxycorreantoside **18**, correantine A **19**, B **20**, C **21**, and 20-epi-correatine B **22**.¹⁴ Three new quinoline alkaloids, glomerulatine A **23** (major), B **24**, and C **25**, have

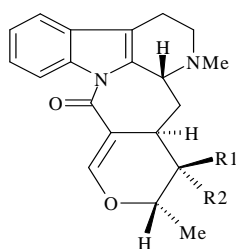
also been isolated from aerial parts of *P. glomerulata*. The Amazonian plants *P. viridis* and *P. carthagenensis* are ingredients of a hallucinogenic beverage made by Indian tribes in the Southwestern Amazon basin. Chemical investigations revealed the presence of *N,N*-Dimethyltryptamine **26**, methyltryptamine **27** and 2-methyl-1,2,3,4-tetrahydro- β -carboline **28**.^{15,16}



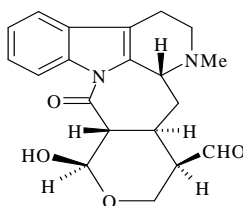
17 : Correantoside; R=H
18 : 10-Hydroxycorreantoside; R=OH



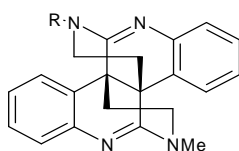
19 : Correantine A



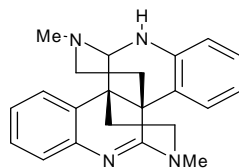
20 : Correantine B; R₁=H, R₂=CHO
22 : 20-epi-Correantine B; R₁=CHO, R₂=H



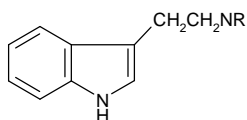
21 : Correantine C



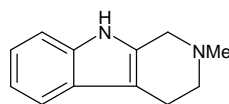
23 : Glomerulatine A, R=Me
24 : Glomerulatine B, R=H



25 : Glomerulatine C

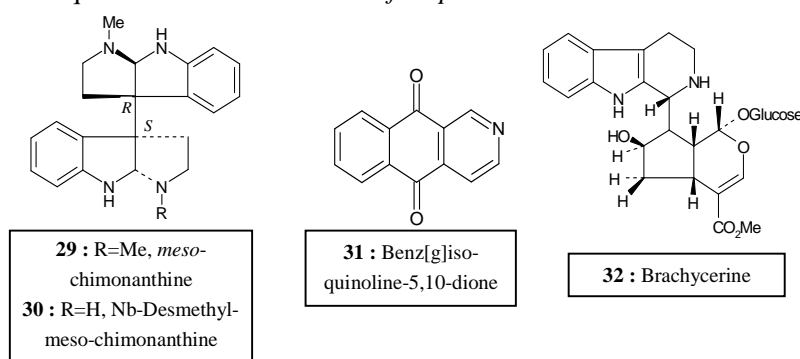


26 : R=Me₂, *N,N*-dimethyltryptamine
27 : R=Me, Methyltryptamine



28 : 2-Methyl-1,2,3,4-tetrahydro- β -carboline

Psychotria lyciiflora. The plant *Psychotria lyciiflora* from New Caledonia contained two dimers, *meso*-chimonanthine **29** and *Nb*-Desmethyl-*meso*-chimonanthine **30**, and hodgkinsine **5** as reported by Jannic *et al.*⁶ Psychotridine **4** was obtained as a major alkaloid component of *P. beccarioides*,¹⁷ while the structurally different alkaloid benz[*g*]isoquinoline-5,10-dione **31** was isolated from the woody parts of *P. computants* based on bioactivity-guided fractionation. The compound showed strong activity *in vitro* against brine shrimp, KB cells, and chloroquine-resistant *Plasmodium falciparum*.¹⁸



Another unusual alkaloid, brachycerine **32**, was isolated from *P. brachyceras*. The compound was found to be restricted to shoots in rooted cuttings and accumulation was not affected by root induction treatment with auxin.¹⁹

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