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Alkaloids Derived from Tryptophan

INTRODUCTION

A very large group of alkaloids—undoubtedly the largest of all—the group of alkaloids arising from the metabolism of tryptophan was thoroughly studied following the isolation, in 1953, of reserpine, the antihypertensive and tranquilizing constituent of the roots of an Apocynaceae, *Rauwolfia serpentina*. Several years later, the therapeutic interest of these indole-type structures was confirmed when the antitumor properties of the binary alkaloids of the Madagascan periwinkle, *Catharanthus roseus*, were demonstrated. In addition to its pharmacological and therapeutic interest, this group of alkaloids is obviously of great chemical interest: the structural variety that it displays, the biosynthetic questions that it raises, and the synthetic challenges that it proposes are all thrilling subjects; the plethora of publications reflects the number of questions that it has inspired.

Tryptophan is a precursor of these alkaloids, but except for simple amines (assimilated with the alkaloids out of habit, even though they do not fulfill the strict and generally accepted definition), it is not the only one: acetate, mevalonate, secologanin, and other elements can be combined with tryptamine, hence the structural variety mentioned above.

Thus four groups of alkaloids can be distinguished, including the tryptamines.

1. Simple Amines and Carboline Alkaloids

In this chapter, we shall only describe the tryptamine derivatives that have hallucinogenic properties (gramine [= 3-dimethylaminomethylindole] is devoid of pharmacological interest); the β -carboline and tetrahydro- β -carboline alkaloids often occur alongside tryptamines, and most of them have the same properties: we

2. Indolines Arising from the Cyclization of Tryptamine

These are essentially the alkaloids of the Calabar bean, and in addition the oligomers from the Calycanthaceae and Rubiaceae (*Psychotria*) are of some interest.

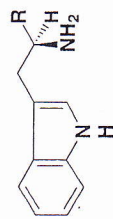
3. Ergoline Derivatives

They are highly specific to a few rare higher vegetables (Convolvulaceae) and to the Ascomycetes fungi. Although they are of fungal origin, they will be covered in the present book, because of their very high therapeutic interest.

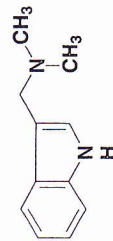
4. Monoterpenoid Indole Alkaloids

Monoterpenoid indole alkaloids are by far the largest group. They incorporate a C₁₀ (or C₉) monoterpenoid unit, and their distribution is limited to a small number of Angiosperm families, mainly the Apocynaceae, Rubiaceae, and Loganiaceae. Based on their biosynthesis, in this group of indole alkaloids we shall include the quinoline alkaloids of the cinchona: they are derived from the same precursor, namely strictosidine.

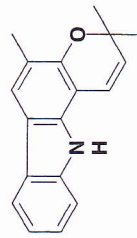
Because they have no applications (or interesting properties), the carbazoles of the Rutaceae, and the canthin-6-ones of the Rutaceae and Simaroubaceae will not be covered. Like the metabolites of phenylalanine and tyrosine, the mycotoxins formed from tryptophan will also be skipped (except for the ergolines: spirodesmin, paspalicine, and so forth).



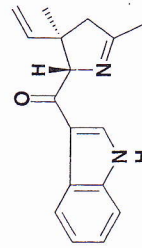
R = H: Tryptamine

R = CO₂H: Tryptophan

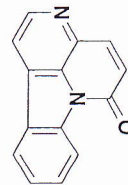
Gramine



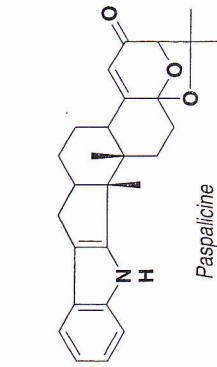
Gitrinbine



Borreline



Canthin-6-one



Paspalicine

Tryptamines, β-Carboline Alkaloids

“Drugs Containing Hallucinogenic Indole Alkaloids”

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1. GENERALITIES

Hallucinogens are substances capable of causing “substantial and transient modifications of perceptions, thought, and mood”, and are classified among psychoactive substances, a less restrictive term applicable to the hallucinogens but also to opium, alcohol, and solvents, and even to the psychoactive component of the action of the Solanaceae alkaloids.

Except for Indian hemp, whose properties are in fact markedly different, hallucinogenic plants owe their activity to nitrogen-containing substances. In most cases the structures responsible are indoles* (p. 970), indoalkylamines, or true alkaloids: tryptamines, carboline, and ergoline alkaloids; in a few rare cases, they are aryl-alkylamines (e.g., mescaline, see peyote) in which some authors see “virtual” indoles. In both cases, we shall note the obvious structural analogy with