

**Alkaloids from S. American species of *Uncaria* (Rubiaceae)**

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The genus *Uncaria* has a pantropical distribution and is found mainly in S.E. Asia although it is also represented in mainland Asia, Africa and S. America. One of the two S. American species, *U. guianensis* (Aubl.) Gmel. is said to be used in folk-medicine in the treatment of intestinal ailments and in promoting wound healing (Ostendorf, 1962). The oxindole alkaloid rhynchophylline has been isolated from this species (Raymond-Hamet, 1952) but there are no other reports on its constituents, nor any on those of the other S. American species, *U. tomentosa* DC.

Both species were collected on recent expeditions to S. America and were made available to use for chemical investigation. The leaves and stems of each species yielded isorhynchophylline and rhynchophylline as the major alkaloids, together with their *N*-oxides, mitraphylline, dihydrocorynantheine, hirsutine and hirsuteine. In addition, *U. tomentosa* was found to contain isomitraphylline, its *N*-oxide and two new alkaloids which were identified as dihydrocorynantheine *N*-oxide and hirsutine *N*-oxide.

Another 14 samples of *U. guianensis* originating from widely separated regions of S. America were obtained from herbarium collections and screened for alkaloids. Of these, 12 resembled the above sample in their alkaloid content and one had the mitraphyllines as major alkaloids. Fewer collections of *U. tomentosa* have been made and only one herbarium sample was obtained for screening. Its alkaloid content was similar to the other sample except that the 9-hydroxy oxindoles isorotundifoline and rotundifoline were present as minor alkaloids.

Both the S. American species have morphological similarities to African and to Asiatic taxa. However, in their alkaloid content they are more closely allied to the Asiatic taxa (unpublished observations). The morphological and chemical affinities between the different geographical groups of species are of interest in the light of divergent theories as to the origin of the Asian, African and S. American continents (van Steenis, 1962; Tarling & Tarling, 1971).

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**The chemotaxonomic significance of alkaloids in the Naucleaeae**

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Some genera of the Rubiaceae (e.g. *Cinchona*, *Cephaelis*) are sources of medicinally important alkaloids. Members of the family produce alkaloids of three major types which although based on either quinoline (e.g. quinine), isoquinoline (e.g. emetine) or indole (e.g. yohimbine) ring systems, are related biosynthetically since all are partially derived from secologanin (Hegnauer, 1973). Oxindole and heteroyohimbine alkaloids are reported only from the tribes Cinchoneae and Naucleaeae in which the tribal delimitation has been debated (Bremekamp, 1966). The Naucleaeae in particular, are in a state of taxonomic confusion (Bakhuizen van den Brink, 1970) and are currently being revised. *Mitragyna* and *Uncaria*, traditionally

placed in the Naucleaeae are good sources of oxindole and heteroyohimbine alkaloids and thus it seemed possible that a knowledge of the alkaloids in other members of the Naucleaeae might assist in unravelling generic relationships. To this end, over 100 Naucleaeae leaf samples from herbarium material were screened for alkaloids and species from the following genera were examined:

*Adina*, *Anthocephalus*, *Breonia*, *Cephalanthus*, *Metadina*, *Myrmeconauclea*, *Nauclea* (*Sarcocephalus*) and *Neonauclea*.

The results indicate that oxindoles or heteroyohimbines are not widespread in the rest of the tribe, only being found in several species of *Cephalanthus* and one of *Neonauclea*. The majority of the samples of *Neonauclea*, together with those of *Nauclea*, *Metadina* and *Myrmeconauclea*, contained pyridino-indolo-quinolizidinone alkaloids, also reported from species of *Mitragyna* and *Uncaria* (Phillipson, Hemingway & others, 1974). However, the latter two genera have morphological and anatomical affinities with the Cinchoneae which also includes genera producing heteroyohimbines and oxindoles. Inclusion of *Cephalanthus* in the Naucleaeae has been questioned (Bremekamp, 1966) and considering its isolated position perhaps it would be better placed in a separate tribe. The presence and nature of the alkaloids of *Mitragyna* and *Uncaria* tends to support the taxonomic idea that these genera together with *Cephalanthus*, stand apart from the rest of the Naucleaeae and that their exclusion would result in a taxonomically homogeneous tribe. Hence differences in alkaloid content proved useful in assessing the taxonomic relationships, although further information is required on the distribution of indole and quinoline alkaloids, especially in members of the Cinchoneae as well as of the Naucleaeae.

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#### Methylating and demethylating enzymes in *Papaver somniferum* latex

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Tracer work has established that the formation of the hydrophenanthrene phthalideisoquinoline and benzyloisoquinoline groups of alkaloids involves a number of methylation and demethylation steps. Spenser (1966) reported that methionine was the most efficient donor for both *O*- and *N*-methyl groups of the alkaloids.

The presence of methylating enzymes was investigated in whole latex as well as latex which was fractionated to 1000 *g* × 30 min and supernatant fractions. In the preliminary experiments the latex was incubated with methionine (<sup>14</sup>C-methyl) in presence and in absence of co-factors intended to shift the equilibrium to the formation of *S*-adenosyl-L-methionine together with norlaudanosoline. The activity extracted using chloroform was taken as a measure of the total organic soluble methylation products (including alkaloids), formed by the latex at the end of the incubation period. The extraction was done after preliminary precipitation of the latex protein by acid followed by readjustment of the pH to 8.0-8.5. The radioactivity in the organic layer was found to be dependent on the amount of latex used and was considerably increased by inclusion of the co-factors in the incubation mixture implying preliminary formation of *S*-adenosyl-L-methionine which was more efficient in this respect as methyl donor.

On repeating the experiments with *S*-adenosyl-L-methionine (methyl <sup>14</sup>C) it was found that the activity in the organic layer was considerably increased by inclusion of norlaudanosoline