Letters to the Editors

ETHNOPHARMACOLOGY OF KRATOM AND THE MITRAGYNA ALKALOIDS

Sirs,

The letter from Karl L.R. Jansen and Colin J. Priest (1988) regarding the pharmacological effects of Mitragyna speciosa Korth. raises a number of interesting points. In the first place it cannot be concluded that because mitragynine has a methoxy substitution at C(9) corresponding to a hydroxy substitution at C(4) in the indole unit of psilocybin and lysergic acid amide that the pharmacological actions must be similar. This was never suggested by Beckett et al. (1965). It should be noted that there are no C(9)-OH indole alkaloids in any of the species of Mitragyna although there are C(9)-OH oxindole alkaloids. None of these alkaloids are reported to have any analgesic activity although, as reported by Zarembo et al. (1974) mitragynine pseudoxindole does. However, this compound does not occur naturally and the A and B corresponding oxindole isomers are only found in traces, the former only during some months (Shellard et al., 1978). The pharmacological activity of mitragynine must obviously depend upon its configuration. Mitragynine has the allo configuration but speciociliatine (epiallo), speciogynine (normal) and mitraciliatine (pseudo) have no reported analgesic properties.

Nevertheless, there is this contradiction between the activity of “kratom” leaves which are chewed as a stimulant and the depressant activity of mitragynine which is the main alkaloid found in “kratom” leaves but which is not found in any of the other species of Mitragyna. But this is not an unknown feature of many plants, e.g. Panax ginseng C.A. Meyer. Medical herbalists could give examples of many more such as Filipendula ulmaria and it is clear evidence of their claim that the therapeutic effect of plant extracts can be quite different from that of isolated constituents. It may be that the other alkaloids present in Mitragyna speciosa have a marked stimulant effect but this is most unlikely.

However, there is a possible explanation. In 1963 when our group at Chelsea College (now King's College), University of London, was trying to isolate large amounts of mitragynine from “kratom” leaves it was found that when the powdered leaf was extracted with ethanol it was never possible to obtain a clean, white sample, whether the semi-alcoholate or a salt. This was overcome by extracting the plant material with ethyl acetate which left behind a dark, sticky residue which because of its non-alkaloidal nature was ignored by us at the time. It was always my intention to return to this but the
opportunity never materialised. Evidence for the presence of latex in this leaf was substantiated by the anatomical study of the leaf which showed laticiferous cells particularly in the mid-rib (Shellard et al., 1965). It might well be that a study of this latex would be useful.

I would like to mention one historical fact which could have some bearing on the question of finding a suitable treatment for addiction to opiates. When I was in Bristol in 1956—1957 a pharmacist friend purchased an old, historic pharmacy and found in the cellar hundreds of bottles of a reddish-brown liquid clearly labelled as an "Opium substitute". They had obviously been in the cellar since 1924 when the Dangerous Drugs regulations came into force and, of course, they were destroyed. But I did have the opportunity of testing for alkaloids which were absent and I noted that the label indicated that the preparation was based on an extract of a species of Uncaria. Unfortunately I cannot now remember the name of the species or find the notes I made at the time, but the close botanical relationship between the genera Uncaria and Mitragyna may not be without significance.

References


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