

LETTERS TO THE EDITOR

MONO AMINO OXIDASE (MAO) INHIBITORY
ACTIVITY OF INDOLE-3-ACETAMIDO-
4'-ARYLCARBOXYLIC ACID ALKYLESTERS

IN connection with our synthesis of cysticidal compounds, we synthesized a series of compounds having substituted *p*-amino benzoates and salicylates joined, *via.* an amidic link to the carboxy group of indole 3-acetic, propionic and butyric acid. The cysticidal activity of these compounds have been reported elsewhere¹. 3-(2-amino butyl indole) has been reported as a potent MAO inhibitor². Since our compounds had an indolic nucleus, we tested them for possible MAO inhibitory activity. The compounds have shown MAO inhibitory activity of an order equivalent to that possessed by pheniprazine³ and ipronizid⁴ (well known MAO inhibitors).

Experimental

The following compounds were tested for MAO inhibitory activity:

(1) 2-Methyl indole 3-acetamido (3'-hydroxy)-4'-methylbenzoate (2) 2-Methyl-indole-3-acetamido (3'-hydroxy)-4'-ethyl benzoate (3) Indole-3-acetamido-(3'-hydroxy)-4'-methyl benzoate (4) Indole-3-acetamido-4'-ethyl benzoate, (5) 2-methyl indole-3-acetamido-4'-methyl benzoate, (6) 2-methyl-indole-3-acetamide 4'-ethyl benzoate, (7) Indole-3-acetamido-4'-methyl benzoate (8) Indole-3-propionamido-4'-methyl benzoate, (9) Indole-3-propionamido-4'-ethyl benzoate, (10) Indole-3-butyramido-4'-methyl benzoate (11) Indole-3-butyramido-(3'-hydroxy)-4'-methyl benzoate, (12) Indole-3-butyramido-4'-ethyl benzoate.

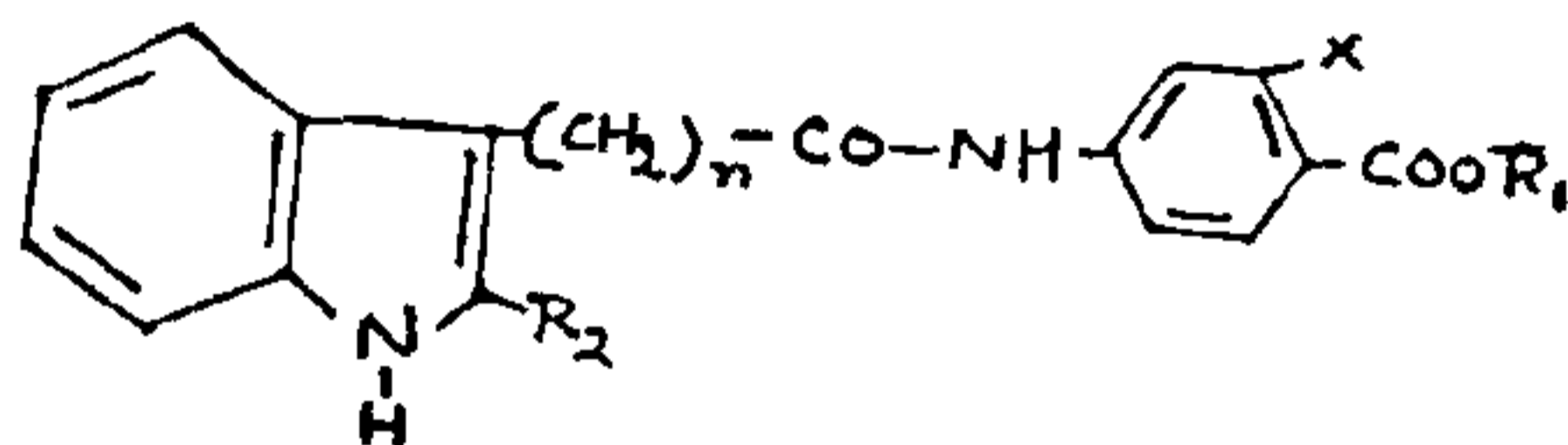
MAO activity was determined by the spectrophotofluorometric method of Krajl⁵ in rat brain using kynuramine as the substrate. The amount of 4-hydroxyquinoline which is formed from the spontaneous cyclization of the intermediate aldehyde generated during the deamination of kynuramine in 1N NaOH was measured fluorometrically in an Amino-Bowman Spectrophotofluorometer (activation frequency 315 m μ and fluorescence frequency at 380 m μ). Decrease in optical density provides a direct measurement of MAO inhibition.

Rats weighing approximately 100-150 g were killed by decapitation. Brains were quickly removed and homogenized in ice-cold 0.25 M sucrose with the help of Potter-Elvehjem homogenizer with a glass tube and Teflon-pestle. The enzyme was partially purified by subjecting the homogenate to differential

centrifugation upto 16,000 \times g. The 16,000 \times g residue which exclusively consisted of mitochondrial fraction, was suspended in 0.25 M sucrose to make a 10% (w/v) suspension.

The reaction mixture in a final volume of 2.0 ml contained 1.0 ml phosphate buffer (0.5 M, pH 7.4), 0.4 ml preparation, 20 μ g of kynuramine and an appropriate amount of the compound to be tested so that the final concentration of the compound in 2.0 ml was 5×10^{-5} M. After 10 minutes preincubation in a water bath at 37°C, the reaction was started by the addition of substrate. After an incubation of 30 minutes the reaction was stopped by the addition of 1.0 ml 10% (w/v) trichloroacetic acid. Tubes were centrifuged at 800 \times g for 15 minutes, and a suitable eluot of the supernatant was taken in 1 N NaOH. The 4-hydroxyquinoline formed during the incubation period was measured fluorometrically. Decrease in O.D. provided a direct measure of enzyme inhibition in experiment containing 3-indole-PAS esters. The MAO inhibitory activity is reported in Table I.

TABLE I



Sl. No.	X	R ₁	R ₂	n	MAO inhibitory activity(%)
1.	OH	CH ₃	CH ₃	1	58.30
2.	OH	C ₂ H ₅	CH ₃	1	60.47
3.	OH	CH ₃	H	1	58.38
4.	H	C ₂ H ₅	H	1	57.99
5.	H	CH ₃	CH ₃	1	60.47
6.	H	C ₂ H ₅	CH ₃	1	62.66
7.	H	CH ₃	H	1	58.98
8.	H	CH ₃	H	2	61.9
9.	H	C ₂ H ₅	H	2	67.42
10.	H	CH ₃	H	3	63.2
11.	OH	CH ₃	H	3	64.3
12.	H	C ₂ H ₅	H	3	72.9

a. The compounds were dissolved in propylene glycol.

b. Compounds were used at the final concentration of 5×10^{-5} M.

c. Each experiment was done in duplicate. Values in the table are mean of two separate experiments.

Structure activity relationship

An examination of enzyme inhibitory activity in relation to the structure shows the following pattern.

1. A substitution at position 2 of the indole nucleus does not show any appreciable effect on inhibitory activity.

2. The presence of a -OH group or its absence in the benzene of the side chain does not affect the inhibitory activity.

3. It is clearly brought out that increase in the side chain from acetyl to butyryl at the 3-position of indole, causes a gradual increase in the inhibitory activity, and finally, the carboethoxy derivatives are more active than the carbomethoxy derivatives.

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CHEMICAL EXAMINATION OF THE HEARTWOOD OF *ABROMA AUGUSTA* LINN. F.
THE root and root-bark of *Abroma augusta* Linn. F. are used as emmenagogue, uterine tonic and in dysmenorrhoea¹. The leaves, stem-bark and heartwood of this plant are used in the treatment of gonorrhoea and in painful menstruation. Although the roots, leaves and stem-bark of *A. augusta* have been investigated by several workers²⁻⁶, yet no phytochemical work has been done on the heartwood of this plant. We now report the results of systematic chemical investigation of the heartwood of this plant.

The dried and powdered heartwood was successively extracted with petroleum ether (60°-80°) and chloroform.

The petroleum ether (60°-80°) extract was chromatographed over Brockmann alumina using petroleum ether (60°-80°), benzene and chloroform as eluents. The fraction eluted with benzene on evaporation left a white solid (0.002%) which crystallised from methanol in shining flakes (m.p. 136°-137°). It gave positive Liebermann-Burchardt test for sterol and its IR spectrum showed absorption at 3400 cm⁻¹ (-OH-stretching). The identity of this sterol as β -sitosterol has been confirmed by m.m.p. determi-

nation, co-TLC with authentic sample of β -sitosterol and by the preparation of its acetate (m.p. 128°) and benzoate, (m.p. 145°).

The concentrated chloroform extract of the heartwood was chromatographed over Brockmann alumina. The benzene: chloroform (1:1) eluted fraction, furnished a white solid (0.005%) m.p. 112°. It does not respond to Liebermann-Burchardt test for sterol and triterpene. The IR spectrum shows absorption peaks at 3420 (-OH-stretching), 2940, 2860 (C-H stretching) 1465 (-CH₃-bending), 1060 (C-O stretching due to primary alcohol) and doublet at 730 and 720 cm⁻¹ [-(CH₂)_n bending vibration due to straight chain methylene]. These data indicated the compound as octacosane-1, 28-diol (Lit. m.p. 112°) which was confirmed by its acetate⁷ (m.p. 81°).

The authors wish to express their sincere thanks to the University Grants Commission, New Delhi for financial support and to Dr. S. P. Ghosh of Indian Association for the Cultivation of Science, Calcutta for IR spectra.

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CONE-IN-CONE STRUCTURE IN THE UPPER FLYSCH SERIES (UPPER CRETACEOUS) MALLA JOHAR AREA PITHORAGARH DISTRICT, UTTAR PRADESH

CALCAREOUS cone-in-cone structures are minor features of some shales and are characterised by abundance of right circular cones (Pettijohn)³. These structures are of much help in establishing the diagenetic history of the sedimentary succession (Franks)¹. This note records the occurrence of calcareous cone-in-cone structure from the Upper Flysch Series of Upper Cretaceous age (see Heim and Gansser)², Sancha Malla area, Pithoragarh district, Uttar Pradesh. It is the first record of this structure from India.