

animals made severely diabetic by intravenous administration of alloxan monohydrate (45 mg kg⁻¹ on three successive days). On the basis of these results, it appears that the leaves of *Azadirachta indica* contain a potentially useful oral hypoglycaemic constituent which acts in a similar manner to the sulphonylureas.

In addition to its antidiabetic activity, an aqueous extract of neem leaves was found to possess mild diuretic properties in water-loaded rats (100-125 g). Mean urine output from animals dosed orally with 200 mg kg⁻¹ leaf extract was 5.3 ml during 0-6 h, compared with a mean control urine output of 3.6 ml during the same time period. Aqueous extracts of neem leaf also produced non-specific inhibition of natural and induced tone in smooth, cardiac and skeletal muscle in isolated muscle preparations. No local anaesthetic activity was found in neem extracts using the guinea-pig wheal and rabbit corneal reflex tests.

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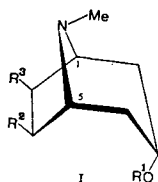
Alkaloids of the roots of *Erythroxylum monogynum* Roxb.

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E. monogynum Roxb. is a tree of Indian origin; the leaves contain cinnamoylcocaine and ecgonine (Chopra & Ghosh, 1938) and the wood constitutes a prolific source of diterpenoids (Fairlie, McCrindle & Murray, 1969).

An ether extract of the alkaline root-bark, submitted to column chromatography at pH 6.8 and preparative t.l.c. on alumina with CHCl₃ as solvent, afforded crystalline fractions which by mass spectroscopy were shown to contain components of molecular weights 335, 351, 361, 367 and 393. The compound giving M⁺335 had m.p. 120° and furnished a picrate, yellow prisms from aqueous alcohol, m.p. 201°; it was characterized as 1 α H, 5 α H-tropan-3 α -yl 3,4,5-trimethoxybenzoate I; R¹ = (MeO)₃C₆H₂·CO, R² = R³ = H. It possessed ester properties ν max (KBr disc) 1700 cm⁻¹ and after hydrolysis with Ba(OH)₂ solution gave rise to 3,4,5-trimethoxybenzoic acid and tropine. The hydrolysis products, or their derivatives, were confirmed by comparison with authentic samples (i.r. spectroscopy, m.p. and m.m.p., R_B values) and by elemental analysis. N.m.r. spectroscopy of the parent base, τ (CDCl₃) 4.8 (1H,t), confirmed the 3 α -orientation of the ester linkage (Evans & Major, 1968; Parelo, Longevialle & others, 1963). The product of the esterification of 3,4,5-trimethoxybenzoyl chloride and tropine, purified by chromatography, proved identical with the natural product (m.s., i.r., n.m.r. and m.p. and mixed m.p. of picrates). Compared against atropine the base had a low activity when tested on isolated guinea-pig ileum.



The fraction giving M⁺ 361 was identified as 1 α H, 5 α H-tropan- 3 α -yl 3,4,5-trimethoxy-cinnamate (picrate, i.r., n.m.r. and comparison with an authentic sample); this base I; R¹ = (MeO)₃C₆H₂·CH:CH·CO, R² = R³ = H has been reported previously as a constituent of *E. ellipticum* leaves. (Johns, Lamberton & Sioumis, 1970). A CHCl₃ extract of the original partition column made alkaline with ammonium hydroxide solution contained a mixture of bases, two of them having the chromatographic properties (3 systems) and colour reactions of tropine and ψ -tropine. Esterification of the mixture with tigloyl

chloride gave a number of products, two of which corresponded (t.l.c. 2 systems) to the tigloyl esters of tropine and ψ -tropine.

Other fractions, some of which are consistent in molecular weights and spectroscopic properties with esters of other tropanols (e.g. I; R¹ = H, R² and R³ = H or OH) and trimethoxybenzoic and trimethoxycinnamic acids are currently under investigation.

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Preliminary studies concerning the metabolism of hyoscyne and hyoscyamine in the Solanaceae

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The aerial parts of *Solandra grandiflora* Sw. and *Anthocercis viscosa* R.Br. contain esters of tropine and nortropine as principal alkaloids; little or no hyoscyne, apohyoscyne, norhyoscyne and oscine has been found in the specimens examined (Evans, Ghani & Woolley, 1972; Evans & Tregust, 1973).

To study the metabolism of hyoscyne in the aerial parts of these plants (–)-hyoscyne sulphate solution was infiltrated into shoots of intact *S. grandiflora* plants during 3 to 5 h. Shoots were harvested after 2,4,8 and 16 days and subsequently analysed. In addition to the normal alkaloids of the plants the injected shoots contained, in all cases, apohyoscyne, (±)-norhyoscyne, oscine (all characterized by t.l.c. and by mixed m.p. and i.r. spectrum of picrate). (±)-Hyoscyne was isolated from all the injected shoots. It may be inferred that the new metabolites arose from hyoscyne and that racemisation of the optically active bases is in keeping with the normal occurrence of atropine and nortropine in the plant. In another experiment, hyoscyne-G-¹⁴C fed as the sulphate solution to intact *A. viscosa* plants gave rise to the production of labelled apohyoscyne, norhyoscyne and oscine in addition to unchanged hyoscyne.

Hyoscyamine metabolism was studied by the separate infiltration of hyoscyamine-G-¹⁴C solution and unlabelled hyoscyamine sulphate solution into the alkaloid-free scions of *S. grandiflora* grafted on tomato stocks. Analysis of dried shoots, harvested 21 days after treatment, afforded atropine (t.l.c. and i.r. spectrum, mixed m.p. and radioactivity measurement of the picrate), nortropine and tropine (t.l.c., radioactivity measurement).

These results indicate that in the aerial parts of *Solandra*, atropine, nortropine and tropine can arise from hyoscyamine. Hyoscyne, which is of little significance in the normal alkaloid spectra of *Anthocercis* and *Solandra* is subjected to secondary transformation (racemization, demethylation, dehydration and hydrolysis) when injected into the intact shoots. Such findings supplement observations for other genera (Romeike, 1960; 1964; Neumann & Tschoepe, 1966; Hamon & Youngken, 1971) that atropine and hyoscyne are not necessarily the end-products of plant metabolism.

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