Table 1. Dissolution of CaG in water and saliva.

Dissolution medium	Time (min) for 50% dose (Ca) to dissolve α-isomer with citric acid	α-isomer without citric acid	β-isomer with citric acid	β-isomer without citric acid
water	6·6*	14·5*	5·8*	17·5*
saliva	2·4**	2·9**	2·3*	3·1*

Water: means of 4 tablets. Saliva: means of 4 tablets in 4 individuals. Significance of differences: $*P<0{\cdot}01$, $**0{\cdot}05>P>0{\cdot}01$.

Discrimination between CaG isomers in animal and clinical work has been referred to above although doubt exists concerning the strict identity of the isomers used. Table 1 shows that dissolution of the β-isomer in saliva is accelerated by citric acid more than that of the α-isomer although the expected general effect of citric acid is seen in water with both isomers equally. We also conclude that water and saliva are not interchangeable in dissolution studies and that dissolution rate of CaG can be modified by formulation for example by inclusion of citric acid. Future study will require much better separation and definition of isomers before definitive clinical work can be undertaken.

REFERENCES

BOWEN, W. H. (1972). *Caries Res.*, **6**, 43–51.
BROOK, A. H., GAWTHORPE, J. & WINTER, G. B. (1973). *Helv. Odont. Acta*, **17**, 55.
FEDEROFF, Y. A. (1965). *Rep. Acad. Sci.* USSR, **161**, 244–247.
GRENBY, T. H. (1973). *Helv. Odont. Acta*, **17**, 54–55.
STEPHEN, K. W., BEELEY, J. A., MACFADYEN, E. & BOWEN, W. H. (1973). *Ibid.*, **17**, 54.
WILLIAMS, C. H. (1960). *Analyt. chim. Acta.*, **22**, 163–171.

Pharmacological studies on the leaves of *Azadirachta indica*

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Azadirachta indica A.Juss (syn *Melia azadirachta* Linn.) is a large evergreen tree found growing in tropical and subtropical climates. It is indigenous to India and the Malay Archipelago. In addition, the tree is widely cultivated as an ornamental shade tree and has been naturalized in such countries as Nigeria, Saudi Arabia and the Soudan. In India, where it is known as the neem tree, the bark, leaves and fruit have been used from time immemorial in the treatment of such diverse complaints as constipation, fever, arthritis, worms and skin disorders.

Despite the popularity of the neem tree in folk-lore medicine, very little work has been carried out on its pharmacological properties apart from a study by Rao, Sukumar & others (1969) which indicated that neem leaves possess some antiviral activity. The present report concerns itself with other pharmacological properties possessed by neem leaves.

Young tender leaves were dried to constant weight at 40° and ground into a fine powder. A 10% w/v aqueous extract was prepared and tested for hypoglycaemic activity in rabbits (1·0–1·5 kg) previously fasted for 24 h but allowed free access to water. Following oral administration of the aqueous extract, a marked fall in blood glucose concentration was observed. This effect was both dose and time related, a maximum reduction in blood glucose level of 27% occurring 3·0 h after administration of a dose of extract equivalent to 200 mg kg^{-1} dried powdered leaf. Blood glucose concentrations returned towards control levels after 12 h. A similar hypoglycaemic effect was observed in fasted rats and to a lesser extent in guinea-pigs following oral dosing.

Antidiabetic activity was dependent on the presence of functioning pancreatic beta-cells, since neem leaf extracts did not produce hypoglycaemia in totally pancreatectomized rats, or

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.

REFERENCE

RAO, A. R., SUKUMAR, S., PARAMASIVAM, T. V., KAMALAKSHI, S., PARAMSHURAMAN, A. R. & SHANTHA, M. (1969). *Indian J. med. Res.*, **57**, 3–6.

Alkaloids of the roots of *Erythroxylum monogynum* Roxb.

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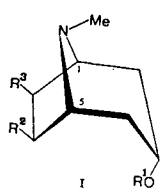
E. monogynum Roxb. is a tree of Indian origin; the leaves contain cinnamoylcocaine and ecgonine (Chopra & Ghosh, 1938) and the wood constitutes a prolific source of diterpenoids (Fairlie, McCrindle & Murray, 1969).

An ether extract of the alkaline root-bark, submitted to column chromatography at pH 6·8 and preparative t.l.c. on alumina with $CHCl_3$ 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 1α H, 5α H-tropan-3α-yl 3,4,5-trimethoxybenzoate I; $R^1 = (MeO)_3\ C_6H_2{\cdot}CO$, $R^2 = R^3 = H$. 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_E values) and by elemental analysis. N.m.r. spectroscopy of the parent base, τ ($CDCl_3$) 4·8 (1H,t), confirmed the 3α-orientation of the ester linkage (Evans & Major, 1968; Parello, 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.



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The fraction giving M^+ 361 was identified as 1α H, 5α H-tropan- 3α-yl 3,4,5-trimethoxycinnamate (picrate, i.r., n.m.r. and comparison with an authentic sample); this base I; $R^1 = (MeO)_3C_6H_2{\cdot}CH{:}CH{\cdot}CO$, $R^2 = R^3 = H$ has been reported previously as a constituent of *E. ellipticum* leaves. (Johns, Lamberton & Sioumis, 1970). A $CHCl_3$ 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