Of the methyl substituted procaine congeners, 2-diethylaminoethyl-3 5-dimethylbenzoate hydrochloride was most effective having a therapeutic index of 64·1 and a protective index of 28·5.

2-Diethylaminoethyl-2,3-dimethylbenzoate hydrochloride and 2-diethylaminoethyl-2,3,5,6-tetramethylbenzoate hydrochloride had higher protective indices, but lower therapeutic indices compared with procaine hydrochloride.

Compared with procaine hydrochloride, 2-diethylaminoethyl-2,5-dimethylbenzoate hydrochloride has slightly higher therapeutic index (37·4), but a much higher protective index.

The present study reveals that methyl substitution at position 3 and 5 in the benzene ring of procaine yields a compound which has much higher protective and therapeutic indices compared with the parent substance procaine.

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## Orally Effective Hypoglycaemic Agents from Plants

SIR,—Hypoglycaemic agents from *Allium cepa* Linn. (the domestic onion), *Ficus bengalensis* Linn. and *Eugenia jambolana* Lam. have already been reported by us (1961). The present communication describes two more orally effective hypoglycaemic principles extracted from *Allium sativum* Linn. (garlic) and from an Indian indigenous plant, *Ficus religiosa* Linn.

TABLE I

BIOLOGICAL ASSAY OF ORALLY EFFECTIVE HYPOGLYCAEMIC AGENTS FROM *Allium sativum* AND *F. religiosa.* COMPARED WITH TOLBUTAMIDE

| Substance administered | Dose | Blood sugar response mg./100 ml. Initial average values for six rabbits | 4 hr. pool average values for six rabbits | Mean reduction per cent | Mean hypoglycaemic potency as per cent of tolbutamide |
|---|---|---|---|---|---|
| Tolbutamide (Albert David and Co.) | 0·5 g. | 100 | 74·98 | 25 ± 2·1 | 100 |
| Total ethyl ether (34–36°) extract from 50 g. dry garlic powder .. | 0·5 g. | 117·3 | 100·03 | 14·72 ± 3·5 | 58·88 |
| Total water extract from 50 g. dry root bark powder of *F. religiosa*.. | 2·5 g. | 117·9 | 95·52 | 18.97 ± 4·34 | 75·9 |

The hypoglycaemic effect of the different fractions of garlic extracts was reported by Laland and Havrivold (1933). *F. religiosa* Linn. is used throughout India as a natural remedy for diabetes mellitus as mentioned by Chopra (1933).

Sun dried cloves of garlic and the root bark of *F. religiosa* were thoroughly dried and extracted separately with different solvents in soxhlets. Only the water extract of *F. religiosa* and the ethyl ether extract of garlic were found to exhibit sufficient hypoglycaemic activity, on oral administration to rabbits, compared to a standard dose of tolbutamide (0·5 g./rabbit). The results of the biological assay of these extracts on groups of normal male albino rabbits weighing 2 kg. with fasting 18 hr. blood sugar levels of 100–125 mg./100 ml. are given in Table I. The biological assay was made by a procedure similar to that of Marks (1926). Blood sugar was determined by the micromethod of Folin and Malmros (1929).

Both these extracts were found to be effective in controlling the hyperglycaemic response of glucose feeding (1 g./kg.) in glucose tolerance experiments on normal fasting rabbits, as will be evident from Fig. 1. The drugs concerned were fed 1 hr. before the administration of glucose to facilitate their absorption.

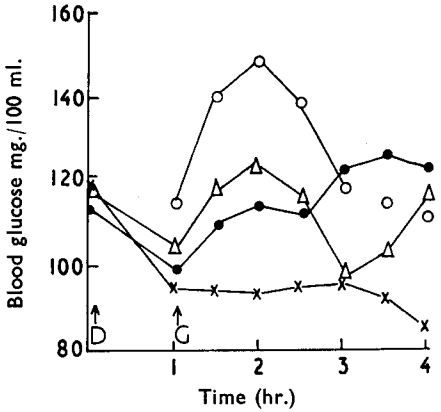


FIG. 1. Effects of the hypoglycaemic agents on the glucose tolerance of normal fasting rabbits. (X——X) tolbutamide; (●——●) *Allium sativum*; (△——△) *Ficus religiosa*; (○——○) control. Dose same as given in the Table I. Each curve is a mean of results from six rabbits. D = drug, G = glucose.

The results, Table I and Fig. 1, show that, *Allium sativum* and *F. religiosa* contain orally effective hypoglycaemic agents.

A detailed report on the separation and isolation of the orally effective hypoglycaemic agents from these natural sources will be published elsewhere.

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