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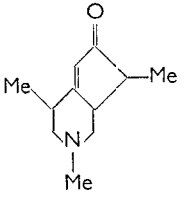
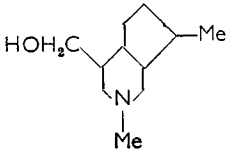
Hypoglycaemic properties of tecomine and tecostanine

SIR,—Tecomine (I) and tecostanine (II) are two alkaloids isolated by Hammouda & Motawi (1959) and Hammouda, Plat & Le Men (1963a) from the leaves of *Tecoma stans* (Juss.). The leaves of the various species of *Tecoma*



Tecomine (I)



Tecostanine (II)

have long been used orally by the natives of Mexico as antidiabetic remedies (Colin, 1926; 1927). The structures of the two alkaloids have also been elucidated (Hammouda, Plat & Le Men, 1963b; Jones, Fales & Wildman, 1963).

The present communication describes the biological assay for hypoglycaemic properties of the two alkaloids compared with tolbutamide. Normal healthy albino rabbits weighing 1·5–2 kg fasted for 12 hr were injected with tecomine and tecostanine salt solutions in isotonic saline. Their hypoglycaemic potency was calculated and related to that of tolbutamide given orally and measured by the procedure outlined by Marks (1926) for the biological assay of insulin. Blood sugar was determined by the method of Nelson (1944).

The results (Table 1) show tecomine and tecostanine to be potent hypoglycaemic agents when given intravenously. The average lethal dose was found to be 300 mg/kg in mice.

TABLE 1. HYPOGLYCAEMIC ACTION OF THE ALKALOIDS

Substance administered	Dose mg/kg	Route	Blood sugar response mg/100 ml		Time of maximal response hour : min	Mean reduction %	Hypoglycaemic potency of tolbutamide %
			Initial†	Maximal†			
Tolbutamide	250	Oral	100·1	73·7	3 : 50	26 ± 2	—
Tecomine citrate ..	20*	i.v.	98·3	52·3	3 : 14	47 ± 3·5	179
Tecostanine hydrochloride	20*	i.v.	104·9	48·6	3 : 23	49 ± 3	186

† Average of four rabbits.
* Calculated as the free base.

The two alkaloids represent a new nucleus not investigated before for hypoglycaemic effect. Further work on their detailed action on blood sugar, their beneficial effects in diabetes and their structure activity relationships is now in progress.

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Beta sympathetic inhibitory receptors in the small intestine of the guinea-pig

SIR,—The sympathetic inhibitory receptors of the gut of the cat, rat, rabbit, and dog were defined by Ahlquist (1948) as alpha receptors, but it has since been demonstrated that beta receptors also are present in the small intestine of the dog (Ahlquist & Levy, 1959) and rabbit (Furchgott, 1960). Activation of either type of receptor causes an inhibition of the gut.

In the guinea-pig, McDougal & West (1954) showed that the sympathetic inhibitory receptors on the intramural cholinergic neurones have the properties of alpha receptors, and more recently, Harry (1964) in this department has distinguished alpha inhibitory receptors in the circular smooth muscle layer. The results described below (Wilson, 1960) formed part of a communication to the British Pharmacological Society in January, 1960: they give evidence for the presence of beta inhibitory receptors in the longitudinal smooth muscle layer of the guinea-pig gut.

Isolated preparations of guinea-pig proximal small intestine were suspended at 36°, in Krebs solution containing 1 in 10,000 sodium metabisulphite as an antioxidant and bubbled with a mixture of 95% oxygen and 5% carbon dioxide. Longitudinal contractions were produced at 4 min intervals by direct stimulation of the smooth muscle with histamine or methacholine. Graded doses of noradrenaline, adrenaline, isoprenaline or phenylephrine were added to the organ bath 2 min before the next addition of agonist drug and caused an inhibition of the longitudinal contractions. The four sympathomimetic amines produced parallel log dose-inhibitory response curves, but the slope of the curves for the inhibition of histamine was steeper than the slope of the curves for the inhibition of methacholine. Estimates of the pA_2 values of the sympathomimetic amines (Table 1) showed a more pronounced inhibition of histamine than of methacholine, with a ten- to twenty-two-fold difference in potency for the inhibition of the two agonists. The sequence of inhibitory potency of the sympathomimetic amines was isoprenaline the most active, followed by noradrenaline, then