Table 1

| Fibre type | Sodium chloride | Acetic acid | Quinine | Sucrose | Saliva |
|---|---|---|---|---|---|
| I | + | + | − | + | + |
| II | + | + | + | + | + |
| III | − | + | − | + | + |
| IV | + | (+) | − | − | − |
| V | − | + | + | − | − |
| VI | − | + | − | − | + |

compared with the chemoceptive fibres. A comparison of the chemoceptive response of the palatal nerves with that from the nerves innervating the lips, the barbels and the gill rakers gives us the impression that the palatal nerves are the most important taste nerves of this species.

That human saliva is such a powerful stimulant of the palatal organ gives us, of course, a certain aspect on the angler's habit of spitting on the bait.

JIHEI KONISHI
YNGVE ZOTTERMAN

Department of Physiology,
Veterinärhögskolan, Stockholm 51.

## Pharmacology of the Alkaloidal Fraction from the Bark of the Jamaican Shade Tree *Pithecolobium samath* Benth.

A PHARMACOLOGICAL screening programme of extracts of plants used as folk medicines in Jamaica for the preparation of the so-called 'bush teas' is being carried out in collaboration with a group under Prof. L. J. Haynes at the Department of Chemistry, and with Dr. P. C. Feng at the Department of Physiology, University College of the West Indies, Jamaica. The shade tree, *Pithecolobium samath* Benth., was selected for detailed study. The main alkaloid from its bark, pithecolobine, had already been isolated by Wiesner *et al.*[1], who have given its partial structure[2].

A crude alkaloidal fraction was isolated from the powdered bark of the shade tree by extraction with dilute hydrochloric acid. The extract was made alkaline and then washed with chloroform, and these washings were then extracted with dilute hydrochloric acid. The acid extract was made alkaline and re-extracted with chloroform. The chloroform was evaporated to give an oil. Paper chromatography of this oil in several solvent systems showed one major component, presumably identical to pithecolobine, and only traces of a second component were disclosed with Dragendorff's reagent[3].

This fraction (referred to as pithecolobine) when injected intraperitoneally into mice (40 γgm./gm. body-weight, *BALB/C* × *C57* mice) produced characteristic convulsions within 2–4 min. The stages were: first hypersensitivity to auditory stimuli, followed by muscular twitching and vertical head tremor, clonus first appeared in the hind limbs and then became more generalized with jumping. Between convulsions the animal appeared flaccid with apparent paralysis of the fore and hind limbs. Clonic attacks were followed by rapid respiration, gasping, exophthalmos and death. With lower doses the severe clonic attacks did not occur and surviving animals were subdued for up to 90 min.

The $LD_{50}$ at room temperature (20°) for pithecolobine injected intraperitoneally was 40 γgm./gm. body-weight, the $LD_{50}$ was approximately halved at both 4° and at 36°. Doses of 12 γgm./gm. body-weight of pithecolobine reduced the quinalbarbitone sleeping time of mice by 20 per cent; higher doses (12–18 γgm./gm. body-weight) increased it by up to 100 per cent. The toxicity of pithecolobine for mice was approximately doubled by the doses of quinalbarbitone (450 γgm./gm. body-weight) used for sleeping-time determination. When mice were given pithecolobine intraperitoneally (14 γgm./gm. body-weight) the rectal temperature, normally 37° C., dropped to 33° C.; when given quinalbarbitone alone it dropped to 29° C. and when given both it dropped to 26° C. Intravenous pithecolobine reduced the arterial blood pressure in the anæsthetized cat (4 mgm./kgm.) and rat (1·5 mgm./kgm.) by about 20 per cent for 5 min., both before and after vagotomy. In the anæsthetized rat, hypotensive doses of pithecolobine caused a marked increase in the amplitude and decrease in the rate of respiration. Perfusion of the spinal cord of the frog[4] with pithecolobine (15 γgm./ml.) reduced or abolished the electrically stimulated reflex contractions of the femoral biceps.

The most striking peripheral effect of pithecolobine is its local anæsthetic activity. It is apparently twice as potent as cocaine in the frog lumbar plexus test for local anæsthetics[5]. The intradermal weal test on guinea pigs[5] showed that injection of 1–3 mgm. of pithecolobine caused local anæsthesia for up to 8 hr. Similar results have been obtained in man. Pithecolobine did not produce significant corneal anæsthesia[6] in guinea pigs or rabbits. Pithecolobine appeared to have a generalized depressant effect on isolated organ preparations; for example, on the electrically stimulated phrenic nerve diaphragm[7], on the contractions of the guinea pig ileum induced by acetylcholine, histamine, nicotine and barium, on the contractions of the rat fundus strip induced by 5-hydroxytryptamine[8], and on the Langendorff preparation of the isolated rabbit heart.

The nature of the convulsions caused by pithecolobine and its effects on respiration, sleeping-time, and possibly temperature, suggest that this substance has some action on the brain stem. These pharmacological actions of pithecolobine are of particular interest because of the very unusual structure[2] of this alkaloid. Chemical studies of the alkaloids of the shade tree are under way at the University College of the West Indies and we hope to investigate fully both the pharmacology and biochemistry of pure alkaloids from this source.

We wish to thank Prof. A. C. Frazer for his interest and encouragement, and Dr. R. Schneider, Dr. M. R. A. Chance and Dr. K. Sargeant for valuable advice and help. This investigation was supported by the Tropical Products Institute, Department of Scientific and Industrial Research.

*Note added in proof.* Further work suggests that the local anæsthesia produced by intradermal injections of pithecolobine is due to damage to nerve endings.

B. E. LEONARD
H. S. A. SHERRATT

Department of Medical Biochemistry and Pharmacology, University of Birmingham.

[1] Wiesner, K., MacDonald, D. M., Valenta, Z., and Armstrong, R., *Canad. J. Chem.*, **30**, 761 (1952).
[2] Wiesner, K., and Orr, D. E., *Tetrahedron Letters*, **16**, 11 (1960).
[3] Munier, R., and Machboeuf, M., *Bull. Soc. Chim. Biol.*, **31**, 1144 (1949).
[4] Angelucci, L., *Brit. J. Pharmacol.*, **11**, 161 (1956).
[5] Bülbring, E., and Wajda, I., *J. Pharm. Exp. Therap.*, **85**, 78 (1945).
[6] Chance, M. R. A., and Lobstein, H., *J. Pharmacol. Exp. Therap.*, **12**, 344 (1957).
[7] Bülbring, E., *Brit. J. Pharmacol.*, **1**, 38 (1946).
[8] Vane, J. R., *Brit. J. Pharmacol.*, **12**, 344 (1957).