A PRELIMINARY NOTE ON THE ALKALOIDS OF *ASPIDOSPERMA EXCELSUM* BTH.

BY J. N. BANERJEE*†, J. J. LEWIS* and G. W. G. SHARP

From the Pharmacological Laboratories, Pharmacy Department, University of Nottingham

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THE results of work on the alkaloids of the barks of *Aspidosperma spp.* have recently been reported[1,2,3,4]. Some preliminary observations have now been made on the actions of the alkaloids of the bark of *Aspidosperma excelsum* Bth.

The total alkaloids were extracted from the dried powdered bark by classical methods and purified. These appeared to contain indolic bases. A 1 per cent. solution of the alkaloidal hydrochlorides in the appropriate saline was used.

The pharmacological properties of the total alkaloids of *Aspidosperma excelsum* bark were investigated by the methods outlined in previous papers[1,2,3,4]. These were qualitatively almost identical with those of the total alkaloids of *Aspidosperma oblongum* ADC[1,2] which were also found to contain indolic bases[5]. Thus the alkaloids of *Aspidosperma excelsum* antagonised the spasmogenic actions of acetylcholine, histamine and barium on smooth muscle preparations of the guinea-pig and rabbit small intestine, and antagonised the spasmogenic actions of acetylcholine on the frog rectus abdominis muscle. On the frog and rabbit isolated perfused hearts, we observed depression of tonus, amplitude and frequency, and a well marked auricular-ventricular block. On the perfused blood vessels of the rabbit's ear and rat's hind quarters, there was reversal of the constrictor action of 0·1 μg. to 1·0 μg. of adrenaline hydrochloride. Antagonism to the vasodilator action of acetylcholine was shown on the perfused blood vessels of the rabbit's ear. 0·5 to 1·0 mg. of the alkaloids had a dilator effect on the blood vessels of the rabbit's ear, but constricted those of the rat's hind quarters. In the chloralosed cat the alkaloids caused a prolonged lowering of the blood pressure (Fig. 1) and there was reversal of the pressor reponse to adrenaline (Fig. 2). Antagonism was shown to the pressor response to adrenaline hydrochloride on the spinal cat, but no adrenaline-reversal was seen. In both chloralosed and spinal cats antagonism to adrenaline could be overcome by adminstration of larger doses of adrenaline. The alkaloids (2 mg. by intraperitoneal injection) were found to lower the body temperature of normal mice, weighing 24 to 25 g.) by 3° C., and at a dose level of 3 mg. to protect mice against the lethal effects of a potentially toxic dose of adrenaline hydrochloride. A local anæsthetic action was shown using the frog plexus anæsthesia method[6,7]. No antimalarial action could be shown against *Plasmodium*

* Present address: Department of Materia Medica, University of Glasgow.
† Nottingham University Research Scholar.

berghei in mice, by 5 mg. of the total alkaloids given by intraperitoneal injection.

When investigating the actions of the alkaloids upon the electrocardiogram of rats and mice anæsthetised with pentobarbitone, a reversible bundle branch block was observed after intraperitoneal injection of the drug. This effect was not observed with the *Aspidosperma oblongum* alkaloids.

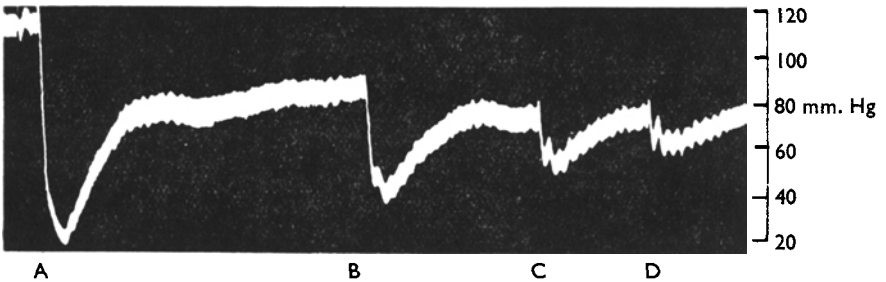

FIG. 1. Effects of the total alkaloids of *Aspidosperma excelsum* on the arterial blood pressure of a chloralosed cat weighing 2·8 kg. At "A" 5 mg., at "B" 2·5mg., at "C" 1·0 mg., and at "D" 0·5 mg. of the total alkaloids was injected into the jugular vein.

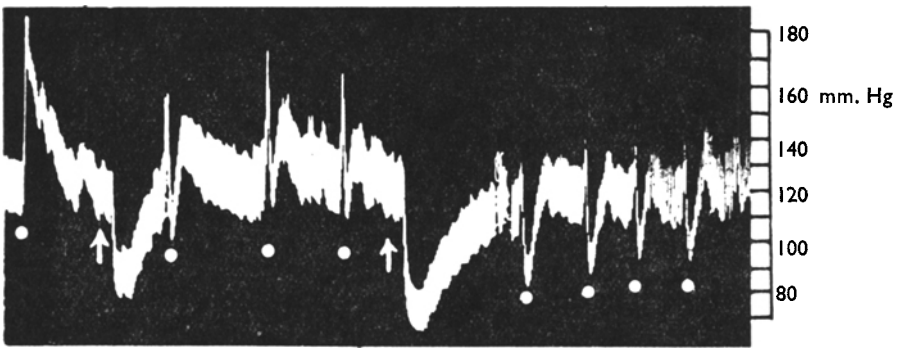

FIG. 2. Effects of the total alkaloids of *Aspidosperma excelsum* on the pressor response to injected adrenaline hydrochloride of a chloralosed cat weighing 3·0 kg. At white dots 4 μg. of adrenaline hydrochloride was injected into the jugular vein. At the arrows 5 μg. of alkaloids was injected.

In frogs 1 mg. of the total alkaloids when injected into the dorsal lymph sac caused miosis, depression of respiration and muscular weakness. Recovery ensued. In mice subcutaneous injection of 100 mg. per kg. caused general depression of movement and activity; the eyes were closed and the pupils slit-like. Recovery ensued. Chemical and pharmacological studies on these alkaloids are being continued.

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REFERENCES

1. Banerjee and Lewis, *Nature, Lond.*, 1953, **171**, 802.
2. Banerjee and Lewis, *J. Pharm. Pharmacol.*, 1954, **6**, 246.
3. Banerjee and Lewis, *ibid.*, 1954, **6**, 466.
4. Banerjee and Lewis, *ibid.*, in press.
5. Banerjee, Thesis, Nottingham University (1954).
6. Sollman, *J. Pharmacol.*, 1918, **11**, 1.
7. Bülbring and Wajda, *ibid.*, 1945, **85**, 78.