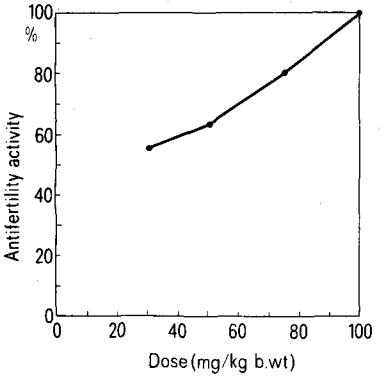
Effect of the sesquiterpene from the petroleum ether extract of the plant *Aristolochia indica* Linn. on fertility in female mice

No. of mice used	Day of administration	Dose administered in mg/kg b.wt	Mice showing antifertility activity (%)
20 (control)	1, (6–7)	–	0.0
12	1	100	91.7
10	6–7	30	55.5
10	6–7	50	63.6
10	6–7	75	80
10	6–7	100	100



Graph showing percentage of antifertility activity at different dose levels in mice.

tion. The ovary showed prominent corpus albicans. The nonaborting females in each case were allowed to go to term.

The extract exerted 91.7% anti-implantation activity, where laparotomy on day 6 revealed the absence of implantation sites. The ovary showed corpus albicans. No toxic effect was observed at the dose levels used. The litters of the nonaborting females were observed for any morphological abnormalities. No deformities were observed upto the F_1 generation.

1 The authors wish to thank Dr S. C. Pakrashi and his associate Mr P. P. Ghosh Dastidar of Medicinal Chemistry Department for isolating the compound for this study. Thanks are also due to Director-General of Indian Council of Medical Research for granting a Junior Research Fellowship to C.S.

2 R. N. Chopra, S. L. Nayer and I. C. Chopra, in: Glossary of Indian Medicinal Plants, p. 24. Council of Scientific and Industrial Research, New Delhi 1956.

3 K. R. Kirtikar and B. D. Basu, in: Indian Medicinal Plants III, p. 2123. L. M. Basu. Allahabad 1935.

4 K. P. Biswas and A. Ghosh, Bharatiya Bonousadhi IV, p. 385. Calcutta University, India 1973.

5 A. Pakrashi, B. Chakrabarty and A. Dasgupta, Experientia *32*, 394 (1976).

A centrally induced vasodepressor response after intravenous administration of whole venom of *Naja mossambica pallida* in cats[1]

R. K. Raina[2], D. Njoroge, J. N. Ng'ang'a and B. V. Telang

Division of Pharmacology and Therapeutics, Department of Medicine, P. O. Box 30588, Nairobi (Kenya), 2 May 1977

Summary. Naja mossambica pallida venom administered i.v. (300 μg/kg) produces an initial brief fall in blood pressure, due to a direct myocardial depressant effect, and a sustained fall due to central depressant effect.

I.v. administered snake venoms generally cause a precipitous fall in the blood pressure followed by a partial recovery and then a gradual or a rapid descent of systemic arterial pressure. In *Dendroaspis Jamesoni* venom, a central locus of action for the hypotensive response was suggested[3,4]. In this paper evidence is presented for a central locus for the hypotensive response after i.v. administration of *Naja mossambica pallida* venom.

Materials and methods. Cats (2.5–3.5 kg) were anaesthetized with ether followed by i.v. chloralose (80 mg/kg). Carotid artery blood pressure was recorded by a Statham transducer (P23D) and the heart rate on a Grass Polygraph (Model 79-8P-40). Artificial respiration at a pressure of 15 cm of water/kg and rate of 20/min was maintained by an electronic ventilator (SRI, England). The rectal temperature was maintained between 36 and 37 °C throughout the experiment. The efferent pathways of the hypotensive response were determined in spinalized cats (C-2). The action of snake venom on central vasomotor areas was assessed according to method described by Telang et al.[4].

Drugs used. Atropine sulphate (Sigma, London), mepyramine maleate (May & Baker, England), pentolinium tartrate (May & Baker, England) 1,1-dimethyl-4-phenylpiperazinium iodide (DMPP, K & K Laboratories Inc. USA), sodium nitrite[5] (B.D.H. analar grade). Dessicated whole venom was obtained from Mr J. H. Leakey, Baringo Snake Farm, P.O. Box 1141, Nakuru, Kenya.

Results and discussions. In control experiments, the mean blood pressure was 135 ± 2.5 mm Hg (mean ± SE). I.v. administration of snake venom (300 μg/kg) produced a biphasic vasodepressor response (figure 1A). An initial brief fall (61.6 ± 7.5 mm Hg) and a prolonged fall (59.2 ± 5.8 mm Hg). The blood pressure did not return to normal levels even after 2 h. In spinalized cats (N = 7), mean basal blood pressure 71.4 mm Hg ± 5.5 mm of Hg, after i.v. administration of the venom (300 μg/kg), the prolonged fall in blood pressure was completely

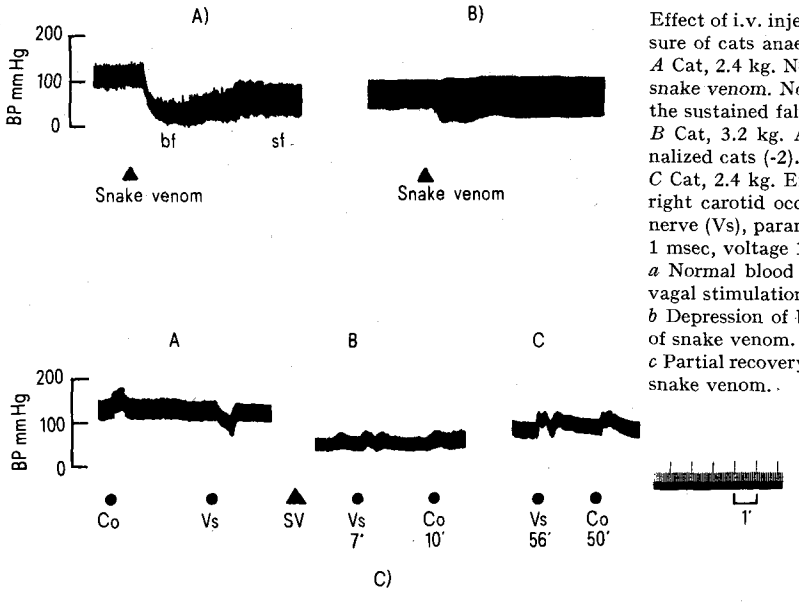
1 This study was supported by University of Nairobi research grants (670–376). We also thank Mr E. Njogu for photographic assistance.

2 Permanent address: Department of Pharmacology, Government Medical College, Jammu 180001 (India).

3 R. K. Raina, J. N. Ng'ang'a, D. K. Njoroge and B. V. Telang, Toxicon, in press (1977).

4 B. V. Telang, R. J. M. Lutunya and D. Njoroge, Toxicon *14*, 133 (1976).

5 R. Scivoletto, A. J. O. Toledo, A. C. Gomes Da Silva and D. Nigro, Archs int. Pharmacodyn. *223*, 333 (1976).



Effect of i.v. injection of snake venom (300 µg/kg) on the blood pressure of cats anaesthetized with ether-chloralose (80 mg/kg).
A Cat, 2.4 kg. Normal record of blood pressure after i.v. injection of snake venom. Note the initial brief fall (bf) the partial recovery and the sustained fall (sf).
B Cat, 3.2 kg. Absence of biphasic vasodepressor response in spinalized cats (-2).
C Cat, 2.4 kg. Effect of snake venom on blood pressure response to right carotid occlusion (Co) and central stimulation of right vagus nerve (Vs), parameters of stimulation: frequency 10 Hz, pulse width 1 msec, voltage 10 V.
a Normal blood pressure response to carotid occlusion and central vagal stimulation. Duration of stimulation in both were 30 sec.
b Depression of both responses (7–10 min) after i.v. administration of snake venom.
c Partial recovery of the response (56–59 min) after administration of snake venom.

blocked (figure B) in all the cats but the effect of the venom on the initial brief fall was not consistent, and in 3 preparations the initial brief fall in blood pressure (56.7 ± 5.8 mm Hg) was noted. Similar initial brief hypotensive response was noted in bilateral cervical vagotomized (N=2) and spinalized cats (N = 4).
Pretreatment i.v. with atropine (2 mg/kg) and mepyramine (5 mg/kg) did not significantly alter the venom-induced hypotension. In cats (N = 4) pretreated with i.v. pentolinium (5 mg/kg), administration of whole venom resulted in an immediate steep fall in blood pressure and a fatal response in all cats. The snake venom has no effect on contraction of nictitating membrane or on vasopressor response to i.v. administration of DMPP. The influence of the venom on the peripheral vasculature was studied by its influence on vasodepressor response of i.v. administered sodium nitrite (5 mg/kg), the venom had no effect on this response. The results of experiments (N = 2) on the effect of whole venom (300 µg/kg) on central vasomotor responses (figure C) indicated that these responses to central vagal stimulation and carotid occlusion respectively were depressed with partial recovery within 59 min.

The present investigation reveals that i.v. administration of *Naja mossambica pallida* venom causes a biphasic vasodepressor response, the initial brief fall in blood pressure which does not seem to be due to peripheral vasodilatation, as pretreatment with atropine mepyramine does not abolish it and also as the venom does not influence the sodium nitrite-induced hypotension. Spinal cord transection with or without bilateral cervical vagotomy does not consistently alter this response. In another study to be reported, the present authors[6] have shown the direct depressant effect of the Naja venom on myocardium, and it is quite likely that this may be responsible for the initial brief fall. The prolonged hypotensive response is probably due to depression of vasomotor centre since it is absent in spinalized cats and confirmed by abolition of central vasomotor response by venom. The fatality noted in pentolinium-pretreated cats may be due to combination of effects of loss of peripheral sympathetic tone by ganglion blockade and direct myocardial depressant effect of the venom.

6 R. K. Raina, J. N. Ng'ang'a and B. V. Telang, Agressologie, accepted for publication (1977).

Comparison of human adult and fetal hemoglobin: Aminophenol-induced methemoglobin formation[1]

M. Wind and A. Stern

Department of Pharmacology, Stella and Charles Guttman Laboratories for Human Pharmacology and Pharmacogenetics, New York University School of Medicine New York (N.Y. 10016, USA), 5 February 1977

Summary. Human fetal hemoglobin was more susceptible to methemoglobin formation in the presence of aminophenols than was adult hemoglobin. This was due to the intrinsic properties of the proteins rather than the presence of methemoglobin reductases.

Newborn susceptibility to drug-induced methemoglobinemia, cannot be fully accounted for on the basis of a decrease in methemoglobin reductase activity in their red cells. Since fetal hemoglobin is both spontaneously and chemically transformed to methemoglobin more readily than adult hemoglobin[2,3], perhaps the changes observed are due to intrinsic properties of the proteins.

In this communication, we report our comparative studies on human fetal and adult hemoglobin. These studies reveal that fetal hemoglobin exhibits an enhancement in methemoglobin formation in the presence of aminophenols, when compared to adult hemoglobin. Aniline, which can be metabolized to p-aminophenol[4] produces significant methemoglobinemia in the newborn[5].