

- CARLSSON, A. & WALDECK, B. (1965). *J. Pharm. Pharmac.*, **17**, 243-244.
- COYLE, J. T. & SNYDER, S. H. (1969). *Science, N.Y.*, **166**, 899-901.
- EVETTS, K. D., URETSKY, N. J., IVERSEN, L. L. & IVERSEN, S. D. (1970). *Nature, Lond.*, **225**, 961-962.
- FUXE, K. & UNGERSTEDT, U. (1968). *Europ. J. Pharmac.*, **4**, 135-144.
- GLOWINSKI, J. & AXELROD, J. (1964). *Nature, Lond.*, **204**, 1318.
- HÄGGENDAL, J. & HAMBERGER, B. (1967). *Acta physiol. scand.*, **70**, 277-280.
- IVERSEN, L. L. (1967). "The uptake and storage of noradrenaline in sympathetic nerves." Cambridge: University Press.
- MALMFORS, T. & SACHS, CH. (1968). *Europ. J. Pharmac.*, **3**, 89-92.
- NOBLE, E. P., WURTMAN, R. J. & AXELROD, J. (1967). *Life Sci.*, **6**, 281.
- SNYDER, S. H., GREEN, A. I. & HENDLEY, E. D. (1968). *J. Pharmac. exp. Ther.*, **164**, 90-102.
- STONE, C. A., PORTER, C. C., STAVORSKI, J. M., LUDDEN, C. T. & TOTARO, J. A. (1964). *Ibid.*, **144**, 196-204.
- THOENEN, H. & TRANZER, J. P. (1968). *Arch. exp. Path. Pharmac.*, **261**, 271-288.
- URETSKY, N. J. & IVERSEN, L. L. (1970). *J. Neurochem.*, **17**, 269-278.

Effects of 6-hydroxydopamine on the perfused rat mesentery preparation

We have recently shown in the pithed rat that after pretreatment with 6-hydroxydopamine, an agent producing chemical sympathectomy (Thoenen & Tranzer, 1968), supersensitivity develops to injected noradrenaline (Finch & Leach, 1970). Similar results have been obtained in the spinal cat by Haeusler, Haefely & Thoenen (1969), who observed a 10-30 fold increase in the responses to noradrenaline. In contrast to the cardiovascular responses, the isolated heart exhibited only a 3.5 times greater sensitivity to noradrenaline. It was, therefore, decided to investigate whether 6-hydroxydopamine could produce supersensitivity in the vascular beds.

Male C.S.E. rats, 300-350 g, were given intravenously 6-hydroxydopamine (A. B. Kistner, Gotenborg) (2×50 mg/kg on day 1 and 2×100 mg/kg on day 7). Perfusion experiments were made on day 10. Mesenteric vessels were isolated and perfused with Krebs solution (McGregor, 1965). Fibres of the periarterial nerve plexus were stimulated at supramaximal voltage (30-40 V), pulse duration 1 ms and a frequency of 6-25 Hz repeated every 2 min. To investigate changes in sensitivity to exogenously administered drugs, noradrenaline and adrenaline (as base) were injected into the perfusate every 3 min in doses of 0.01-1.0 μ g.

After pretreatment with 6-hydroxydopamine, the vasoconstrictor responses of the mesenteric preparation to sympathetic nerve stimulation were abolished at low frequencies of stimulation (6, 12 Hz) and markedly reduced at 25 Hz. Noradrenaline sensitivity after treatment with 6-hydroxydopamine was increased by 10-12 times (Fig. 1A). Similar results were obtained for adrenaline. When desipramine (10^{-8} g/ml) was added to the perfusion fluid, no further increase in sensitivity to noradrenaline occurred in the preparations pretreated with 6-hydroxydopamine (Fig. 1B). Control preparations, however, showed potentiated responses similar in extent to those seen in 6-hydroxydopamine-treated preparations.

These results suggest that 6-hydroxydopamine produces chemical sympathectomy of the mesenteric blood vessels. Supersensitivity to injected noradrenaline also occurred and there was no further potentiation after desipramine pretreatment. It would seem, therefore, that chemical sympathectomy abolishes the normal physiological uptake process by day 10 and produces a pre-junctional supersensitivity to noradrenaline. These results are only in partial agreement with those reported by McGregor & Phelan (1969) who found that 6-hydroxydopamine abolished the vasoconstrictor responses to nerve stimulation but did not alter the noradrenaline sensitivity of the perfused mesenteric arteries. Their treatment with 6-hydroxydopamine (30 mg/kg, i.p.) produces only an incomplete depletion of endogenous catecholamines

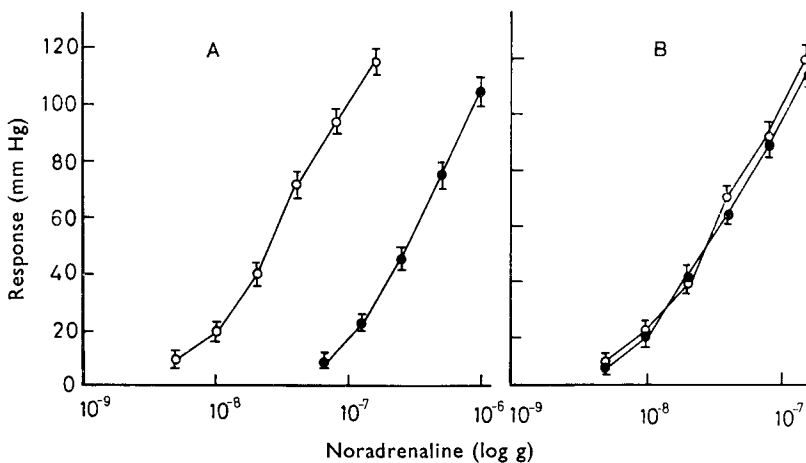


FIG. 1. After 6-hydroxydopamine the vasoconstrictor responses of mesenteric vessels to injected noradrenaline was increased. Each point represents the mean value (\pm s.e. as vertical bars). (A) \bullet — \bullet control responses (6), and \circ — \circ ten days after the first injection of 6-hydroxydopamine (4). (B) Effect of desipramine (10^{-8} g/ml) in the perfusion fluid. \bullet — \bullet control responses (6), and \circ — \circ ten days after the first injection of 6-hydroxydopamine (4). Figures in brackets in the legend indicate the number of individual observations.

(Lavery & Phelan, 1969) and there is evidence that the doses we used are more effective in destroying sympathetic nerve endings (Thoenen & Tranzer, 1968; Clarke & Jones, 1969; Finch & Leach, 1970).

In conclusion our results suggest that the increased cardiovascular reactivity to catecholamines, after treatment with 6-hydroxydopamine is at least partially due to supersensitivity of the vascular beds.

School of Studies in Pharmacology,
University of Bradford,
Bradford, 7, Yorkshire, U.K.
April 15, 1970

L. FINCH
G. D. H. LEACH

REFERENCES

- CLARKE, D. E. & JONES, C. J. (1969). *Europ. J. Pharmac.*, **7**, 121–124.
FINCH, L. & LEACH, G. D. H. (1970). *J. Pharm. Pharmac.*, **22**, 354–360.
HAEUSLER, G., HAEFELY, W. & THOENEN, H. (1969). *J. Pharmac. exp. Ther.*, **170**, 50–61.
LAVERY, R. & PHELAN, E. L. (1969). *Proc. Univ. Otago med. Sch.*, **47**, 18–19.
MCGREGOR, D. D. (1965). *J. Physiol., Lond.*, **177**, 21–30.
MCGREGOR, D. D. & PHELAN, E. L. (1969). *Proc. Univ. Otago med. Sch.*, **47**, 19–21.
THOENEN, H. & TRANZER, J. P. (1968). *Naunyn-Schmiedeberg's Arch exp. Path. Pharmac.*, **261**, 217–288.

Identity of peyocactin, an antibiotic from peyote (*Lophophora williamsii*), and hordenine

A variety of medicinal uses have been claimed (LaBarre, 1960; Schultes, 1940) for the well-known hallucinogenic peyote cactus, *Lophophora williamsii* (Lemaire) Coulter. McCleary, Sypherd, & Walkington (1960) recently isolated peyocactin, a water-soluble crystalline substance, from an ethanol extract of peyote and found it to be inhibitory *in vitro* against 18 strains of penicillin-resistant *Staphylococcus aureus* and effective in mice against fatal staphylococcal infection. Since there appeared to be no report in the literature elucidating the structure of peyocactin, it became an objective to characterize this antibiotic substance.