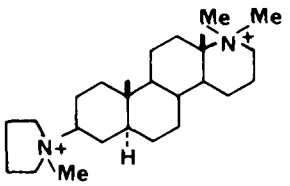
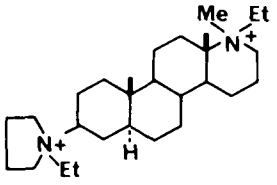
NEUROMUSCULAR AND AUTONOMIC ACTIONS OF FOUR CHANDONIUM ANALOGUES

P. Teerapong*, I.G. Marshall*, A.L. Harvey*, H. Singh, D. Paul, T.R. Bhardwaj, N.K. Ahuja, *Department of Physiology and Pharmacology, University of Strathclyde, Glasgow G1 1XW and Department of Pharmaceutical Sciences, Panjab University, Chandigarh 160014, India

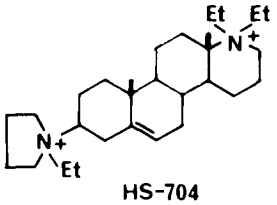
Of the several compounds tested in an azasteroid series, chandonium iodide possessed the greatest neuromuscular blocking potency (Gandiha et al., 1974). Four new analogues of chandonium have been tested for neuromuscular and autonomic blocking activities in the anaesthetized cat.



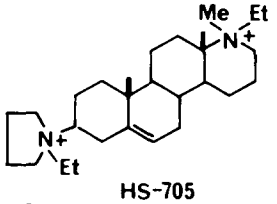
HS-692



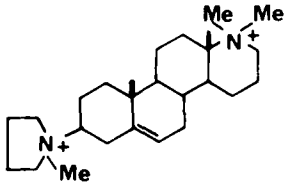
HS-693



HS-704



HS-705



Chandonium

All four compounds exhibited neuromuscular blocking activity of rapid onset and short duration, these characteristics being indistinguishable from those of chandonium. The order of potency relative to chandonium (1.0) was HS-692 (0.5) > HS-693 (0.25) > HS-704 (0.1) = HS-705 (0.1). All four compounds were antagonized by neostigmine (100 µg/kg).

At neuromuscular blocking doses none of the compounds exhibited any ganglion blocking activity and no marked changes in blood pressure or heart rate were observed. However the compounds depressed the response of the heart rate to vagal stimulation. The degree of vagal inhibition produced by equieffective neuromuscular blocking doses was HS-693 (86%) > HS-705 (55%) = HS-704 (55%) > HS-692 (28%) > chandonium (9%). The vagal inhibition produced by HS-693 was particularly striking and long outlasted the neuromuscular block.

Thus, of the new analogues of chandonium tested, HS-692 possesses the most desirable spectrum of activity i.e. powerful but short-lasting neuromuscular block, no ganglion block and the least vagolytic action. This compound appears worthy of further study as part of the attempt to find an ideal muscle relaxant for use in surgery.

Gandiha, A., Marshall, I.G. & others (1974). J. Pharm. Pharmac., 26, 871-877.

Supported by the Scottish Hospitals Endowment Research Trust, Colombo Plan and the Council of Scientific & Industrial Research, New Delhi.