—SHORT COMMUNICATIONS

A COMPARATIVE STUDY OF THE CENTRAL MUSCLE
RELAXANT ACTIVITY OF BUTYROPHENONES

S.K. RASTOGI*, J.N. SINHA** and K.P. BHARGAVA

Department of Pharmacology, K.G. Medical College, Lucknow-3, India

Accepted July 10, 1973

Haloperidol has been reported to possess neuroleptic, analgesic, antiemetic and hypotensive properties (1 and 2). In a comparative study, Bhargava and Srivastava (3) have demonstrated a potent central muscle relaxant activity of haloperidol against strychnine and tetanus toxin induced facilitation of the linguomandibular polysynaptic reflex (LMR). Reported here in are the relative potencies of four butyrophenones for inhibiting the LMR.

The present study was carried out on 45 adult cats (3.0–4.5 kg) of both sexes. The animals were anaesthetized with chloralose (80 mg/kg i.p.), bilaterally vagotomized and maintained on positive pressure artificial respiration. The right carotid artery was cannulated and the blood pressure was recorded through a mercury manometer on a smoked Rymograph paper. The linguomandibular polysynaptic reflex (LMR) was elicited by stimulating the root of the tongue as described by King and Unna (4). Inhibition of LMR was taken as a criterion for central muscle relaxant activity. Inhibition of the responses of the gastrocnemius muscle to electrical stimulation of the peripheral cut end of the sciatic nerve was taken as a criterion for peripheral muscle relaxant activity in all the experiments. The experimental procedures have been described in our earlier publications (5 and 6). The drugs were injected intravenously and the percentage reduction of linguomandibular reflex was determined with at least three dose levels of each drug. The results were subjected to probit analysis by the method of Finney (7), and the ED 50 and standard error were calculated.

The results are summarized in Table 1. Among the butyrophenones, haloperidol and trifluoperidol, exhibited transient hypotension and selectively inhibited the polysynaptic linguomandibular reflex (LMR) without affecting the sciatic gastrocnemius response (SGR). Haloperidol was found to be the most potent compound ($ED_{50} 0.63 \pm 0.01$ mg/kg i.v.) for inhibiting the LMR with a long duration of action of 80 min. Next in order of potency was trifluoperidol ($ED_{50} 2.22 \pm 0.02$ mg/kg i.v.) with a duration of action of 75 min. As compared to mephesisin the relative potencies of haloperidol and trifluoperidol were 27.58 and 7.82 respectively.

* Lecturer, Department of Pharmacology, G.S.V.M. Medical College, Kanpur, India

** IUPHAR Fellow, Department of Pharmacologie, Faculte de Medecine, PARIS 75006

TABLE 1. Effect of i.v. administration of mephenesin and butyrophenone derivatives on linguomandibular reflex (LMR) and sciatic gastrocnemius response (SGR).

	Central muscle relaxant activity		Peripheral muscle relaxant activity	
	ED ₅₀ (mg/kg i.v.) ± S.E.	Activity ratio	Duration of action	Inhibition of sciatic nerve stimulation-induced gastrocnemius response
Mephenesin (Control)	17.38 ± 0.045	1	10 min	No effect
Haloperidol	0.63 ± 0.01	27.58	80 min	No effect
Trifluoperidol	2.22 ± 0.02	7.82	75 min	No effect
Pipamerone*	—	—	—	No effect
Droperidol*	—	—	—	No effect

*Transient inhibition during the phase of hypotension

Pipamerone and droperidol were found to induce severe hypotension (60–90 mm of HG) and transiently inhibited the linguomandibular reflex. In the doses tested these agents did not however affect the SGR.

The inhibition of polysynaptic linguomandibular reflex (LMR) has been shown to be a good criterion for the central muscle relaxant activity (2). The results of the present study, therefore, clearly demonstrate the presence of potent central muscle relaxant activity in haloperidol and trifluoperidol.

Acknowledgements: The authors are grateful to the Council of Scientific and Industrial Research (CSIR), New Delhi, India for financial assistance, McNeil Laboratories, Fort Washington, U.S.A., for providing trifluoperidol and to Dr. Paul Janssen of Janssen Pharmaceutica, Belgium, for pipamerone and droperidol.

REFERENCES

- 1) JANSSEN, P.A.J.: *Int. J. Neuropharmacol.* **1**, 145 (1962);
- 2) BHARGAVA, K.P. AND SRIVASTAVA, R.K.: *Br. J. Pharmacol. Chemother.* **25**, 751 (1965a);
- 3) BHARGAVA, K.P. AND SRIVASTAVA, R.K.: *Br. J. Pharmacol. Chemother.* **25**, 74 (1965b);
- 4) KING, E.E. AND UNNA, K.R.: *J. Pharmacol. exp. Ther.* **11**, 293 (1954);
- 5) SINHA, J.N., JAJU, B.P. AND SRIMAL, R.C.: *Japan. J. Pharmacol.* **16**, 250 (1966);
- 6) SINHA, J.N., SRIMAL, R.C., DIXIT, K.S., CHANDRA, O. AND BHARGAVA, K.P.: *Japan. J. Pharmacol.* **16**, 120 (1966);
- 7) FINNEY, D.J.: *Probit analysis* 2nd Ed., Cambridge University Press, London, (1952)