SUPPORTING INFORMATION

Inhibition of DOI-induced head twitches demonstrates 5-HT_{2A} antagonist activity

Results

Pretreatment **1, 2, 5, 7, 12, 26,** and **31** dose-dependently reduced the head twitch response induced by (±)-DOI (2 mg/kg, i.p.) in rats.[8] Doses inhibiting this response by 50% were as follows: **1** (0.02 ± 0.004 mg/kg, i.p.), **2** (0.001 ± 0.0003 mg/kg, s.c.), **5** (0.15 ± 0.05 mg/kg, s.c.), **7** (0.001 ± 0.00008 mg/kg, s.c.), **12** (0.005 ± 0.0005 mg/kg, i.p.), **26** (0.2 ± 0.15 mg/kg, p.o.) and **31** (0.02 ± 0.002 mg/kg, p.o.).

Method

Male Sprague Dawley rats (210-370g; Bantin and Kingman, Hull, U.K.) were pretreated with test compounds according to the injection routes and pretreatment times reported in the Table and placed in a perspex observation box either immediately afterwards or 30 min after dosing in the case of compounds administered orally. After the specified pretreatment time had elapsed all animals received (±)-DOI (2 mg/kg, i.p.) and the number of head twitches were recorded for the following 20 minutes. Details of drug formulations and routes of administration are given below. Drugs dosed i.p. and s.c. were administered in a volume of 1ml/kg whereas drugs given orally were dosed at 3 ml/kg. Each determination was carried out 7 times.

Table Antagonist studies – vehicle, routes of administration and pretreatment times

Antagonist	Vehicle	Route	Pretreatment
1	25% PEG300, pH 5-6	i.p.	30
2	water, pH 7	s.c.	30
5	water, pH 6-7	s.c.	30
7	water, pH 7	s.c.	30
12	20% PEG 400, pH 7	i.p.	30

26	20% Peg 400, pH 4-5	p.o.	60
31	20% Peg 400, pH 7	p.o.	60

Abbreviations are as follows: s.c. = subcutaneous; i.p. = intraperitoneal; p.o. = oral; min = minimal amount; PEG = polyethylene glycol (molecular weight either 300 or 400 as specified). Pretreatment times are given in minutes.