

CF 25-397 (9, 10-Didehydro-6-methyl-8 β -[2-pyridylthiomethyl]ergoline), a new central dopamine receptor agonist

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There is increasing evidence that several ergot derivatives stimulate dopamine receptors in the central nervous system. Bromocriptin (2-Br- α -ergokryptine, CB 154) induces contralateral turning in rats with unilateral lesions in the substantia nigra and produces stereotypies in normal rats. In mice, bromocriptin inhibits reserpine-induced catalepsy and increases motor activity (Johnson, Loew & Vigouret, 1976). CF 25-397 (9,10-Didehydro-6-methyl-8 β -[2-pyridylthiomethyl]ergoline) is a new, non-peptide ergot derivative which seems to exert central dopamine-like actions which differ from the effects of bromocriptin or L-DOPA and appear to be more selective.

CF 25-397 induced dose-dependent contralateral turning in rats with 6-hydroxydopamine lesions in the substantia nigra from a dose of 1 mg/kg. However, even at doses 30 times greater, stereotypies were barely detectable (Figure 1). In mice, CF 25-397 inhibited catalepsy induced by reserpine (5 mg/kg i.p., given 17 h before administration of CF 25-397), the ED₅₀ for this effect was 0.55 mg/kg s.c. No motor stimulation was observed; on the contrary, CF 25-397 (2.5 to 10 mg/kg s.c.) slightly reduced motor activity.

The fact that the contralateral turning induced by CF 25-397 could be blocked by pimozide (1 mg/kg i.p.) indicates that the compound possesses central dopamine receptor stimulant activities. Unlike other central dopamine receptor agonists, CF 25-397 does not induce stereotypies in the rat. These results suggest that its action on the nigro-striatal system is highly selective. Based on these pharmacological findings it is anticipated that CF 25-397 may provide a new and more

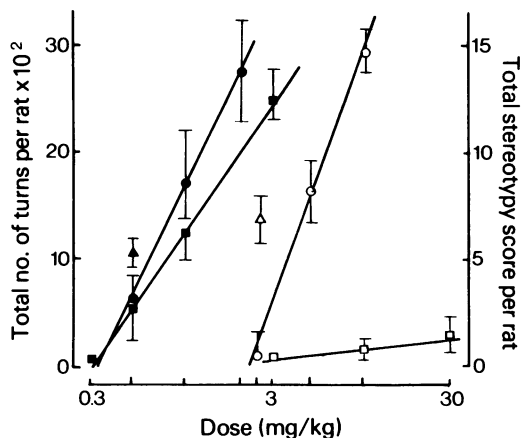


Figure 1 Induction of turning behaviour and stereotypies after subcutaneous injection of CF 25-397, bromocriptin or apomorphine in rats. Solid symbols: means \pm s.e. means of the total number of turns in groups of six rats lesioned according to Ungerstedt & Arbuthnott (1970). Open symbols: means \pm s.e. mean of the total stereotypy score in groups of six rats, rated according to Costall, Naylor & Olley (1972). (■) CF 25-397 tartrate; (●) bromocriptin mesilate; (▲) apomorphine hydrochloride.

selective treatment for patients suffering from extrapyramidal disorders.

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