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## Investigation of the psychopharmacological profile of mianserin, A 5-HT<sub>2A/2C</sub> receptor antagonist

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### Abstract

**Aim:** The present study was undertaken to investigate whether mianserin by blocking 5-HT<sub>2A/2C</sub> receptor can modulate the behaviours dependent on the functional status of the nigrostriatal DAergic system.

**Material and method:** Mianserin in the dose range 1.25 to 20 mg/kg i.p. did not produce motor incoordination, ataxia or muscular hypotonia. But these doses produced a hunch-back posture with abdomen clearly lifted up from the floor. Mianserin at 5, 10 and 20 mg/kg i.p. doses acts as a 5-HT<sub>2A</sub> receptor blocker as evident by the antagonist effects of these doses on 5-HT<sub>2A</sub> agonist ergometrine induced wet dog shake behaviour.

**Results:** Mianserin at 1.25, 2.5 and 5 mg/kg i.p. did significantly antagonise 5-HT<sub>2C</sub> receptor agonist fluoxetine induced PEs and 10 and 20 mg/kg i.p. mianserin abolished fluoxetine induced PEs. Thus 1.25 to 20 mg/kg doses of mianserin possess significant 5-HT<sub>2C</sub> receptor blocking activity. Mianserin at 5, 10 and 20 mg/kg i.p. doses does not block presynaptic D2 DA autoreceptors as with these doses it failed to antagonise low dose (0.1 mg/kg) apomorphine induced catalepsy. Mianserin at 5, 10 and 20 mg/kg i.p. doses is devoid of postsynaptic D2 and D1 DA receptor blocking activity as at these doses it did not antagonise apomorphine induced SB and did not produce catalepsy in rats.

**Conclusion:** Mianserin at 5, 10 and 20 mg/kg doses blocks the 5-HT<sub>2C</sub> receptors on the nigrostriatal DAergic neurons and remove the inhibitory influence of 5-HT on the nigrostriatal DAergic neurons which further causes increase in intraneuronal synthesis of DA and hence intraneuronal stores of DA. So pretreatment with 5, 10 and 20 mg/kg i.p. makes more DA available for release and resultant potentiation of dexamphetamine SB and antagonism of haloperidol catalepsy.

**Keywords:** Apo morphine, auto receptors, mianserin

### Introduction

Mianserin, a tetracyclic compound, was introduced for treatment of depressive illness in 1976 [1, 2]. There are 7 main types of 5-hydroxytryptamine (5-HT, serotonin) receptors with subtypes of these for a total of at least 14 different 5-HT receptors [3]. The antidepressant mianserin, on the basis of radioligand binding and behavioural studies, is considered to be a 5-HT<sub>2A/2C</sub> receptor antagonist [4, 5].

In the present study we have determined the dose range at which mianserin exerts 5-HT<sub>2A</sub> and 5-HT<sub>2C</sub> receptor blocking activity by studying the effect of its pretreatment on ergometrine-induced wet dog shake (WDS) behaviour and fluoxetine-induced penile erections in rats. The wet dog shake (WDS) behaviour in rats and the head twitch response (HTR) in mice are 5-HT<sub>2A</sub> receptor mediated behaviours [6]. Ergometrine induces the WDS behaviour in rats and HTR in mice by directly stimulating the central 5-HT<sub>2A</sub> receptors [7, 8]. Direct or indirect activation of central 5-HT<sub>2C</sub> receptors [originally designated as 5-HT<sub>1C</sub> receptors [9] induces penile erections in rats [10]. Fluoxetine induces penile erections in rat either indirectly via its 5-HT uptake blocking activity or directly by stimulating the 5-HT<sub>2C</sub> receptors [10, 13].

Also tweak of 5-HT<sub>2</sub> receptor work by different medications has been appeared to impact DA work in SN and VTA just as in the terminal areas and answered to adjust the power of practices dependant on the useful status of nigrostriatal DAergic frameworks viz. DA agonist initiated generalized conduct (SB) [14] and neuroleptic prompted catalepsy [15].

Mianserin, as effectively expressed, is a 5-HT<sub>2A/2C</sub> receptor foe [4, 5], contingent upon its overwhelming opposing activity on 5-HT<sub>2A/2C</sub> receptor is probably going to regulate the movement of the nigrostriatal DAergic neurons and henceforth the power of practices subject to the useful status of the nigrostriatal DAergic framework [16]. It was accordingly thought beneficial to research the psychopharmacological profile of mianserin relating with the impacts of its pretreatment on practices reliant on the useful status of the nigrostriatal DAergic framework.

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## Materials and Methods

The trial conventions were endorsed by the Institutional Animal Ethics Committee and led by the Indian National Science Academy Guidelines for the utilization and care of trial creatures.

### Animals

Albino rodents of either sex (gauging 100-180 g), reared in the Central Animal House Facility of the Institute, were utilized. The creatures were housed under standard conditions, kept up on a 12 hr light/dull cycle and had let loose access to food and water to the hour of experimentation. Each gathering comprised of 10 creatures. Every creature was utilized just a single time. All observations were made between 10 and 17 hrs at 27°-30 °C. Observations were made blind with respect to the treatments used.

### Drugs

Drugs used were mianserin hydrochloride (Torrent, India), apomorphine hydrochloride (Sigma, USA), dexamphetamine sulphate (Kock-Light laboratories Ltd, UK), haloperidol (Senorm injection, Sun pharmaceuticals, India), ergometrine maleate (Sigma) and fluoxetine hydrochloride (Sun Pharmaceuticals). Haloperidol injection solution was diluted to required strength with distilled water. Apomorphine was dissolved in distilled water containing 0.2 mg/ml ascorbic acid, while the remaining drugs i.e. mianserin, d-amphetamine, ergometrine and fluoxetine were dissolved in distilled water only. The volume of drug injection was 2 ml/kg body weight for all the drugs. Doses refer to the forms mentioned and were selected on the basis of previous studies conducted in our laboratory and those reported in literature.

### Scoring of wet-dog shake (wds) behaviour in rats

For observation of the WDS behaviour, the animals were placed individually in open-topped perspex cages (30×20×20cm) immediately after the injection of ergometrine. The number of head shakes and whole body shakes were counted for 2 min at 10-min intervals between 10 and 122 min after administration of ergometrine. The 2- min scores were accumulated to give a total number of head and whole body shakes per rat and the total number scored by each rat in the group was taken to compute the mean value of the group. Mianserin was injected 1 hr before ergometrine. Control group received the requisite distilled water (2 ml/kg i.p.) 1 hr before receiving ergometrine. Mianserin was tested in the dose range of 1.25 to 20 mg/kg.

**Mianserin on fluoxetine induced penile erections (pes) in male rats:** The methodology followed was similar to that of Berendsen and Broekkamp (80). For observation of distilled water (DW 2 ml/kg i.p, control group), FLU (10 mg/kg) induced PEs the rats were placed in individual perspex cages (30×20×20cm) immediately after the injection of DW (2 ml/kg), FLU (10 mg/kg). The number of PEs induced by DW (2 ml/kg), FLU (10 mg/kg) was counted between 5 and 60 min observation period. The total number of PEs scored by each rat in the group was taken to compute the mean value of the group. Mianserin was injected 1 hr before fluoxetine. Control group received the requisite distilled water (2 ml/kg i.p.) 1 hr before receiving fluoxetine. Mianserin was tested in a dose range of 1.25 to 20 mg/kg.

**Catalepsy testing in rats:** For observation and measurement

of catalepsy the animals were placed in individual perspex cages (30×20×20cm), 30 min before drug treatment to allow adaptation to the new environment. Animals were tested for catalepsy according to the method of Costall and Naylor (152) by placing both front limbs of the animal over an 8 cm high wooden block and measuring the time that the animal maintained this posture. The animals were considered cataleptic if they maintained this imposed posture for more than 10 sec. Animals were tested for catalepsy 1.0, 2.0, 3.0 and 4.0 hrs after treatment with mianserin (1.25 to 20 mg/kg), haloperidol (1 mg/kg) and distilled water (2 ml/kg body weight i.p., control group).

### Mianserin on catalepsy induced by hal and small dose of apo in rats:

For observation and measurement of catalepsy the rats were placed in individual perspex cages (30×20×20cm), 30 min before drug treatment to allow adaptation to the new environment. Catalepsy was assessed by putting both front appendages of the creature over a 8 cm high wooden square and estimating the ideal opportunity for which the creature kept up the forced stance.

Scoring, altered from that of Costall and Naylor (152), was as per the following: keeping up the forced stance 0-10 sec (0); 11-30 sec (1); 31-60-sec (2); 61-120 sec (3); 121 sec and the sky is the limit from there (4). Creatures were tried and scored for catalepsy 1 and 2 hrs after HAL or little portion APO treatment. Catalepsy score of every creature in the gathering, at the individual testing time stretch, was taken to figure the mean estimation of the gathering for that specific planning.

Mianserin was injected 1 hr before HAL or small dose of APO while the control groups received distilled water (2 ml/kg i.p.) 1 hr before receiving HAL or small dose of APO. Mianserin was tested in the dose range of 1.25 to 20 mg/kg.

### Mianserin on stereotyped behavior (sb) induced by high doses of the da agonists in rats:

For observation of SB, the rats were placed in individual cages made of wire netting, measuring 30×20×20cm, 30 min before drug treatment to allow adaptation to the new environment.

The power of SB was surveyed over a 30 sec perception period at 10 min stretches all through its length, utilizing the scoring where occasional sniffing =score 1, consistent sniffing =2, intermittent gnawing, chewing or licking =3 and constant gnawing, biting or licking =4. The most extreme power of SB scored by each rodent in the gathering was taken to register the mean estimation of the gathering. Mianserin or haloperidol (HAL) was infused 1 hr before apomorphine (APO) or dexamphetamine (DAM) treatment. Control bunches got refined water (2 ml/kg body weight i.p.) 1 hr before accepting APO or DAM. Mianserin was tested in the dose range of 1.25 to 20 mg/kg while HAL was tested in the dose of 0.5 mg/kg.

## Results

In preliminary experiments it was observed that animals treated with 1.25 to 20 mg/kg mianserin appeared sedated, but the motor activity of the animals was similar to the control animals. All the mianserin treated animals appeared to adopt a hunch back posture with abdomen clearly lifted up from the floor. Mianserin in the dose range of 1.25 to 20 mg/kg i.p., did not produce motor incoordination, ataxia or muscular hypotonia or inhibit righting reflex. Further, in the dose range of 1.25 to 20 mg/kg i.p., mianserin did not induce WDS behaviour or catalepsy or SB in rats. As, at doses of 40 and 80

mg/kg mianserin had produced ataxia, motor incoordination and muscular hypotonia, for subsequent studies it was therefore used in the dose range of 1.25 to 20 mg/kg. Mianserin (1.25 to 20 mg/kg) did not induce SB in rats. DAM (5 and 10 mg/kg) induced dose-dependent SB in rats. Pretreatment with 1.25 and 2.5 mg/kg did not significantly affect SB induced by 5 and 10 mg/kg DAM. Pretreatment with 5, 10 and 20 mg/kg mianserin significantly increased the intensity of SB induced by 5 and 10 mg/kg DAM. Pretreatment with 0.5 mg/kg HAL abolished the SB induced by 5 and 10 mg/kg DAM.

**Table 1:** Effect of mianserin (MIAN) and HAL pretreatment on DAM induced SB in rats.

Study 6	Treatment dose mg/kg	Intensity score Mean $\pm$ SEM
I. A. 1.	DW + DAM 5	1.6 $\pm$ 0.16
2.	MIAN 1.25 + DAM 5	1.9 $\pm$ 0.16
3.	MIAN 2.5 + DAM 5	1.7 $\pm$ 0.15
4.	MIAN 5 + DAM 5	2.9 $\pm$ 0.10*
5.	MIAN 10 + DAM 5	3.3 $\pm$ 0.15**
6.	MIAN 20 + DAM 5	3.1 $\pm$ 0.10**
B. 1.	DW + DAM 5	1.5 $\pm$ 0.16
2.	HAL 0.5 + DAM 5	0.0
II.A. 1.	DW + DAM 10	$\pm$ 0.16
2.	MIAN 1.25 + DAM 10	2.9 $\pm$ 0.10
3.	MIAN 2.5 + DAM 10	$\pm$ 0.00
4.	MIAN 5 + DAM 10	$\pm$ 0.16*
5.	MIAN 10 + DAM 10	3.8 $\pm$ 0.13**
6.	MIAN 20 + DAM 10	3.9 $\pm$ 0.10**
II.B. 1.	DW + DAM 10	3.0 $\pm$ 0.0
2.	HAL 0.5 + DAM 10	0.0

## Discussion

The predominant effects of mianserin on 5-HT neuronal systems are mediated mainly through 5-HT<sub>2A/2C</sub> receptor antagonist action. In the present study conducted in rats, we have investigated how mianserin through its 5-HT<sub>2A/2C</sub> receptor blocking activity modulate the behaviours dependent on the functional status of the nigrostriatal DAergic system.

In the present study, since pretreatment with 5, 10 and 20 mg/kg doses of mianserin significantly antagonized the WDS behaviour induced by ergometrine in rats, it indicates that 5, 10 and 20 mg/kg doses of mianserin possess 5-HT<sub>2A</sub> receptor blocking activity. Our findings concur with the reports cited in literature stating that mianserin pretreatment antagonised the head shakes and the head twitches induced by 5-methoxytryptamine (5-MT) in rats. 5-MT induces HTR by direct stimulation of 5-HT<sub>2</sub> receptors. Mianserin also inhibits the HTR to 5-HTP (precursor of 5-HT) in rats and mice.

In our study, pretreatment with 1.25, 2.5 and 5 mg/kg mianserin significantly antagonised whereas 10 and 20 mg/kg mianserin abolished 5-HT<sub>2C</sub> receptor mediated PEs induced by fluoxetine. This indicates that 1.25 to 20 mg/kg doses of mianserin possess 5-HT<sub>2C</sub> receptor blocking activity. Our observations concur with the findings of Jenck et al. [11] that mianserin pretreatment antagonised mCPP induced PEs in male rats and that mCPP induced responses viz yawning and PEs which are mediated through stimulation of 5-HT<sub>1C</sub> (now 5-HT<sub>2C</sub>) receptor were attenuated by mianserin.

We postulate that pretreatment with 5, 10 and 20 mg/kg mianserin may be having predominant 5HT<sub>2C</sub> receptor blocking activity than 5HT<sub>2A</sub> receptors located on the cell bodies and axonal terminals of the nigrostriatal DAergic neurons, removes the inhibitory influence of 5HT on the nigrostriatal DAergic neurons. Our observations that pretreatment with 5, 10 and 20 mg/kg doses of mianserin

which block the 5HT<sub>2</sub> receptors antagonised haloperidol catalepsy is in agreement with the observations that pretreatment with 5HT antagonists having high affinity for 5HT<sub>2</sub> receptors viz methysergide and cyproheptadine [14] antagonised the cataleptic effect of neuroleptics haloperidol, molindone, pimozide and fluphenazine. Further, our observations are also in agreement with the observations that mianserin had antagonised haloperidol catalepsy in rats and also in agreement with that the selective 5-HT<sub>2C</sub> receptor antagonist SB-228357 significantly reversed haloperidol catalepsy whereas the 5-HT<sub>2A</sub> and 5-HT<sub>2B</sub> receptor antagonists MDL-100907 and SB-215505 respectively did not reverse haloperidol induced catalepsy. This suggests a role of 5-HT<sub>2C</sub> receptors in the anticataleptic action of SB-228357. In our study, mianserin in low doses of 1.25 and 2.5 mg/kg had no effect on haloperidol induced catalepsy.

our findings that pretreatment with 5, 10 and 20 mg/kg mianserin which block 5HT<sub>2C</sub> receptors did not influence apomorphine stereotypy but did potentiate dexamphetamine SB concur with the observations that pretreatment with methysergide a 5HT<sub>2</sub> antagonist failed to influence apomorphine SB but did enhance metamphetamine SB in rats. Further our findings that pretreatment with mianserin potentiate dexamphetamine SB in rats also concur but not with observations that mianserin did not enhance dexamphetamine induced SB in rats.

In our study, pretreatment with 5, 10 and 20 mg/kg mianserin antagonized the 5-HT<sub>2A</sub>-receptor-mediated WDS behaviour induced by ergometrine and the 5-HT<sub>2C</sub>-receptor-mediated penile erections induced by fluoxetine. This indicates that at these doses mianserin acts as a 5-HT<sub>2A</sub> and 5-HT<sub>2C</sub> receptor antagonist. However, on the basis of following observations, we contend that mianserin-induced potentiation of dexamphetamine stereotypy and antagonism of haloperidol catalepsy resulted due to the blockade of 5-HT<sub>2C</sub> receptors by mianserin. The SN and striatum has a high density of 5-HT<sub>2C</sub> mRNA and receptors and a low density of 5-HT<sub>2A</sub> receptor binding sites [4]. The 5-HT<sub>2C</sub>-receptor-mediated inhibitory effect of 5-HT on nigrostriatal DAergic transmission is therefore likely to predominate over the 5-HT<sub>2A</sub>-receptor-mediated facilitatory effect of 5-HT on nigrostriatal DAergic transmission. Consequently, disinhibition of the nigrostriatal DAergic pathway is more likely to occur due to mianserin induced blockade of 5-HT<sub>2C</sub> receptors. In addition, our contention is supported by the findings that the 5-HT<sub>2A</sub> receptor antagonists amperozide and MDL-100,907 had no effect on amphetamine-induced SB, and haloperidol-induced catalepsy was reversed by 5-HT<sub>2C/2B</sub> receptor antagonist SB-228357 but was not affected by the selective 5-HT<sub>2A</sub> and 5-HT<sub>2B</sub> receptor antagonists MDL-100,907 and SB-215505, respectively.

Our observations that pretreatment with the 5-HT<sub>2A/2C</sub> antagonist mianserin antagonised haloperidol catalepsy concurs with the observation of Gelders that the 5-HT<sub>2A/2C</sub> receptor antagonist ritaserin co-administered with haloperidol in schizophrenic patients decreased the extrapyramidal side effects of haloperidol. Antipsychotics possessing high degree of 5-HT<sub>2</sub> antagonistic activity in addition to D2 DA receptor blocking activity e.g. risperidone are less prone to produce extrapyramidal symptoms (EPS). Our findings and the clinical reports suggest that co-administration of 5-HT<sub>2A/2C</sub> receptor antagonists viz mianserin, with haloperidol in schizophrenia will prove beneficial as this drug will decrease the EPS of haloperidol.

Further, mianserin, a 5-HT<sub>2A/2C</sub> receptor antagonist can be used at low dose (15 mg/day) for the treatment of neuroleptic induced akathisia (NIA) as well as alternative option for sufferers from NIA for whom established antiakathic agents (beta blockers, anticholinergics, benzodiazepines) have been found to have limited therapeutic value or are contraindicated. Mianserin can also be useful as addition to ongoing neuroleptic treatment which may be associated with a significant improvement in neuroleptic induced dysphoria and psychosis. Further, our observations that mianserin antagonised haloperidol catalepsy indicates a role of it in the treatment of idiopathic parkinsonism and mianserin potentiated dexamphetamine SB suggests its use as an adjuvant along with l-dopa might prove beneficial by enhancing its antiparkinsonian effect of l-dopa and it might permit decrease in dose and hence side effects of l-dopa.

### Conclusion

Based on findings of Present study it can be concluded that Mianserin in the dose range 1.25 to 20 mg/kg i.p. did not produce motor incoordination, ataxia or muscular hypotonia. But these doses produced a hunch-back posture with abdomen clearly lifted up from the floor. Mianserin at 5, 10 and 20 mg/kg i.p. doses acts as a 5-HT<sub>2A</sub> receptor blocker as evident by the antagonist effects of these doses on 5-HT<sub>2A</sub> agonist ergometrine induced wet dog shake behaviour. Mianserin at 1.25, 2.5 and 5 mg/kg i.p. did significantly antagonise 5-HT<sub>2C</sub> receptor agonist fluoxetine induced PEs and 10 and 20 mg/kg i.p. mianserin abolished fluoxetine induced PEs. Thus 1.25 to 20 mg/kg doses of mianserin possess significant 5-HT<sub>2C</sub> receptor blocking activity. Mianserin at 5, 10 and 20 mg/kg i.p. doses does not block presynaptic D<sub>2</sub> DA autoreceptors as with these doses it failed to antagonise low dose (0.1 mg/kg) apomorphine induced catalepsy. Mianserin at 5, 10 and 20 mg/kg i.p. doses is devoid of postsynaptic D<sub>2</sub> and D<sub>1</sub> DA receptor blocking activity as at these doses it did not antagonise apomorphine induced SB and did not produce catalepsy in rats. Mianserin at 5, 10 and 20 mg/kg doses blocks the 5-HT<sub>2C</sub> receptors on the nigrostriatal DAergic neurons and remove the inhibitory influence of 5-HT on the nigrostriatal DAergic neurons which further causes increase in intraneuronal synthesis of DA and hence intraneuronal stores of DA. So pretreatment with 5, 10 and 20 mg/kg i.p. makes more DA available for release and resultant potentiation of dexamphetamine SB and antagonism of haloperidol catalepsy.

### References

1. Brogden RN, Heel RC, Speight TM, Avery GS. Mianserin: A review of its pharmacological properties and therapeutic efficacy in depressive illness. *Drugs*. 1978; 18:273-301.
2. Hollister LE, Claghorn JL. New antidepressants. *Annu Rev Pharmacol Toxicol*. 1993; 32:165-77.
3. Hoyer D, Hannon JP, Martin GR. Molecular, pharmacological and functional diversity of 5-HT receptors. *Pharmacol Biochem Behav*. 2002; 71:533-54.
4. Baldessarini RJ. Drug therapy of depression and anxiety disorders. In: Brunton LL, Laso JS, Parker KL, eds. *Goodman and Gilman's the pharmacological basis of therapeutics*. 11<sup>th</sup> ed. New York: McGraw-Hill, 2006, 429-59.
5. Meltzer HY, Nash JF. Effects of antipsychotic drugs on serotonin receptors. *Pharmacol Rev*. 1991; 43:587-604.
6. Martin GR, Humphrey PP. Receptors for 5-hydroxytryptamine: current perspectives on classification and nomenclature. *Neuropharmacology*. 1994; 33:261-73.
7. Bapat TR, Gada VP, Nandal NV, Balsara JJ, Chandorkar AG. Behavioural evidence for direct stimulation of rat brain 5-hydroxytryptamine receptors by ergometrine. *Indian J Pharmacol*. 1985; 17:108-12.
8. Balsara JJ, Bapat TR, Nandal NV, Gada VP, Chandorkar AG. Head-twitch response induced by ergometrine in mice: behavioural evidence for direct stimulation of central 5-hydroxytryptamine receptors by ergometrine. *Psychopharmacology (Berl)*. 1986; 88:275-8.
9. Zifa E, Fillion G. 5-Hydroxytryptamine receptors. *Pharmacol Rev*. 1992; 44:401-58.
10. Berendsen HHG, Jenck F, Broekkamp CL. Involvement of 5-HT<sub>1C</sub> receptors in drug induced penile erections in rats. *Psychopharmacology (Berl)* 1990; 101: 57-61.
11. Jenck F, Moreau JL, Mutel V, Martin JR, Haefely WE. Evidence for a role of 5-HT<sub>1C</sub> receptors in the antiserotonergic properties of some antidepressant drugs. *Eur J Pharmacol* 1993; 231: 223-9.
12. Berendsen HH, Broekkamp CL. Comparison of stimulus properties of fluoxetine and 5-HT receptor agonists in a conditioned taste aversion procedure. *Eur J Pharmacol*. 1994; 253:83-9.
13. Chen Y, Peng L, Zhang X, Stolzenburg JU, Hertz L. Further evidence that fluoxetine interacts with a 5-HT<sub>2C</sub> receptor in glial cells. *Brain Res Bull*. 1995; 38:153-9.
14. Balsara JJ, Jadhav JH, Muley MP, Chandorkar AG. Effect of drugs influencing central serotonergic mechanisms on methamphetamine-induced stereotyped behavior in the rat. *Psychopharmacology (Berl)*. 1979; 64:303-07.
15. Thorat VM, Gaonkar RK, Bhosale KB, Balsara JJ. Effects of dexfenfluramine on dopamine dependent behaviours in rats. *Indian J Physiol Pharmacol*. 2005; 49:39-48.
16. Alex KD, Pehek EA. Pharmacologic mechanisms of serotonergic regulation of dopamine neurotransmission. *Pharmacol Ther*. 2007; 113:296-320.