NEUROPHARMACOLOGICAL PROFILE OF TRANS-01 A POLYHERBAL FORMULATION IN MICE

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Summary

In the present study TRANS-01, a polyherbal formulation was explored for its CNS activity. The CNS activity was tested using mice in several experimental models like exploratory behavior, muscle relaxant activity and pentobarbitone sodium-induced sleeping time tests. The formulation at 200, 400 and 600 mg/kg showed significant dose dependent anxiolytic activity in hole board test and insignificant effect on pentobarbitone induced slleing time and muscle coordation.. Whereas Trans –01 at 800 mg/kg showed significant Sedative effect in hole board test and motor incoordination and muscle relaxant activity in traxction and rota rod tests respectively.

Keywords: TRANS-01; Neuropsychopharmacology; CNS effects; Hole board

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Introduction

Drugs acting in the central nervous system were among the first to be discovered by the primitive human and are still the most widely used group of pharmacological agents. The CNS acting drugs are invaluable therapeutically, because they can produce specific physiological and psychological effects. From the vast array of Materia Medica of the indigenous system so many plants have been reported to have activity against CNS disorders and thus act as very useful remedies for the alleviation of human suffering.

The investigational drug Trans-01 consists of Valeriana wallichii 120mg, Convolvus microphyllus 80mg, Plumbago zylanica 20mg, Boswellia serrata 40mg, Acorus calamus 10mg. There are reports for some of the ingredients of this formulation demonstrating the sedative and anxiolytic activities like antagonism of strychnine induced convulsion, sedative and tranquilizing effect of *Acorus calamus* [1]. *Convolvulus microphyllus* has been used since time immemorial as nerve tonic for improvement of memory, alleviating stress [2,3]. *Valerian Wallichii* has specific CNS activities [4].

These facts justify our interest in further studies of this formulation. The pharmacological activities of this plant extract are currently being studied in our laboratory. The purpose of the present study was to characterize the putative anxiolytic and sedative effects in mice using various animal models.

Materials and methods

Animals

Swiss albino mice of either sex (weighing between 20 and 25 gm) and albino (Wistar) rats of either sex (180–200 gm) were used for the study. They were maintained under standard environmental conditions and were fed a standard pellet diet with water *ad libitum*.

Drugs and chemicals

Diazepam (Ranbaxy Labs. New Delhi), Pentobarbitone sodium (National chemicals, Mumbai) were used for the present study.

Pentobarbitone sodium induced sleeping time

Swiss albino mice were divided into four groups (10 in each). The Trans-01 at doses of 100, 200, 400, 600 and 800 mg/kg and vehicle (10 ml/kg) was administered orally to each group. 1 hr after the administration, each animal was injected with pentobarbitone sodium (40-mg/kg i.p.). The sleeping time was noted by recording the time interval between the loss and return of righting reflex [5].

Muscle relaxant activity

30° Inclined screen test

Swiss albino mice (male) 1 hr after administration of either control vehicle (10 ml/kg), Diazepam (5 mg/kg) or TRANS-01 (100, 200 and 300 mg/kg) were left on the screen and the 'fall off' time was noted down when the mouse fall from the inclined screen. Normal mice generally fall off within 3–5 min[6]

Rotarod test

Untreated fresh mice were placed on a horizontal wooden rod (32 mm diameter) rotating at a speed of 5 rpm. The animals remaining on the rod for 3 min or more in two successive trials were selected for the test and were divided into 6 groups of 6 animals each. The first 4 groups were given TRANS-01 (200, 400, 600 and 800 mg/kg) while the fifth and sixth groups received control vehicle (10 ml/kg p.o) and Diazepam (5 mg/kg i.p.) respectively. The respective treatment was carried for 30 days and after 1 hr of the last dose animals were placed on the rod to note the time taken for the mice to fall from the rotating rod [6, 7].

Exploratory behavior test

Head board test

The hole-board apparatus consisted of gray wooden panels (40 cm × 40 cm, 2.5 cm thick) with 16 equidistant holes 3 cm in diameter in the floor. The board was positioned 15 cm above a table. Animals were placed singly in the center of the board facing away from the observer and animal behavior and head-dip numbers were recorded over 5 min. Mice subjected to this test were administered Trans-01 (200, 400, 600 and 800mg/kg, p.o.) for 30 days, and the final treatment was administered 1 h before hole-board testing on the 30th day. The number of times they dipped their heads in to the holes during 5-min was counted[8].

Statistical analysis

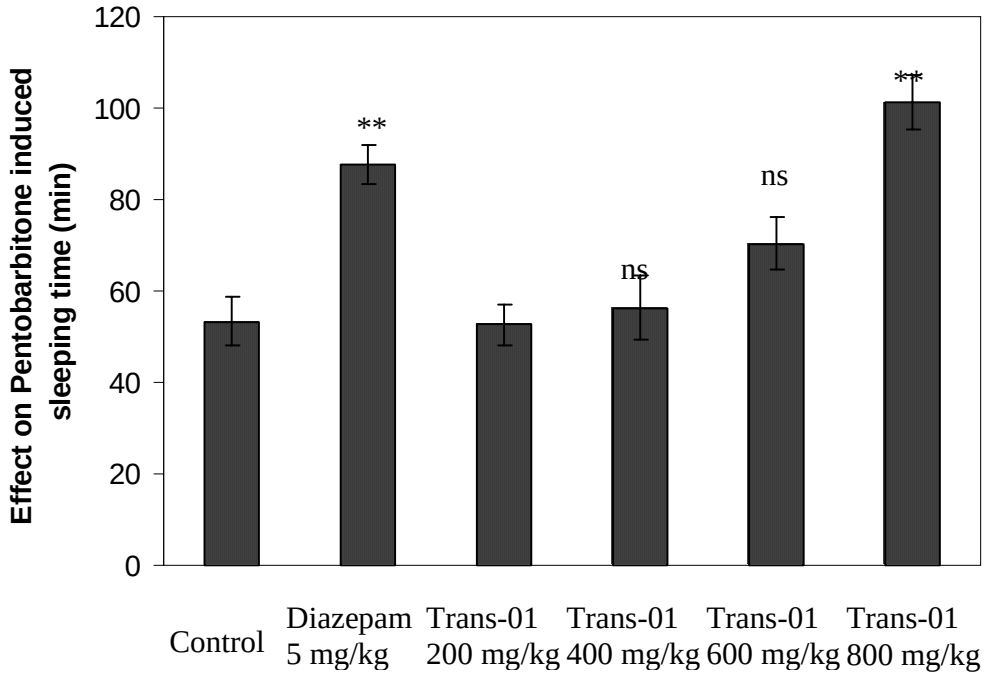
Results were expressed as mean±SEM. Statistical significance was analyzed by ANOVA followed by Tukey's post hoc test. $P<0.05$ was considered to be statistically significant.

Results

Effect on Pentobarbitone sodium induced sleeping time

The Trans-01significantly potentiated the pentobarbitone sodium induced sleeping time at 800 mg/kg which was compareable to diazepam and the other tested doses did not alter significantly when compared to control (Fig.1).

Fig. 1 Effect of Tans-01 on pentobarbitone induced sleeping time in mice following treatmentfor 30 days



(Figure 1)Values are expressed as mean ± S.E.M (n = 6). ^{ns}- statistically non significant, $^{**}p < 0.01$when compared to control group (ANOVA followed by Tukey's post hoc test)

Effect on muscle coordination

In both traction test and rota rod tests, TRANS-01 at 800 mg/kg produced significant failure in traction and motor inco-ordination in animals. Whereas the other tested doses did not produce any significant effect.

Table 1 Effect of Tans-01 on muscle coordination in mice following treatment for 30 days

Groups	Time taken in Sec	
	Rota rod test	**30^0 inclined test**
Control	180.6 ± 1. 6	180.2 ± 2.16
Diazepam 5 mg/kg	29.65 ± 3.21**	23.74 ± 1.11**
Trans-01 200 mg/kg	169.7 ± 2.4	159.7 ± 0.16
Trans-01 400 mg/kg	162.3 ± 1.26	153.2 ± 1.26
Trans-01 600 mg/kg	148.7 ± 3.21	148.7 ± 2.16
Trans-01 800 mg/kg	102.7 ± 1.26*	99.7 ± 0.26*

(Table 1)Values are expressed as mean ± S.E.M (n = 6). ^{ns}- statistically non significant, $^{*}p<0.05$, $^{**}p<0.01$, ***p<0.001 when compared to control group (ANOVA followed by Tukey's post hoc test)

Effect on exploratory behavioral pattern

Mice treated with TRANS-01 (200, 400 and 600 mg/kg), showed significant increase in exploratory behavior and head dips dose dependently when compared to control. However, Trans-01 at 800 mg/kg showed decrease in head dips as compared to control (Table 2).

Table 2 Effect of Tans-01 on exploratory behavioral pattern in mice following treatment for 30 days

Groups	No. of dips in 5 min
Control	17.6 ± 1. 6
Diazepam 2 mg/kg	54.65 ± 3.21***
Trans-01 200 mg/kg	29.7 ± 2.4*
Trans-01 400 mg/kg	38.3 ±2.26**
Trans-01 600 mg/kg	49.7 ± 3.11**
Trans-01 800 mg/kg	11.7 ± 1.16

(Table 2)Values are expressed as mean ± S.E.M (n = 06). ^{ns}- statistically non significant, $^{**}p < 0.01$when compared to control group (ANOVA followed by Tukey's post hoc test)

Discussion

The present experimental work indicated that the TRANS-01 has significant psychopharmacological activity.

The head-dipping behavior of mice observed in a hole-board apparatus is sensitive to changes in the emotional state of the animal, and an increase in head-dipping behavior reflects an anxiolytic state in animals[9]. Consistent with the previous report, diazepam significantly increased head-dip counts in the present study. Trans-01 also increased head-dip counts dose dependently which help to claim that Trans-01 has an anxiolytic-like activity. On contrary to this Trans-01 at 800 mg/kg showed decrease in head dips, which may indicate that at higher doses it may show sedative effect, which was also evident from its potentiation of sodium pentobarbital induced sleep. This activity may be contributed to its central nervous system depressant effect[10]. However, this test is not specific because compounds that interfere with biotransformation of pentobarbital by cytochrome P450 complex can show the same effects of central nervous system depressant drugs [11]. Nevertheless, the animals treated with Trans-01 in Traction and rota rod tests at a dose of 800 mg/kg produced significant muscle incoordination exhibiting significant muscle relaxant activity.

Thus it may be inferred that Trans at higher doses may act as general depressant whereas at lower doses behaves as an anxiolytic. However detailed studies are required to further ascertain the same and probe its mechanism of action in general depressant activity.

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