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STUDY OF ANTIDEPRESSANT LIKE EFFECT OF *CORIANDRUM SATIVUM* AND INVOLVEMENT OF MONOAMINONERGIC AND GABANERGIC SYSTEM

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ABSTRACT
The aim of this study was to examine possible mechanism of action of aqueous extract of *Coriandrum sativum* seed central nervous system of mice. We investigated the antidepressant-like mechanism of *Coriandrum sativum* by the combination of the Sulpiride (a selective dopamine D_2 receptor antagonist), Prazosin (a α_1 adrenoceptor antagonist), and Baclofen (GABA agonist). The results show that *Coriandrum sativum* (200 mg/kg, 400mg/kg, p.o.), significantly reduced the immobility time during Tail Suspension Test (TST). We also investigated the antidepressant-like mechanism of *Coriandrum sativum* by the combination of Sulpiride (a selective dopamine D_2 receptor antagonist), Prazosin (a α_1 adrenoceptor antagonist), and Baclofen (GABA agonist). The immobility time after treatment with *Coriandrum sativum* (200 mg/kg, 400mg/kg, p.o.) in TST was augmented by Sulpiride, Baclofen, Prazosin. Our findings support the view that *Coriandrum sativum* exerts antidepressant-like effect. And the mechanism of action of *Coriandrum sativum* may be related to the increase in Nor adrenaline and serotonin levels in the hippocampus and frontal cortex.

KEYWORDS: Tail Suspension Test, immobility time, nor adrenaline and serotonin levels.

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INTRODUCTION

Depression, anxiety is a common, debilitating, life-threatening illness with a significant incidence in the population. Numerous antidepressants, antianxiety compounds are now available, presumably acting via different mechanisms including serotonergic, noradrenergic and/or dopaminergic systems.

Coriandrum sativum L. Apiaceae (Umbelliferae) (coriander, also known as cilantro, cilantrillo, Arab parsley, Chinese parsley, Mexican parsley, Dhania and Yuen sai), is an annual herb commonly used in Middle eastern, Mediterranean, Indian, Latin American, African and Southeast Asian cuisine[1]. In the Indian traditional medicine, coriander is used in the disorders of digestive, respiratory and urinary systems, as it has diaphoretic, diuretic, carminative and stimulant activity. Its use is recommended in urethritis, cystitis, urinary tract infection, urticaria, rash, burns, sore throat, vomiting, indigestion, nosebleed, cough, allergies, hay fever, dizziness and amoebic dysentery[2].

Coriandrum sativum L. has been recommended for relief of anxiety and insomnia in Iranian folk medicine. Nevertheless, no pharmacological studies have thus far evaluated its mechanism of action on central nervous system[3].

The major classes of drugs that are used to treat depressive illness are: tricyclic antidepressants, selective serotonin reuptake inhibitors, atypical antidepressants, and monoamine oxidase inhibitors. Tricyclic antidepressants block the reuptake of monoamines (most often noradrenaline and serotonin) into nerve terminals[4]. Imipramine is a tricyclic antidepressant with a preferential effect on noradrenaline (NA) reuptake[5] and extensively used clinically. It was therefore of interest to use as standared in this study. Indications of the effects of serotonin (5-HT), noradrenaline (NA),GABA on the pathology and treatment of Depression[6], make it interesting to investigate if a extract of *Coriandrum sativum* exert any effect in the TST model. In presence of Sulpiride (a selective dopamine D_2 receptor antagonist), Prazosin (an α_1 adrenoceptor antagonist),

and Baclofen (GABA agonist) . These mechanisms are interesting in the context of depression[7] and it was valuable to know whether *Coriandrum sativum* could exert an effect in the TST,. The aim of the present study was to measure the effect of acute treatment with Sulpiride, Prazosin and Baclofen on tail suspension test, in order to study the predictive mode of actio of these two extract of Coriandrum Sativum.

MATERIAL AND METHOD

Animals

Male albino mice weighting 25–35 g were housed in cages of 5 at 22 ± 1 ◦C in a 12-h light/dark cycle. Tap water and food pellets were available as libitum. Groups of 6–11 mice were randomly assigned to different treatment groups and tested in a counterbalancing order. Animals were naive to experiment conditions[7].

Preparation of aqueous extract

Dried coriander seeds were homogenized to a fine powder. Hundred grams of powdered coriander was infused in 500 ml cold distilled water for 24 h, brought to the boil, then removed from the heat source and allowed to infuse for 15 min. The extract was filtered, then concentrated over the water bath and brought to dryness under vacuum[8].

Preparation of Fixed oil extract

The seeds of the *Coriandrum sativum* were ground in mixer. The 100gm of powdered material was macerated with 500ml of Diethyl ether for 2 hrs. The solvent was evaporated. The yield of the extract was 1.02% w/v.

The toxicity study was carried out according the test procedure described in OECD Guideline (425) to estimate acute oral toxicity of drug. The drug extracts are safe and non toxic for use.

Screening method

Tail suspension test

The tail suspension test was the method for assessing the antidepressant effect of the extract. Thirty minutes after the single drug or vehicle injection, mice were subjected to the test[9, 10].

A cord of about 50 cm in length was stretched between two mental tripods at a height of ca 70 cm, to which the mice were attached by the tail with sticky tape. After the initial period of vigorous motor activity, the mice become still and the immobility time was measured with a stopwatch, for a total duration of 4 minutes.

Experimental protocol shows in table no .1 all observations on TST carried on after 14 successive days of drug administration[9].

Statistical analysis

Statistical analysis of data was carried out by one way ANOVA followed by Dunnett t- test. Values are expressed as mean ± SEM, $P<0.001$ is considered as criterion of significance.

RESULT

In this present study, 300mg/kg and 600mg/kg of Aqueous extract and 6ml/kg, 8ml/kg of Diethyl ether extract of seeds of *Coriandrum sativum* have been used for TST. These doses administered for 14 successive days produced significant antidepressant effect in TST (Table no.2). The efficacies of the extracts were found to be comparable to fluoxetine (SSRI) and Imipramine (Tricyclic antidepressant). Both the extract shows significantly shows antidepressantlike effect.

Sulpiride, Prazosin and Baclofen alone significantly increased the immobility time as compared to control group when tested with TST. Pretreatment of animals with Sulpiride, Prazosin and Baclofen significantly blocked in decreased immobility time elicited by aquous extract and diethyl ether extract of *Coriandrum sativum* .(Table No. 3)

In TST model, treatment of aqueous extract and Diethyl ether extract of coriandrum seeds in combination with Sulpiride (a selective dopamine D_2 receptor antagonist), showed 64% & 61% reduction in immobility time when compared with individual drug Sulpiride resp. Further the combination with Prazosin (a α_1 adrenoceptor antagonist), showed 34% & 61% reduction in immobility time when compared with individual drug Prazosin which was statistically significant.

Aqueous extract of *Coriandrum sativum* combine with Baclofen it showed 25% decrease in immobility time and Diether ethyl extract showed 50.3% decrease in immobility time when compare with baclofen.

DISCUSSION

Tail suspension test are currently most widely used models of animal depression[10]. And it has been validated for use with rat and mice. The indices of depression in these models were “Immobility Time” Shorter immobility time, stronger antidepressant effect.

This suggests that both these extract might produce antidepressant like effect by interacting with, dopamine D_2, and α1 adrenoceptors receptor. Thereby, aqueous extract and Diethyl ether extract of coriandrum seeds increasing the level of noradrenalin, dopamine and decrease level of GABA.

Antidepressant like effects of both extract were significantly reversed by the treatment of animal with Sulpiride (a selective dopamine D_2 receptor antagonist), Prazosin (a α_1 adrenoceptor antagonist), and Baclofen (GABA agonist) when tested in TST. This suggests that both the extract of *Coriandrum sativum* might produce antidepressant like effect by interacting with α_1

adrenoceptors, dopamine D_2 receptor, and GABAergic receptor, hence increasing level of norepinephrine, dopamine, and decreasing GABA levels in brain of mice.

CONCLUSION

The finding in the current study shows that extracts of seeds of *Coriandrum sativum* displays a behavioral profile consistent with an antidepressant like action.

Both the extract of seeds of *Coriandrum sativum* might produce antidepressant effect through interaction with adrenergic system, dopaminergic system and GABAnergic system.

On the other hand , it was observed that Diethyl ether extract of seeds of *Coriandrum sativum* showed more significant antidepressant effect than that of Aqueous extract when statistically significant difference compared to the control group of animal.

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Table 1: Experimental protocol for combination study

Groups	No.of animals	Dose
Control+Sulpiride	6	D/W+ 50mg/kg
Control+Prazosine	6	D/W + 62.5mg/kg
Control+Baclofen	6	D/W + 10mg/kg
Test 1 + Sulpiride	6	200mg/kg + 50mg/kg
Test 1+ Prazosine	6	200mg/kg+ 62.5mg/kg
Test 1+ Baclofen	6	200 mg/kg+ 10mg/kg
Test 2+ Sulpiride	6	0.8ml/kg+50 mg/kg
Test 2+ Prazosine	6	0.8 ml/kg +62.5 mg/kg
Test 2+ Baclofen	6	0.8ml/kg + 10 mg/kg

Test 1: Aqueous extract of *Coriandrum sativum*
Test 2: Diethyl ether extract of *Coriandrum sativum*

Table 2: Effect of various extract of seeds of *Coriandrum sativum* on immobility period in TST

Drug treatment for 14 days p.o.	No. of animals	Dose (mg/kg)	Immobility time(s) (mean ± SEM)
Control(distilled water)	6	10ml	188 ± 6.75
Fluoxetine	6	20	109.16 ± 25.48
Imipramine	6	15	150.16 ± 6.49
AECS	6	200	137.66 ± 31.86
AECS	6	400	130.5 ± 8.26
DEECS	6	0.4ml/kg	135.5 ± 21.14
DEECS	6	0.8ml/kg	140.83 ± 14.49

Table 3: Effect of combination of extracts of *Coriandrum sativum* seeds with Sulpiride, Baclofen and Prazosin on immobility period in tail suspension test

Drug treatment for 14 days p.o.	No.of animals	Dose	Immobility time(s) (mean ± SEM)
Control (distilled water)	6	10 ml	192 ± 11.9
AECS	6	300 mg/kg	102 ± 20.49
DEECS	6	6 ml/kg	115.5±31.86
Vehicle + Sulpiride	6	50 mg	234.33±18.27^{ab}
AECS + Sulpiride	6	300mg/kg + 50 mg/kg	136.83 ± 8.18^{a}
DEECS + Sulpiride	6	6 ml/kg + 50mg/kg	83 ± 13.82^{b}
Vehicle + Prazosine	6	62.5 µg	225.8 ± 14.41^{ab}
AECS + Prazosine	6	300mg/kg+ 62.5µg/kg	150.0 ± 6.26
DEECS + Prazosine	6	6 ml/kg + 62.5µg/kg	87.33 ± 9.4
Vehicle + Baclofen	6	10 mg/kg	189.5 ± 8.11*^{b}
AECS + Baclofen	6	300mg/kg + 10 mg/kg	142.83 ± 2.31^{c}
DEECS + Baclofen	6	6 ml/kg + 10 mg/kg	94 ± 5.50^{c}

AECS = Aqueous extract of seeds of *Coriandrum sativum*
DEECS = Diethyl ether extract of seeds of Coriandrum Sativum

Statistical analysis of data was carried out by one way ANOVA followed by Dunnett t- test. Values are expressed as mean ± SEM, P<0.001 is considered as criterion of significance. P<0.001 as compared to control, *P>0.05 as compared to control , ^{a}P< 0.001 as compared to test 1, ^{b}P< 0.001 as compared to test 2 , ^{c}P< 0.01 as compared to control

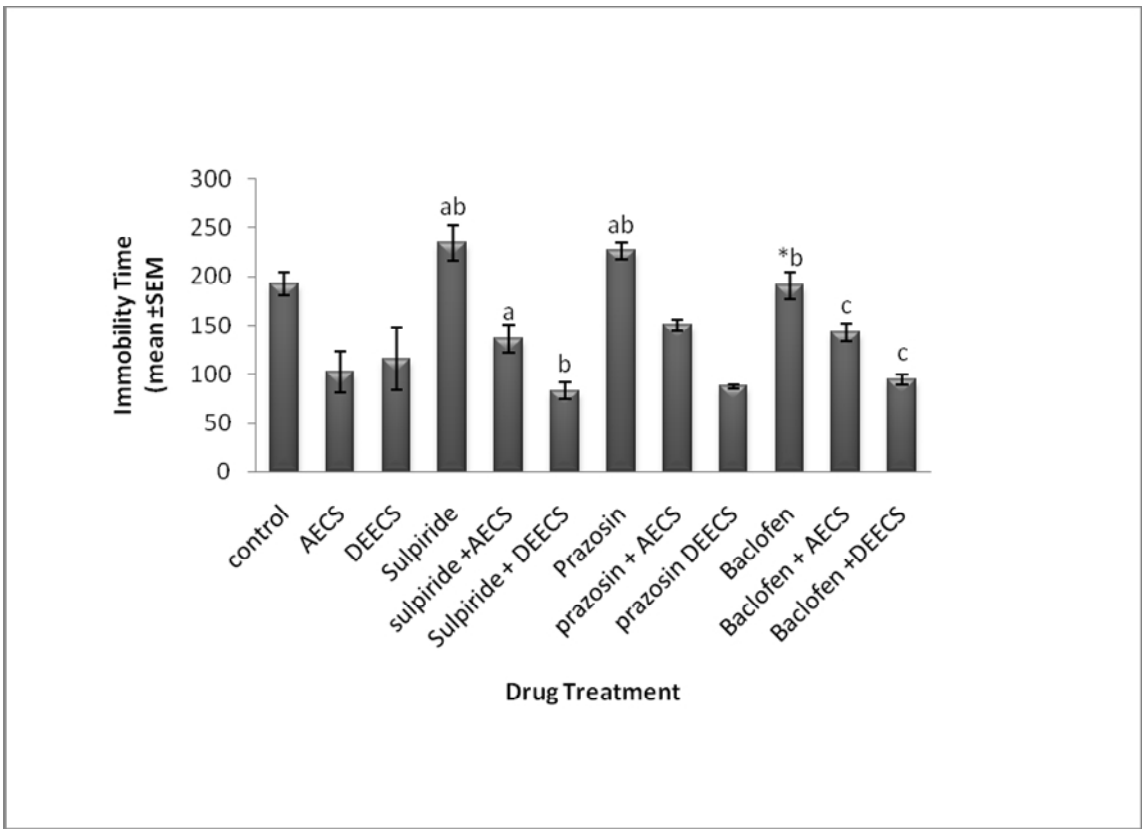

Fig 1: Effect of combination of extracts of C.S with Sulpiride, Baclofen and Prazosin in TST

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