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ANXIOLYTIC AND ANTIDEPRESSANT ACTIVITY OF PETAL OF *CROCUS SATIVUS* VAR. 'CASHMERIANUS'

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ABSTRACT: *Crocus sativusvar*. 'cashmerianus' (Iridaceae)is worldwide known as "Saffron" contains than volatile and aroma-containing compounds mainly terpenes, terpene alcohol, and their esters. The bitter taste and a hay-like fragrance of saffron are due to presence picrocrocin and safranal. Traditional anxiolytic and antidepressant effects of *C. sativus* var. 'cashmerianus' was evaluated using successive extracts in elevated plus maze test and forced swim test in rat sat doses level of 50, 100 and 200 mg/kg/p.o., Whereas diazepam (1mg/kg/p.o.) was used as standard drugs. Successive methanol and aqueous extracts of petals of *C. sativus* at a dose of 200 mg/kg/p.o. (1^{st}, 3^{rd} and 7^{th} day) were shows significant (*P <0.05) as like diazepam increased the percentage of time spent and arm entries in the open arms and decreased the closed arms entries and duration in closed arm in elevated plus maze. The results for antidepressant activity using forced swim test shown that the ethyl acetate, methanol and aqueous extracts of petals of *C. sativus* var. cashmerianus at a dose of 200 mg/kg significantly increased the climbing and swimming time, however decreased the immobility time as similar like imipramine. The results are shown good potential of petal of *Crocus sativus* var. 'cashmerianus' as anxiolytic and antidepressant like action.

INTRODUCTION: *Crocus sativus* var. 'cashmerianus'is a stem less perennial herb belonging to Iridaceae family, generally known as Kesar in India , Saffron (worldwide) and locally Zafranin Kashmir region in India. Saffron is produced worldwide at an annual rate of 50 tons with a commercial cost of about 50 million dollars. *C. sativus* var. 'cashmerianus' comprises of the red stigma (dried), purple color petal with a yellowish style is attached.

It is mainly cultivated in China, Egypt, France, Greece, Iran, Italy, Israel, Morocco, Spain, Turkey, Mexico and Kashmir in India [1]. It is most expensive spice and used for cooking, staining, medicine, cosmetics [2]. Traditionally, used as aphrodisiac, an antispasmodic, carminative, expectorant, stomachic and hypolipaemic effect, petals possesses antidepressant, cardio-tonic and stimulant effects [3-4].

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Anxiety and depression are central nervous system disorders and badly affects routine life. Physical symptoms of anxiety disorders are appeared due to release of stress hormones like adrenaline and cortisol, which have an effect on almost every organ in the human body. Untreated anxiety disorders can lead to depression which may result in increased blood pressure, heart palpitations, chest pain, rapid breathing or breathlessness, sweating, increased muscle tension or irritability, and decreased intestinal blood flow resulting in nausea or diarrhea. Regular use of benzodiazepines type drugs causes addiction, confusion, aggression, excitement, physical dependence, tolerance, deterioration of cognitive functioning, psychomotor impairment and anterograde amnesia [5].

These are some of the factors that caused interest in many researchers to evaluate new compounds from plant origin in the hope to identifying other anxiolytic drugs with fewer unwanted side effects. In present study, anxiolytic and antidepressant activities are assessed using well established animal models like elevated plus maze test (EPMT), light and dark test (L and DT) and forced swim test (FST) of the successive extracts of petals of *Crocus sativus* var. 'cashmerianus' in rats.

MATERIAL AND METHODS

Plant Material: *Crocus sativus* var. "Cashmerianus" petals collected from Pampore, area of Srinagar district in Kashmir (India). It is identified by Prof. A.R. Naqshi, Taxonomist, University of Kashmir, Srinagar. The petals were dried under shade and powdered as coarsely.

Preparation of Extracts: The coarse powder of petals of *C. sativus* var. "Cashmerianus" was subjected to continuous extraction in a Soxhlet apparatus using petroleum ether, chloroform, ethyl acetate, methanol separately and lastly decoction using water as solvent.

Experimental Animal used: Animals Albino rats (Wistar strain) of either sex (180- 200 g) were obtained from the animal house of Indian Institute of Integrative Medicine (IIM), Jammu. Animals were kept under the laboratory conditions (25 ± 2°C, 12 h light). They were provided with standard rodent pellets diet. Food was withdrawn 12 h before the experimental work and water was provided *ad libitum*. After a 7 days of acclimatization period, animal were randomly selected for different experimental groups (6 animal/ group) and used for activities. This Institution is approved for carrying out animal studies (Approval No.801/03/ca/CPCSEA) and the protocol for the present study was approved by Institutional Animal Ethical Committee [Approval no. FIAEC (Pharm. Sc.) APPROVAL/2011/02]

Drugs: Diazepam was obtained from Ranbaxy Lab. Ltd., HPSIDC-Baddi, Solan (India). Sodium carboxy methyl cellulose was purchased from CDH-Laboratory Reagent Pvt. Ltd. Post Box. No. 7138, New Delhi-110002 (India). Diazepam and extracts were suspended in a 1% sodium carboxy methyl cellulose solution. All drugs were prepared immediately before use and were given orally. Control rats received 1% aqueous sodium carboxy methyl cellulose solution only. The effect of the drugs was estimated 60 minutes after drug administration. Drug dose, pre-treatment time and selection of 1% sodium carboxy methyl cellulose solution as vehicle were based on findings in preliminary experiments or taken from the literature. Tests were performed only after the rats had been acclimatized to the above environment for at least 7 days. All experiments were carried out between 09:00 and 16:00 h. In each experiment apparatus was cleaned using 5% ethanol before introducing the next animal to preclude the possible cueing effects of odors left by previous subjects.

Methods:

Anxiolytic and Antidepressant Activities:

Elevated Plus-maze Test: The wooden maze consists of two open arms (50 x 10 cm) and two closed arms of the same size enclosed with 40 cm high walls and a central square of 10 x 10 cm. The maze was 60 cm above the floor.

A slight raised edge on the open arms (0.25 cm) provided additional grip for the animals, whereas open arm activity was further encouraged by testing under dim red light (4 x 25 W). The experiment was conducted as described [6-7] in sound proof room during the dark phase of the light cycle (9 –16:00 h). To facilitate adaptation to new surroundings, rats were transported to the laboratory at least 1 h prior to testing.

The trial was started by placing an animal on the central platform of the maze facing an open arm. Standard 5 min test duration was used and between subjects, the maze was thoroughly cleaned by 5% ethanol with damp and dry towels.

were randomly allocated to the following groups: vehicle control, diazepam (1 mg/kg po, successive extracts were selected as 50, 100 and 200 mg/kg/p.o. Similarly, study was carried out on 1st, 3rd and 7th day for acute, subacute and chronic model. In acute study 60 min. after the first dose, in subacute 60 min. after the 3rd dose and in chronic study 60 min. after the last dose on the 7th day of drug or vehicle administration.

The animal was placed at the central platform of the maze facing an open arm. Standard 5 min test duration was used and between subjects, the maze was thoroughly cleaned with damp and dry towels. The experiments were performed with an observer unaware of the treatment of the rats inside the room. The following parameters are classically measured in this test: frequency and duration (s) of arm visits, separately for open and closed arms. Rat was considered to have entered an arm when all four paws were on the arm. The percentage of entries into open arms (open arm entries/total arm entries×100; % open arm entries) and the percentage of time spent in open arms (open arm time/total arm time×100; % open arm time) are used as traditional indices of the anxiety [8-9].

Forced Swimming Test: The forced swim test was performed as described by Porsolt *et al.* [10]. The rats were forced to swim individually in a glass cylinder, filled with water to a height of 40 cm under natural light controlled conditions. The temperature of the water was adjusted to 25 ± 2°C. The animals were trained 24 h before the test start (15 min individually) and the test was performed for 5 min in next day. The water was changed between swims by different rat.

During the test time, sampling technique was used to score the durations of climbing time, swimming, and immobility time. Immobility time was measured when the rat was in an upright position on the surface with its front paws together and making only those movements which were necessary to keep it afloat.

RESULTS AND DISCUSSION:

Elevated Plus Maze Test:

Effect of Diazepam and Successive Extracts Petals of *C. sativus* var. *Cashmerianus* in Rats: The doses of successive petals extracts of *C. sativus* var. *Cashmerianus* (SECS) were administered to different groups of rats on 1st, 3rd and 7th days of experiment with 50, 100 and 200 mg/kg/p.o. for this activity.

Doses of drugs for different groups of EPM test were selected as- control group treated with vehicle (5 ml/kg), DZ mean diazepam (1mg/kg/p.o.) as standard drug, test groups were treated with PECS-50, PECS-100 and PECS-200 treated with petroleum ether (40-60°C) extract of petals of *C. sativus* var. *Cashmerianus* at dose of 50 mg/kg, 100 mg/kg and 200 mg/kg/p.o. respectively.

CECS-50, CECS-100 and CECS-200 treated with chloroform extract of petals of *C. sativus* var. *Cashmerianus* at dose of 50 mg/kg, 100 mg/kg and 200 mg/kg/p.o. respectively. EECS-50, EECS-100 and EECS-200 treated with ethyl acetate extract of petals of *C. sativus* var. *Cashmerianus* at dose of 50 mg/kg, 100 mg/kg and 200 mg/kg/p.o. respectively. MECS-50, MECS-100 and MECS-200 treated with methanol extract of petals of *C. sativus* var. *Cashmerianus* at dose of 50 mg/kg, 100 mg/kg and 200 mg/kg/p.o. respectively.

AECS-50, AECS-100 and AECS-200 treated with aqueous extract of petals of *C. sativus* var. *Cashmerianus* at dose of 50 mg/kg, 100 mg/kg and 200 mg/kg/p.o. respectively. Successive extracts of *C. sativus* var. *cashmerianus* and standard drug diazepam significantly increased the open arm time and increase the entries in open arm **Fig. 1-2** and at the same time decreased the latency time but there was no significant difference observed in immobility time as compared to control **Fig. 3.**

Among all the test extracts, ethyl acetate extract was found to be more effective *viz*. increased open arm time and entries versus control, chloroform, methanol and aqueous had intermediate and petroleum ether extract was found to be least active as compared to control. The values are expressed as $^{a}p<0.01$ vs. control group. All the groups' datas were statistically analyzed by ANOVA followed by Tuckey test.

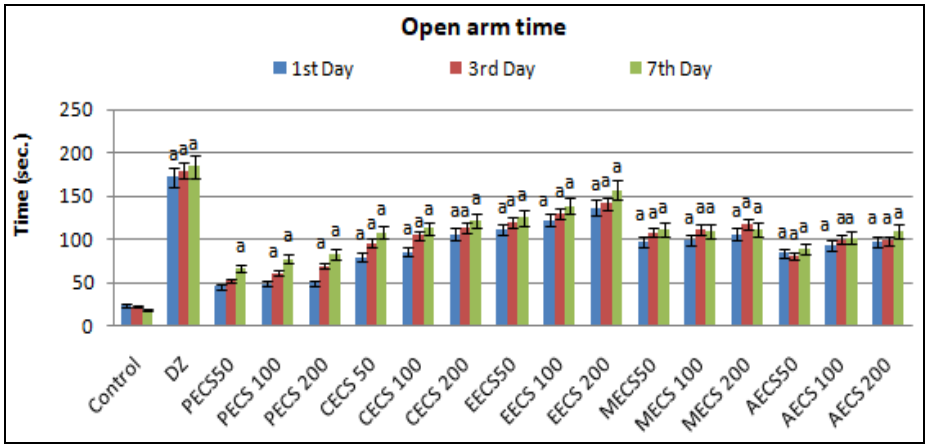

FIG. 1: EFFECTS OF DIAZEPAM AND SECS ONOPEN ARM TIME IN EPM TEST IN RATS. Results are expressed as means ± S.E.M., n = 6 per group. ap<0.01 vs. control group. Statistically analysed by ANOVA followed by Tucky test.

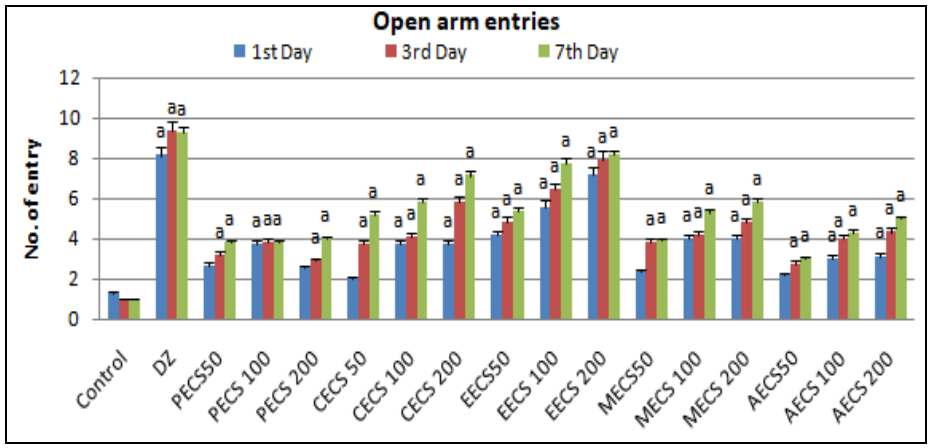

FIG. 2: EFFECTS OF SECS ONOPEN ARMENTRIES IN EPM TEST IN RATS. Results are expressed as means ± S.E.M., n = 6 per group. ap<0.01 vs. control group. Statistically analyzed by ANOVA followed by Tucky test.

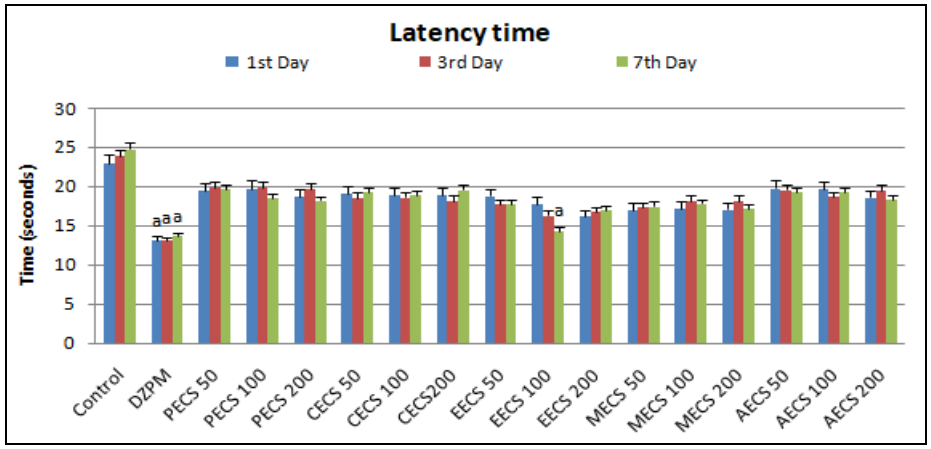

FIG. 3: EFFECTS OF SECS ON LATENCY TIME IN EPM IN RATS. Results are expressed as means ± S.E.M., n = 6 per group. [a]p<0.05 vs. control group. Statistically analyzed by ANOVA followed by Tucky test.

Forced Swim Test:

Successive Extracts of Petals of *C. sativus* var. *Vashmerianus* on Forced Swim Test of Tats: The effect of diazepam (1mg/kg) as standard drug and successive extracts of petals of *C. sativus* var. *cashmerianus* were evaluated in rats using forced swim test. Successive extracts of petals of *C. sativus* var. *cashmerianus* at doses of 50, 100 and 200 mg/kg were tested and some behavioral defense parameters of this test (swimming, climbing and immobility time) were observed. The results of all doses of ethyl acetate extracts, higher doses (200mg/kg) of chloroform, methanol and aqueous extracts showed significant increase in the

climbing and swimming time whereas, decreased the immobility time similar to that of diazepam **Fig. 4**. The successive ethyl acetate extract was found to be most promising and comparable to the standard drug .The results were statistically significant ($^aP<0.01$) vs. control. Experimental data were analyzed by ANOVA followed by Tucky test.

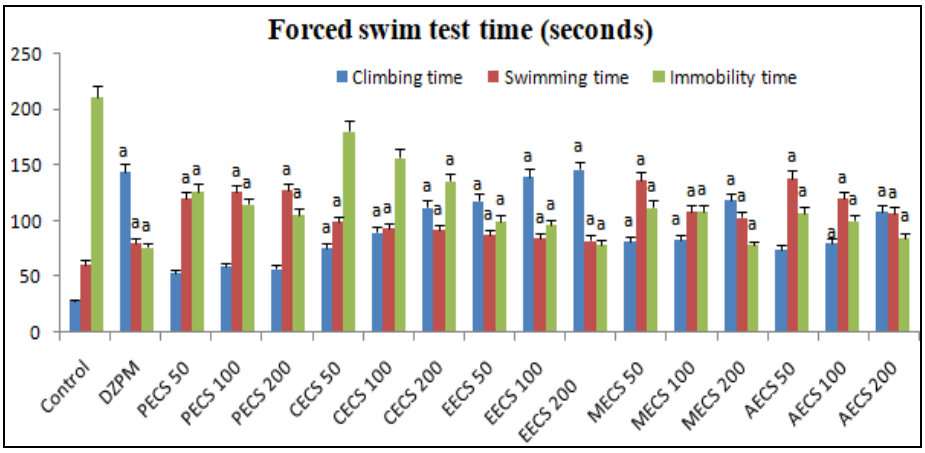

FIG. 4: EFFECTS OF DIAZEPAM AND SECS ON FORCED SWIM TEST PARAMETERS IN RATS. Results are expressed as means ± S.E.M. (n=6). The values $^ap<0.05$ vs. control group, all groups compared with control. Data statistically analyzed by ANOVA followed by Tucky test.

DISCUSSION AND CONCLUSION: The results supported the traditional uses of *Crocus sativus* var. *cashmerianus* in the management of nervous and cerebral disorders including anxiety and depression. *C. sativus* var. *cashmerianus*is rich sources of flavonoids like quercetion, luteolin etc that have antioxidant, antianxiety and antidepressant effects.

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CONFLICTS OF INTEREST: There are no conflicts of interest.

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