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Antidepressant activities of *Sambucus ebulus* and *Sambucus nigra*

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Abstract. – OBJECTIVE: Many pharmacological activities have been reported in *Sambucus (S.)* genus. The aim of present study was to investigate antidepressant activities of different parts of *S. ebulus* and *S. nigra*.

MATERIALS AND METHODS: Antidepressant activity of methanolic extracts were evaluated by forced swimming test (FST) and tail suspension tests (TST) in male Swiss albino mice.

RESULTS: Extracts showed very good antidepressant activity in both FST and TST. They shortened remarkably the immobility period in both FST and TST and exhibited a dose dependent activity. Extracts in all tested doses showed significant activity as compared to control group ($p < 0.001$). *S. nigra* showed better activity than *S. ebulus*. Its leaf extract at 1200 mg kg^{-1} showed the same activity as imipramine in FST ($p > 0.05$). Its fruit extract at 1200 mg kg^{-1} showed far better activity than imipramine in FST ($p < 0.001$). *S. ebulus* fruit extract in 1200 mg kg^{-1} showed significant activity which was so better than imipramine at 10 mg kg^{-1}, in decreasing immobility period in TST ($p < 0.001$). No mortality was observed after 48 hours at 3 g kg^{-1}.

CONCLUSIONS: Our report indicated the *S. ebulus* and *S. nigra*. extracts were safe and showed remarkable antidepressant activity in FST and TST in mice. These results introduced these plants as easily accessible source of natural antidepressant.

Key Words:
Antidepressant, Forced swimming test, Tail suspension test, *Sambucus ebulus* and *Sambucus nigra.*

Introduction

Depression constitutes the second most common chronic condition in clinical practice and will become the second leading cause of disease burden worldwide by the year 2020[1]. Approximately two-thirds of patients respond to the currently available treatments but the magnitude of improvement is still disappointing[2]. Although there are many effective antidepressants available today, the current armentarium of therapy is often inadequate with unsatisfactory results in about one third of all subjects treated[2]. This necessitates the development of newer and more effective antidepressants from traditional medicinal plants whose psychotherapeutic potential has been assessed in a variety of animal models[3]. Genus of *Sambucus (S.)* L. belongs to Caprifoliaceae and included eighteen species in all over the world, among them six species distributed in subtropical areas of America, Eurasia and Africa. Four species of the genus *Sambucus* are growing in Iran. Of these species, *S. ebulus* and *S. nigra* extensively growth in moist grasslands or forest margins on Northern coast of Caspian Sea. Iranian traditional medicine uses the leaves, fruits and rhizomes of *S. ebulus* in treating some inflammatory cases such as, bee and nettle bites, arthritis, and sore-throat[4,5]. In addition, it has been reported to be an insect repellent, antihemorrhoid, antiprotozoal, antigiardial, antibacterial toward Helicobacter pylory, convenient in treatment of burns and infectious wounds, edema, eczema, urticarial, the cold and scolices of Hydatid cysts[6-8]. To the best of the author's knowledge, antidepressant activity of *S. ebulus* and *S. nigra* have not been reported to date and nothing was found about mechanism or antidepressant activity of this plant. Therefore, the aim of the present work is to determine the antidepressant activity by forced swimming test (FST) and tail suspension test (TST) in order to understand the usefulness of these plants in medicine.

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Materials and Methods

Plants Materials and Preparation of Extracts

S. ebulus and *S. nigra* materials were collected from north of Iran. After identification by Dr. Bahman Eslami voucher (No. 1395 and 1396) have been deposited in the Faculty of Pharmacy Herbarium. Plants materials were dried and coarsely ground. Plants materials were extracted by percolation using methanol. The resulting extract was concentrated over a rotary vacuum until a crude solid extract was obtained which was then freeze-dried for complete solvent removal.

Animals

Male Swiss albino mice (20 ± 2 g) were randomly housed in groups of 10 in polypropylene cages at an ambient temperature, 25 ± 1°C and 45-55% relative humidity, with a 12 h light: 12 h dark cycle (lights on at 7 a.m.). The animals had free access to standard pellet and water and *libitum*. Experiments were conducted between 8:00 and 14:00 h. The experiments were conducted according to the norms of Committee for the Purpose of Control and Supervision of Experiments in Animal. Mice were divided into six different groups (n = 10 per group) and tested in FST and TST.

Forced Swimming Test

The mouse was dropped into a glass cylinder (20 cm in height and 12 cm in diameter) containing 8-cm-deep water at 24-25°C and left there for 6 min. The duration of immobility during the final 4-min interval of the swimming test was measured[9,10]. Control group was treated with Tween 80 plus 0.9% (w/v) saline solution. The other groups received an *i.p.* injection of extracts (200-1200 mg kg^{-1}) in Tween 80 plus 0.9% (w/v) saline solution and imipramine (10 mg kg^{-1}) (from Darupakhsh Co., Tehran, Iran), one hour before the experiment.

Tail Suspension

Male mice are housed in plastic cages for at least 10 days prior to testing in a 12h light cycle with food and water freely available. Animals are transported from the housing room to the testing area in their own cages and allowed to adapt to the new environment for 1 h before testing. Groups of 10 animals are treated with the extract (200-1200 mg kg^{-1}) by *i.p.* injection 30 min prior to testing. For the test the mice are suspended on the edge of a shelf 58 cm above a table top by adhesive tape placed approximately 1cm from the tip of the tail. The duration of immobility is recorded for a period of 5 min. Mice are considered immobile when they hang passively and completely motionless for at least 1 min. Imipramine (10 mg kg^{-1}) was used as positive control[9,10].

Non-Fatal Dose

Three mg kg^{-1} doses of extracts were injected to separated groups of seven. After 48h, any mortality was considered as the maximum non-fatal dose[10].

Statistical Analysis

Experimental results are expressed as means ± SD. The data were analyzed by analysis of variance ($p < 0.05$) and the means separated by Duncan's multiple range test.

Results and Discussion

There are many published papers that showed polyphenolic compounds such as flavonoids have antidepressant activity[11,12]. Because of high polyphenol and flavonoids contents of *Sambucus* extracts, they were nominated for assay of antidepressant activity. Behavioral despair was proposed as a model to test for antidepressant activity. It was suggested that mice or rats forced to swim in a restricted space from which they cannot escape are induced to a characteristic behavior of immobility. This behavior reflects a state of despair which can be reduced by several agents which are therapeutically effective in human depression[13]. Table I showed the result of effect of extract on the duration of immobility during FST. All of extracts in all tested doses showed significant activity as compared to control group ($p < 0.001$). *S. nigra* showed better activity than *S. ebulus*. *S. nigra* leaf extract at 1200 mg kg^{-1} show the same activity as imipramine at 10 mg kg^{-1} in FST ($p > 0.05$). *S. nigra* fruit extract at 1200 mg kg^{-1} showed far better activity than imipramine in FST ($p < 0.001$). TST has been described as a easy mean of evaluating potential antidepressants[14]. The immobility displayed by rodents when subjected to an unavoidable and inescapable stress has been hypothesized to reflect behavioral despair which in turn may reflect depressive disorders in humans. Clinically

Table I. Antidepressant activities of *S. ebulus* and *S. nigra* in FST and TST.

Group	Dose (mg kg^{-1})	Duration of immobility (s)[a,b], FST	Duration of immobility (s)[a,b] TST
Control	–	191 ± 18	110.5 ± 12
S. nigra fruit	200	87 ± 12	85.5 ± 15.1
	400	76.8 ± 3.3	72.2 ± 8.3
	800	72 ± 7.3	60.3 ± 6.2
	1200	8.5 ± 3.8***[c]	44 ± 3.8
S. nigra leaf	200	131 ± 5	97.4 ± 15.7
	400	74 ± 12.9	77.8 ± 11
	800	48.8 ± 7.4	42 ± 11
	1200	37.8 ± 10.3[ns,c]	20 ± 15.7
S. ebulus flower	200	220 ± 11.5	122.5 ± 17
	400	134 ± 13.7	99.8 ± 14
	800	129 ± 14	61.4 ± 11
	1200	84 ± 1	54 ± 6.5
S. ebulus fruit	200	134 ± 16	76.3 ± 4.3
	400	78.6 ± 14	71.6 ± 8.7
	800	53.8 ± 17	44.5 ± 9.5
	1200	41.7 ± 15	8.5 ± 3.5***[c]
Imipramine	10	37 ± 12	15 ± 2.1

[a]Data are expressed as mean ± SD (n = 10). [b]All groups were different from control group with $p < 0.001$. [c]Groups are different from imipramine ([ns]$p > 0.05$,***$p < 0.001$).

effective antidepressants reduce the immobility that mice display after active and unsuccessful attempts to escape when suspended by the tail. All extracts in all tested doses showed significantly and dose dependently decreased in the immobility time as compared to control mice ($p < 0.001$). *S. ebulus* fruit extract in 1200 mg kg^{-1} showed significant activity which was so better than imipramine at 10 mgkg^{-1}, in decreasing immobility period ($p < 0.001$) (Table I). The nonfatal doses of *S. nigra* and *S. ebulus* extracts were over 3 g kg^{-1}. No mortality was observed after 48 hours.

Conclusions

Our studies indicate that *S. nigra* and *S. ebulus* extracts showed good antidepressant activity. It produced dose dependent effect on both FST and TST. Further investigations of individual compounds and the mechanisms of activities are needed.

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Conflict of Interest

The Authors declare that there are no conflicts of interest.

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