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EVALUATION OF ANTIDIABETIC, ANTIEPILEPTIC AND ANXIOLYTIC ACTIVITIES OF *SALVIA BUCHARICA* AND *HYOSCYAMUS INSANUS*

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ABSTRACT

Salvia bucharica (Lamiace) and *Hyoscyamus insanus* (Soalanaceae) are two important medicinal plants of Balochistan, Pakistan. Current study was carried out to evaluate the traditional claim of the plants for the treatment of diabetes, epilepsy and depression. Anti-diabetic activity was carried out on rabbits by producing hyperglycemia with glucose solution (2 g/kg, p.o.). For anti-epileptic activity strychnine induced seizures method in mice were used. Anxiolytic activity was determined by using light- dark test on mice. In anti-diabetic activity methanolic extract of *S. bucharica* and *H. insanus* at oral dose of 300mg/kg produced significant ($p<0.05$) results as compared with standard drug. In anti-epileptic activity both plants at 300mg/kg produced significant effects as duration onset of seizures were significantly increased. In light-dark test both plants produced significant anxiolytic effects at 250 and 500 mg/kg oral doses as compared with control and standard drug. In conclusion results of current study reveals that the methanolic extract of *S. bucharica* and *H. insanus* produced significantanti-diabetic, anti-epileptic, Anxiolytic activities.

Keywords: Alhagi maurorum, Analgesic, CNS depressant

INTRODUCTION

Diabetes is a chronic disease of the breakdown of biomolecules such as proteins, fats and carbohydrates [1, 2]. Diabetes can be due to low amount of insulin or its malfunctioning [2]. A statistical data showed, 2.8% of the world's population are affected and will elevate ahead 5.4% by 2025 [3]. Diabetes is a disease that affects many people in the 21st century and is known as the fifth leading cause to death [4].The crippling disease is responsible for mass number of morbidities globally. People suffering from diabetes lack insulin and so leads to increase blood glucose level [5]. About 90 to 95% of cases is of type 2 diabetes in which the body does not produce enough insulin [6]. According to World Health Organization by the year 2025 this disease around 300 million or more is expected to be elevated [7].

Recently herbal medicines are used due to their wide varieties of features, the use of natural health products as complementary or alternative approaches to existing medicines is growing in fame [8] Several ethnopharamacological studies reveals the potential effects herbal medicines [9]. Literature reveals that, the evaluation of sugar lowering action of medicinal plants used traditionally confirms the antidiabetic effects in various animal models [10, 11, 12].

Salvia bucharica (Lamiaceae) is a perennial plant of Pakistan, Afghanistan and Central Asia [14] Plant grows in Quetta, herboi and zairat Balochistan, Pakistan. Local name is `sursunda. In the local region its given to cure liver aliments [15, 16],its decoction is employed for kidney pain, colic pain, jaundice, fever, and hypertension [16, 17].

Hyoscyamus insanus (Solanaceae) locally called khohi Bhang is a medicinal plant of balochistan [18], this plant possesses analgesic affect through using it as poultice of fresh leaves on area with pain. The smoke is inhaled for the treatment of asthma. In order to increase body weight, seeds of this plant are used by females [19].This plant is containing alkaloids namely hyoscyamine (atropine), hyoscine and apoatropin [20].

MATERIAL AND METHODS

Plant material

Plant material was collected from Jhal Magsi and Hanna urak, Quetta district of Baluchistan Pakistan. The plants were identified and voucher specimen no.G-575 and 576 were deposited in the pharmacognosy department, Faculty of Pharmacy, Baluchistan University Pakistan. The fresh leaves and stem were cut downed

into small pieces. The chopped material was macerated with methanol for two weeks (twice) at 25 ^{O}C. The methanolic extract was filtered and evaporated under reduced pressure in rotary evaporator.

Antidiabetic activity

During this study the rabbits were divided into4 groups of 5 each. Control (non treated), *S. bucharica* and *H. insanus* crude extract 300mg/kg treated group, and standard drug glimepiride 3mg/kg treated group. Anti diabeteic activity was carried on according to method described by Tamboli et al., 2012 [21]. In this study, glucose solution (2 g/kg, p.o.) was introduced 30 min after vehicle/drug administration. Blood samples were collected after 30 minutes of glucose load. For blood glucose levels glucometer (Abott) was used.

Antiepileptic activity

The mice were divided into three groups each with five mice. Methanolic extracts obtained from the plants were administered at doses of 250 & 500 mg/kg *orally.* First group was treated with vehicle (saline) and Group II was treated with Divalproex sodium 300mg/kg. Group III, was treated with 250& 500mg/kg orally. All the drug treatment was given thirty minutes before the injection of Strychnine (3 mg/kg *Sc*). Individual plastic cage was prepared for observation of each animal lasting 45 minutes. The commencement of general clonus was recorded and tonic clonic convulsions were studied. Protection of the animals from mortality was recorded [22].

Light-dark Test

Anxiety model Light-Dark Box Test [23] was carried on to evaluate the anxiolytic action of the plant extracts (light-dark box test). The instrument possesses light and dark compartments. Light dark box is a rectangular box of 46 X 27 X 30 cm, which is divided into 2 compartments. A central opening (7 X 7 cm) on the floor level is placed for the joining of the two compartment. For this experiment, albino mice were divided into four groups, each group comprising of five animals. Vehicle (saline5ml/kg), standard (diazepam 2 mg/kg) and extract (250 and 500mg/kg) were introduced p.o. After 30 minutes of drug administration, each mouse was placed individually in the illuminated part of the light/dark box. Total time spent in the light and dark compartment were recorded.

RESULTS

Antidiabetic activity

In antidiabetic activity, mean level of blood glucose for control (vehicle treated) group was 104$\pm$3.17,for diabetic animal (glucose 2g/kg treated group) the mean sugar level

was 199.22±2.63, for *S. bucharica* crude extract 300mg/kg treated group were 158.6±0.4, for *H. insanus* crude extract 300mg/kg treated group were 128.42±3.51 and for standard drug (glimipride 3 mg/kg) treated group level was 155.1±0.45.Results shows that *S. bucharica* and *H. insanus* crude extract showed significant anti diabetic action.

Antiepileptic activity

In antiepileptic activity of *S. bucharica* and *H. insanus* crude extract showed significant results. For control (vehicle treated group) the mean strychnine induced onset of seizures was 103.76 ±2.39 seconds, for *S. bucharica* 300mg/kg crude extract onset was 316.24±6.67 seconds, for *H. insanus* crude extract 300mg/kg treated group onset was 295.8±3.96 seconds , forDivalproex sodium 300mg/kg onset was 340.24±1.60 seconds.

Anxiolytic activity

Light and dark test

In Light and dark test for control (0.5ml saline treated group), the mean time spent in light was 3.34±0.005 minutes and time spent in dark was 6.27±0.005, for *S. bucharica* 250mg and 500 mg/kg the time spent in light was 2.42± 0.008 and 1.51±0.018, and the time spent in dark was7.18±0.009 and8.09±0.018 minutes respectively, for *H. insanus*250mg and 500 mg/kg the time spent in light was 1.54±0.001and 1.56±0.007, and the time spent in dark was 8.06±0.017and 8.04±0.007minutes respectively, for diazepam (2mg/kg) the time spent in light was 2.06±0.005 and the time spent in dark was 7.54±0.005.

Table 1: Antidiabetic action of *S. bucharica* and *H. insanus* crude extract on rabbits

Treatment	Dose mg/kg orally	Mean blood glucose level ±S.E.M
Control	0.5ml/kg saline	104±3.17
Diabetic control	Glucose2g/kg	199.22±2.63
S. bucharica	300 mg/kg	158.6±0.40
H. insanus	300 mg/kg	128.42±3.51
Glimepiride	3mg/kg	155.1±0.45

Values are mean ± SEM; n=5; * = Significant results (*P*<0.05), ** = highly significant results (*P*<0.01).

Table 2: Anti epileptic activity: Effect of *S. bucharica* and *H. insanus*on onset of seizures using strychnine

Treatment	Dose mg/kg orally	Onset of seizures using strychnine ±S.E.M
Control	0.5 ml saline	103.76±2.39
S. bucharica	300 mg/kg	316.24±6.67
H. insanus	300 mg/kg	295.8±3.96
Divalproex sodium	250mg/kg	340.24±1.60

Values are mean ± SEM; n=5; * = Significant results (*P*<0.05), ** = highly significant results (*P*<0.01).

Table 3: Anxiolytic action: Light and dark action of *S. bucharica* and *H. insanus*crude extract on mice

Treatment	Dose mg/kg orally	Time spent in light	Time spent in dark
Control	0.5ml saline	3.34±0.005	6.27±0.005
S. bucharica	300 mg/kg	2.42± 0.008	7.18±0.009
	500 mg/kg	1.51±0.018	8.09±0.018
H. insanus	300 mg/kg	1.54±0.001	8.06±0.017
	500 mg/kg	1.56±0.007,	8.04±0.007
Diazepam	2mg/kg	2.06±0.005	7.54±0.005

All values are mean ± SEM; n=5; * = Significant results (*P*<0.05), ** = highly significant results (*P*<0.01).

DISCUSSION

Alternative therapies are common know a days and one of the most important method is self-medication of herbal drugs. Currently much focus is drawn for the search of new drugs in the management anxiety disorders. Medicinal plants can provide better opportunities for the treatment of such diseases. The result of current study shows that these plants showed Anti-hyperglycemic effect and this may be due to the presence of phyto-constituents such as tannins, saponins and flavonoids.These substances are frequently implicated for its antihyperglycemic effects [21].

Glucose intestinal absorption inhibition or enhancerelease of insulin by pancreatic beta cells may be one of the possible mechanisms for this anti-hyperglycemic effect, as previously reported that flavonoids (gallocatechin) are responsible for increased utilization of peripheral glucose [21].

Result of current study shows that methanolic extract of leaves of *S. bucharica* and *H. insanus* exerts significant ($p<0.05$) anticonvulsant effects against strychnine-induced seizures as compared with control and standard drug treated group. Mechanism behind anticonvulsant effects is may be the involvement of antagonism (direct) of strychnine-sensitive glycine receptors, brainstem, spinal cord and higher brain, thereby repealing spinal reflexes and causing enhanced muscle tone,motor disturbance, tonic convulsions, hyperaction of sensory, visual and acoustic perception and death through spinal or respiratory paralysis or by cardiac arrest [24].

Result of light/dark test shows that methanolic extract of leaves of *S. bucharica* and *H. insanus* showed significant ($p<0.05$) anxiolytic effects. In this test, anxiety is produced by the conflict among the inclination to search and the first leaning to sidestep the unaware [25] and it is determined by number of moves in to and the time spent in the light chamber [26,27], increase in member and time spent reflect

anxiolytic effects. Results revealed methanolic extract of leaves of *S. bucharica* and *H. insanus* produced anxiolytic effect as evident by increased time spent in the light chamber [28]. The anxiolytic agents are responsible to enhance the response to GABA, by enabling the opening the GABAA-activated chloride channels [29]. Methanolic extract of leaves of *S. bucharica and H. insanus* showed may produce effects similar benzodiazepine-like substance.

CONCLUSION

Methanolic extract of leaves of *S. bucharica* and *H. insanus* showed significant anti-diabetic, anti-epileptic, Anxiolytic activities, however further studies are required to evaluate the exact mechanism on large number of animals and toxicological studies are also required to check the safety profile of the both plants.

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