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Central Nervous System Depressant Effect of *Senna occidentalis* Linn. (Fabaceae) Leaf Extract in Mice

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Authors' contributions

This work was carried out in collaboration between all authors. Author AUC identified the species of plant, designed the study, wrote the protocol and wrote the first draft of the manuscript. Authors MYD, TSM and MIH managed the literature searches and analyses of the data while authors AUC, TSM and YAA managed the experimental process. All authors read and approved the final manuscript.

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ABSTRACT

Senna occidentalis has been used in traditional medicine in Nigeria for managing various ailments in traditional medicine. This study was aimed at evaluating the central nervous system depressant effect of ethanol leaf extract of *Senna occidentalis* in mice. Thirty mice of either sex were taken and divided into five groups of six animals each. First group was considered as negative control in diazepam-induced sleeping time (normal saline + diazepam), second, third, fourth and fifth as test groups (with 20 mg/kg, 40 mg/kg, 80 mg/kg and 100 mg/kg doses of the extract + diazepam). All the drugs were administered intraperitoneal (i.p). The extract showed significant decrease in the

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onset of sleep at doses of 20 mg/kg, 40 mg/kg and 80 mg/kg ($p<0.05$; One-way ANOVA). The number of head dips have significantly decreased at $p<0.05$ for all the graded doses of the extract. Beam walking test for motor deficits, showed significant increase in the number of foot slips at the same graded doses at $p<0.05$ with no significant difference in the time taken to complete the task. The study showed that leaf ethanol extract of *Senna occidentalis* possess CNS depressant effect, and serve as a good sedative as such, can save patients from many doses of anesthetic medication usually administered during surgery in conventional medicine when used.

Keywords: CNS depressant; Senna occidentalis; motor deficits; traditional medicine.

1. INTRODUCTION

Insomnia is defined as persistent difficulty in falling sleep which affects function of humans. It can induce significant psychological and physical disorder. Sedatives are drugs that reduces activity and have a calming, relaxing effect. At higher doses, sedatives usually cause sleep thereby putting the body in a state of calmness [1]. Drugs used mainly to induce sleep are called hypnotics. The difference between sedatives and hypnotics, then, is usually the amount of the dose; lower doses have a calming effect and higher doses induce sleep [2]. Recent studies have shown that herbal drugs exert good sedative and hypnotic effect on the central nervous system [3].

Senna occidentalis (Linn.) formally *Cassia occidentalis* is a weed of the leguminosae (Fabaceae) family. *Senna* is a low branching annual shrub and grows to about three feet high. *Senna* has compound leaves with narrow linear to oval shaped dark green leaflets. In summer, it has yellow pea-like flowers which are flowed by brown pods with brown seeds. It can be found in open pastures and in field cultivated with cereals such as soya beans [4].

Fig. 1. *Senna occidentalis* in its natural habitat
Source: Bali Town, July, 2014

The plant is known as "*Rai doore*" or "*Rairai*" by Hausa people and "Siyi banje" by Yoruba people in Nigeria. The plant's tissues contain a host of photoactive chemicals that may support its numerous applications in folk medicine. Extracts or powdered leaves are used as an analgesic, antibacterial, anti-hepatotoxic, antifungal, antiinflammary, antiseptic, antiparasitic, antiviral, carminative, diaphoretic, emmenagogue, febrifuge, insecticidal, immune-stimulant, laxative, purgative, pseudorific, and vermifuge [5].

This study was carried out in order to scientifically screen the leaves extract of *Senna occidentalis* for some behavioral effect in mice and hence, predicts its possible CNS depressant effect in albino mice model.

2. MATERIALS AND METHODS

2.1 Plant Collection, Identification and Preparation

The leaves of *S. occidentalis* were collected from Daniya in Bali Community, Taraba State, Nigeria in 2016, and identified at the Department of Science Laboratory Technology, Federal Polytechnic, Bali, Nigeria by a taxonomist Mr. Cletus A.U, where a voucher number was deposited for the plant. The materials were allowed to dry for 2 weeks under a shade. They were later on reduced to powdered by using pestle and mortar. The powdered leaves were then weighed and extracted with absolute ethanol using cold maceration techniques. It was evaporated to dryness to get a black residue with a yield of 14.3% w/w, and then stored for further use in the desiccators.

2.2 Experimental Animals

Thirty Swiss albino mice of both sexes with body weight ranging from 18 to 24 g were kept in the Department of Science Laboratory Technology, Bali Taraba State. The mice were grouped and housed in cages (38x23x10 cm) with stainless

steel wire mesh covers, floored with wood shavings to absorb urine, fecal matter and spilled water and maintained under standard laboratory conditions (temperature 25 ± 2℃) relative humidity 45%, with dark/light cycle 12/12 h). They were allowed free access to standard diet and water *ad libitum*. The mice were acclimatized to laboratory conditions for 7 days before commencement of the experiments.

2.3 Diazepam-induced Sleeping Time in Mice

Mice of either sex were divided into five groups of six mice each. Animal in group I received normal saline (10 mL/kg) and served as negative control, while groups II, III, IV and V received the extract doses of 20, 40, 80 and 100 mg/kg (i.p.) respectively. Thirty minutes after treatment, all animals were given diazepam (2 mg/kg). Each mouse was observed for the onset and duration of sleep with the criterion of sleep being loss of righting reflex. The time from the loss of righting reflex to recovery was recorded as sleeping time [6].

2.4 Exploratory Behavior in Mice

The study was done using the hole-dip test on the hole-board [7]. It was carried out using wooden board (40x40 and with four equidistant holes (1cm diameter; 2 cm depth). Mice of either sex were divided into five groups of six each. Animals in group 1 receive normal saline (10 mL/kg; i.p) and served as positive control, group 2 received 2 mg/kg diazepam while those in groups III, IV and V received the extract at doses of 20, 40 and 80 mg/kg i.p respectively. Thirty minutes after treatment, each mouse was placed at one corner of the board and allowed to move about and dipped its head into the holes indicating exploratory behavior. The number of times the mice dipped their heads into the holes during the 5 minutes period was counted and recorded.

2.5 Beam Walking Test for Motor Coordination Deficits in Mice

The study was done according to method described by [7]. Mice were trained to travel from a start platform along a ruler (80 cm long and 3 cm wide) inclined at 30° above the bench by metal supports and attached to a metal box. Trials were performed for each mouse, and were designed such that the mice tested would be aware that there was a box that could be reached.

Mice of either sex were divided into five groups of six each. Group I received normal saline 10 mL/kg i.p, group II received 2 mg/kg diazepam, while groups III, IV and V received 20, 40, and 80 mg/kg of extract respectively. Thirty minutes after, each mouse was placed at one end of wooden beam (8 mm in diameter, 60 cm long and elevated 30° above the bench by metal supports), and allowed to walk to the box within a maximum of 60 s. The time taken on the beam, number of falls, and the number of slips were recorded.

Fig. 2. Beam walking test

3. RESULTS

The ethanol extract of *S. occidentalis* produced an increase in the mean onset of sleep in the diazepam induced sleep at 20 mg/kg ($p<0.05$).

Similarly, there were decrease in the mean duration of sleep from 20 to 80 mg/kg ($P<0.05$) in all the groups except in group I (Table 1). The ethanol extract *S. occidentalis* and diazepam (2 mg/kg; standard drug used) decreased the number of head dips in exploratory behavior test in mice as compared to the control (normal saline) group at $P<0.05$ (Table 2). The extract at all the tested doses and diazepam (2 mg/kg) increased the number hind limb slips in motor coordination test in mice. The test groups that were administered the extract doses and diazepam were significantly different while at doses of 40 and 80 mg/kg the groups were also significantly different at $p<0.05$ (ANOVA) compared to control (normal saline) group. There was no statistical difference in the time taken to complete the task between the extract treated, diazepam and the extract groups. Similarly, none of the animals fell down from the beam walk in all the groups (Table 3).

Table 1. Effect of ethanol leaf extract of *S. occidentalis* on diazepam-induced sleep in mice

Treatment (mg/kg)	Mean onset of sleep (min)	Mean duration of sleep (min)	Number slept/mice
N/Saline (10 mL/kg + D)	5.66 ± 0.65	120.00 ± 25.00	6/6
SO 20 + D	3.59 ± 0.31	242± 20.96**	6/6
SO 40 + D	3.50 ± 0.30**	253.00 ± 10.76 **	6/6
SO 80 + D	3.45 ± 0.29	259.00 ± 20.36**	6/6
SO 100 + D	2.90 ± 0.21**	264.00 ± 17.40**	6/6

*Values are mean± SD, n = 6, SO = Senna occidentalis, significant difference from control group at **p< 0.05 (ANOVA), D= Diazepam 2 mg/kg, N = Normal*

Table 2. Effect of ethanol leaf extract of *S. occidentalis* and diazepam on exploratory behaviour in mice

Treatment (mg/kg)	Number of head dips
Normal saline (10 mL/kg)	8.50 ± 2.09*
D 2	12.96 ± 1.67*
SO 20	14.33 ± 1.72
SO 40	16.66 ± 1.87
SO 80	20.67 ± 2.02*

*Values are mean ± SD, n = 6, SO = Senna occidentalis, D = Diazepam, *p< 0.05, significant difference from controls (ANOVA)*

Table 3. Effect of ethanol leaf extract of *S. occidentalis* and diazepam (D) on motor coordination

Treatment (mg/kg)	Number of hind limb slips	Time taken for the task(s)	Number of falls/mice
Normal saline (10 mL/kg)	0.00	8.90 ±1.59*	0/6
Diazepam 2	5.30 ± 0.12	35.70 ± 0.91*	0/6
SO 20 + D	10.67 ± 0.19	25.60 ± 2.67	0/6
SO 40 + D	14.67 ± 0.21	20.7 ± 3.50	0/6
SO 80 + D	18.00 ± 1.38	15.70 ±1.39*	0/6

*Results are mean±SD, D = Diazepam, *p< 0.05 significant difference (ANOVA), SO = Senna occidentalis*

4. DISCUSSION

The extracts have significantly decrease on the onset of sleep, and increased the duration of sleep dose-dependently. This shows that the extract potentiated the diazepam-induced sleep, which may be attributed to an action on the central mechanisms involved in the regulation of sleep or an inhibition of diazepam metabolism [8-9].

It has also been reported that activation of $GABA_A$ (Gamma-amino butyric acid) receptor in the CNS known to favour sleeping [10], and the study on antinociceptive activity of *S. occidentalis* extract indicated that the extract had significant central antinociceptive action revealing the involvement of the CNS in anti-nociception [11]. Also demonstration of muscle relaxant effect by the rotor rod study indicated that the *S. occidentalis* extract induced neurological deficit accompanied with taming or calming effect in mice [11], thereby supporting its CNS-depressant effect.

The hole-board test is a measure of exploratory behavior in mice therefore, an agent that decreases this parameter reveals a sedative behavior [12]. The decrease in exploratory behavior in mice as seen by the reduction in number of head dips can be exploited to predict the central depressant activity of the extract [13]. Also, agents that diminished the number of head dips in this test are considered to have propensity for antipsychotic activities [14]. Thus showed that the extract possess central depressant activity and may have calming effect. Similarly, the extract significantly increased the number of foot slips in mice, but not statistically significant effect on the time taken to complete the task on the beam. Beam walking test assess benzodiazepine-induced ataxia as a predictor of

sedative effects by measuring the extent of motor deficits caused by damage to the motor cortex, and it is highly defined by the extent of foot slips [15-17]. Also, the extract might have its effect via peripheral neuromuscular blockage [18]. Some bioactive compounds such as alkaloids and tannins had been reported to be presence in methanol fraction of the leaf of *S. occidentalis* [19]. Therefore, it can be said that theses biological active compounds were responsible for some of these pharmacological properties observed, hence, may be of benefit in some CNS disorders due to its observed depressant and sedative properties in mice.

5. CONCLUSION

This study showed that ethanol leaves extract of *Senna occidentalis,* possess depressant and sedative activities in mice, and can be use as a sedative drug in traditional medicine. The plant therefore, represents a source for new drug discovery. However, it is suggested here that the compound(s) responsible for this behavior in animal model should be investigated.

CONSENT

It is not applicable.

ETHICAL ISSUE

The animals use in this research work, was in accordance with animal in research rules of the National Health Institute.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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