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Full Length Research Paper

Central nervous system stimulant effect of the ethanolic extract of *Kigelia africana*

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CNS stimulant effect of the ethanolic stem bark extract of *Kigelia africana* was studied in mice using the barbiturate induced sleeping time and the Rota rod bar to check the extract's effect on muscle coordination. The results showed that the extract at all doses tested reduced the duration of sleeping time when compared to the control group that received distilled water. This difference in sleeping time was significant ($p<0.0001$ at all doses tested) and this was also found to be dose dependent. Its effect was also compared with caffeine (a known stimulant) and the extract gave a shorter duration of sleeping time compared to caffeine, ($p<0.05$ at 400 mg/kg dose) indicating better stimulant properties. In comparison with diazepam the extract at all doses tested, also gave a shorter duration of sleep ($p<0.0001$). On the Rota rod, the extract had no sedative effect as the animals maintained their balance on the rod through the entire period of the experiment.

Key words: *Kigelia africana*, barbiturate induced sleeping time, motor coordination.

INTRODUCTION

Kigelia africana (Lam) Benth, Family: Bignoniaceae is abundant in the tropics and is widely used in Southern Nigeria as a herbal remedy for various ailments such as diarrhoea, malaria, rheumatism, retained placenta and dizziness (Gill, 1992). The stem bark in particular has a wide reputation in folk medicine for the treatment of malaria, rheumatism, wounds, ulcers, retained placenta, venereal diseases, diarrhoea and to combat infections (Burkill, 1985).

To our knowledge there are no available reports on the bioactivity of the ethanolic stem bark extract of *K. africana* with the exception of recent reports that described the antibacterial activity of the fruits (Grace et al., 2002) and the antidiarrhoeal activity of the aqueous leaves extract (Akah, 1996). As part of our pharmacological screening of this plant, we previously demonstrated that the ethanolic extract of *K. africana* analgesic and anti-inflammatory activities (Owolabi and Omogbai, 2007).

The purpose of the present study was to investigate its use as a remedy for dizziness and drowsiness (sedation) via barbiturate induced sleeping time and the Rota rod to check its effect on muscle co-ordination using mice. A wide range of experimental tests is used for the evaluation of centrally active drugs, such as CNS depressants and CNS stimulants.

Tests used include, estimation of changes in spontaneous locomotor activity, muscle co-ordination, prolongation or reduction of barbiturate-induced sleeping time, change in body temperature, amongst others. Most centrally active drugs affect some or all of these tests. The plant *K. africana* was thus subjected to the test on muscle co-ordination and barbiturate-induced sleeping time to provide a pharmacological basis for its folkloric use as a CNS stimulant.

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Abbreviations: CNS - Central nervous system, GABA - Gamma-aminobutyric acid, I.P - Intra peritoneal, K.A - Ethanolic extract of *Kigelia africana,* S.C – S ubcutaneous possesses

MATERIALS AND METHODS

Plant material

The fresh stem barks of the *K. africana* tree were collected in Okhoro village, Egor local government area, Edo State, Nigeria and identified by Alhaji Alasa Abubakar, a herbarium curator of the de-

department of Pharmacogonosy, University of Benin, Edo State, Nigeria. Botanical authentication was confirmed at the Forestry Research Institute, Ibadan, Nigeria, where a voucher specimen (No: FHI107654) was deposited for future reference. Immediately after collection, barks were cut into small pieces and dried under sunlight. The dried barks were pulverized into a smooth powder using impact mill, weighed and kept for further analysis.

Drugs and chemicals

Phenobarbitone (Sigma-Aldrich), Diazepam (Roche, Nigeria), Pentobarbitone (Sigma-Aldrich), Caffeine, Tween 80 and Absolute ethanol (Sigma-Aldrich).

Stock solutions of the various drugs and the ethanolic extract of *K. africana* were prepared fresh for each experiment.

Animals

Swiss mice (20 – 30 g) of either sex kept at the Laboratory Animal House of the Department of Pharmacology and Toxicology, University of Benin were used.

The animals maintained under standard environmental conditions had access to standard diet (Ladokun feeds, Ibadan, Oyo State, Nigeria) and water *ad libitum.* Animals were housed in a cage with a twelve hour light-dark cycle. All experiments were performed after an overnight fast and conformed to acceptable protocols for use of animals in experiment.

Ethical approval

Approval for the use of the animals was obtained from the ethical committee on the use of animals, Faculty of Pharmacy, University of Benin, Edo State, Nigeria.

METHODS

Extraction of plant material

The powdered material (500 g) was packed in a column jar and extracted with 2.0 litres of absolute ethanol via cold extraction for 72 h. The extract was evaporated to dryness in vacuo (40^{o}C) giving a yield of 3.78%. The concentrated extract was stored in air tight containers, labelled and refrigerated at 4^{o}C prior to use.

Barbiturate induced sleeping time

The animals were divided into 6 groups of 5 mice per group. Groups A, B and C received the ethanolic extract at 100, 200 and 400 mg/kg doses intraperitoneally. Group D received distilled water (10 ml/kg I.P) and served as the control group, group E received diazepam (0.1 mg/kg S.C) and group F, caffeine (20 mg/kg S.C). All treatments were done 30 min prior to intraperitoneal injection of pentobarbitone (40 mg/kg). The onset of sleep and duration of sleeping time for each animal was determined and mean for each group calculated.

The sleeping time is the time interval between onset of loss of righting reflex and regain of righting reflex.

Motor coordination

The effect of the extract on muscle co-ordination was determined via the use of the Ugo Basile Rota rod bar. Swiss albino mice were divided into 5 groups of 5 animals each after an initial screening.

This screening involved placing each mouse on the Rota rod prior to treatment, any mouse that fell off before the cut off time of 2 min was excluded from the experiment. The ethanolic extract (100, 200 and 400 mg/kg) were administered intraperitoneally to groups A, B and C, group D received distilled water (10 ml/kg I.P) and served as the control group, while the reference drug, phenobarbitone at a dose of 30 mg/kg was given intraperitoneally to group E. The animals were placed on the Rota rod bar prior to treatment and at 0.5, 1, 2, 3, 4 and 5 h after treatment. The time in seconds for the mouse to fall off within the cut off time of 120 s was noted.

Statistical analysis

All data were expressed as mean $\pm$SEM. Where applicable, the data were analysed statistically by Student's t-test using graph pad instant version 2.05a. The level of significance was $P < 0.05$ and n represents five per group.

RESULTS

In the barbiturate induced sleeping time, the extract caused a significant ($p<0.0001$) reduction of the duration of sleeping time at all doses tested and delayed the onset of sleep when compared to the control group (Table 1). The delay in onset was significantly different from the control ($p<0.0001$ and $p<0.05$ at 200 and 400 mg/kg doses respectively).

The reduction in duration of the sleeping time and a delay of the onset of sleep produced at the 400 mg/kg dose of the extract was significantly ($p<0.05$) lower than that produced by caffeine (30 mg/kg) indicating better CNS stimulant effect.

In comparison with diazepam (0.1 mg/kg), a known sedative, its effect was also significantly ($p<0.0001$ at all doses tested) lower than that produced by diazepam.

The effect of the extract on motor coordination is shown in Table 2. The extract had an enhancing effect on muscle co-ordination of the mice at all doses tested as the animals maintained their balance on the Rota rod bar. This is in contrast to the effect of phenobarbitone (the standard reference drug) which had a sedative effect thus shortening the time spent on the Rota rod bar. This effect of phenobarbitone was significantly different from the control group ($p<0.001$ and $p<0.05$ at the 30 and 60^{th} min respectively) . However from the 120 to 240^{th} min, though the duration spent on the Rota-rod was shorter, it was found not to be statistically significant.

DISCUSSION

Two tests were employed in evaluating the CNS stimulant effect of the ethanolic extract of *K. africana.* This was necessary to substantiate its folkloric use in situations of dizziness and drowsiness (sedation) (Gill, 1992) . A wide variety of agents have the capacity to excite the function of the CNS, such that calming or drowsiness (sedation) is inhibited. Sedation indicates a decrease in activity, moderate excitement and drowsiness (Balter and Uhlehuth, 1992). CNS stimulants include caffeine and amphet-.

Table 1. The effects of the ethanolic extract of *K. aficana*, distilled water, caffeine and diazepam on barbiturate induced sleeping time

Treatment (mg/kg)	Onset of sleep (min)	Duration of sleep (minutes)
Control(10ml/kg distilled water)	15.4 ± 0.24	206.6 ± 9.4
K.A (100)	19.4 ± 2.29	82.0 ± 10.9 [a]
K.A (200)	30.6 ± 1.33 [a]	80.4 ± 15.6 [a]
K.A (400)	22.6 ± 2.98 [b]	67.8 ± 8.70 [a]
Caffeine (20)	9.2 ± 0.49 [a]	117.0 ± 13.2 [b]
Diazepam (0.1)	12.2 ± 0.37 [a]	263.4 ± 21.8 [a]

Values are mean onset and duration of sleep ± SEM, (n = 5 mice per group). There was a dose-dependent reduction of the duration of sleep by the extract, [a] P<0.0001, [b]P<0.05 in comparison with the control group while diazepam prolonged the sleeping time ([a]P<0.0001) when compared with the control. The extract also delayed the onset of sleep, ([a]P<0.0001 and [b]P<0.05 at 200 and 400 mg/kg doses respectively), in comparison with the control that received distilled water.

Table 2. The effects of the ethanolic extract of the stem bark of *K. africana,* distilled water, and phenobarbitone on motor coordination in mice

Treatment (mg/kg)	Time	Spent on	The Rota	Rod at:		
	30 mins	1 h	2 h	3 h	4 h	5 h
Control(10ml/kg distilled water)	120.0± 0.1	120.0 ± 0.1	120.0 ± 0.1	120.0 ± 0.1	120.0 ± 0.1	120.0± 0.1
K.A (100)	120.0 ± 0.1	120.0 ± 0.1	120.0 ± 0.1	120.0 ± 0.1	120.0 ± 0.1	120.0± 0.1
K.A (200)	120.0 ± 0.1	120.0 ± 0.1	120.0 ± 0.1	120.0 ± 0.1	120.0 ± 0.1	120.0± 0.1
K.A (400)	120.0 ± 0.1	120.0 ± 0.1	120.0 ± 0.1	120.0 ± 0.1	120.0 ± 0.1	120.0± 0.1
Phenobarbitone(30)	37.6±14.3[a]	71.4±21.8[b]	106.6±13.4	89.2±18.9	97.6±22.4	120.0± 0.1

Values are Mean time in seconds spent on the Rota rod ± SEM, (n = 5 mice per group). The extract at different doses used had no significant effect on the mean times spent on the Rota rod, while phenobarbitone significantly decreased the time ([a]P<0.001, [b]P<0.05) between 30 min and 60 min in comparison with the control group.

amine. The results obtained indicate that the extract possess CNS stimulant effect as shown by its ability to reduce the duration of the barbiturate induced sleeping time. There was a dose-dependent reduction of the duration of sleep by the extract, (p<0.0001) in comparison with the control. Induction of sleep was by pentobarbitone a well known barbiturate that produces all degrees of depression of the CNS, ranging from mild sedation to general anesthesia. Pentobarbitone in particular potentiates GABA-induced increases in chloride conductance and depresses voltage- activated Ca^{2+} currents (Beckstead et al., 2000). The effect of *K. africana* as a CNS stimulant was found to be better than caffeine, a known stimulant. This can be seen from the result via its ability to delay the onset of sleep better than caffeine which also delayed the onset in comparison with the control. Both the extract and caffeine shorten the sleeping time, but however when both were compared the extract's effect was found to be better than that of caffeine. This reducetion in sleeping time at the 400 mg/kg dose of the extract was significantly (p<0.05) lower than that produced by caffeine (30 mg/kg).

Caffeine, a mild stimulant is the most widely used psychoactive drug in the world (Silverman et al., 1999). It increases nor-epinephrine secretion and enhances neural activity in numerous brain areas. Many of its effects are believed to occur by means of competitive antagonism at adenosine receptors. Tolerance occurs rapidly to the stimulating effects of caffeine, thus a mild withdrawal syndrome has been produced. Herein lies the advantage of herbal remedies such as the plant *K. africana* which most times are devoid of these withdrawal syndromes (Silverman et al., 1999). In comparison with diazepam (0.1 mg/kg), a known sedative, its effect was also significantly (p<0.0001 at all doses tested) lower than that produced by diazepam. The extract's CNS stimulant effect was further confirmed by its ability to maintain the ani-mals on the Rota rod, thus indicating muscle co-ordination.

The results obtained in this study indicate that the extract possesses CNS stimulant properties which probably act via competitive antagonism at adenosine recaptors leading to increase in nor-epinephrine secretion and enhanced neural activity in numerous brain areas since the extract's effect was compared to caffeine. This could provide a rationale for the use of this plant in situations of dizziness, drowsiness and sedation in folk medicine.

Conclusion

The results suggest that the ethanolic extract of *K. africa*

na has a potential CNS stimulant effect that can be explored for therapeutic advantage as an alternative treatment in medical conditions associated with dizziness, drowsiness and sedation.

Further work is in progress to monitor activity in a familiar and novel environment where the activity of the animals is minimal, to further confirm its stimulant effect on the central nervous system.

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