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Acute and Sub-Acute Evaluations of *Parsonsia straminea* Stem Bark Ethanol Extract Impact on Some Behavioral Parameters in Mice

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Objectives: The plant *Parsonsia straminea* (P.S) have little or no ethnopharmacological records but local claims; as such its behavioral impact determination leads this study. The study team is poised at assessing the changes in behaviors such as: Motor coordination, anxiety, and depression in single dose and repetitive dose(s) exposure.
Methodology: *Ethical consideration*. The study proposal was submitted to the Research Ethics Committee of the University of Port Harcourt, Nigeria and approval was given. *Plant collection and crude drug extraction.* The plant was sourced from the Wilberforce rain forest of Nigeria and herbarium identification number, NDUP/21/001 was given in the Department of Pharmacognosy and Herbal Medicine, Niger Delta University, Nigeria. The collected plant was processed for ethanol extraction according to the method described by Trease and Evans. *Design.* The study was designed into single (acute) and repetitive (sub-acute) treatments/exposures in all study methods. The acute were administered via oral and intraperitoneal route to ascertain safety and possible onset difference. The acute treatment groups: group, 1(VEH), 2 (100 mg/kg), 3 (200 mg/kg), 4 (400 mg/kg), 5 (800 mg/kg), 6 (1000 mg/kg) doses and sub-acute treatment groups include group: 1

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(VEH), 2 (50 mg/kg), 3 (100 mg/kg), 4 (200 mg/kg), 5 (400 mg/kg) and 6 (800 mg/kg) treatment for 15 days (n=5), motor coordination (open field test, cataleptic test), depression (light & dark box test), memory function test (B-maze) and sleeping time test was applied to both acute and sub-acute.
Results: Data from the P.S stem bark extract showed significant motor coordination, prevents sleep onset, and no depression potential in both acute and sub-acute treatments.
Conclusion: The P.S stem bark extract proves stable impact on the CNS as it is indicated in behaviors evaluated in the animal model. However, beside all that are stated above, the extract of *P. Straminea* stem bark suggests usefulness in control of narcolepsy, cataplexy and sleep paralysis symptoms.

Keywords: Caffeine; catalepsy; diazepam; light and dark; open field; Parsonsia straminea; phenobarbitone; sleeping time; tail suspension.

1. INTRODUCTION

Behavioral change among young people in this part of the world is owed to consumption of substances including drugs. Some of the acclaimed reasons for indulging into the consumption of these substances is sue for happiness which is lacking in the societal governance system. It is worthy of note that some substance in the guise of drug, therapeutics, and poisons in its natural, semi-synthetic and synthetic forms are without impacts on the behavior of the consumer(s) depending on the dose [1,2]. The previous statement implies, the famous toxicology quote “every substance is poison”, what makes the difference between poison and therapeutic is the dose. Signs of behavioral changes include: depression, euphoria, manic-depression, hallucinations, ataxia, among other behavioral changes. These behavioral changes could be noticed and un-noticed depending on the period and the dosages exposed [3]. Despite, the wide claim of safety or less additive records of natural products does not rule out the changes in behaviors such as: motor coordination, anxiety, obsessive behaviors, depression among others [4,5,6]. Behavioral integrity is known to be the sane characteristic factor of every individual as it is a thing of caution in every substance of consumption especially among humans. Behavioral check is a necessity especially among the present day young people as well as the advanced aged being associated with gross use of drugs, leading record of addiction, abuse and death globally [4,2,7].

The need for this study is to establish scientific record about the plant *Parsonsia straminea* (P.S) because it has little or no ethnopharmacological records; however, its recorded to have its origin in New south Wales and Queensland of the Australian rain forest. It is commonly known as silkpod, monkey rope vine which belong to the Apocynaceae family [8,9,10,11]. The plant was accidently identified by means of local use for seizure control in the Wilberforce Island of Bayelsa State, Nigeria. Thus, this study is aimed at the screening for P.S stem-bark extract possible behavioral influence using the animal model. This is necessary because indicates a means of controlling herbal drug induced behavioral changes among other pharmacological check measures.

2. METHODOLOGY

1. Plant collection and crude drug extraction. The plant was sourced from the Wilberforce rain forest of Nigeria and herbarium identification number, NDUP/21/001 was given in the Department of Pharmacognosy and Herbal Medicine, Niger Delta University, Nigeria. The collected plant was processed for ethanol extraction according to the method described by Trease and Evans as reported [12].

2. Animal. Mice were the animal used in this study; which were raised in the animal house unit of the Department of Pharmacology and Toxicology, Niger Delta University, Nigeria in accordance with the prescribed international standard practice as instituted by the ethical research committee, NDU/PHARM/AEC/22/019A.

3. Design. The study was designed into single (acute) and repetitive (sub-acute) treatments/exposures of *P.straminea* stem-bark extract in all study methods as expressed in the table below) [13].

Table 1. Study treatment protocol

Group (n=5)	Dose For Acute Treatment (1 day)	Dose For Sub-Acute Treatment (15 days)
1	0.2 D.h2O (VEH)	0.2 D.h2O (VEH)
2	100 mg/kg	50 mg/kg
3	200 mg/kg	100 mg/kg
4	400 mg/kg	200 mg/kg
5	800 mg/kg	400 mg/kg
6	1000 mg/kg	800 mg/kg

Open-Field Test (OFT): The effect of *P. straminea* stem bark on the motor function in mice were determined using the open field apparatus. Drawn squares lines on the platform of the apparatus were used as counting techniques by determining the number of cross squares in a coordinated pattern. This method was adjusted according to Gould et al [14,15]. The study cage was cleaned and sprayed with 70% ethanol after each assessment to avoid bias.

Catalepsy: The plant *P.straminea* was evaluated for its motor coordination potential using wooden block of 3 cm height. The "animals in various groups were subjected to the evaluation by placing the fore paw of the mouse onto the block and time the duration of stay on the block in seconds. The scoring of catalepsy was not necessary because of absence of induction of catalepsy" [16].

Light/Dark Box (LDB) Test: The assessment of anxiety-inducing potential of *P.straminea* stem-bark extract in the animal model was conducted according to the adjusted light /dark method as described by Crawley and Goodwin, [1]. It was simple box of 36 cm long and 33 cm wide, 30 cm deep with two partitions painted white and black separately with one larger than the other. Between the compartment is a barrier with little opening at the lower part allow access of the mice. Furtherly the larger compartment painted white color, open and illuminated by a 60-W lamp placed 50 cm above the compartment. The smaller compartment painted black color and had a cover especially during the evaluations. The mice were placed in either compartment for observation of the choice entries and record was analyzed in the according to the total time spent in each compartment, [15].

Tail Suspension Test: Briefly, *P. straminea* stem-bark extract was assessed for depression by the use of the tail suspension test technique as described by Andreasen et al. [17].

B-Maze: Cognition evaluation of the *P.straminea* stem-bark extract described by the Attar study group [18] modified. Barnes maze was employed to assess cognitive deficits in learning and memory of mice. Furtherly, "the maze was made from a circular, 13-mm thick, white PVC slab with a diameter of 48 cm. Twenty holes with a diameter of 1.75 cm were made on the perimeter at a distance of 1 cm from the edge". This circular platform was then mounted on top of a rotating stool, 35 cm above the ground and balanced and the study was conducted in 4 days as described by Pitts [19], modified.

Pentobarbitone-Induced Sleeping Time: Mice in this study were randomly divided into groups (n=5) as described above: "saline-treated group as control, P. straminea treated groups as described above, diazepam (5 mg kg-1, p.o.) group and caffeine (16 mg kg-1, p.o.) group. Sodium pentobarbitone (50 mg kg-1) was intraperitoneal administered 60 min after treatment of test drugs. Two parameters were recorded: sleep onset and duration of sleep" [20].

4. Statistically analysis. Data presented as mean ± standard error of mean (SEM), using graph pad prism 8.3, ANOVA followed by multiple comparison post hoc test (tukey). Differences between mean value compared with control group were considered significant at $P<0.05$.

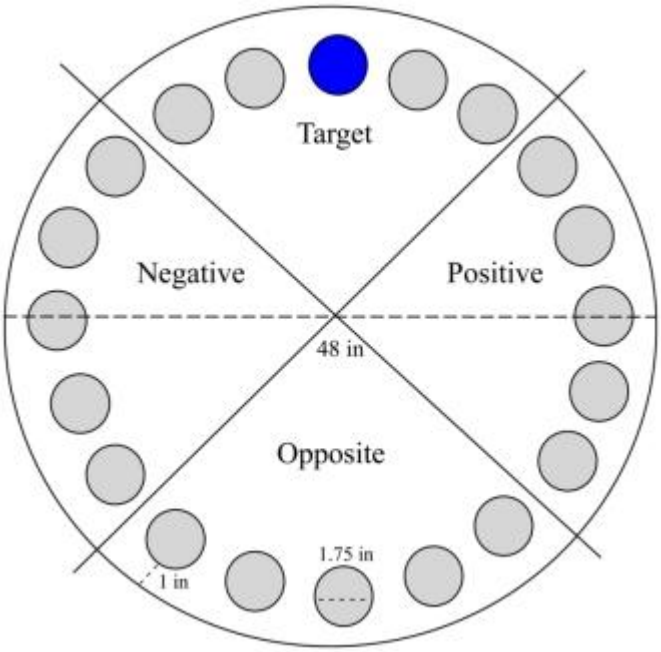

Fig. 1. Study protocol. The small ball shapes all round in the board platform are the holes with blue colored hole indicating the point where clue is kept as recognition target for the animal to assess it cognitive ability. Adapted from Attar et al., [18] study approach

3. RESULTS

1. Acute Treatment

Motor coordination evaluations: Motor coordination also known as motor function activities. These evaluations are ensured in this study to assess the motor function interference potential of *P. straminea* stem-bark extract.

Open field test: Table 2 showed an assessment of acute motor function using the open field model with interest in oral (p.o) and intraperitoneal (i.p) route of administration which showed significant (P<0.002) hyperactivity when compared with the control group at 200 to 800 mg/kg of the i.p route of administration. It was also noted that at 1000 mg/kg showed immobility significantly (P<0.0001) when compared with the control group within the 5 min of the study duration.

Catalepsy: Table 3 showed an assessment of acute function using the cataleptic technique with interest in oral (p.o) and intraperitoneal (i.p) route of administration which showed statistical significant (P<0.0001) less mobile at dose 1000 mg/kg (i.p) when compared with the control group within the 120 sec. of the study duration.

Anxiety Evaluations: Light/Dark model: The Fig. 2a result of the p.o route of treatment which showed statistical significant (P<0.0001) entry into the light compartment when compared with the dark compartment. However, no significant difference between the test groups and control group. Fig. 2b showed difference in between the test groups and the control group with more entry into the light compartment of the test groups but however, showed difference significantly (P<0.0001) compared with the dark compartment. Which implies that *P. straminea* stem-bark extract indicates no anxiety/depression inducing potential.

Depression evaluation: Tail suspension study: Table 4. Acute tail suspension study revealed statistical significant (P<0.002) with more struggling time (ST) compared to immobile time (I.T) in the p.o route. Contrary to the p.o route, i.p route revealed significant (P<0.001) I.T at 1000 mg/kg compared to S.T within a study period of 5 min.

Phenobarbital induced sleep time evaluation: Sleeping time assessment: Fig. 3a and 3b showed statistical significant (P<0.001) increased onset to sleep in the test groups compared to the control group as well as the 5 mg/kg diazepam group. The effect is even comparable to the stimulant 200 mg/kg caffeine group.

Table 2. Acute open field test

Group	Treatment (mg/kg)	Oral route (N)	Intraperitoneal route (N)
1	VEH 0.2 ml	72.6±6.1	72.6±2.3
2	PS 100	75.0± 2.1	76.0±2.0
3	PS 200	80.0±2.8	91.4±1.1**
4	PS 400	74.2±6.0	90.8±2.0**
5	PS 800	56.6±6.5	95.6±1.9**
6	PS 1000	86.8±2.7*	0****

*Data showed increased coordinated mobility compared with control group significantly *=significant (P<0.048), **= significant (P<0.002), ****= significant (P<0.0001). VEH=Vehicle/control, PS= P.Straminea Stem Bark Extract. N. Number of lines crossed accurately within 300 sec*

Table 3. Acute cataleptic evaluation

Treatment (mg/kg)	Oral route	Intraperitoneal route
	Duration (120 sec)	**Duration (120 sec)**
VEH	1.24	1.24
PS 100	1.22	1.18
PS 200	2.94	2.92
PS 400	3.82	1.63
PS 800	3.36	1.31
PS 1000	4.16	47.86****

*Data showed mild cataleptic sign in higher doses of both routes of administration****= significant (P<0.0001). VEH=Vehicle/control, PS= P.Straminea Stem Bark Extract. Time spent on the wooden block as an indication catalepsy was measured within 120 sec*

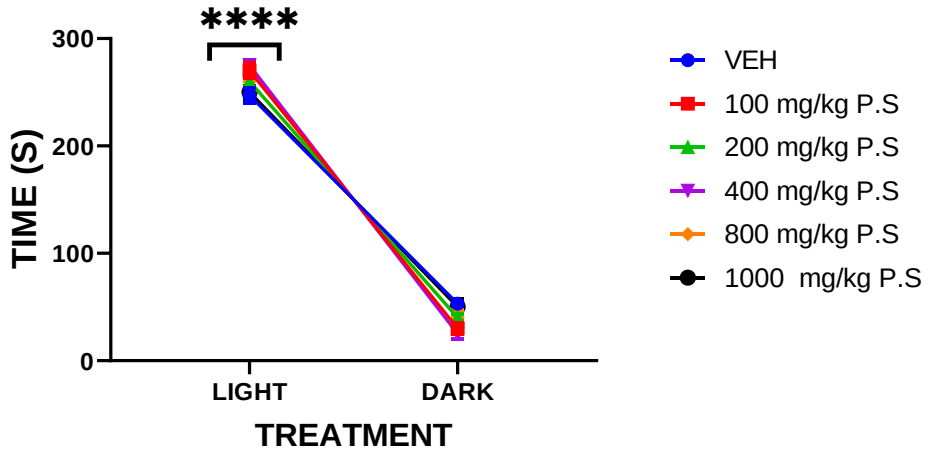

Fig. 2a. light and Dark. Oral route. Data indicates absence of depression with all doses of the plant extract of the oral route of administration making more rounds in the light compartment. **= significant (P<0.0001). VEH=Vehicle/control, PS= *P. straminea* Stem Bark Extract**

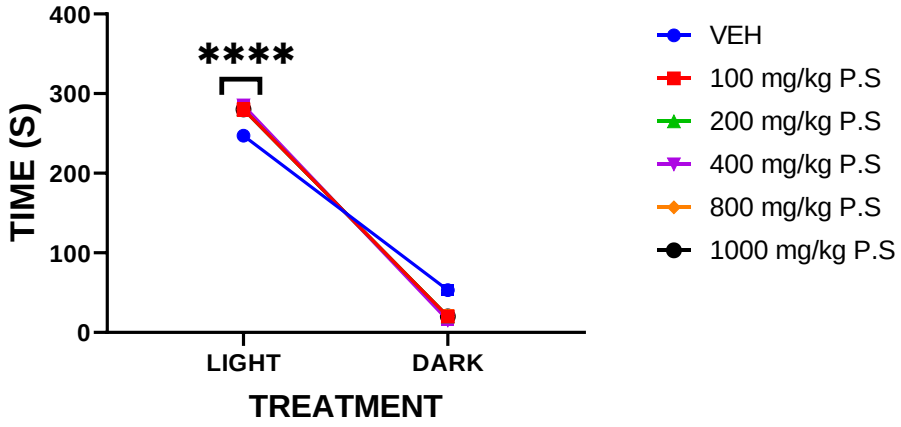

Fig. 2b. light and Dark. Intraperitoneal route (I.P). Data indicates absence of depression with all doses of the plant extract of the i.p route of administration making more rounds in the light compartment. **= significant (P<0.0001). VEH=Vehicle/control, PS= *P. straminea* Stem Bark Extract**

Table 4. Acute tail suspension test

Treatment (mg/kg)	Oral route		Intraperitoneal rote	
	S.T (min)	I.T (min)	S.T (min)	I.T (min)
VEH	5	0	5	0
PS 100	3.22	1.78	2.45	2.55
PS 200	2.95*	2.05	2.46	2.54
PS 400	2.95*	2.05	3.17**	1.83
PS 800	3.12**	1.88	2.23	2.77
PS 1000	2.95*	2.05	0.58	4.02***

*Data showed better struggling time compared with immobility time. *=significant (P<0.0483), **= significant (P<0.002), ***= significant (P<0.001). VEH=Vehicle/control, PS= P. straminea Stem Bark Extract. The measure of symptomatic depression was determined by struggling and immobility time (min) within 5min.*

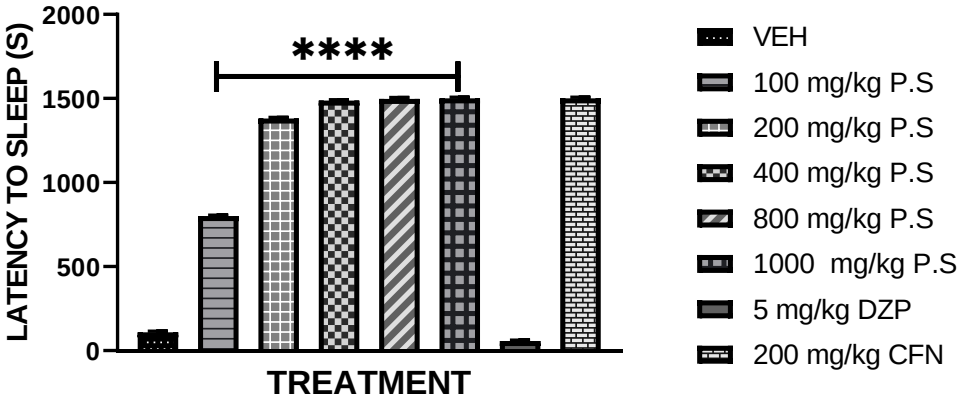

Fig. 3a. Oral route. showed increased latency to sleep in all doses of the plant extract significantly, **= (P<0.0001). VEH=Vehicle/control, PS= *P. straminea* Stem Bark Extract. DZP= diazepam, CFN =caffeine**

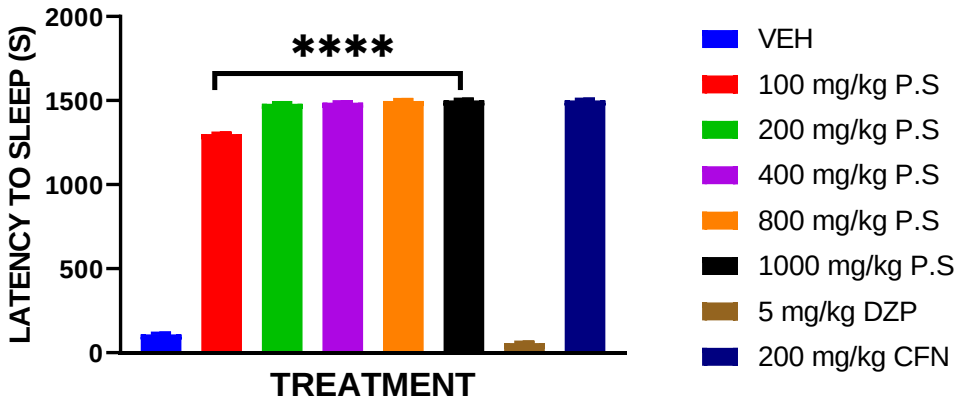

Fig. 3b. Intraperitoneal route. showed increased latency to sleep in all doses of the plant extract significantly, **= (P<0.0001). VEH=Vehicle/control, PS= *P. straminea* Stem Bark Extract. DZP= diazepam, CFN = Caffeine**

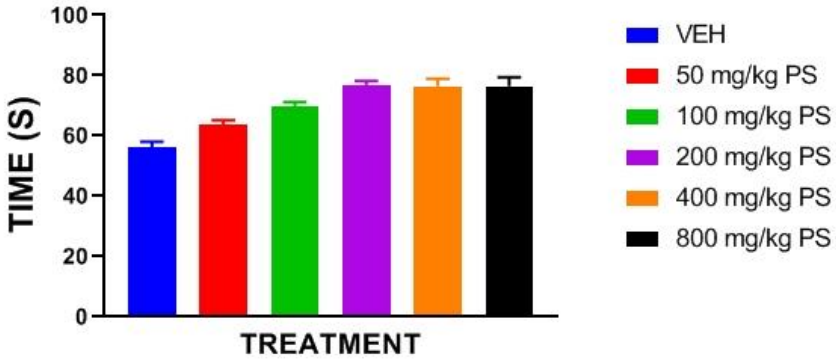

Fig. 4. Sub-Acute Open Field test. showed little or no significant different with the control. VEH=Vehicle/control, PS= *P. straminea* Stem Bark Extract. Motor function activities measured by open field (P>0.05)

2. Sub-Acute Treatment

Motor coordination: Open field test: Fig. 4 showed an assessment of sub-acute open field with interest in oral (p.o) route of administration only. Being that route difference has been tested in the acute above. This study result showed no statistical significant difference between the test group and the control group.

Catalepsy: Fig. 5 sub-acute result revealed delayed movement significantly (P<0.0001) in 100 to 800 mg/kg compared with control. Its worthy of note from the graph, delayed difference is 0.5 sec. between the aforementioned test groups and the control. Thus, not enough to indicate cataleptic effect or potential.

Anxiety assessment: Light/Dark model: The Fig. 6 sub-acute anxiety assessment result revealed that the p.o route of treatment which showed statistical significant (P<0.0001) entry into the light compartment compared with the dark compartment. Which implies that *P.straminea* stem-bark extract indicates no anxiety/depression inducing potential.

Depression Evaluation: Tail suspension study: Fig. 7. Sub-acute tail suspension assessment revealed statistical significant (P<0.0001) more struggling time(ST) compared to immobile time (I.T) within the observation period of 5 min. This result implies that the stem bark extract of *P. straminea* possesses no depression inducing effect.

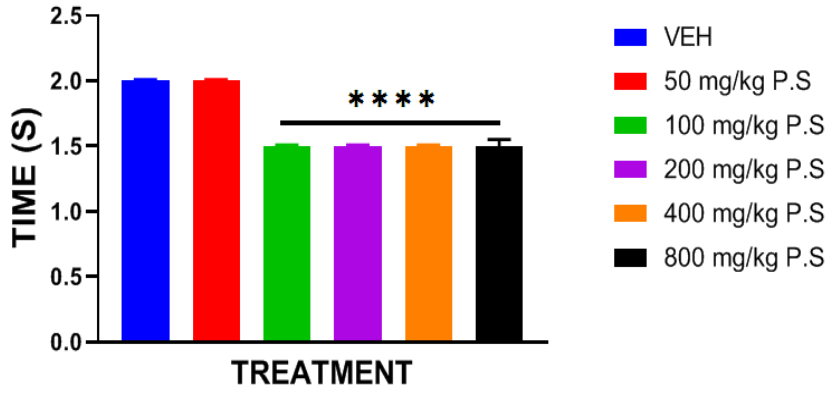

Fig. 5. Catalepsy scoring. showed significant reduction in time taken to inclined to the measuring device **** P<0.0001. VEH=Vehicle/control, PS= *P. straminea* Stem Bark Extract. Motor function activities measured by catalepsy

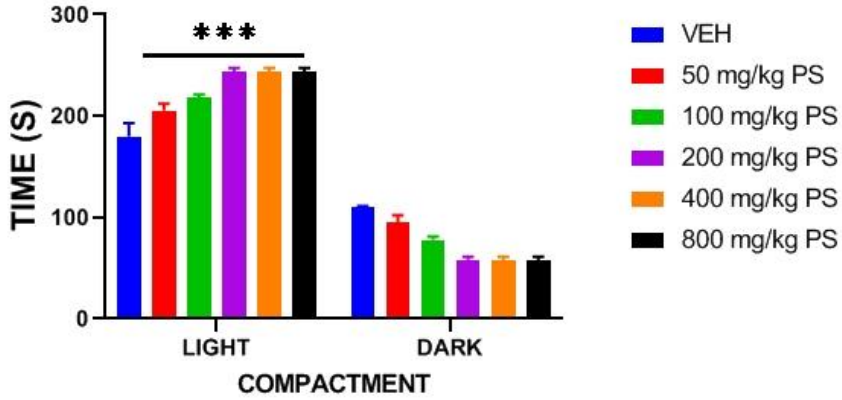

Fig. 6. Sub-Acute Light and Dark Test. Data indicates absence of depression with all doses of the plant extract of the oral route of administration making more rounds in the light compartment. *= significant (P<0.001). VEH=Vehicle/control, PS= *P.Straminea* Stem Bark Extract**

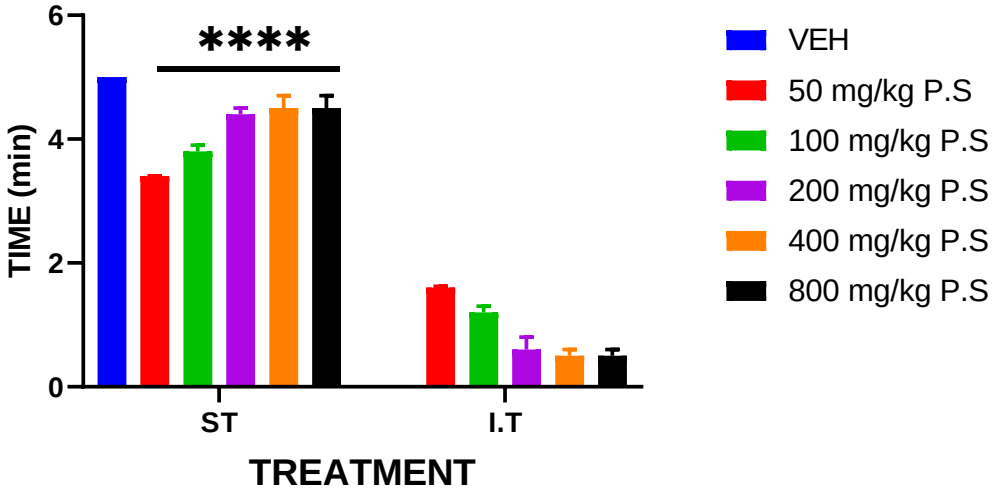

Fig. 7. Tail suspension test. showed more struggling time compared with the immobility time, **** P<0.0001. VEH=Vehicle/control, PS= *P.Straminea* Stem Bark Extract

Table 5. Sub-acute Barnes maze test: Escape latency

Parameters	VEH	50 mg/kg PS	100 mg/kg PS	200 mg/kg PS	400 mg/kg PS	800 mg/kg PS
DAY 1	56.5±0.5	57.1±0.5	57.1±0.5	56.1±0.5	57.1±0.5	55.9±0.5
DAY2	54.0±1.0	55.0±1.0	56.0±1.0	55.0±1.0	55.0±1.0	55.0±1.0
DAY3	53.5±0.5	54.5±0.5	54.0±0.5	53.5±0.5	54.5±0.5	54.5±0.5
DAY4	53.0±1.0	53.0±1.0	53.0±1.0	52.0±1.0	53.0±1.0	53.0±1.0

Data evaluation statistically indicates no difference. VEH=Vehicle/control, PS= P.Straminea Stem Bark Extract. Barnes maze, memory measured with escape latency in days showed not significant (P>0.05).

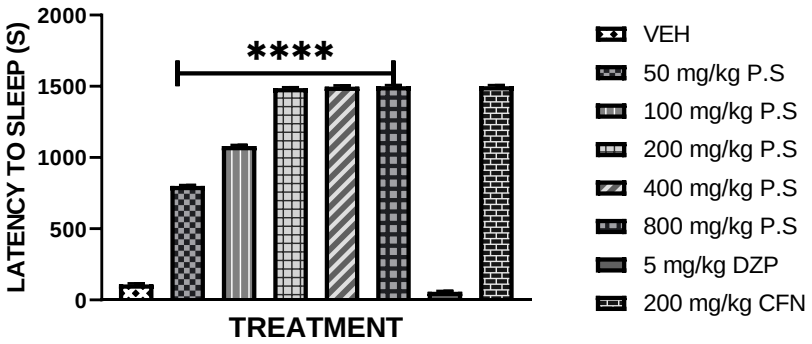

Fig. 8. Sleeping time. showed increased latency to sleep in all doses of the plant extract significantly, **= (P<0.0001). VEH=Vehicle/control, PS= *P.Straminea* Stem Bark Extract. DZP= diazepam, CFN =caffeine**

Memory function test: This result from Table 5 for the assessment of memory function in the sub-acute study revealed no statistical significant difference when compared with the control group.

Sleeping time: Sleeping time assessment: Fig. 8 sub-acute study showed statistical significant (P<0.001) increased latency to sleep in the test groups compared to the control group as well as the 5 mg/kg diazepam group. The effect is even comparable to the stimulant 200 mg/kg caffeine group.

4. DISCUSSION

Personality change is of medical concern and remains a risk factor for the sane society, haven't known that lots of factors are responsible for behavioral change ranging from mental illness to physical illness [21]. Among the factors, include certain side effects of medication as well as drug induced psychosis are among leading causes of behavioral change in this part of the globe. Human behavior is a major determinant of health [22] as such pharmacovillance on all drugs and medications should be a prime check factor to make a distinct pharmacological profile of every drug or medication to aid health, mentally and physically stable society. It is worthy of note that some drugs or chemicals penetrates the central nervous system rapidly and some others, poorly penetrate. This is likely to be its lipid solubility / water-phobic nature or strength as well as level of exposure of the drug to the brain or the allied tissues. The stem bark extract of *P. straminea* have shown to have no negative motor coordination potential at acute and sub-acute level of exposures in open field and cataleptic methods of motor function evaluation (Tables 2, 3, Figs. 4 & 5). This is also an indication that the stem bark extract of *P. straminea* at the dose range of 50 to 1000 mg/kg do not deregulate or desensitize the catechole-aminergic system as shown in similar study [23]. Most substances that depresses the central nervous system [24] usually ends in addiction and abuse which calls for serious check in pharmacovigilance and ethno-pharmacological profiling [25]. The stem bark extract of *P. straminea* through the light and dark box and tail suspension methods have implied that there is little or no central depressive/apprehensive potential and such cannot aid depression or anxiety as evidenced in the motor coordination results as relative confirmatory test. The light and dark box device is also used to evaluate or measure the presence

of induced anxiety in the animal model. This result can be said of the plant extract to possess anti-anxiogenic prospect (Fig. 2a, b; Table 3, Figs. 6 & 7). Barnes maze test used for the measurement of memory function proves the stem bark extract of *P. Straminea* to be devoid of memory impairment at subacute level of exposure as revealed in this study (Table 5). This again implies that crude drug of *P. straminea* do not impede or deplete acetylcholine or the cholinergic system among other memory associated biological managers (Table 5). The stem bark extract of *P. Straminea* proves none sedating ability that could be comparable to a 200 mg/kg of caffeine in all doses used in this study (Figs. 3a, 3b & 8). The action of the extract implies the possibilities of its lipophilic nature and similarity to the mechanism of action of caffeine as it proves to prevents the onset of drowsiness believed to be induced by adenosine [26,27]. Caffeine by one of its actions is thought to antagonize the adenosine receptors, also inhibition of phosphodiesterase [26,27], release of calcium from store intracellularly and benzodiazepine receptor antagonism, [28]. This also inform us on the bases of the good motor coordination among the test doses of the stem bark extract of *P. straminea.*

5. CONCLUSION

The plant extract of *P. straminea* stem bark has given an impression of positive impact on some of the behaviors (motor coordination, depression/anxiety, memory function and hypnosis/sedation) by not depressing but keeping stable the Central Nervous System (CNS), after acute and sub-acute exposure of various doses of the stem bark extract of *P. straminea*. However, beside all that are stated above, the extract of *P. straminea* stem bark maybe usefulness in control of narcolepsy, cataplexy and sleep paralysis symptoms.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

It is not applicable.

ETHICAL APPROVAL

The study proposal was submitted to the Research Ethics Committee of the University of Port Harcourt, Nigeria and approval identity, UPH/CEREMAD/REC/MM76/003 was given.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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