WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 11, Issue 17, 21-31. Research Article ISSN 2277– 7105

EVALUATION OF SPONDIANTHUS PREUSII EFFECT ON MOVEMENT DIFFICULTY IN ANIMAL MODEL

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Article Received on
30 October 2022,
Revised on 20 Nov. 2022,
Accepted on 10 Dec. 2022
DOI: 10.20959/wjpr202217-26522

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ABSTRACT

Background: Movement disorders populates among the advanced aged groups with some genetically enroot disease conditions such as the -cerebral autosomal dominant arteriopathy as well as -subcortical infarct and –leukoencephalopathy. No cure but management exist for theses neurological disorders by a way of symptomatic treatments, physiotherapeutic measures and brain stimulations. Medicinal plant has been prioritized on the bases of supplementary medicine, *Spondianthus preusii* represents one of the alternatives. **Methods:** Ethical approval was secured for animal research. The animal grouping includes: -A=Normal control; -B= standard control (bromocriptine 2.5mg/kg); -C= 100mg/kg, 200mg/kg and 400mg/kg Methanol fraction; -D= 100mg/kg, 200mg/kg, and 400mg/kg n-hexane fraction; -E= 100mg/kg, 200mg/kg and 400mg/kg of n-butanol fraction; -F= 100mg/kg, 200mg/kg and 400mg/kg ethylacetate fraction; -G= 100mg/kg, 200mg/kg and 400mg/kg aqueous fraction of *S. presuii* extract to animals respectively. The study was designed into groups as acute treated with aqueous, methanol, n-hexane, n-butanol, ethyl acetate fractions of *S. preusii* and sub-acute treated with n-butanol and n-hexane *S. preusii*. ***Grip strength determination:*** The grip strength test was manually formulated using 4.0mm wire of 20 cm length and was fixed to both ends of a wooden pole in the laboratory as part of the improvisation. The treated animals in respective groups were individually clamped into the set-up with their fore-arms and immediately timed for when it will let off the grip and such time values were recorded as grip strength within time range of 300 seconds After 30 minutes administration of chlorpromazine. ***Cataleptic evaluation:*** The various groups were treated respectively as started above. After 30 minutes administer chlorpromazine to all

groups. Observe the animals for catalepsy 10, 30 and 60 minutes. Score the animals according to the criteria below: 0 = if animal moves normally when placed on the table; 1 = if animal moves only when touched; 2 = if animal fails to correct posture when fore paws are placed on the 3 cm high wooden block; 3 = if animal fails to remove fore paws when placed on the 9 cm high wooden block; 4= no movement at all. **Result:** The n-butanol, and n-hexane fractions of *S.preusii* suggested inhibitory potentials against the cataleptic inducing agent, chlorpromazine at mid and lower doses in both factions in acute and sub-acute studies. **Conclusion:** The plant fractions (n-butanol and n-hexane) has shown to potentiate anti-cataleptic effect.

KEYWORDS: Catalepsy, spondianthus preusii, movement disorders.

BACKGROUND OF STUDY

The term movement disorders describe the group of nervous system- (neurological)-conditions that causes either increased movements or reduced or slow movements. These movements may be voluntary -or- involuntary.

Movement disorders populates among the advanced aged groups with some genetically enroot disease conditions such as the -cerebral autosomal dominant arteriopathy as well as -subcortical infarct and -leukoencephalopathy that are basically characterized by family and or personal history of migraines, episodes of stroke like features before sixty (60) years of age accompanied with -dementia, -behavioral disturbances as well as cognition.

Some of the variants of movement disorder includes: -Parkinson's disease, -ataxia,-dystonia,-essential tremor, -Huntington's disease, -restless leg syndrome, -Tourette syndrome, -Multiple system atrophy.

Parkinson's disease (PD). PD remains a central nervous system (CNS) disorder having great influence on the motor coordination centers in the brain. It manifests as retrogressive loss of muscular function in a gradual fashion causing muscle stiffness, trembling of the muscle, slow movement and or inability to gain balance. It may also cause other symptoms not related to movement such as reduced sense of smell, constipation, acting out dreams and a decline in cognition. (Zoghbi et al., 2009; Mayo Clinic, 2022).

- Ataxia. This movement -disorder affects the part of the brain that controls coordinated-movement leading to loss of total control of the motor system which mostly presents as -

clumsy balance, -limb movements, among others. Among major factors linked to the cause of ataxia includes - genetic, and -degenerative disorders (NH, 2020, Mayo Clinic, 2022).

- Essential tremor. This movement disorder is characterized by uncontrollable rhythmic shaking of the body parts.
- Huntington's disease. This is mostly associated with inherited neurological disorders characterized by uncontrolled movements, -loss of cognition and psychiatric disorder.
- Restless leg. This condition is mostly best described as uncomfortable sensation of the legs with much discomfort alleviation followed by movement.
- Tourette syndrome. This is a neurological condition that starts between childhood and teenage years and is associated with repetitive movements and -vocal sounds.
- Multiple system atrophy. This is rare neurological disorder that affects many brain systems and progressively worsens. It manifests like -ataxia or -parkinsonism. It can also cause -low blood pressure, -impaired bladder function and -acting out dreams.

It is important to note that at present, no cure but management exist for theses neurological disorders by a way of symptomatic treatments, physiotherapeutic measures and brain stimulations. The resolution of WHO to achieve greater health status among the global population has created more room for alternative medicine to promote access to health care service within every economic reach either in the underdeveloped world or the developing nations (WHO, 2021; Veeresham, 2012). Medicinal plant has been prioritized on this bases as it has been giving place in the formal sector through the ministry of health of the various nations of concern. *Spondianthus preusii* of the family phyllanthaceae commonly found in tropical African nations (Léonard & Nkounkou, 1989).

The plant parts such as the leaves and the bark has been traditionally claimed to be useful in managing neurological challenges such arthritis and wound healing (Venkatesan et al., 2015). Thus, this study is aimed determining the extent of movement promotion in a state of movement difficulty as will be demonstrated by the study methods.

METHOD AND MATERIALS

Ethical approval: The study proposition was subjected to evaluation by the Committee of Research and Ethics in the Department of Pharmacology and Toxicology, Niger Delta University, Wilberforce island, Nigeria with reference identity NDU/PCO/REC/081222.

Plant Collection: The leaves of Spondiathus presuii were collected in February, 2020 from the premise of college of Health Sciences, Niger Delta University, Wilberforce Island, Bayelsa State. The collected leaves were sorted carefully to avoid it been mixed with other plants.

Plant Preparation: Fresh leaves of Spondiathus presuii were dried under the air condition ($16^{O}C$) in a clean room. The leaves were allowed to dry properly for more than a week. The dried leaves were blended properly with a blender (Kenwood 1800 watt.co, Germany). Double maceration was done with each of the solvents for extraction in this study. The filtrate was filtered into an empty weighed beaker and was then placed in a water bath and was allowed to dry at ($55^{o}C$) temperature. The dried extract was weighed and stored in a refrigerator until it was used. This procedure was done for N-Hexane, N-butanol, methanol, ethylacetate, and distilled water respectively.

Experimental Animals: In this study, wistar rats were procured from the animal breeding and research unit of the Department of Pharmacology and Toxicology, Faculty of pharmacy, Niger Delta University Wilberforce Island, Bayelsa state. The wistar rats were given standard rodent feed and tap water. All rats in the study were handled in accordance with the institutional guidelines for care and use of laboratory animals in biomedical research as promulgated by the Guide for the Care and Use of Laboratory Animals, 8th edition (NRCC, 2022).

Drugs and chemicals: Distilled water, N-hexane, ethylacetate, methanol, N-butanol, chloroform, bromocriptine 2.5mg, normal saline, chlorpromazine 25mg/ml.

Experimental Design

Acute Study: Adult wistar rats were used for this study and were divided into seven (7) groups A (A1-A5), B (B1-B5), C (C1-C5), D (D1-D5), E (E1-E5), F (F1-F5), G (G1-G5) with each group containing five (5) rats.

- The group A (Normal control) were pretreated with 0.2ml of sterile water (water for injection).
- Group B (standard control) -were pretreated with bromocriptine (2.5mg/kg of body weight).
- Group C (test) -were pretreated with 100mg/kg, 200mg/kg and 400mg/kg Methanol fraction of *S. presuii* extract to animals respectively.

- Group D (test)-were pretreated with 100mg/kg, 200mg/kg, and 400mg/kg n-hexane fraction of of *S. presuii* extract to animals respectively.
- Group E (test)-were pretreated with 100mg/kg, 200mg/kg and 400mg/kg of n-butanol fraction of of *S. presuii* extract to animals respectively.
- Group F (test)-were pretreated with 100mg/kg, 200mg/kg and 400mg/kg ethylacetate fraction of of *S. presuii* extract to animals respectively.
- Group G (test)-were pretreated with 100mg/kg, 200mg/kg and 400mg/kg aqueous fraction of of *S. presuii* extract to animals respectively.

The individual groups were treated with chlorpromazine (25mg/kg of body weight) thirty (30) minutes after pretreatment (i.p). The results obtained from the experiment were recorded.

Subacute Study: Adult wistar rats were used for the subacute study and were divided into four (4) groups A (A1-A5), B (B1-B5), C (C1-C5) and D (D1-D5) with each group containing five (5) animals.

- The rats in group A were treated with sterile water (water for injection) 0.2ml/day.
- Group B (B1-B5) were treated with bromocriptine (2.5mg/kg/day).
- Group C (C1- C5) was treated with a combined dose of 100mg/kg n-butanol fraction of spondiathus presuii and bromocriptine (2.5mg/kg), 200mg/kg and 400mg/kg respectively.
- Group D (D1-D5) was treated with a combined dose of 100mg/kg n-hexane fraction of spondiathus presuii and bromocriptine (2.5mg/kg), 200mg/kg and 400mg/kg respectively.

This procedure was repeated for fourteen (14) days. The drugs were administered with oral gastric tube orally. The animals (rats) were weighed on the third (3rd), seventh (7th), tenth (10th) and thirteenth (13th) day of the experiment to determine the weight variations.

The animals (wistar rats) muscle coordination was determined using adjusted grip strength method.

Chlorpromazine (25mg/kg) was administered intraperitonally to all the group. Results obtained from the subacute study and the grip strength (the base line [before administration of chlorpromazine], Ten minutes (10), twenty (20) and sixty (60) minutes) after the administration was recorded. On the night of the fourteen (14) days, animals were sacrified.

Grip strength determination: The grip strength test was manually formulated using 4.0mm wire of 20 cm length and was fixed to both ends of a wooden pole in the laboratory as part of the improvition. The treated animals in respective groups was individually clamped into the set-up with their fore arm and immediately timed for grip strength within time range of 300 seconds After 30 minutes administer chlorpromazine (Takeshita et al., 2017).

Cataleptic evaluation: The various groups were treated respectively as started above. After 30 minutes administer chlorpromazine or haloperidol to both groups. Observe the animals for catatonia 10, 30 and 60 minutes. Scoring was improvised in the study according to the criteria below: -0 = if animal moves normally when placed on the table; -1 = if animal moves only when touched; -2 = if animal fails to correct posture when fore paws are placed on the -3 cm high wooden block; -3 = if animal fails to remove fore paws when placed on the 9 cm high wooden block; -4= no movement at all.

Statistics: All generated data were statistically analyzed using graph pad prism 8.0 software.

RESULTS

Acute Evaluation

Brief description of the movement scoring or rating: 0= Movement without a Push; 1= Movement with A Single Push; 2=Movement with A 6cm Block Elevation of the Fore Arms; 3= Movement with A 9cm Block Elevation of the Fore Arms; 4= No Movement at All.

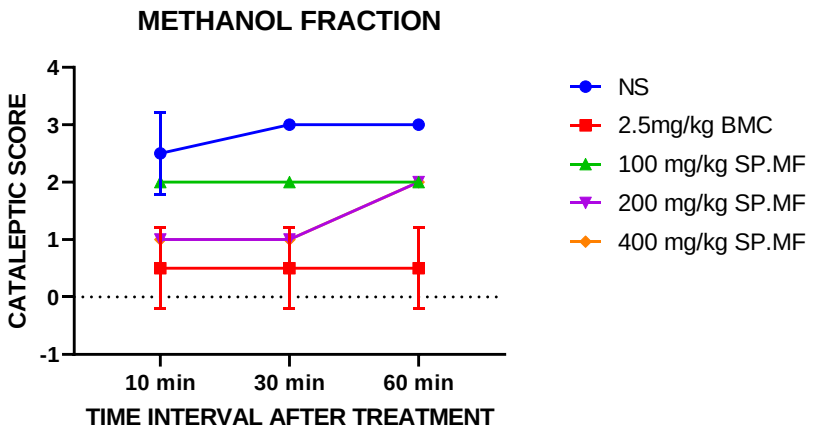

Figure 1: Methanol fraction of S.preusii.

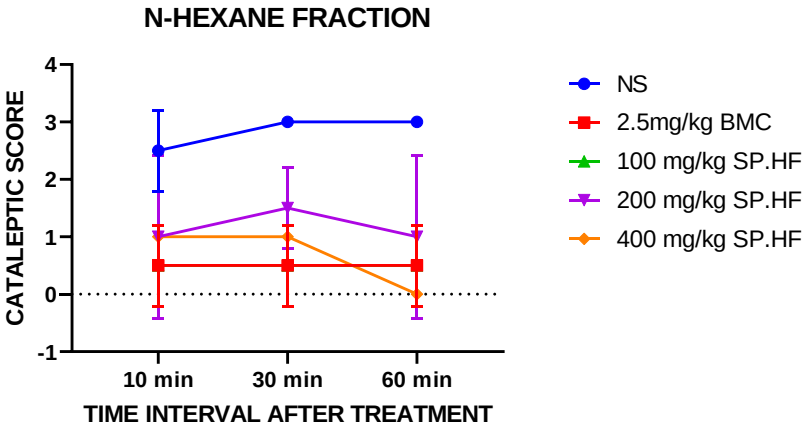

Figure 2: N-hexane fraction of S.preusii.

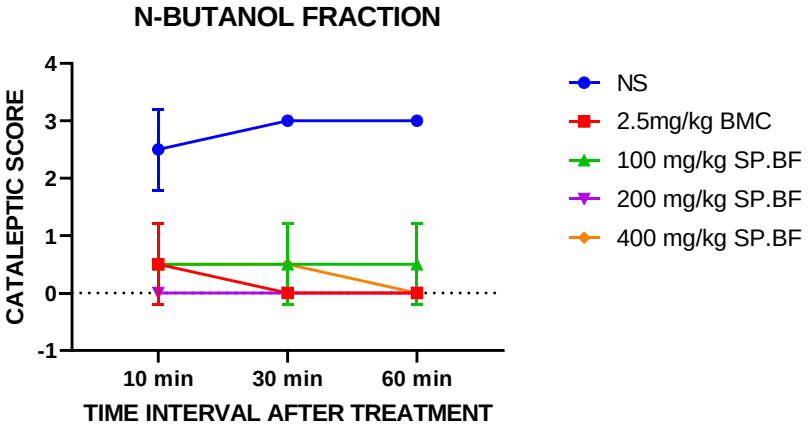

Figure 3: N-butanol fraction of S.preusii.

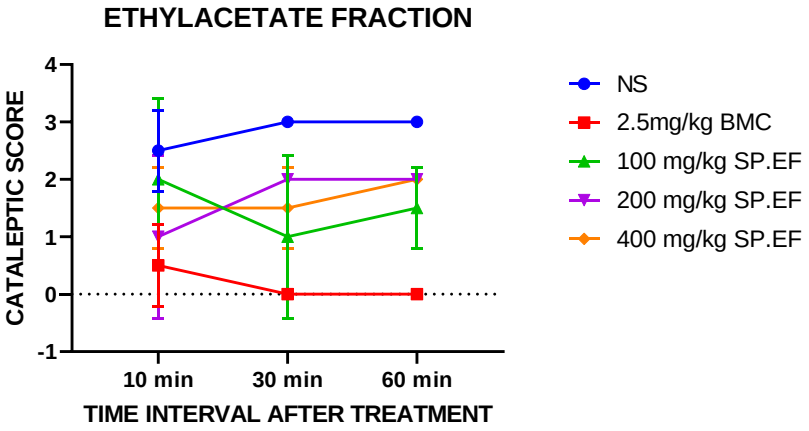

Figure 4: Ethylacetate fraction of S.preusii.

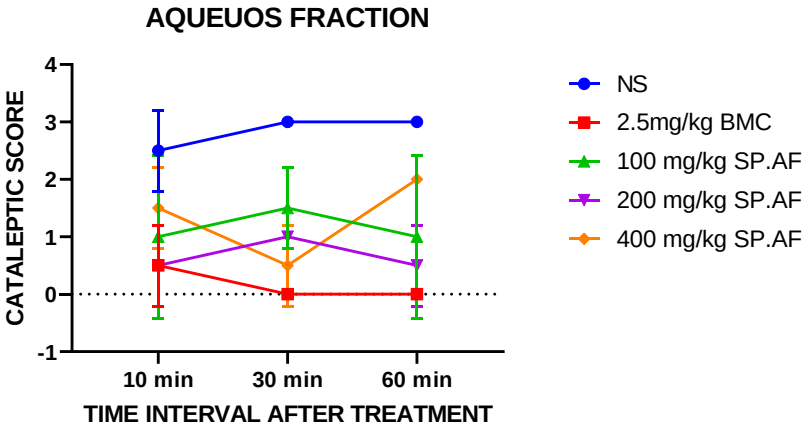

Figure 5: Aqueous fraction of S.preusii.

SUBACUTE EVELUATION

Cataleptic Evaluation

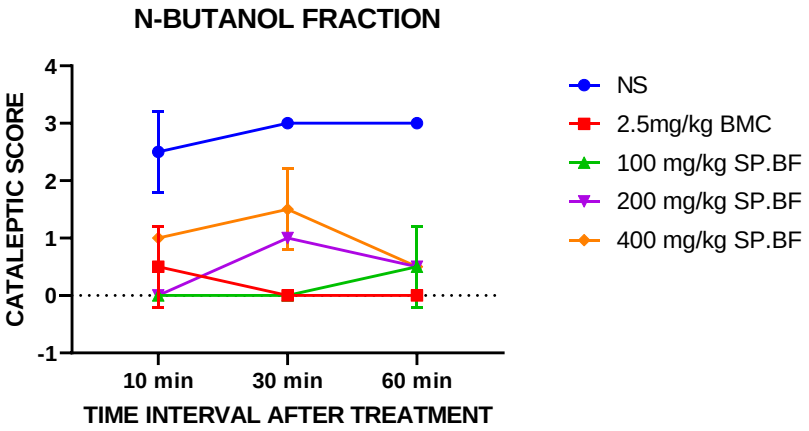

Figure 6: N-butal fraction of S.preusii.

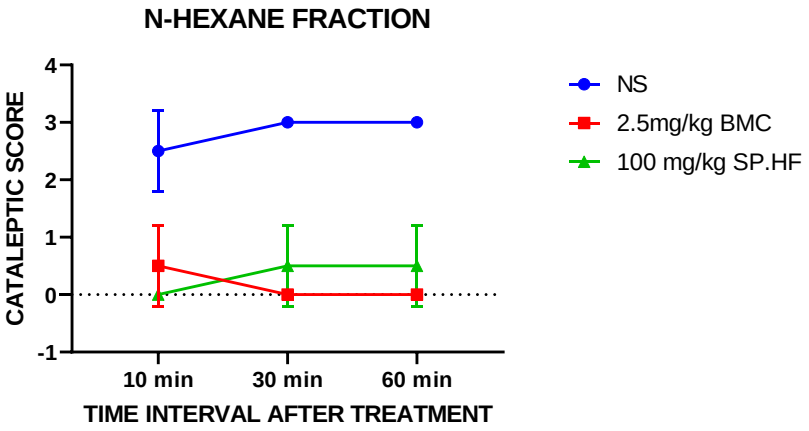

Figure 7: N-hexane fraction of S.preusii.

Sub-Acute Evaluation

Comparison of Grip Strength

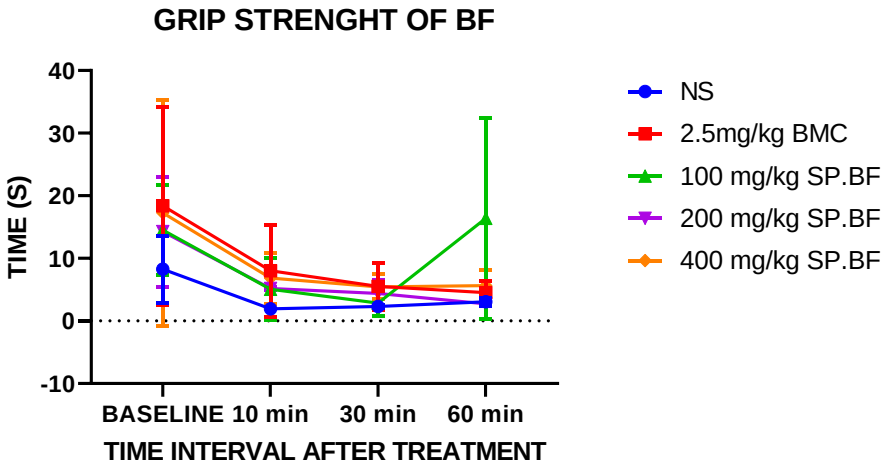

Figure 8: N-butanol fraction of S.preusii.

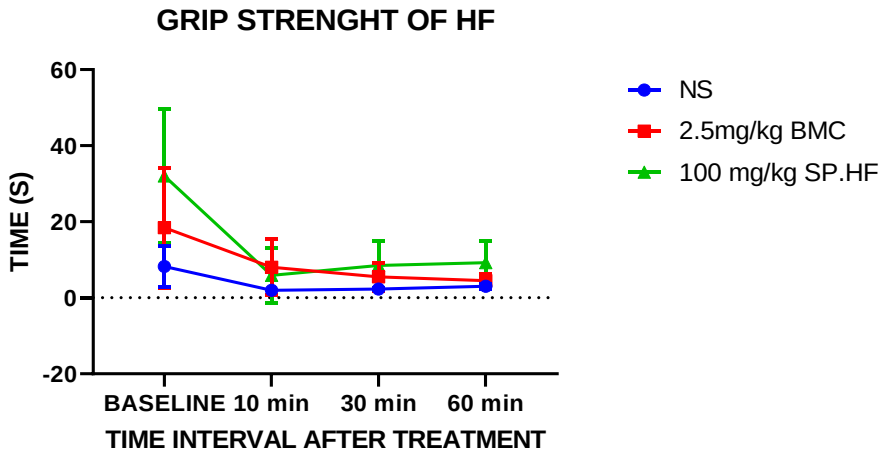

Figure 9: N-hexane fraction of S.preusii.

DISCUSSION

What possibly describes body movement difficulties in mammal ranges from -spasms, -stiffness, -jerking, -shaking, -flaccid which indicates neurological health concerns with inclination to genetic-conditions as well as some medications and environmental or occupational factors. Some anti-psychotics such chlorpromazine and haloperidol have make a mark in this regards owing to their extrapyramidal side effects (Joy et al., 2006; Leucht et al., 2008) among users of these drugs in both the human and animal population. Be it as it may, the drug mechanism of action, especially chlorpromazine is not clearly understood by most authorities but it is un-arguably accepted to be a psychotropic agent with influence on the reticular activating center (RAS), as well as the vomiting center, among other sub-cortical

structures that mostly results as sedative, anti-emetic, body weakness effects. It is also perceived to have a form interaction with the GABA receptor complex relatively contributing to its sedating property. Chlorpromazine seems to have better opposing influence on some nervous system pathways especially the adrenergic as well passively in cholinergic system at the peripheral level with passive ganglionic blocking action, -anti-histaminic action and – anti-serotonergic action. These extrapyramidal side effects could be controlled with a dopaminergic agonist such as the bromocriptine a D2 receptor agonist that interact partly with primary use for the treatment of acromegaly, as well as hyperprolactinemia with association of amenorrhea, infertility, hypogonadism, prolactin-secreting-adenoma and also movement difficulties as mostly associated with Parkinson's disesase. Bromocriptine is also an alkaloid derivative with two peptide groups of its tripeptide moiety. That is also known to be a derivative of lysergic acid (Fischer & Ganellin, 2006).

Looking at the study outcome, figure 2, 3, 7 and 9 has demonstrated similarity in the result with the standard group (2) bromocriptine at mid and lower doses 100 mg/kg and 200 mg/kg respectively. It maybe deduced that these both fractions (n-butanol and n-hexane) likely interact with doperminergic receptor on the bases of the presence of alkaloid in the phytochemistry of S. preusii (Gabriel et al.2017, Zbarsky et al., 2005). The fractions naturally got eliminated as a result of mortality among other groups except the n-butanol and n-hexane fraction as found in the sub-acute groups. I suppose this is a clear evidence of important medicinal phytochemical in the aforementioned fraction as such the result is significant with respect to these two fraction. It will be in our view to conduct more detailed study with these two fractions for further ethnopharmacological contribution.

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