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Further studies on the anticonvulsant potential of extracts from *Ceiba pentandra* (L.) Gaertn in a rat model of convulsion

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ABSTRACT

Background: The leaf and stem extracts of *Ceiba pentandra* (L.) Gaertn. (Malvaceae) has been documented traditionally for the management of convulsions. However, only the anticonvulsant effect of the ethanolic leaf extract has been studied. Aim and Objectives: This current study was to investigate the anticonvulsant properties of extracts from various parts of *C. pentandra* to justify their folkloric use and also to ascertain the most potent extract for further study. Materials and Methods: The aqueous leaf extract (CPALE), aqueous stem extract (CPASE), ethanolic leaf extract (CPELE) and ethanolic stem extract (CPESE) of *C. pentandra* were evaluated in the pentylenetetrazole (PTZ)-induced convulsion test in rats. Also, a combination of CPASE and carbamazepine (CZP) was investigated for any potential pharmacologic interactions (synergy, additivity or antagonism). Results: The various extracts (30-300 mg/kg, p.o.) demonstrated varying degrees of anticonvulsant effects by significantly delaying the onset and reducing the frequency and duration of PTZ-induced convulsions in a dose-dependent manner. CPESE and CPASE were the most active of the four extracts while CPELE was the least. Again, isobolographic analysis of combination of the CPASE and carbamazepine demonstrated synergistic activity in reducing the frequency of convulsions. Conclusion: The present findings justify the folkloric use of *C. pentandra* and the ethanolic and aqueous stem extracts possess the most active anticonvulsant properties.

Keywords: *Ceiba pentandra*, Anticonvulsant activity, Pentylenetetrazole, CompuSyn, Isobologram, Carbamazepine.

INTRODUCTION

Ceiba pentandra (L.) Gaertn is a tropical tree of the family Malvaceae (previously Bombacaceae). It is one of the plants known in African traditional medicine for the management of several conditions including epilepsy and mental ill health [1-4]. The stem decoction is used for the management of epilepsy in parts of Oyo and Osun States of Nigeria [4]. Again, the stem and leaf extracts made by maceration are also used in the treatment of convulsions in Nigeria [5].

In a previous study, the hydroethanolic (70%) leaf extract was shown to have significant anticonvulsant effects in murine models [6]. This is the only known anticonvulsant study although various parts of the plant are documented in folklore for management of epilepsy and convulsions [4, 5]. As part of a broad research underway to isolate the active constituents responsible for the anticonvulsant effect, there is the need to investigate the anticonvulsant properties of extracts from various parts of *C. pentandra* to establish the most potent extract from which fractions can be obtained for further study. This research will also justify or otherwise the folkloric use of these other parts in convulsion management. In this study, we report the anticonvulsant activity of ethanolic and aqueous leaf and stem extracts of *C. pentandra* and also the anticonvulsant effect of a combination of the aqueous stem extract and carbamazepine.

MATERIALS AND METHODS

Plant collection and extraction

Plant collection

The leaves and stem of *Ceiba pentandra* were collected from Ayikuma, Akuapem-Mampong in the Eastern region of Ghana (N 05.945991°; W 0.015529°) on the 1st of November 2024. They were authenticated by Mr. Peter Atta Adjei Junior and a voucher specimen (CPMR 5275 for the stem and

CPMR 5203 for the leaves) have been deposited in the herbarium of the Center for Plant Medicine Research (CPMR), Ghana.

Preparation of Ceiba pentandra extracts

The harvested leaf and stem samples were thoroughly washed with distilled water, blotted, air-dried for 14 days and were pulverized with a hammer mill into a course powder.

Ethanolic leaf and stem extracts

Over the course of 7 days, 200 g each of the course powder was cold macerated in 2000 ml of 70% (v/v) ethanol at room temperature. The mixture was then filtered several times with a cotton wool and the filtrate was freeze dried to obtain a final yield of 10.66% (w/w) and 2.94% (w/w) *Ceiba pentandra* ethanolic leaf extract (CPELE) and *Ceiba pentandra* ethanolic stem extract (CPESE) respectively.

Aqueous leaf and stem extracts

An amount of 200 g each of the powdered samples was weighed into a water trough and 2000 ml of distilled water was added, placed on a heating mantle and allowed to boil at 100ºC for 45 minutes. It was allowed to cool, filtered with cotton wool and then dried at 70^0C in a hot oven for 3 days to obtain a yield of 5.96% (w/w) *Ceiba pentandra* aqueous stem extract (CPASE) and 28.23% (w/w) *Ceiba pentandra* aqueous leaf extract (CPALE).

Animals

Male albino rats (100-150 g) were purchased from Center for Plant Medicine Research (CPMR), Mampong, Ghana. They were housed at room temperature in groups of six in plastic cages with wire mesh to ensure proper ventilation in the Pharmacology Laboratory of the Department of Pharmaceutical Science, Central University, Ghana. The cages were packed with soft wood shavings as bedding material and to help with easy cleaning. Rats were fed twice daily and clean water was provided *ad libitum*. All experiments were conducted in accordance with the National Institute of Health Guidelines for the Care and Use of Laboratory Animals (NIH Publication No. 85 - 23, 1985, revised 1996) [7]. All protocols used in this study were reviewed and duly approved by the institutional review board (IRB) of Central University, Ghana (Protocol number: CUIRB/33/12/24).

Acute toxicity studies

Albino rats were randomly divided into five groups (*n=3*). The animals were fasted overnight, but with access to water *ad libitum*, and then treated orally with CPASE in doses of 100, 300, 1000, and 3000 mg/kg of body weight. The other group served as the control and received 10 mL/kg of vehicle (distilled water) orally. Observation for signs of toxicity were performed at 0, 15, 30, 60, 120, 180 minutes and 24 h after administration. The assessment of behavior and physiological function was carried out similarly to the primary observation procedure (Irwin test) originally described by Irwin [8].

Anticonvulsant activity assessment

Pentylenetetrazole-induced convulsion test

The method used by Homayoun et al. [9] was modified and used. Animals were put into sixteen groups (n = 6). Twelve groups received CPELE, CPALE, CPESE and CPASE at 30, 100 and 300 mg/kg, *p.o.*. Three groups received carbamazepine (CZP; 1, 3 and 10 mg/kg, *p.o.*) and the last group received normal saline (10 ml/kg). Each rat was pretreated with a daily dose of these selected doses for seven days. One h after the administration on the last day, a pre-tested dose of pentylenetetrazole (100 mg/kg) was dissolved in the vehicle and injected intraperitoneally (i.p) into the rats to induce convulsions. The animals were placed individually in an observation chamber—clear Plexiglas boxes (30 cm × 18.5 cm × 21.5 cm) with a camera positioned a few meters above the chamber—and videotaped for 30 minutes. The videos were later scored with JWatcher™ Version 1.0 (a public domain software by University of California, Los Angeles, USA and Macquarie University, Sidney, Australia available at http://www.jwatcher.ucla.edu/) to determine the onset, frequency and duration of convulsions for each rat.

Isobolographic analysis of a combination of CPASE and Carbamazepine

Dose-effect curve for each drug alone in reducing the frequency of convulsions in the PTZ test was established and their respective ED_{50}s in inhibiting frequency of convulsions were determined. The ED_{50}s were then combined in various ratios (2:2, 1:1, ½ : ½, and ¼ : ¼) by serial dilution. Rat (n = 5) received these dose combinations for a week and the effect on the frequency of convulsions were investigated in the PTZ-induced test. The Chou-Talalay method for drug combination (CompuSyn) [10], based on the median-effect equation was then used to determine the combination index (CI).

Analysis of data

Statistical analyses were done with GraphPad Prism for Windows version 8 (GraphPad Software, San Diego, CA, USA). All values are expressed as mean ± S.E.M (n=4-6). Data were analyzed using one-way ANOVA. All ANOVAs were followed by Tukey's multiple comparison test when statistical significance was reached (i.e., $P < 0.05$).

RESULTS

Acute toxicity test

No mortality was recorded and there were no general changes in behavior and physiological function. However, there were sedation and ataxia in animals that received the 1000 mg/kg and 3000 mg/kg.

Anticonvulsant activity assessment

Anticonvulsant effect of CPELE on pentylenetetrazole-induced convulsion test

Rats that received various doses of CPELE showed a reduction in the duration of convulsions (figure 1A) although they were not statistically significant. However, all the dose of CPELE significantly in a dose-dependent manner reduced the frequency of convulsions (30 mg/kg: $P = 0.0022$, 100 mg/kg: $P = 0.0003$ and 300 mg/kg: $P = 0.0006$; figure 1B) compared with the vehicle group. Carbamazepine, which was the standard drug, significantly delayed the onset ($P = 0.0016$) and reduced the frequency ($P = 0.0003$) and duration ($P = 0.0086$) of convulsions (figure 1 A and B).

Anticonvulsant effect of CPALE on pentylenetetrazole-induced convulsion test

The extract at 300 mg/kg delayed the onset ($P = 0.0090$; figure 2A), reduced the duration ($P = 0.0359$; figure 2A) and frequency ($P = 0.0433$; figure 2B) of convulsions. Carbamazepine at the tested dose of 10 mg/kg significantly delayed the onset ($P = 0.0017$) and reduced duration ($P < 0.0001$) and frequency ($P = 0.0042$) of convulsions (figure 2 A and B).

Anticonvulsant effect of CPESE on pentylenetetrazole-induced convulsion test

All doses (30-300 mg/kg) significantly reduced the duration and frequency of convulsions ($P < 0.0001$; figure 3 A and B). The 300 mg/kg dose also delayed the onset of convulsions ($P = 0.0462$; figure 3A). Carbamazepine at the tested dose of 10 mg/kg significantly delayed the onset ($P = 0.0069$) and reduced the duration ($P < 0.0001$) and the frequency ($P < 0.0001$) of convulsions (figure 3 A and B).

Anticonvulsant effect of CPASE on pentylenetetrazole-induced convulsion test

Ceiba pentandra aqueous stem extract at all the doses tested reduced the duration of convulsions significantly (30 mg/kg: $P = 0.0029$ and 100-300 mg/kg: $P < 0.0001$; figure 4A). Again, the 300 mg/kg was able to significantly delay the onset of convulsions ($P = 0.0001$; figure 4A) and also caused a significant reduction in frequency of convulsions ($P = 0.0229$; figure 4B). Carbamazepine, which was the standard drug, significantly delayed the onset ($P = 0.0006$) and reduced the frequency ($P = 0.0092$) and duration ($P < 0.0001$) of convulsions (figure 4 A and B).

Anticonvulsant effect of carbamazepine in the pentylenetetrazole-induced convulsion test

Pentylenetetrazole (100 mg/kg, i.p) induced convulsions in all animals in the vehicle group. Carbamazepine at all the doses tested significantly reduced the duration (1-3 mg/kg: $P < 0.0001$; figure 5A) and the two higher doses delayed the onset (3 mg/kg: $P = 0.0227$, 10 mg/kg: $P = 0.0144$; figure 5A) of convulsions compared with the vehicle. Again, the 10 mg/kg caused a significant reduction in frequency of convulsions ($P = 0.0297$; figure 5B).

The doses for 50% of the maximal effect (ED_{50}) for each drug on pentylenetetrazole-induced convulsion test

The dose-response curves for the four different extracts and carbamazepine were plotted for the onset, duration and frequency of convulsions in the pentylenetetrazole-induced convulsion test for all the extracts and the anticonvulsant effect potency (ED_{50}) for each drug was determined and tabulated (table 1).

Anticonvulsant effect of CPASE-CZP combination on frequency of pentylenetetrazole-induced convulsion test

The ED_{50} of frequency of *Ceiba pentandra* aqueous stem extract (30.26 mg/kg) and that of carbamazepine (1.935 mg/kg) were combined in different ratios and the ability of these combinations to reduce frequency of convulsions were tested in the PTZ-induced convulsion test. CPASE-CZP combinations significantly reduced the frequency of convulsions in all the dose ratios (0.25x; $P = 0.0007$, 0.5x-2x; $P < 0.0001$; figure 6A). Again, comparing the effects of the combinations with CPASE alone, the combined doses were superior to even the highest dose of the extract (CPASE-CZP: 0.5x; $P = 0.0014$, 1x; $P = 0.0001$, 2x; $P < 0.0001$, CPASE: 300 mg.kg; $P = 0.0031$; figure 6B). Furthermore, the combinations showed a more significant effect in reducing frequency of convulsions than even the highest dose of carbamazepine which is a known standard anticonvulsant agent (CPASE-CZP: 0.5x; $P = 0.0043$, 1x; $P = 0.0005$, 2x; $P = 0.0003$, CZP: 10 mg/kg; $P = 0.0023$; figure 6C).

Isobolographic analysis of a combination of CPASE and Carbamazepine

Following the findings that the combined effect of CPASE and carbamazepine is superior to either agent alone, isobolographic analysis (using compuSyn) was performed to study the nature of interaction between the two agents. The Chou-Talalay method for drug combination based on the median-effect equation was used to determine the combination index (CI). According to figure 7, the combination data point falls below the additivity line and again the combination index (CI) indicates synergy in reduction of frequency at all effect levels (table 2). All the dose-reduction indices (DRIs) were greater than one and the greater DRI value indicates a greater dose reduction for a given therapeutic effect.

Table 1: The doses for 50% of the maximal effect (ED_{50}) on onset, frequency and duration of PTZ-induced convulsion test for each extract

Convulsion parameter	ED50 (mg/kg)				
	CPELE	CPALE	CPESE	CPASE	CZP
Onset	Ns	126.1	98.74	155.1	4.547
Duration	Ns	89.55	122.0	38.55	1.986
Frequency	65.18	133.4	23.22	30.26	1.935

Ns, non-significant (CPELE did not have a significant effect on onset and duration of convulsions)

Table 2: Two-drug combination effect of CPASE and CZP on frequency of PTZ-induced convulsions

Drug combo	CI value at the various effect levels		Dose reduction index (DRI)
			CPASE, CZP
CPASE-CZP	ED50	0.29152	6.31630, 7.50756
	ED75	0.41037	3.43312, 8.39667
	ED90	0.64238	1.86602, 9.39107
	ED95	0.90995	1.23263, 10.1339

CI, combination index; CI = 1, additivity; CI < 1, synergism; CI > 1, antagonism

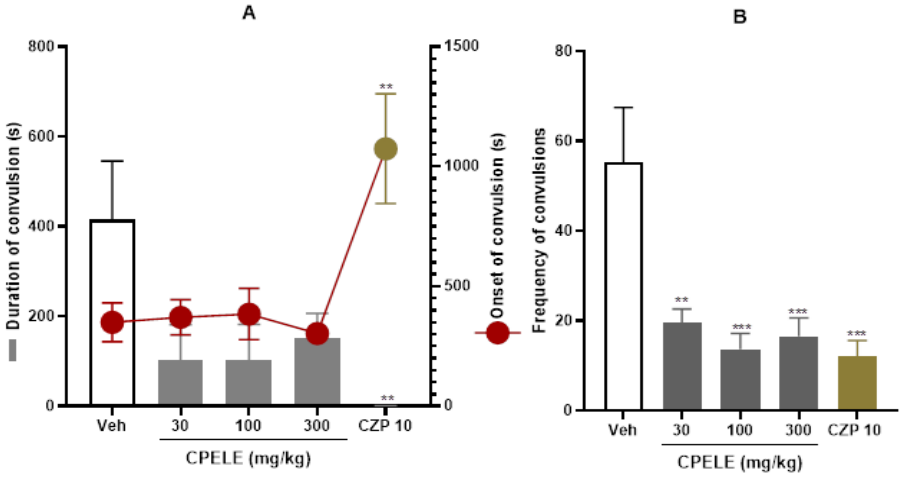

Figure 1: Effect of CPELE (30, 100, 300 mg/kg *p.o.*) and carbamazepine (CZP 10 mg/kg *p.o.*) on onset & duration (A) and frequency (B) of 100 mg/kg PTZ-induced convulsion in rats. Each point/column is the mean ± S.E.M. (n = 4-6). $^{**}P < 0.01$, $^{***}P < 0.001$, versus vehicle (Veh) group; 1-way ANOVA with Tukey's *post hoc* test.

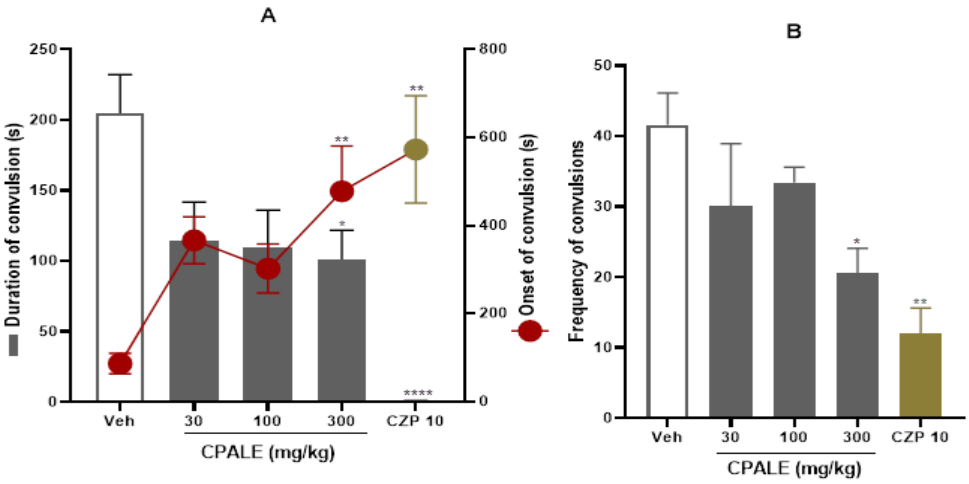

Figure 2: Effect of CPALE (30, 100, 300 mg/kg *p.o.*) and carbamazepine (CZP 10 mg/kg *p.o.*) on onset & duration (a) and frequency (b) of 100 mg/kg PTZ-induced convulsion in rats. Each point/column is the mean ± S.E.M. (n = 4-6). $^{*}P < 0.05$, $^{**}P < 0.01$, $^{****}P < 0.0001$, versus vehicle (Veh) group; 1-way ANOVA with Tukey's *post hoc* test.

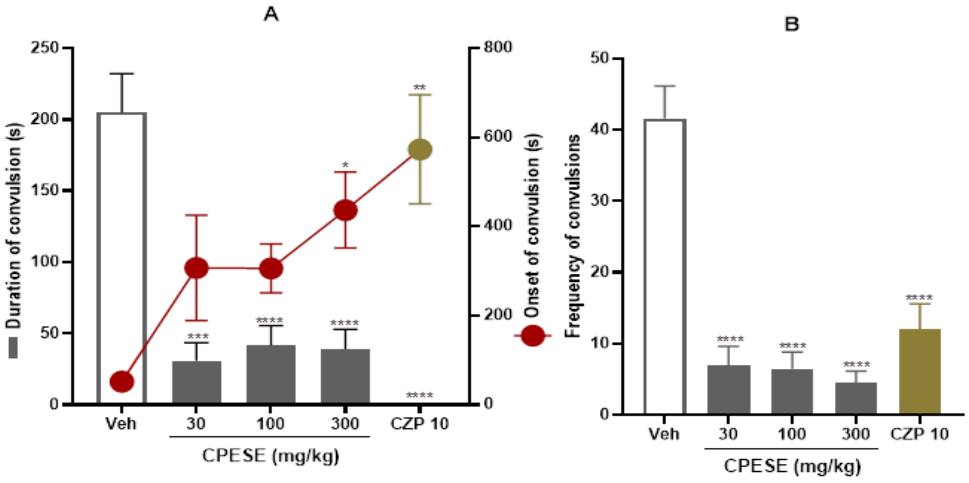

Figure 3: Effect of CPESE (30, 100, 300 mg/kg *p.o.*) and carbamazepine (CZP 10 mg/kg *p.o.*) on onset & duration (A) and frequency (B) of 100 mg/kg PTZ-induced convulsion in rats. Each point/column is the mean ± S.E.M. (n = 4-6). $^{*}P < 0.05$, $^{**}P < 0.01$, $^{****}P < 0.0001$, versus vehicle (Veh) group; 1-way ANOVA with Tukey's *post hoc* test.

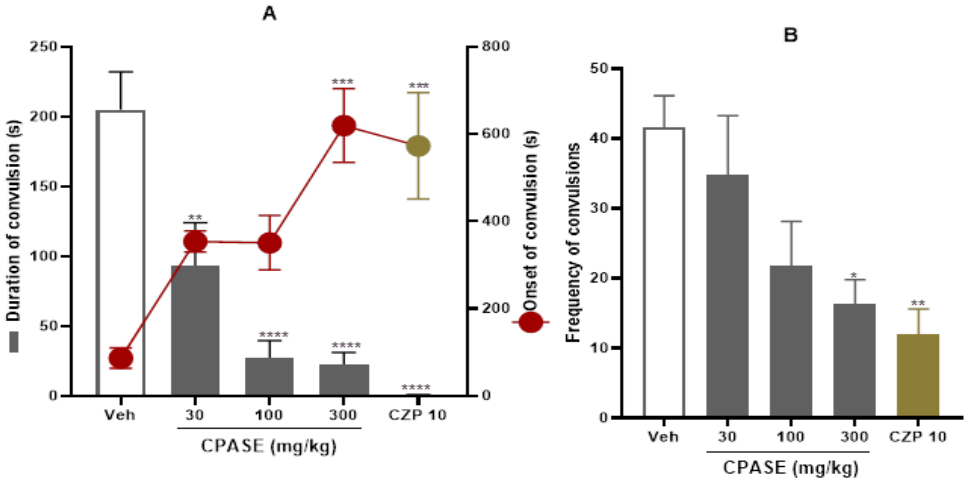

Figure 4: Effect of CPASE (30, 100, 300 mg/kg *p.o.*) and carbamazepine (CZP 10 mg/kg *p.o.*) on onset & duration (A) and frequency (B) of 100 mg/kg PTZ-induced convulsion in rats. Each point/column is the mean ± S.E.M. (n = 4-6). $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$, $^{****}P < 0.0001$, versus vehicle (Veh) group; 1-way ANOVA with Tukey's *post hoc* test.

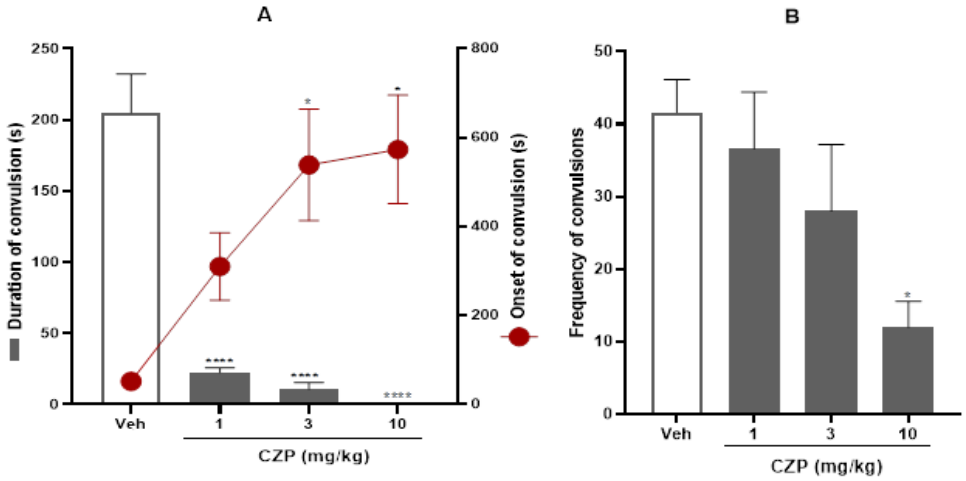

Figure 5: Anticonvulsant effect of carbamazepine (1-3 mg/kg *p.o.*) on onset & duration (A) and frequency (B) of 100 mg/kg PTZ-induced convulsion in rats. Each point/column is the mean ± S.E.M. (n = 4-5). *P < 0.05, **P < 0.01, ***P < 0.001, ****P < 0.0001, versus vehicle (Veh) group; 1-way ANOVA with Tukey's *post hoc* test.

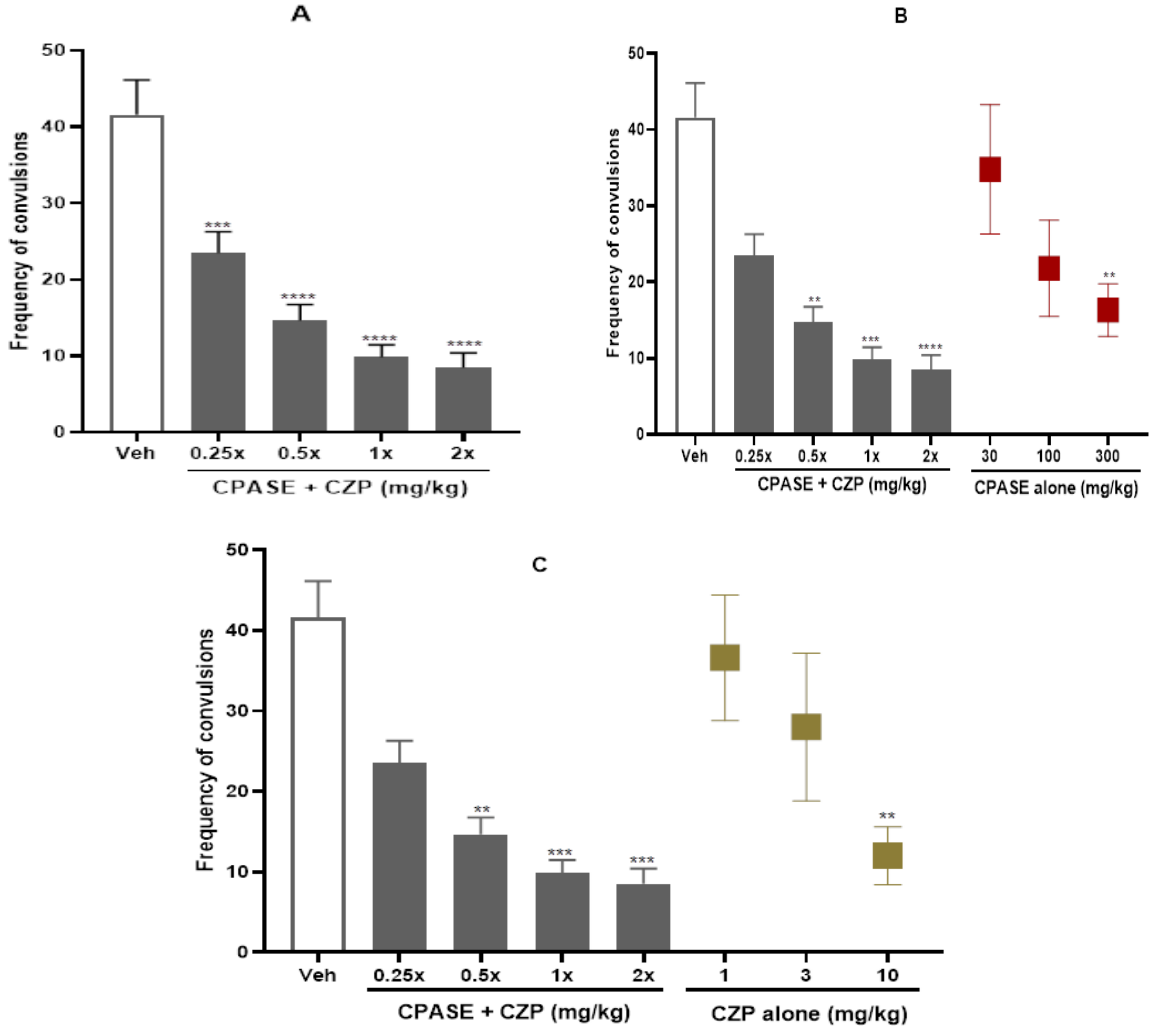

Figure 6: Effect of combined doses of CPASE-CZP alone (6A), combined doses with the extract alone (6B) and combined doses with carbamazepine alone (6C) on frequency of PTZ-induced convulsion test. Each point/column is the mean ± S.E.M. (n = 5-6). *P < 0.05, **P < 0.01, ***P < 0.001, ****P < 0.0001, versus vehicle (Veh) group; 1-way ANOVA with Tukey's *post hoc* test. CPASE-CZP combined ratios (0.25x; 1/4:1/4, 0.5x; 1/2:1/2, 1x; 1:1, 2x; 2:2).

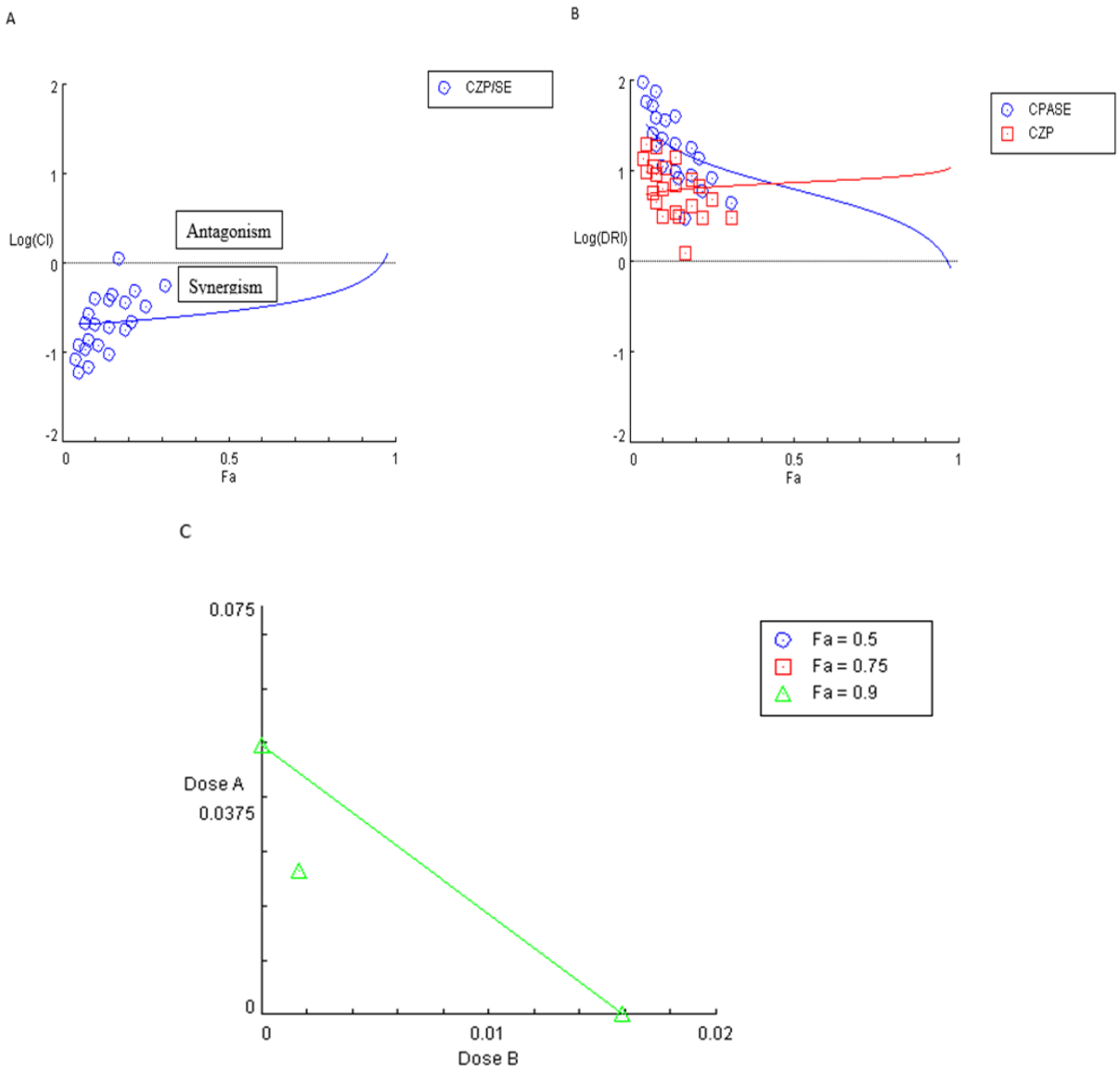

Figure 7: Isobologram analysis of combination of CPASE and CZP on frequency of PTZ-induced convulsions. A, combination index plot; B, dose reduction index plot; C, normalized isobologram at 90% dose-effect level.

DISCUSSION

The goal of research into medications for the treatment of epilepsy is to achieve complete remission of seizures without adverse events and although new antiepileptic drugs (AEDs) have been developed, more AEDs are needed to achieve better care of patients with epilepsy [11]. The use of traditional alternative medicines is prevalent in Ghana. According to research by Kretchy et al. [12], almost 60% of respondents (n = 1364) reported using herbal medicinal products that have been registered by the Ghana Food and Drugs Authority to cure diseases including neurological and psychiatric disorders. There is therefore the urgent need to conduct thorough scientific research into the standardization and use of herbal medicinal products and this will provide basis for the integration into the healthcare system in Ghana. Isolated compounds from these plant species could also serve as important lead molecules against potential drug targets. One such plant is *Ceiba pentandra* a well-known plant for its anticonvulsant effect in traditional medicine [4, 5].

This current study is part of a broad research underway to isolate the active constituents responsible for the anticonvulsant effect. In this study, we have investigated the anticonvulsant properties of four extracts from the leaf and stem (which are the parts document in folklore for the management of convulsions) and also the anticonvulsant effect of combination of CPASE and carbamazepine.

In the search and development of novel AEDs, animal models play an essential role. The pentylenetetrazole seizure test is one of the traditional acute test protocols used to characterize anticonvulsant and/or proconvulsant properties of compounds [13]. PTZ induces clonic convulsions at low doses and both clonic and tonic convulsions are seen at higher doses. Hence agents which are able to abolish PTZ induced convulsions would be effective against generalized tonic clonic convulsions. Again, PTZ is also used to investigate candidate compounds that lower or elevate the seizure threshold [14].

All the extracts tested in this study demonstrated significant anticonvulsant activity in the PTZ-induced convulsion test. Rats that received the ethanolic leaf extract demonstrated a significant reduction in frequency of convulsions at all the doses tested. This is consistent with previous study by Sarfo et al. [6] where the hydroethanolic leaf extract showed significant anticonvulsant activity in mouse model of PTZ-induced convulsion. The results indicate that extracts from the stem and leaf of *Ceiba pentandra* can control generalized tonic clonic convulsions and also raise the seizure threshold and justifies the folkloric use of the stem and leaf in the management of epileptic convulsions.

Following the finding that all the four extracts delayed the onset and reduced the frequency and duration of convulsions, their respective ED_{50}s were calculated to ascertain the most potent extract in

abolishing the onset, frequency and duration of PTZ-induced convulsions. The results show that the ethanolic stem extract is the most potent in delaying the onset and reducing the frequency of convulsions whilst the aqueous stem is the most potent in reducing the duration of convulsions. Hence it can be concluded that amongst the two parts of the plant that are known for the traditional management of convulsions, the stem extract is more active compared with the leaf and should be considered for any further study.

Studies have shown that about 30% of patients are refractory to the known AEDs. Combination therapy has been suggested for such patients [11]. Findings from Margolis et al [15] suggest that combining two or more antiepileptic drugs with different mechanisms of action results in an enhanced effectiveness. Three-drug combination therapy with AEDs abolished seizures in about 15% of patients with refractory focal epilepsy [16]. Drug combination in epilepsy management is not limited to only orthodox AEDs. In fact, most people in the developing countries take herbal medicines in conjunction with their orthodox drugs. One study reported that about 16% of patients with epilepsy were treated with integrated medicine of both orthodox AEDs and herbal medicine [17]. A combination of *Gastrodiae rhizoma* a plant used in Chinese folklore for the management of convulsions with carbamazepine reduced the auto-induction of carbamazepine which could enhance the therapeutic effect of carbamazepine [17]. Several studies suggest that a combination of carbamazepine and ginkgo biloba, turmeric and *Ajuga bracteosa* may help improve therapeutic outcomes of carbamazepine [18-20]. Hence the current study also investigated the potential pharmacodynamic interaction (synergism, additivity or antagonism) between the aqueous stem extract of *Ceiba pentandra* and carbamazepine.

The aqueous stem extract (CPASE) when combined with carbamazepine significantly reduced the frequency of convulsions and the efficacy of this combination was superior to either CPASE or carbamazepine alone. The best-known method for studying combination effect is the isobolographic analysis [10]. This method of analysis known as the Chou-Talalay method for drug combination is based on the median-effect equation, derived from the mass-action law principle. The analysis provides the combination index (CI) which offers quantitative definition for additive effect (CI = 1), synergism (CI < 1), and antagonism (CI > 1) in drug combinations. The Isobolographic analysis showed that the CI was less than one and hence the interaction between CPASE and CZP is a synergistic effect. According to [21] agents that interact synergistically do so because they have different mechanisms of action whereas those with similar mechanisms of action seem to produce additive effects. Hence, this effect suggests that carbamazepine and CPASE each may exert its anticonvulsant effect through different mechanisms. The dose reduction index (DRI) from the analysis were greater than one for CPASE and CZP at all the given effect levels and this implies that the dose of each agent may be reduced for instance 6-fold and almost 8-fold at the 50% dose effect level for CPASE and CZP respectively. Hence this combination enhances the chance for a drastic reduction in drug toxicity (such as sedation, dizziness from both CZP and CPASE) whilst providing better efficacy.

One of the challenges of traditional alternative medicines is with regards to their safety. In fact, there are documents to support the fact that herbal drugs considered safe for the past decades have proven to be associated with some adverse effects [22]. Toxicity studies of extracts from *Ceiba pentandra* have been proven according to several published articles to be very safe [6, 23-25]. To our knowledge no toxicity study exists in literature about stem extracts of *Ceiba pentandra* hence in this current study the Irwin's test was used to screen aqueous stem extract of *Ceiba pentandra* to evaluate any neurotoxicity, CNS stimulation, CNS depression as well as autonomic effects associated with the crude extract. According to the results, no mortalities were observed after 24 h and therefore the LD_{50} of the aqueous stem extract is above 3000 mg/kg. Again, rats did not show any neurotoxic and CNS stimulant features. However, at higher doses sedation and ataxia which are CNS depressant effects were observed. These findings conform with that of Sarfo et al. [6] where the ethanolic leaf extract also demonstrated sedative activities and a reduction in motor coordination. Generally based on the current and previous toxicity studies, it can be stated that extracts from *Ceiba pentandra* have low potential for toxicity.

CONCLUSION

This current study has shown that extracts from *Ceiba pentandra* have anticonvulsant properties in rat models of PTZ-induced convulsion with the most potent agents being CPASE and CPESE. The results have also established a potential synergy between the aqueous stem extract and carbamazepine. The research justifies the use of the stem and leaf of *Ceiba pentandra* in convulsion management in African traditional medicine. A study is currently underway to isolate and characterize active compounds from CPASE and CPESE through bioassay-guided fractionation technique.

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Conflict of interest

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REFERENCES

1. Friday ET, James O, Olusegun O, Gabriel A. Investigations on the nutritional and medicinal potentials of *Ceiba pentandra* leaf: A common vegetable in Nigeria. Plant Physiol Biochem. 2011;3:95–101.
2. Ngounou FN, Meli AL, Lontsi D, Sondengam BL, Atta-Ur-Rahman, Choudhary MI, et al. New isoflavones from *Ceiba pentandra*. Phytochemistry. 2000;54(1):107–10.
3. Onyenso AI. Ethnobotanical survey of medicinal plants in homegardens in Abia State, South-eastern Nigeria. Int J Agric Food Sci. 2019;2(2):243–5.
4. Wahab OM, Wahab OM. Ethnomedicinal antiepileptic plants used in parts of Oyo and Osun States, Nigeria. Bot Res Int. 2019;8(4):77–81.
5. Ichoron N, Tyoer S, James EJ, Igoli JO. A survey of medicinal plants used as traditional medicine in Ukum and Ogbadibo Local Government Areas of Benue State, Nigeria. Plants Environ. 2019;1(1):5–11.
6. Sarfo A, Abotsi WKM, Ekuadzi E, Woode E. *Ceiba pentandra* (L.) Gaertn hydroethanolic leaf extract exhibits anticonvulsant properties in mouse models. Phytomed Plus. 2022;2(2):100263.
7. Bayne K. Revised guide for the care and use of laboratory animals available. The Physiologist. 1996;39(4):199.

8. Irwin S. Drug-induced convulsions. Psychopharmacologia. 1968;13:222–57.
9. Homayoun M, Shafieian R, Seghatoleslam M, Hosseini M, Ebrahimzadeh-Bideskan A. Protective impact of *Rosa damascena* against neural damage in a rat model of pentylenetetrazole-induced seizure. Int J Pharm Sci. 2020;10(6):574–83.
10. Chou TC. Drug combination studies and their synergy quantification using the Chou-Talalay method. Cancer Res. 2010;70(2):440–6.
11. Lee SK. Old versus new: Why do we need new antiepileptic drugs? J Epilepsy Res. 2014;4(2):39–44.
12. Kretchy IA, Koduah A, Opuni KFM, Agyabeng K, Ohene-Agyei T, Boafo EA, et al. Prevalence, patterns and beliefs about the use of herbal medicinal products in Ghana: A multi-centre community-based cross-sectional study. Trop Med Int Health. 2021;26(4):410–20.
13. Giardina WJ, Gasior M. Acute seizure tests in epilepsy research: Electroshock- and chemical-induced convulsions in the mouse. Curr Protoc Pharmacol. 2009;45:5.22.1–5.22.20.
14. Sills GJ, Brodie MJ. Antiepileptic drugs: Preclinical drug development in epilepsy. Encycl Basic Epilepsy Res. 2009;1:97–103.
15. Margolis JM, Chu BL, Wang ZJ, Copher R, Cavazos JE. Effectiveness of antiepileptic drug combination therapy for partial-onset seizures based on mechanisms of action. JAMA Neurol. 2014;71(8):985–93.
16. Wu C, Wu H, Zhou Y, Liu X, Huang S, Zhu S. Effectiveness analysis of three-drug combination therapies for refractory focal epilepsy. Neurotherapeutics. 2024;21(3):e00345.
17. Yip KL, Zhou X, Chook P, Leung PC, Schachter S, Mok VCT, et al. Herb-drug interaction of *Gastrodiae rhizoma* on carbamazepine: A pharmacokinetic study in rats. Epilepsy Res. 2020;165:106376.
18. Ahmad E, Jahangir M, Ishtiaq S, Haider HMF, Shah PA, Bukhari NI. Carbamazepine shows plasma and tissue pharmacokinetic interactions with *Ajuga bracteosa* extract in rats. Planta Med Int Open. 2021;8(1):e10–8.
19. Pagotto GL, Dos Santos LMO, Osman N, Lamas CB, Laurindo LF, et al. Ginkgo biloba: A leaf of hope in the fight against Alzheimer's dementia: Clinical trial systematic review. Antioxidants. 2024;13(6):651.
20. Dhir A. Curcumin in epilepsy disorders. Phytother Res. 2018;32(10):1865–75.
21. Matsumura N, Nakaki T. Isobolographic analysis of the mechanisms of action of anticonvulsants from a combination effect. Eur J Pharmacol. 2014;741:237–46.
22. George P. Concerns regarding the safety and toxicity of medicinal plants: An overview. J Appl Pharm Sci. 2011;1(6):40–4.
23. Amani GN, Stanislas ZO, Yomalan K, Anthelme NBS. Acute and subacute toxicities of an aqueous leaves extract of *Ceiba pentandra* and its ethanolic fraction in Wistar rats. J Pharmacogn Phytochem. 2024;13(3):23–30.
24. Gandhare B, Kavimani S, Rajkapoor B. Acute and subacute toxicity study of methanolic extract of *Ceiba pentandra* (Linn.) Gaertn. on rats. J Sci Res. 2013;5(2):315–24.
25. Muhammad HL, Kabiru AY, Busari MB, Mann A, Abdullah AS, Usman AT, et al. Acute oral toxicity study of ethanol extract of *Ceiba pentandra* leaves as a glucose lowering agent in diabetic rats. J Acute Dis. 2016;5(3):237–43.

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