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# Anticonvulsant activity and mechanism of actions of fractions of *Ipomoea asarifolia* (Desr) (Convolvulaceae) ethanol leaf extract

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## Abstract

**Background:** Preparation of *Ipomoea asarifolia* (Desr) (Convolvulaceae) is widely used in traditional African medicine for the treatments of different kinds of ailments such as syphilis, malaria, convulsions and rheumatism.

**Aim:** The anticonvulsant properties of fractions of leaf of *Ipomoea asarifolia* (Desr); *n*-butanol (BF), chloroform, *n*-hexane and residual aqueous fractions (RAF) were evaluated on animals.

**Results:** The RAF at dose of 75 mg/kg ( $P < 0.01$ ) with 33% quantal protection and 83% protection against mortality is the most active fraction when compared with BF at 300 mg/kg ( $P < 0.01$ ) with no quantal protection and 83% protection against mortality; the anti-seizure activity could be because of the presence of saponins (23.3%) and flavonoids (43.92%). The RAF may also owes its anticonvulsant activity via GABAergic pathway as flumazenil at 2 mg/kg significantly ( $P < 0.05$ ) blocked the activity of RAF, via glutamatergic pathway with RAF ( $P < 0.05$ ) significantly reversing the proconvulsive activity of ketamine at 200 mg/kg as compared to ketamine alone. Opioidergic pathway may also be implicated as naloxone 1 mg/kg significantly ( $P < 0.05$ ) reduced the anticonvulsant effect of RAF.

**Conclusions:** BF and RAF of leaf of *Ipomoea asarifolia* have shown anticonvulsants activities in PTZ-induced seizures. RAF was observed to be the most active fraction of *Ipomoea asarifolia* extract which probably exerts its action through GABAergic, glutamatergic and opioidergic pathways.

**Keywords:** GABAergic, Glutamatergic, Opioidergic, *Ipomoea asarifolia*, Convulsions, Quantal protection

## Background

Epilepsy is a neurological disorder that affects 2–5% of the global population; about 67 million people have epilepsy (Angus-Leppan and Parsons 2008). In Nigeria, epilepsy affects 3.1–37 per 1000 population (Owolabi et al. 2019). Main cause of epileptic seizure is the imbalance between the excitatory (glutamatergic) and the inhibitory (GABAergic) drive at the synaptic level. Seizures in epilepsy are generated by abnormal synchronous discharge in a group of neurons (Fisher et al. 2005). However, the

exact cellular mechanisms through which seizures are generated in epilepsy are not well understood.

Plants are good source of new compounds with potential therapeutic effects and benefits for the management of debilitating neurological disorders (Bormann and Kellert 1991). Some species of the genus *Ipomoea* have also shown to possess anticonvulsant activities; *Ipomoea stans* (Contreras et al. 1996), *Ipomoea involucreta* (David-Oku et al. 2017) and *Ipomoea carnea* (Rout and Kar 2013).

*Ipomoea asarifolia* belongs to family Convolvulaceae and authority (Desr.) Roem, and Schult is a hairless and succulent perennial weed that grows in hydromorphic soil along inland valley, rivers and streams. The weed is native to tropical America but now commonly found West Africa and Cameroun (Nacoulma 1996). The plant

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and *n*-hexane were used. Ugo Basile current electroshock machine (Model) and diazepam (Roche, Germany) were also used.

#### Acute toxicity studies

The median lethal dose (LD<sub>50</sub>) was determined according to the method described by Lorke (1983). The animals were euthanized at the end of the acute toxicity test.

#### Screening for anticonvulsant activities

##### *Pentylenetetrazole (PTZ)-induced convulsion in mice*

The method described by Swinyard and Kupferberg (1985) was employed to induce convulsion in mice using PTZ. Thirty (30) mice were randomly grouped into five ( $n=6$ ). Group 1 administered with normal saline 10 ml/kg *i.p.* Groups 2–4 were given 75, 150 and 300 mg/kg *i.p.* of chloroform, *n*-butanol and *n*-hexane fractions of ethanol extract of *Ipomoea asarifolia*, respectively, while group 5 received sodium valproate 200 mg/kg. Thirty minutes later, the mice received PTZ 85 mg/kg subcutaneous (Sc) and were observed for another 30 min.

##### *Maximal electroshock-induced convulsion in chicks*

The method earlier described by Swinyard and Kupferberg for induction of electric shock convulsion [16] was used in the study. 50-day-old chicks were randomly grouped in five ( $n=10$ ). Group 1 was administered with normal saline 10 ml/kg *i.p.*, groups 2 to 4 received 75, 150, 300 mg/kg *i.p.* of *n*-hexane, chloroform and *n*-butanol fractions of ethanol extract of *Ipomoea asarifolia*, respectively, while group 5 received 20 mg/kg of phenytoin *i.p.* Maximal electroshock was administered after 30 minutes to induce seizure in the chicks which manifests as tonic hind limb extension (THLE). The ability to prevent this feature or prolong the latency and/or onset of the THLE was considered as an indication of anticonvulsant activity (Swinyard 1969; Sayyah et al. 2002).

##### *Effects of flumazenil on anticonvulsant effects of RAF of ethanol leaf extract of Ipomoea asarifolia on PTZ-induced seizures*

The mice were randomly grouped into eight ( $n=6$ ). Group 1 receiving distilled water at 10 ml/kg and PTZ at 85 mg/kg. Groups 2–8 were administered with RAF (75 mg/kg), flumazenil (2 mg/kg), flumazenil (2 mg/kg) and RAF (75 mg/kg), sodium valproate (200 mg/kg), flumazenil (2 mg/kg) and sodium valproate (200 mg/kg), diazepam (5 mg/kg) and flumazenil (2 mg/kg) and diazepam (5 mg/kg) doses, respectively, followed by PTZ (85 mg/kg) after 30 min of injection of the drugs. The responses were recorded within 30 min after PTZ administration.

##### *Effects of ketamine on anticonvulsant effects of RAF of ethanol leaf extract of Ipomoea asarifolia on PTZ-induced seizures*

The mice were distributed into eight groups having six mice each ( $n=6$ ). Group 1 served as control received distilled water 10 ml/kg and PTZ (85 mg/kg). Groups 2–8 received RAF (75 mg/kg), ketamine (5 mg/kg), ketamine and RAF, sodium valproate (200 mg/kg), ketamine and sodium valproate, diazepam (5 mg/kg), and ketamine and diazepam, respectively, followed by 85 mg/kg of PTZ after 30 min. The responses were recorded within 30 min after PTZ administration.

##### *Effects of naloxone on anticonvulsant effects of RAF of ethanol leaf extract of Ipomoea asarifolia on PTZ-induced seizures*

The mice were grouped randomly into 8 containing six mice each ( $n=6$ ). Group 1 served as control received distilled water 10 ml/kg and PTZ (85 mg/kg). Groups 2–8 received RAF (75 mg/kg), naloxone (1 mg/kg), naloxone and RAF, sodium valproate (200 mg/kg), naloxone and sodium valproate, diazepam (5 mg/kg) and naloxone and diazepam, respectively, followed by PTZ (85 mg/kg) after 30 min. The responses were recorded within 30 min after the administration of PTZ.

At the end of the screening for anticonvulsant activities, all the animals were humanely euthanized. Prior to the experiment, simple randomization was used for the groupings of the animals; however, it was concealed to all research team members except 1 person in order to prevent biasness.

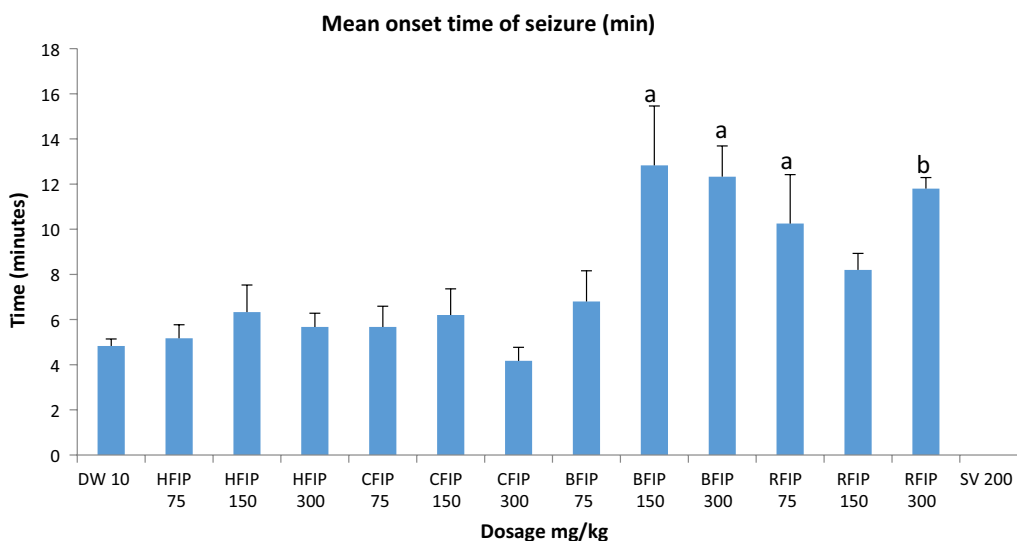
#### Statistical analysis

The data obtained were presented as mean  $\pm$  SEM. One-way analysis of variance (One-way ANOVA) followed by Tukey or Dunnett post hoc tests was conducted using Statistical package for social sciences (SPSS) version 20. Values of  $P < 0.05$  were considered statistically significant.

#### Results

##### *Effects of fractions of n-hexane, chloroform, n-butanol and RAF of crude leaf extract of Ipomoea asarifolia on PTZ-induced seizures in mice*

Figure 2 shows the effects of fractions of chloroform, *n*-butanol, *n*-hexane and RAF of crude leaf extract of *Ipomoea asarifolia* on PTZ-induced seizures in mice. There *n*-hexane and chloroform could not protect the mice from the PTZ-induced seizures, while *n*-butanol at doses of 150 and 300 mg/kg and RAF at doses of 75 mg and 300 mg/kg have significantly ( $P < 0.01$ ) delayed time onset of PTZ-induced seizures by increasing the mean onset



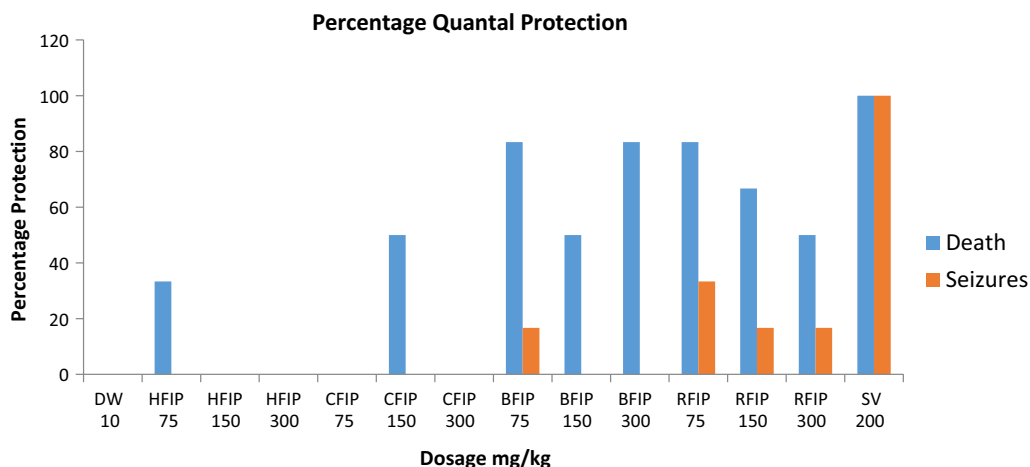
**Fig. 2** The effect of fractions of *Ipomoea asarifolia* on PTZ-induced seizure in mice. DW, distilled water; HFIP, *n*-hexane fraction; CFIP, chloroform fraction; BFIP, *n*-butanol fraction; RFIP, residual aqueous fraction; SV, sodium valproate. a =  $P < 0.01$ , b =  $P < 0.001$

time as compared to the standard. The standard control sodium valproate at 200 mg/kg completely protected the mice from seizure.

**Quantal protection effects of fractions of chloroform, *n*-butanol, *n*-hexane and RAF of crude leaf extract of *Ipomoea asarifolia* against PTZ-induced death in mice**

Figure 3 shows quantal protection against seizure and protection against mortality. There is no protection by *n*-hexane and chloroform fractions at all the tested doses against seizure, while *n*-butanol and RAF have shown

some level of protection at doses of 75 mg for *n*-butanol fraction and at all tested doses of residual aqueous fraction (RAF) compared to the negative standard. Sodium valproate has protected all the mice from seizure as shown above (100%). The *n*-hexane and chloroform fractions have shown low level of protection against death, as only at dose of 75 mg/kg for *n*-hexane and 150 mg/kg for chloroform at 33 and 50%, respectively, compared to the standard drug (sodium valproate) that prevent mice death by 100%. Fractions of *n*-butanol and RAF have shown good level of protection against death, and



**Fig. 3** The quantal protection effect of fractions of *Ipomoea asarifolia* on PTZ-induced seizure in mice. DW, Distilled water; HFIP, *n*-hexane fraction; CFIP, chloroform fraction; BFIP, *n*-butanol fraction; RFIP, residual aqueous fraction; SV, sodium valproate

all the tested doses have shown protection against death. The *n*-butanol at doses of 75, 150 and 300 mg/kg, RAF at doses of 75, 150 and 300 mg/kg have shown 83.33, 50, 83.33, 83.33, 66.67 and 50%, respectively, compared to the standard drug sodium valproate at 200 mg/kg that shows 100% protection.

**Mechanistic studies**

**Effect of flumazenil on RAF of ethanol leaf extract of *Ipomoea asarifolia* on PTZ-induced seizures in mice**

The administration of PTZ has induced myoclonic seizure in all the mice in the negative control group, while the administration of RAF at dose of 75 mg/kg significantly ( $P < 0.05$ ) increased the latency of onset of seizure when compared to the negative control. The standard drug diazepam (5 mg/kg) provided 100% protection against PTZ-induced seizures. On interaction of RAF with flumazenil, there was significant reduction ( $P < 0.05$ ) in the anticonvulsant activity of RAF when compared to RAF alone. Similarly, reduction in the anticonvulsant activity of diazepam was also observed when diazepam was interacted with flumazenil from complete abolishing of seizure to significant ( $P < 0.01$ ) reduction in the activity of diazepam (Table 1).

**Effect of ketamine on RAF of ethanol leaf extract of *Ipomoea asarifolia* on PTZ-induced seizures in mice**

The administration of PTZ-induced myoclonic seizure in all the mice in the negative control group, while the administration of residual aqueous fraction of *Ipomoea asarifolia* (RAF) 75 mg/kg significantly ( $P < 0.05$ ) increased the latency of time onset of seizure when compared to the negative control. The standard drug sodium valproate (200 mg/kg) provided 100% protection against

PTZ-induced seizures. On interaction of RAF with Ketamine, there was significant reduction ( $P < 0.05$ ) in the proconvulsant effect of ketamine as compared to ketamine alone. Similarly, reduction in the anticonvulsant activity of sodium valproate (SV) was also observed when it was interacted with ketamine (Table 2).

**Effect of naloxone on RAF of ethanol leaf extract of *Ipomoea asarifolia* on PTZ-induced seizures in mice**

The administration of PTZ induced myoclonic seizure in all the mice in the negative control group, while the administration of residual aqueous fraction of *Ipomoea asarifolia* (RAF) 75 mg/kg significantly ( $P < 0.05$ ) increased the latency of time onset of seizure when compared to the negative control. The standard drug sodium valproate (200 mg/kg) provided 100% protection against PTZ-induced seizures. On interaction of RAF with naloxone (1 mg/kg), there was significant reduction ( $P < 0.05$ ) in the anticonvulsant activity of RAF when compared to RAF alone. Similarly significant ( $P < 0.01$ ) reduction in the anticonvulsant activity of sodium valproate was also observed when it was interacted with naloxone 1 mg/kg (Table 3).

**Discussion**

The fractions of the ethanol leaf extract of *Ipomoea asarifolia* were subjected to PTZ- and MEST-induced models of seizures. The fractions tested were chloroform, *n*-butanol, *n*-hexane and RAF. *n*-hexane fraction (HF) and chloroform fraction (CF) did not show anticonvulsant effects, while *n*-butanol (BF) and RAF have shown anticonvulsant activities. In the HF fraction, the presence of cardiac glycosides, saponins and steroids was observed, while CF has cardiac glycosides, flavonoids and

**Table 1** Effects of flumazenil on RAF of ethanol leaf extract of *Ipomoea asarifolia* on PTZ-induced seizure in mice

Treatment (mg/kg)	Onset of seizures (min.)	Quantal protection	%Protection against seizures	%Protection against mortality
D/W (10 ml/kg)	4.00 ± 0.26	0/6	0.00	66.67
RAF (75)	10.17 ± 1.70*	1/6	16.67	83.33
FLU (2)	7.17 ± 1.67	0/6	0.00	83.33
FLU (2) + RAF (75)	5.83 ± 0.40 <sup>#</sup>	0/6	0.00	50.00
SV (200)	–	6/6	100.00	100.00
FLU (2) + SV (200)	25.00 ± 1.00**	4/6	66.67	100.00
DZP (5)	–	6/6	100.00	100.00
FLU (2) + DZP (5)	12.60 ± 2.23**	0/6	0.00	100.00

D/W, distilled water; RAF, residual aqueous fraction of *Ipomoea asarifolia*; FLU, flumazenil; DZP, diazepam; SV, sodium valproate

Values are presented as mean ± SEM

\* $P < 0.05$ ; \*\* $P < 0.01$  as compared to D/W group

<sup>#</sup> $P < 0.05$  as compared to RAF group—One-way ANOVA followed by Tukey post hoc test,  $n = 6$

**Table 2** Effects of ketamine on RAF of ethanol leaf extract of *Ipomoea asarifolia* on PTZ-induced seizure in mice

Treatment (mg/kg)	Onset of seizures (min.)	Quantal protection	%Protection against seizures	%Protection against mortality
D/W (10 ml/kg)	4.00 ± 0.26	0/6	0.00	66.67
RAF (75)	10.17 ± 1.70*	1/6	16.67	83.33
KETA (200)	1.17 ± 0.17*	0/6	0.00	83.33
KETA (200) + RAF (75)	2.33 ± 0.67 <sup>#</sup>	0/6	0.00	50.00
SV (200)	–	6/6	100.00	100.00
KETA (200) + SV (200)	17.50 ± 0.50**	4/6	66.67	100.00
DZP (5)	–	6/6	100.00	100.00
KETA (200) + DZP (5)	–	6/6	100.00	100.00

D/W, distilled water; RAF, residual aqueous fraction of KETA; KETA, ketamine; DZP, diazepam; SV, sodium valproate

Values are presented as mean ± SEM

\* $P < 0.05$ ; \*\* $P < 0.01$  as compared to D/W group

<sup>#</sup>  $P < 0.05$  as compared to RAF group—One-way ANOVA followed by Tukey post hoc test,  $n = 6$

**Table 3** Effects of naloxone on RAF of ethanol leaf extract of *Ipomoea asarifolia* on PTZ-induced seizure in mice

Treatment (mg/kg)	Onset of seizures (Min.)	Quantal protection	% Protection against seizures	% Protection against mortality
D/W (10 ml/kg)	4.00 ± 0.26	0/6	0.00	66.67
RAF (75)	10.17 ± 1.70*	1/6	16.67	83.33
NAL (1)	6.00 ± 1.14	0/6	0.00	50.00
NAL (1) + RAF (75)	5.80 ± 0.97 <sup>#</sup>	1/6	16.67	100.00
SV (200)	–	6/6	100.00	100.00
NAL (1) + SV (200)	20.00 ± 5.13**	3/6	50.00	100.00
DZP (5)	–	6/6	100.00	100.00
NAL (1) + DZP (5)	–	6/6	100.00	100.00

D/W, distilled water; RAFI, residual aqueous fraction of *Ipomoea asarifolia*; NAL, naloxone; DZP, diazepam; SV, sodium valproate

Values are presented as mean ± SEM

\* $P < 0.05$ ; \*\* $P < 0.01$  as compared to D/W group

<sup>#</sup>  $P < 0.05$  as compared to RAF group—One-way ANOVA followed by Tukey post hoc test,  $n = 6$

steroids. Qualitative phytochemical analyses of the active fractions (BF and RAF) have shown presence of alkaloids, cardiac glycosides, flavonoids, tannins and saponins. Flavonoids and saponins are known to possess anticonvulsant activities (Saikia et al. 2016; Choudhary et al. 2011). The anticonvulsant activities shown by BF and RAF are seen in PTZ-induced seizure but not observed in MEST, a non-mechanistic seizures model. It was designed to test for drugs that can abolish hind limb tonic extension (HLTE) (Stables and Kupferberg 1997). There is increasing activity of the fractions with increasing polarity as seen with presence of saponins and flavonoids which are polar (BF and RAF). Substance that inhibits voltage-dependent  $\text{Na}^+$  channels can prevent MES-induced tonic extension (Rogawski and Porter 1990). Both RAF and

BF did not have effects on MES-induced seizures which probably show that they do not interfere with voltage-dependent  $\text{Na}^+$  channels. Flavonoids are both polar and non-polar; flavonoid glycosides are soluble in polar solvent while flavonoid aglycones are not, while saponins are polar compounds. Saponins are also known to possess anticonvulsant activity (Singh and Goel 2016). The flavonoids and saponins in BF and RAF are probably responsible for the anticonvulsant activity seen in PTZ-induced seizures. The study has also shown that the RAF is the most active fraction of the leaf extract of *Ipomoea asarifolia* with ( $P > 0.01$ ), 33% quantal protection against seizure and 88.3% protection against mortality. Saponins are also known to bind to  $\text{GABA}_A$  receptor in rat brain (Kim et al. 2001) and it is also shown to inhibit NMDA

receptor mediated epileptic discharge in a cultured hippocampal neuron (Kim and Rhim 2004). Flavonoids have also been shown to act on GABA<sub>A</sub> receptors through the benzodiazepine-binding site, as well as independently of the benzodiazepine-binding site (Chua et al. 2015). However, many flavonoids cause biphasic responses, inhibiting GABA actions at high concentrations and conversely enhancing at low concentrations. Additionally, other flavonoids, at high concentration act as agonist in the absence of GABA by directly gating the receptor (Chua et al. 2015). Some tannins (ellagic acid) have also shown been to possess anticonvulsant activities (Sharma and Kaushik 2018) and alkaloids (Taesotikul et al. 1998). The anticonvulsant activity of RAF can be attributed any of the phytochemical constituents from the plant *Ipomoea asarifolia*.

GABA is known to play a great role as inhibitory neurotransmitter by acting on the GABA<sub>A</sub> receptors leading to influx of chloride ions resulting in hyperpolarisation. GABA<sub>A</sub> receptor is the main receptor that is implicated in seizure disease; it is a pentameric cys-loop ligand gated ionotropic receptor consisting of five subunits of proteins (2 $\alpha$ , 2 $\beta$  and 1 $\gamma$ ). The GABA<sub>A</sub> receptor has two receptor binding sites with benzodiazepine-binding site between gamma and alpha peptide subunits, while the normal GABA binding (picrotoxin) site is between alpha and beta peptide subunits. Enhancement of GABAergic receptors at the hippocampus and dentate gyrus result in brain inhibitory function, while inhibition of GABAergic receptors leads to decrease or blockade of the inhibitory function in the brain allowing glutamatergic excitatory function to takeover. Flumazenil, a non-competitive GABA<sub>A</sub>/benzodiazepine-binding site-specific antagonist of GABA inhibitory function (Brogden and Goa 1998), was used in the interactive studies. PTZ, chemoconvulsant used induced seizure by blocking GABA receptor chloride channel (De Deyn et al. 1992). In the study, RAF alone has significantly ( $P < 0.05$ ) increased the mean onset time of seizure of mice in PTZ-induced seizure leading to increase in seizure threshold as compared to the negative control, but on interacting flumazenil with RAF, it reverses the anticonvulsant effect of the RAF, and since flumazenil is BDZ specific receptor of GABA<sub>A</sub> receptor, it signifies the RAF may act via the BDZ receptor site of GABAergic pathway. The standard drug diazepam a known BDZ receptor site agonist protected the mice completely, but interacting diazepam with flumazenil decreases its activity leading to seizure. This action also supports that fact that RAF may be acting via the GABAergic pathway. It is observed that an agent that blocks PTZ-induced seizures and raises electrical impulse threshold is effective against absence seizure (De Deyn et al. 1992).

Glutamate is brain's major excitatory neurotransmitter that acts on AMPA, NMDA and KA receptors in the brain; this pathway plays a vital role in epilepsy. Activation of metabotropic and ionotropic postsynaptic glutamate receptors can lead to seizures. NMDA receptor is a tetramer that is control by 7 genes, namely GluN1, GluN2A-GluN2D and GluN3A-GluN3B. The tetrameric structure of the receptor is made up of a pair of 2-GluN1 proteins and a combination of any other 2 from the other proteins. Glutamate does not bind with GluN1 protein, the others as glycine and d-serine bind to GluN1 proteins. Agents that act as *n*-methyl-D-aspartate (NMDA) receptors antagonist are good anticonvulsants in many laboratory animals' models of epilepsy (Kumar and Singh 2016). The NMDA receptor has NMDA and phencyclidine binding site (Aram et al. 1989). Ketamine, an NMDA receptor non-competitive antagonist (Dingledine et al. 1999), is used in treatment of seizures (status epilepticus); it blocks the influx of Ca<sup>2+</sup> (Potter and Choudhury 2014). Ketamine combines with phencyclidine binding site on the NMDA receptor and blocks Ca<sup>2+</sup> and Na<sup>+</sup> leading to reduction in epileptiform discharge and neuronal excitability resulting in its anticonvulsant effect (Aram et al. 1989). However, ketamine at high doses has proconvulsant effects. Ketamine, an anesthetic agent is also known to display both anticonvulsant and proconvulsant effects (Moza 2020). Ketamine sits on the ion channel and blocks it which can result to disruption of glutamate functions (Sleigh et al. 2014). As seen in ketamine, it acts as anticonvulsant at lower dose and act as proconvulsant at high dose (Abend and Dlugos 2008). At dose range of 0.5–50 mg/kg, ketamine has shown to be anticonvulsant in a PTZ-induced seizure (Ghasemi et al. 2010); however, experimental evidence has shown that ketamine is proconvulsant in PTZ-induced seizure at higher dose (Dashputra et al. 2012). RAF has significantly ( $P < 0.05$ ) increased the mean onset time of seizure in mice in PTZ-induced seizures as compared to negative control. The ketamine at the dose of 200 mg/kg has significantly reduced ( $P < 0.05$ ) the mean onset time of seizure of mice resulting in decrease in seizure threshold as compared to the negative control, this shows the proconvulsant effect of ketamine at higher dose. On interacting ketamine with RAF, RAF has significantly ( $P < 0.05$ ) reduced the proconvulsant effect of ketamine as compared to ketamine alone. This implies that RAF has block the activity of ketamine an NMDA antagonist and hence the possibility of RAF acting through the glutamatergic pathway.

Opioid receptors are heterotrimeric G-protein couple receptors which belong to the large family of rhodopsin with 7 transmembrane domains. It consists of 3 subunits: alpha, beta and gamma. The opioid receptors are

classified into four different types of receptors, namely mu opioid receptor ( $\mu$ OR), kappa opioid receptor ( $\kappa$ OP), delta opioid receptor ( $\delta$ OP) and opioid receptor like-1 (ORL1). It is a known fact that seizures are also being modulated via the opioidergic pathways (Hong 1991). Studies have shown that morphine an agonist of mu receptor ( $\mu$ OR) has both anticonvulsant and proconvulsant effects at low and high doses, respectively, on chemo-convulsive agents (Foote and Gale 1984). Naloxone is an opioid receptors antagonist and reverses effects mediated via opioidergic pathways. The RAF has significantly ( $P < 0.05$ ) increased the mean onset of time of PTZ-induced seizure; even though naloxone possesses proconvulsant effect, it shows no significant effect on the mean onset time of seizure. This may probably be due to different pathway from PTZ as it acts via GABA. On interacting naloxone with RAF, naloxone has significantly ( $P < 0.05$ ) reduced the anticonvulsant effect of RAF by decreasing the seizure threshold as compared to RAF alone. This suggests that RAF may again owe its anticonvulsant activity via the opioidergic pathway.

## Conclusions

The butanol (BF) and residual aqueous fractions (RAF) of leaf of *Ipomoea asarifolia* have shown anticonvulsant activities in PTZ-induced seizures. This activity is probably due to the presence of saponins and flavonoids in the respective fractions. RAF was observed to be the most active fraction and probably owes its anticonvulsant property via GABAergic, glutamatergic and opioidergic pathways.

## Abbreviations

$\mu$ OR: Mu opioid receptor;  $\kappa$ OP: Kappa opioid receptor;  $\delta$ OP: Delta opioid receptor; ORL1: Opioid receptor like-1; BF: Butanol; RAF: Residual aqueous fractions; NMDA: *n*-Methyl-D-aspartate; PTZ: Pentalenetetrazole; HLTE: Hind limb tonic extension; HF: *n*-Hexane fraction; CF: Chloroform fraction; BF: *n*-Butanol.

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## Author contributions

SSC, ABN, SMC, YJ, AM and LAB were involved in conceptualization; SSS and ABN were involved in experiments; YJ, AM and LAB were involved in supervision; SSC, ABN and SMC were involved in data analysis; SSC, ABN and SMC were involved in writing draft; YJ, AM and LAB revised the manuscript. All authors read and approved the final manuscript.

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## Availability of data and materials

Data will be given on request through the corresponding author.

## Declarations

### Ethics approval and consent to participate

The experimental procedures were carried out strictly in accordance with the "Guide to the care and use of laboratory animals in research and teaching" as detailed in NIH publications volume 25 No. 28 revised in 1996 (National Research Council 2011).

### Consent for publication

Not applicable.

### Competing interests

The authors declare no conflicts of interest.

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