Original Research Article

JOURNAL OF BASIC PHARMACOLOGY AND TOXICOLOGY

Anticonvulsant activity of corn silk (*Stigma maydis*)

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Abstract

Corn silk of *Zea mays* L. (*Stigma maydis*) (Family: Poaceae) is used in Ibibio ethnomedicine for the treatment of various diseases such as CNS disorders. The ethanol corn silk extract of *Z. mays* (170 - 510 mg/kg) was investigated for anticonvulsant activity in mice using pentylene tetrazol and aminophylline-induced convulsion models to assess anticonvulsant activity. The extract was found to significantly ($p < 0.005$ - 0.01) offer protection against PTZ- and aminophylline-induced convulsions in mice. The corn silk extract of *Z. mays* possesses anticonvulsant activity and this supports its use in ethnomedicine for the treatment of central nervous system disorders.

Keywords: *Zea mays*, cornsilk, anticonvulsant

1. Introduction

Zea mays L. (Family: Poaceae) also known as corn or maize, is a large grain plant first domesticated by indigenous people in Mexico about 10,000 years ago [1]. It is an annual grass plant cultivated for human consumption and rearing of animals. It was introduced to Nigeria in the 16th century [1].

Besides its nutritive values of maize grains, the leaves, corn silks, stalk, and inflorescence are also used in ethnomedicine for the treatment of several ailments. The corn silk is used as an antidiabetic or diuretic, and decoction of the silk is consumed for the treatment of urinary troubles and gallstones [2].

Traditionally corn silk was used in many parts of the world for the treatment of cystitis, gout, kidney stones, malaria, prostate hypertrophy, nephritis and heart disorders [3].

Secondary metabolites like flavonoids, saponins, alkaloids, tannins, chlorogenic acid, allantoin, and phytosterols as well as flavonoids such as maysin, apigmaysin, 3-methoxymaysine and ax-4-OH-maysin have also been identified from corn silk [4]. Biological activities include antioxidative [5, 6], diuresis and kaliuresis effect [7], hyperglycemic effect [8], nephroprotective activity [9], antifatigue[10], antidepressant activity [11], antihyperlipidemic activity [12], antidiabetic effects [13, 14], antiinflammatory activity [15, 16, 17], antitumour [16], hepatoprotective [18], antioxidant [4, 19, 20, 21, 22, 23, 24] anticancer [25], α-amylase inhibitory effect [26], antidiabetic and hypolipidemic activities [27, 28, 29]. In this study, we report the anticonvulsant activity of the corn silk extract and fractions of *Zea mays*.

2. Materials and methods

2.1. Plant materials

The fresh corn silk of *Zea mays* was collected in August, 2018 at farmland in Uyo village in Uyo LGA, Akwa Ibom State, Nigeria. The plant was identified and authenticated as *Zea mays* by Dr. Margaret Bassey, a taxonomist in the Department of Botany and Ecological studies, University of Uyo, Uyo, Nigeria. Herbarium specimen was deposited at the Faculty of Pharmacy Herbarium, University of Uyo, Uyo.

2.2. Extraction

The plant parts (corn silk) were washed and air dried on laboratory table for 2 weeks. The dried corn silk were pulverized using a pestle and mortar. The powdered corn silk was macerated in 95% v/v ethanol for 72 hr. The liquid ethanol extract obtained by filtration was evaporated to dryness in a rotary evaporator 40˚C. The extract was stored in a refrigerator at 4 ˚C until used for experiment reported in this study.

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2.3. Animals

The animals (Swiss albino mice) of either sex were used for the experiments. The animals were housed in standard cages and were maintained on a standard pellet feed (Guinea feed) and water *ad libitum.* Permission and approval for animal studies were obtained from the College of Health Sciences Animal Ethics Committee, University of Uyo, Nigeria.

2.4. Determination of median lethal dose (LD_{50})

The median lethal dose (LD_{50}) of the extract was estimated using albino mice by intraperitoneal (i.p.) route using the method of Lorke [30]. This involved intraperitoneal administration of different doses of the extract (100 - 1000 mg/kg) to groups of three mice each. The animals were observed for manifestation of physical signs of toxicity such as writhing, decreased motor activity, decreased body/limb tone, decreased respiration and death. The number of deaths in each group within 24 hr was recorded. The LD_{50} was calculated as geometrical means of the maximum dose producing 0% (a) and the minimum dose producing 100% mortality (b).

$LD_{50} = \sqrt{ab}$

2.5. Anticonvulsant activity

2.5.1. Pentylene tetrazol-induced convulsion

Anticonvulsant effect of the extract was assessed using a modified method of Vellucci and Webster [31] on overnight fasted mice. The mice were divided into five groups of six animals each and treated with 170, 340 and 510 mg/kg of the corn silk extract respectively, phenobarbitone, 40 mg/kg one hr before induction of convulsion. Seizure was induced in each group of mice with pentylene tetrazol (PTZ) (70 mg/kg i.p.). Control group received normal saline. The onset of clonic/tonic convulsion and the mortality rate was recorded and compared with the respective control group. The ability of the plant extract to prevent or delay the onset of the hind limb extension exhibited by the animals was taken as an indication of anticonvulsant activity [32].

2.5.2. Aminophylline-induced convulsion

The extract was evaluated for activity against aminophylline-induced convulsion using the method of Juliet *et al*. [33]. The mice were divided into 5 groups of six animals each and treated with 170, 340 and 510 mg/kg of the extract respectively and phenobarbitone, 40 mg/kg one hr before induction of convulsion. Seizure was induced using aminophylline (280 mg/kg, i.p.). The animals were observed for 120 min after the administration of aminophylline and the following parameters were noted; time to onset of myoclonic jerks in min, time to onset of tonic convulsions in min, time to death during experimental time of 120 min and number of mice dead/alive at 24 hr.

3. Results

3.1. Determination of LD_{50}

The median lethal dose (LD_{50}) was calculated to be 1732.05 mg/kg. The physical signs of toxicity included excitation, paw licking, increased respiratory rate, decreased motor activity, gasping, convulsion and coma which was followed by death.

3.2. Pentylene tetrazol-induced convulsion

Administration of corn silk extract of Z. mays (170 - 510 mg/kg) provided a considerable degree of protection for the mice against seizure induced by pentylene tetrazol. The extract prolonged the time for onset of myoclonic convulsion in a dose-dependent fashion and this was only significant ($p < 0.001$) at the highest dose (510 mg/kg) and comparable to that of the standard drug, phenobarbitone (Table 1). The lower doses (170 and 340 mg/kg) could not offer any considerable protection against onset of myoclonic convulsion. Similarly, the extract exerted a significant ($p < 0.05$ - 0.01) prolongation of time for onset of tonic convulsion in a dose-dependent manner (Table 1). The standard drug, phenobarbitone also offered 100% protection to the animals treated with it.

Table 1. Effect of ethanol extract of *Corn silk* on pentylene tetrazol-induced convulsion

Treatment	Dose (mg/kg)	Onset of myoclonic	Onset of Tonic	No. of deaths
Control normal saline	-	0.49 ± 0.07	1.14 ± 0.02	6/6
Phenobarbitone	40	1.26 ± 0.28[c]	0.00 ± 0.00[c]	6/6
Corn silk extract	170	0.61 ± 0.12	6.08 ± 1.00	6/6
	340	1.01 ± 0.09	13.75 ± 1.87[b]	6/6
	510	1.66 ± 0.52[c]	25.12 ± 0.67[c]	6/6

Data are expressed as Mean ± SEM, Significant at [a]$p < 0.001$, when compared to control. (n=6).

Table 2: Effect of ethanol extract of *Corn silk on* aminophylline-induced convulsion

Treatment	Dose (mg/kg)	Onset of myoclonic	Onset of Tonic	No. of deaths
Control normal saline	-	6.47 ± 0.83	8.26 ± 1.11	6/6
Phenobarbitone	40	23.00 ± 1.20[c]	0.00 ± 0.00[c]	6/6
Corn silk extract	170	3.77 ± 0.28	14.55 ± 1.07[b]	6/6
	340	3.13 ± 0.12	13.47 ± 1.12[a]	6/6
	510	7.40 ± 0.10	13.12 ± 0.02[a]	6/6

Data are expressed as mean ± SEM, significant at [a]$p < 0.001$, when compared to control (n=6).

3.3. Aminophylline-induced convulsion

The administration of *Z. mays* corn silk extract (170 - 510 mg/kg) provided a considerable degree of protection for the mice against seizure induced by aminophylline. The extract offered little or insignificant ($p > 0.05$) protection to the mice against onset of myoclonic convulsion. However, there was a significant ($p < 0.05$ - 0.01) prolongation of time for onset of tonic convulsion at all doses though more pronounced at the lowest dose (170 mg/kg). The standard drug, phenobarbitone also offered 100% protection to the animals treated with it (Table 2).

4. Discussion

Medicinal plants are used in different parts of the world to manage seizures [34]. The Ibibios use corn silk of *Z. mays* in the management of convulsions. Herbs are potential candidates for development of anticonvulsant/antiepileptic drugs which can be used in the management and treatment of this disorder due to their antioxidant activities [35, 36]. The corn silk extract was evaluated for anticonvulsant activity against aminophylline and PTZ-induced convulsion in mice.

The corn silk extract was found in this study to offer significant protection against PTZ-induced convulsion. According to De Sarro *et al.,* [37], pentylene tetrazol (PTZ) is suggested to exert its convulsant effect by inhibiting the activity of gamma aminobutyric acid (GABA) at $GABA_A$ receptors. Gamma aminobutyric acid is the major inhibitory neurotransmitter which is implicated in epilepsy. The enhancement and inhibition of the neurotransmission of GABA will attenuate and enhance convulsion respectively [38, 39]. Phenobarbitone and diazepam, standard antiepileptic drugs, have been shown to exert their antiepileptic effects by enhancing GABA-mediated inhibition in the brain [40, 41]. These drugs are reported to antagonise PTZ-induced convulsion [42] by enhancing GABA neurotransmission. Phenytoin was unable to prevent PTZ- induced seizure because it is thought to exert its antiepileptic effect by blocking sodium ions into brain cells thus inhibiting generation of repetitive action potentials [40]. Since the corn silk extract of *Zea mays* was able to delay PTZ–induced convulsion, this also confirm its CNS anticonvulsive effect.

The corn silk extract was found to offer considerable degree of protection against aminophylline-induced convulsion. The exact mechanisms of seizures induced by aminophylline appear to be diverse, multiple and complex, and also unclear. Evidence suggests that seizures induced by aminophylline, could be the result of adenosine receptor antagonism or due to inhibition of cerebral nucleotidase activity [43, 44], which lower the adenosine content in the brain and eventually lead to a process of disinhibition. However, report has it that di-phenylhydantoin a potent inhibitor of adenosine uptake was ineffective in preventing these seizures [45]. Apart from non-specific adenosine receptor antagonism [46], aminophylline is thought to have inhibitory influence on adenosine synthesis. At higher doses, inhibition of phosphodiesterase activity including mobilization of intracellular calcium ions from labile stores are said to be implicated in aminophylline-induced seizures [47, 48]. However, a report by Ray et al., [49], has implicated oxidative stress due to the generation of free radicals and reactive oxygen species to be responsible for the seizures induced by aminophylline. Corn silk extract has been reported to possess antioxidant activity which could be implicated in its action against aminophylline-induced convulsion.

Secondary metabolites from plants such as flavonoids have been reported to possess antiepileptic activity by modulating the GABAA-Cl-channel complex, as they are structurally similar to benzodiazepines [50]. Some flavonoids, as well as their glycosides, have been reported to exert anxiolytic, sedative, and anticonvulsant effects on the central nervous systems (CNS) [51]. Flavonoids such as rutin, quercetin, and isoquercitrin have been shown to have anticonvulsant effects on experimental epilepsy models [35]. Also, apigenin, a flavonoid, has been characterised as a centrally acting benzodiazepine ligand and was active against picrotoxin-induced convulsions [52]. Corn silk extract has been reported to be rich in flavonoids and other phenolic compounds which are potent antioxidants [4, 19, 20, 21, 22, 24]. These metabolites are likely to act by scavenging free radicals and modulating the GABAA-Cl-channel complex in the CNS, thereby exerting its anticonvulsant activity.

5. Conclusion

The results of this study suggest that the corn silk extract of *Zea mays* possess anticonvulsant activity which maybe due to its phytochemical compounds.

Conflict of Interest

The authors declare that there is no conflict of interest.

Acknowledgements

The authors are grateful to Department of Pharmacology and Toxicology, University of Uyo, Uyo, Nigeria for providing the enabling environment and equipment for the successful completion of this work.

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