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Phyto-pharmacological Benefit of Methanol Whole Plant Extract of *Ocimum canum* Sims. in Chemically-induced Epileptic Rat Model

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Abstract

Objectives: The role of *Ocimum canum* Sim., as a medicinal agent used for the treatment and management of diseases cannot be overemphasized. The aim of the study is to screen the Phytochemical constituents and to evaluate the antiepileptic effect of methanol whole plant extract in Wistar albino rats.

Material and Methods: The whole plant part of *O. canum* was extracted with 85% percentage of methanol and screened for phytochemicals. An acute toxicity study was carried out using Lorke's method and the antiepileptic activity was evaluated using pentylenetetrazole (PTZ) and strychnine in rats. One-way analysis of variance (ANOVA) was used in the analysis of the data.

Results: The phytochemical analysis revealed the presence of saponins, cardiac glycosides, flavonoids, terpenoids, and cardenolides. The intraperitoneal median lethal dose value (LD50) of *O. canum* in rats was 2154 mg/kg. The extract at the dose of 300 and 600 mg/kg body weight protected 40% and 80% of experimental animals against both PTZ and strychnine-induced convulsion; protected 60% and 80% of rats against death induced by strychnine; compared to 100% protection by the standard drug sodium valproate (20mg/kg).

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Antiepileptic, Pentylenetetrazole (PTZ), Strychnine

Conclusion: The antiepileptic investigation suggests that methanol extract of whole plant of *O. canum* has antiepileptic activity which could be employed for the management of epileptic related conditions.

Introduction

Plants have had been a source of food, shelter and medicine. The use of plants medicinally was mostly developed through observing wild animals and trying and failing [1].

The surge in the use of plant in medication formulation is due to the availability, affordability, accessibility, safety, efficiency, and rare side effects of drugs from plants [2]. A lot of drugs listed as conventional medications were derived from plants originally [3]. In Africa, up to 80 % of the population uses traditional medicine for primary health care. Traditional medicine has maintained its popularity in all regions. In Nigeria, Ghana, Mali, and Zambia for example, the first line of treatment for 60 % of children with high fever resulting from malaria, epilepsy and cold is the use of herbal medicines at home [1].

Epilepsy is a major neurological disorder and up to 5% of the world population develop epilepsy in their lifetime [5]. It is a disease that affects about 50 million people across the globe and 85% of this population resides in developing countries, it is the second commonest neurological disorder. The World Health Organization [6] has estimated that 5 million people are diagnosed with epilepsy each year. In Nigeria, the estimated prevalence of epilepsy is 8 per 1000 people indicating a substantial burden of the disease in the country [7]. Available antiepileptic drugs (AED) are synthetic chemicals that have overwhelming side effects such as weight gain, hepatotoxicity, teratogenicity, and withdrawal symptoms [8]. The treatment of epilepsy with available AED is symptomatic as these drugs only prevent seizure and do not cure the underlying disease process in the brain [9]. It is generally estimated that up to 30% of patients are refractory to conventional AED treatment [10]. Although a broad range of newer and more selective agents are currently being used, there is still a need for more selective and less toxic AEDs. Several plants used for the treatment of epilepsy in different systems of traditional medicine have shown activity when tested on modern bioassays for the detection of anticonvulsant activity [4] and many such plants remain to be scientifically investigated.

Figure 1: *Ocimum canum* Sims in its natural habitat

O. canum Sims. (Figure 1) belongs to the family. It is a small herbaceous, erect, perennial, and aromatic plant usually growing 20 – 30 cm tall with some specimens up to 100 cm [11]. The plant is often found in tropical climates, growing on roadsides, in fields, in teak forests, and in open waste place close to settlements. It also often grown as an annual, especially in cooler climates. The entire plant is highly aromatic, with an odour comparable to citrus. As such, it can be used for culinary purposes in similar ways to sweet basil (*O. basilicum*) [11]. The aromatic leaves are used as a flavouring in a range of foods, whilst a cooling drink can be made from the seeds. The plant is gathered from the wild and also often cultivated [11]. Malaysia, and Thailand. Due to the high fragrance nature of the leaves, it is also added to various dishes with fishy or unpleasant smell. Medicinally, the leaves of the plant are used for several ailments. The

The leaves can also be used as a flavouring in salads, sauces, soups etc. The young leaves, which are eaten raw as a vegetable side-dish in Indonesia,

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decoctions are used to treat coughs and for respiratory related conditions, the whole plant is used in baths to treat rheumatism, renal colic, and calcification [12]. Pharmacological investigation which include anaesthetic [13], antimicrobial [14], antioxidant [15], anti-inflammatory [16], anxiolytic [17], and insecticidal effect [18] of the plant has been carried out. This study aimed to scientifically justify the use of this plant for the acclaimed use for the treatment and management of convulsion and related disease in Northeastern Nigeria.

Materials and Methods

Experimental Site

The chemical and pharmacological experiments were conducted in the laboratories of the Department of Pure and Chemistry and Faculty of Pharmacy, University of Maiduguri, Borno State, Nigeria respectively.

Plant Collection and Identification and Preparation

The fresh whole plant *O. canum* was collected from Maiduguri from Konduga Local Government Area, Borno State, Nigeria. The identity of the plant was verified by Professor S.S. Sanusi; a Taxonomist of the Department of Biological Sciences, University of Maiduguri, Borno State, Nigeria. A voucher specimen was deposited at the Herbarium of the Department of Pharmacognosy, Faculty of Pharmacy, University of Maiduguri for future reference. The sample was air-dried under shade for a period of 2 weeks and was size-reduced into coarse powder using mortar and pestle.

Extraction and Preliminary Phytochemical Screening

Two hundred and fifty grammes (250g) of the powdered whole plant was soxhlet extracted using 95% methanol for 6hrs. The obtained solution was then filtered to remove debris, and was concentrated under reduced pressure and the yield was 31g. The extract was transfer into an air-tight container until required for analysis.

The extract was subjected to preliminary phytochemical screening to test for the presence of secondary metabolites, which include: alkaloids, carbohydrates, flavonoids, saponins, tannins, glycosides, (cardiac, steroidal), and terpenes/terpenoids using conventional protocols [19,20,21].

Anticonvulsant Study

Effect of Methanol Whole Plant Extract of *Ocimum canum* on Pentylenetetrazole-Induced Convulsion in Rats

Experimental method of Anticonvulsant study as described by Swinyard *et al*. [22]; Medugu *et al*. [22] and Yakubu *et al*. [24] was adopted in this study. Twenty-five (25) albino rats of both sexes weighing between 100-220 g were used. They were housed in a clean cage and were given food and water *ad libitum*. They were then divided into five groups of five rats and labelled as group A, B, C, D, and E. Group A was given 100 mg/kg of pentylenetetrazole (PTZ) *i.p* and served as the negative control and were not pre-treated. Group B, C, and D were pre-treated intraperitoneally with 300 mg/kg and 600 mg/kg of the extract respectively, 30 minutes before treatment with convulsant (100 mg/kg of PTZ) and Group F was given 5 mg/kg orally of sodium valproate which serve as the positive control as standard anticonvulsant drug. During the experiment the onset of convulsion, number of convulsions per minute, and the duration of convulsions were recorded for 30minutes. Also the number of animals which survived within the period of observation were expressed as percentage (%) protection.

Effect of Methanol Whole Plant Extract of *Ocimum canum* on Strychnine-Induced Convulsion in Rats

The method described by Medugu *et al*. [23] was adopted in this study. In brief, strychnine convulsion was induced by the subcutaneous injection of 1mg/kg of strychnine nitrate in the rats. 30min prior to administration, 2 groups (groups 3 and 4) of 5 animals each were intraperitoneally pre-treated with methanol extract of *Ocimum canum* with doses of 300mg/kg and 600mg/kg. The fourth group was treated with sodium

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valproate (20mg/kg *i.p*) which served as the positive control while the fifth group received normal saline 10ml/kg as the negative control. The rats were observed for tonic extensor jerks of the hind limbs followed by death in 30 minutes. Abolition of tonic extensor jerks of the hind limb was considered an indicator that the extract could prevent strychnine-induced convulsion.

Data Handling

The generated data from the PTZ and strychnine-induced antiepileptic study were express as Mean ± Standard Error of the mean and analyzed by one-way analysis of variance (ANOVA) using Statistical Graphpad Prism Version 9.0 for Windows. Probability value of $P<0.05$ were considered significant.

Results and Discussion

Phytochemical Screening of Methanol Whole Plant Extract of *Ocimum canum*

The phytochemical screening of the methanol extract obtained from the whole plant of *Ocimum canum* revealed the presence of phytochemicals which include flavonoids, terpenoids, cardiac glycosides, cardenolides, carbohydrates, and saponins. The result is presented in Table 2.

Acute Toxicity of Methanol Whole Plant Extract of *Ocimum canum*

The result for acute toxicity (LD_{50}) study obtained is shown in Table 3. The oral and intraperitoneal LD_{50} were $\geqq$5000 mg/kg, as no death was recorded and 3807mg/kg as death occurred at 5000mg/kg dose of the extract respectively.

The Effect of Methanol Leaf Extract of *Ocimum canum* on PTZ-Induced Convulsion in Rats

The methanol extract significantly conferred protection of 40% and 80% against PTZ-Induced convulsion when treated with extract doses of 300 mg/kg and 600 mg/kg respectively in a dose dependent manner. There was also a decrease in the number of convulsion, onset of convulsion while there was a significant increase in time of death. The result of this study is presented in Table 3.The Effect of Methanol Extract of *O. canum* on Strychnine-Induced Convulsion in Rats

The extract of *O. canum* at doses of 300 and 600mg/kg conferred 40% and 80% respectively against strychnine-induced death. The extract acted by significantly ($P<0.05$) prolonging the onset of convulsion and time of death in a dose-dependent manner; while sodium valproate (+ve control drug) had 100% protection effect against strychnine induced convulsion. Result of the study is shown in Table 4.

Table 1: Phytochemical Analysis of *O. canum* Whole Plant Methanol Extract

S/N	Phytochemical Test	Inference
1	Carbohydrates	+
2	Tannins	–
3	Phlobatannins	–
4	Cardiac glycosides	+
5	Flavonoids	+
6	Terpenes	+
8	Saponins	+
9	Soluble starch	–

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10	Alkaloids	_
11	Steroidal nucleus	+

Table 2: Intraperitoneal (IP) Acute Toxicity Effect of *O. canum* whole Plant Methanol Extract

Phase	**Dose (mg/kg)**	**No. of rat**	**Mortality rate** IP route
I	10	3	0/3
	100	3	0/3
	1000	3	1/3
II	600	1	0/1
	1000	1	0/1
	16000	1	0/1
	2900	1	1/1

Ip LD_{50} = 2154 mg/k

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Table 3: Effect of *O. canum* Whole Plant Extract of Methanol on Pentylenetetrazole-induced Epilepsy in Rats

Extract pretreatment (mg/kg	Mean±SEM onset of spasm (min)	Mean±SEM onset of convulsion (min)	Mean±SEM onset of death (min)	Quantal death	Survival (%)
Control Vehicle	7.94±0.32	7.48±1.00	18.20±0.46	1/5	20
Control + 100 mg/kg of PTZ	18.54±0.47	7.32±1.00	17.58±0.25	1/5	20
300 mg/kg + 100 mg/kg of PTZ	11.68±2.07	12.18±0.30	21.34±0.35	2/5	40
600 mg/kg + 100 mg/kg of PTZ	17.68±0.34	18.24±0.41	36.82±10.02	4/5	80
Sodium Valproate (20mg/kg)	7.94±0.32	0.20±0.20	0.00±0.00	5/5	100

Results are in mean±standard error of mean (SEM); n=5; data with the same superscript across columns are statistically not significant (p>0.05)

Table 3: Effect *of O. canum* Whole Plant Methanol Extract on Strychnine-Induced Epilepsy in Rats

Extract pretreatment (mg/kg	Mean±SEM onset of spasm (min)	Mean±SEM onset of convulsion (min)	Mean±SEM onset of death (min)	Quantal death	Survival (%)
Control Vehicle	7.94±0.32	7.48±1.00	18.20±0.46	1/5	20
Control + 100 mg/kg of PTZ	18.54±0.47	7.32±1.00	17.58±0.25	1/5	20
300 mg/kg + 100 mg/kg of PTZ	11.24±0.60	15.20±0.37	24.50±0.21	2/5	40
600 mg/kg + 100 mg/kg of PTZ	6.36±0.16	21.70±70	27.02±0.39	3/5	80
Sodium Valproate (20mg/kg)	7.94±0.32	0.20±0.20	0.00±0.00	5/5	100

Results are in mean±standard error of mean (SEM); n=5; data of same column are all statistically significant (p<0.05)

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The present phytochemical study of the methanol whole plant *O. canum* showed that the plant contains phytochemicals of pharmacological importance and has garnered scientific interest, these includes flavonoids, cardiac glycosides, tannins, saponins, and steroids. This report is supports by the findings of [25] whose study revealed the presence of coumarins, flavanoids, glycosides, phenols, tannins, saponins, and steroids, while alkaloids were not detected. Therapeutic benefits of traditional remedies might depend upon individual or combination of these constituents [26], such as those identified in the extract of this plant.

The most abundant phytochemical detected in the present work is terpenoids. It is one of the most abundant phytochemical found in mostly leaves and seeds of plants as volatile oils. It acts as phyto-alexins in plant direct defense responses which involves herbivores and their natural enemies [27]. They are reported to have neuro-pharmacological activity including anticonvulsant activity [28]. Flavonoids is another interesting class of plants' chemical having broad biological and pharmacological activities which act as powerful antioxidants which helps to protect the human body from free radicals and reactive oxygen species [29]. They have been found to inhibit almost all the mechanisms involved in seizures generation in epilepsy. They have been found to modulate neuronal Na^+ channels [30], Ca^{2+} channels [31], GABAergic pathway glutamatergic pathway and opioid pathway [32].

The intrapertoneal median lethal dose value (LD_{50}) of *O. canum* in mice was 2154 mg/kg. According to Clarke and Clarke [33] any substance whose LD_{50} is greater than 1,000 mg/kg is considered non-toxic and can be said to be a good candidate for further research or as a drug or food.

Protection of the experimental animals against pentylenetetrazole (PTZ)-induced seizure predicts anticonvulsant activity and the delayed onset of seizure indicates that it can raise seizure threshold [34]. The anticonvulsant activity of *O. canum* at doses of 300 mg/kg and 600 mg/kg intraperitoneally (i.p) was studied by PTZ-induced seizure model. Pentylenetetrazole (PTZ) is an antagonist of gamma-aminobutyric acid receptors that induces acute convulsions in rodents [35] and it also reduces the T-type of Ca^{++} currents [36]. Since the methanol whole plant extract of *O. canum* delayed the occurrence of PTZ-induced convulsion, it is likely that it may be interfering with GABAergic mechanism to exert it is anticonvulsant activity.

Strychnine is a known convulsant which directly antagonizes the inhibitory spinal reflexes of glycine [37]. The crude extract of the whole plant of *O. canum* at doses of 300 mg/kg and 300mg/kg protected 60% and 80% of the rats against strychnine-induced death. Strychnine induces convulsion by interfering with postsynaptic inhibition mediated by glycine which is an important inhibitory transmitter of the motor neurons and interneurons in the spinal cord. It acts as a competitive and selective antagonist at all glycine receptors [38]. The ability of the extract to prevent the strychnine-induced seizures amasses the anticonvulsant effects mediated via glycine receptors [39].

Conclusion

The methanol extract of the whole plant of *O. canum* contains saponins, cardiac glycosides, flavonoids, terpenoids, and cardenolides. The whole plant methanol extract had no observable toxic effect on rats within the duration of time evaluated. The anticonvulsant property of the methanol extract was evaluated using two animal models – Pentylenetetrazole and strychnine. The study revealed a significant and promising anticonvulsant effect of the extract which could be attributed to the presence of the individual or synergistic effect of the phytochemicals.

Conflict of Interest

The authors declared no conflicts of interest.

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