ABSTRACT

Alzheimer's disease (AD), the most common form of dementia in the elderly is a neurodegenerative disease that affects 47 millions of people worldwide. The first treatment against Alzheimer's disease are acetylcholinesterase inhibitors; however, these medications are associated with many side effects. Buchholzia coriacea seed popularly called "wonderful kola" because of its usage in traditional medicine to treat variety of illnesses. It's also called memory nut because its suspected to enhance memory and cognition. In this study, we investigated the efficacy of (Aqueous, ethanolic, ethyl acetate & n-hexane fractions) against scopolamine-induced cognitive impairment in experimental of rats. A total of 49 Wistar rats (190 -230g) were used and a total of 7 groups (n=7). Scopolamine (1mg/kg i.p), an amnesic drug was used for impairing memory. 100 mg/kg of each Buchholzia coriacea seed fractions were evaluated for amnesic activity by Morris water maze and Y maze memory model. Donepezil (5mg/kg) was used as standard drug. Animals were sacrificed after 14 days and evaluation of biochemical parameters was done via Malondialdehyde (MDA), Superoxide Dismutase (SOD), reduced Glutathione (GSH), Catalase (CAT). Histopathological analysis was done via H&E stain. All fractions mitigated the neurodegeneration seen in scopolamine alone treated group except for ethyl acetate fraction. Treatment with Buchholzia coriacea fractions significantly decreased escape latency and increased number of crossing for Morris water maze while % alternation was increased in Y maze. The aqueous and hexane fractions did better than the others. The fractions increased the activity of SOD, GSH and CAT while decreasing MDA. These results indicated that the seeds of Buchholzia coriacea might be a promising therapeutic agent for the treatment of cognitive dysfunction in addition to its already established medicinal properties.

KEYWORDS: Buchholzia coriacea, Alzheimers disease, memory loss, scopolamine.

INTRODUCTION

Cognitive dysfunctions are common neurological disorder in clinical practice that may thereby hampering daily activity (Barnes et al. be found to be associated with the Alzheimer's 2011). Memory impairment is attributed to Disease, Epilepsy, Depression, Schizophrenia dysfunction of the cholinergic system, involving and Stroke. Cognitive deficits may be congenital its neurons, neurotransmitters and receptors. or caused by environmental factors such as brain Degeneration of cholinergic neurons, particularly injury (Puri et al. 2017). Dementia is in the basal forebrain, has been found to be characterized by loss of intellectual ability associated with loss of the neurotransmitter leading to disruption of multiple higher cortical acetylcholine (Drever et al. 2011).

functions including memory, reasoning, Scopolamine, an anti cholinergic drug, orientation, learning capacity and emotional causes amnesia in human and also impairs stability. Progressive dementia is associated with learning in animals. Hence, it is widely utilized as Alzheimer's disease, which is a progressive a model for simulating human dementia neurodegenerative disorder associated with loss particularly Alzheimer's disease (Blockhad et al. of neurons and it's characterized by the presence 2006). It has been widely adopted to study of excessive amounts of neuritic plaques cognitive deficits in experimental animals (Ishola containing amyloid β protein and abnormal tau et al., 2013). Hence, we have selected this model protein filaments in the form of neurofibrillary as one of most suitable method to study dementia tangles (Jahanshahi et al. 2016).

Neurodegenerative disorders are clinically characterized by a progressive loss of cognitive abilities, which affect learning and memory dysfunction in experimental animals (Ishola 2013). Scopolamine leads to oxidative stress through impaired acetylcholine
(ACh) release and increased acetylcholinesterase (AChE) activity in the neurons of the central nervous system (CNS) especially the efficacy of Buchholzia coriacea (Nagede et al. 2017). It is understood that free radicals increase oxidative stress in brain leading to memory impairment. However, its precise mechanism is still not clear.

Treatment of dementia of Alzheimer type is usually via using acetylcholinesterase (AChE) inhibitors such as donepezil and memantine, an N-methyl-d-aspartate receptor (NDMAR). The present study is aimed at evaluating the efficacy of Buchholzia coriacea (Aqueous, ethanolic, ethyl acetate and n-hexane extracts) against scopolamine-induced dementia and to stress in brain leading to memory impairment. validate its traditional claim as memory enhancer. Hence, searching for a possible cure, adjuvant anti-amnesic therapies or memory enhancers is mandatory. The use of small pieces, dried and pulverized into coarse herbal and natural extract in the treatment of powder. Extraction was done by cold maceration.

Buchholzia coriacea belongs to the family Capparidaceae and is widely distributed in several tropical countries (Obembe et al. 2012). The plant was named after R.W Buchholz who collected them in Cameroon in the late 19th century (Keay et al. 1989). It is a forest tree with large, glossy leaves and conspicuous cream white flowers in racemes at the end of the branches. This seeds have medicinal value thus called “wonderful kola” because it is used in traditional medicine to treat variety of illnesses. The seeds or kernels of involved preliminary phytochemical screening of this plant are edible (can be eaten raw or cooked) the crude extracts. The different qualitative and quantitative chemical tests were performed in order to establish the chemical composition of the plant. Phytochemicals analyzed were alkaloids, phenols, flavonoids, saponins, terpenoids, steroids, tannins, carbohydrates. The proximate analysis of Buchholzia coriacea seed was done to establish its nutritional profile based on the following parameters; moisture content, total solid, crude fat, ash content, percentage nitrogen, crude protein, hypoglycemic (Adisa et al. 2015; Lenka et al. 2009), anti inflammatory (Umeokoli et al. 2016), antibacterial and antimicrobial (Ezekiel et al. 2009).

MATERIAL AND METHOD

Plant collection and extraction

The fresh seeds were bought from a market in Abuja, FCT and were authenticated by a taxonomist, Dr Tola Oyebanji of the Department of Botany, University of Loughborough, Northern Ireland. The voucher number is LUH 8022. The fruits were grated into small pieces, dried and pulverized into coarse powder. Extraction was done by cold maceration.

The plant material was extracted in distilled water, ethanol, ethyl acetate and n-hexane respectively for 72 hours with intermittent shaking at 2 h interval. The extract was then filtered using Whatman No. 1 filter paper. The filtrate was concentrated using a rotary evaporator (Rota vapor R 210, Büchi). The yield was determined and the extract stored in a refrigerator at 4°C in sample containers prior to use.

The aqueous extract was dried using a freeze dryer.

Phytochemical Analysis

In this study, the preliminary screening involved preliminary phytochemical screening of the crude extracts. The different qualitative and quantitative chemical tests were performed in order to establish the chemical composition of the extract. The phytoconstituents determined were alkaloids, phenols, flavonoids, saponins, terpenoids, steroids, tannins, carbohydrates.

Proximate Analysis

The proximate analysis of Buchholzia coriacea seed was done to establish its nutritional profile based on the following parameters; moisture content, total solid, crude fat, ash also called a memory nut, however, this is yet to content, percentage nitrogen, crude protein,
content, percentage nitrogen, crude protein, crude fiber, carbohydrate and caloric value. These parameters were determined using standard method in official methods (2000). The caloric value of the sample was estimated using (100mg/kg). certain to multiply the value of crude protein, lipid and carbohydrate respectively and taking the sum of the product (Onwuka et al., 2005). The AOAC methods of various parameters are as follows: Crude protein 955.04 (2.4.03), crude fiber 962.09 (4.6.01), moisture. 934.01 (4.1.03), ash 942.05 (4.1.10), Crude fat 920.39 (4.5.01) and carbohydrate by difference.

**Acute Toxicity Test**

Five groups of Rats of both sexes with each group containing five rats were used. Four groups were treated orally with varying doses of the *Buchholzia coriacea* fruit extract at 250, 500, 1000 and 2000 mg respectively. Group 5 was given an equivalent volume of distilled water to serve as control. The animals were observed for toxic signs like excitability, dullness, diarrhea and death over 72 h. Ethical approval was obtained from the College of Medicine of the University of Lagos with number: CMUL/HREC/04/19/511.

**Experimental Animals**

Male Sprague- Dawley rats with average weight of 190-230g were used as test animals. They were obtained from the Laboratory Animal Unit of the College of Medicine, University of Lagos, Nigeria. The animals were housed in cages at room temperature and under a light period of 16-18 hours daily for a period of 2 weeks prior to the commencement of the experiment. Standard commercial rat pellets and water were provided *ad-libitum*. The laboratory animals were used in accordance with laboratory practice regulation and the principle of humane laboratory animal care as documented by Zimmermann (1983).

**Drugs**

Scopolamine hydro bromide (BOC Sciences, USA, CAS-114-49-8) was used in this study. Scopolamine was dissolved in saline (NaCl 0.9%) at final concentrations of 1 mg/kg, and was injected intraperitoneally.

**Experimental Design**

The animals were administered 1mg/kg of these parameters were determined using scopolamine for 2 weeks (Imam et al., 2016) standard method in official methods (2000). The caloric value of the sample was estimated using (100mg/kg).

**Extracts:** Aqueous, ethanol, ethyl acetate and n-hexane extracts were used in order to determine the most effective.

**Rats:** A total of 49 male S-D rats were used. They were divided into 7 groups, 7 per cage.

**Broadly grouped:** normal control, negative control and treatment groups.

**Group I:** Positive Control (distilled water only)

**Group II:** Negative control (Scopolamine (1mg/kg) i.p.

**Group III:** Donepezil (5mg/kg) oral + Scopolamine (1mg/kg) i.p.

**Group IV:** Aqueous extract (100mg/kg) orally+Scopolamine (1mg/kg) i.p.

**Group V:** Ethyl acetate extract (100mg/kg) orally+Scopolamine (1mg/kg) i.p.

**Group VI:** Hexane extract (100mg/kg) orally+Scopolamine (1mg/kg) i.p.

**Group VII:** Ethanolic extract (100mg/kg) orally+Scopolamine (1mg/kg) i.p.

All these groups received the corresponding treatment for 14 consecutive days. On each day, 30 minutes after the various treatments, scopolamine (1 mg/kg i.p.) was injected to all groups except the control group that received distilled water. The behavioral tests were performed 30 min after the injection of scopolamine.

**Behavioural Assessment**

**Y-maze test:**

Y-maze test was used to evaluate short-term memory of rats by recording spontaneous alternation in a single session on day 13 & 14. The maze used in this study was a Y-maze made of plywood with three identical arms (35 cm length × 8 cm height × 15 cm width) mounted at 120 degrees to one another in a single piece. Each arm of the Y-maze was decorated with a different
letter (A, B, or C) in order to be differentiated (Ma et al., 2007). One hour after the last treatment and 30 min after scopolamine injection (except for the distilled water group), each rat, previously naïve to the maze, was placed at the end of one arm and were allow to move freely through the maze during 5 minutes. The number of arm entries was recorded for each rat. An arm entry was noted when a rat entered an arm of the maze with all its paws. Specific sequences of arm transitions (ABC, BCA, or CAB but not BAB or CAC or CBC) were recorded as a spontaneous alternation that reflects short-term memory. The total number of arm entries reflects general locomotor activity. The arms of the maze were cleaned between sessions with 10% ethanol. The percentage of spontaneous alternation was defined according to the following equation: percentage of spontaneous alternation = \[\left(\frac{\text{Number of alternations}}{\text{Total arm entries} - 2}\right) \times 100\] (Ma et al. 2007; Nadege et al. 2017). The effect on alternation behaviour was studied based on two parameters viz: % alternation and number of entries.

The Morris Water Maze (MWM) Task:

The MWM test was used to evaluate spatial and long-term memory of rats. The MWM was performed as previously described by Morris in 1984 with little modifications (Morris, 1984; Nadege et al. 2017). The MWM consisted of a black circular pool (100 cm diameter, 50 cm height). The pool was located in a room with various visual cues (pictures, shelters, curtains, lamps, fans, etc.). The position of the pool and that of the cues were maintained all the days of the experiment. The pool was filled with water at the temperature of 25 ± 2°C. The MWM was virtually divided into four equal quadrants: North, South, East, and West. A platform (11 cm diameter and 16 cm height) was centered in the South–East quadrant 1 cm below the water surface. The water was whitened by addition of liquid milk so that the platform was invisible at water surface. The position of the platform was unaltered during the training session. The 1st day of the MWM test (day 10th of drug treatment), 1 h after drug administration and 30 min after scopolamine injection, each rat received an acclimatization session during where the rat was placed inside the MWM for swimming for 60 s. During the acquisition phase (days 11–13 of drug treatment), 30 min after scopolamine injection, each rat was released into the pool, head facing the wall. The cutting time for each trial was 60 s. Each rat that did not find the platform during the time was gently guided to it and allowed for 15 s. Each animal had 3 training sessions per day of 5 min interval. After each trial each rat was taken to its cage and was allowed to dry up under a 60 watt bulb.

During each trial session, the time taken to reach the platform (escape latency) was recorded with stopwatches. In the retention phase (day 14 of drug treatment), the platform was removed from the pool (Probe test). Each rat individually was placed into the MWM. The latency time taken to reach the place of the formal platform and the time spent in the target quadrant was recorded during 60 s using stopwatches.

Tissue Preparation

At the end of each sacrifice, the brains were immediately removed from the skull, rinsed and then weighed. Each brain was divided into two cerebral hemispheres. Brain homogenate was prepared from one half with 50 mM Tris/HCl buffer for the assessment of brain malondialdehyde MDA and reduced glutathione levels GSH, Superoxide dismutase SOD and catalase CAT.

Biochemical Assays

On day 14 following the MWM test, rats were decapitated under light chloroform anaesthesia. In each group, the brain of a sub set of animal was used for histopathological analysis and the other for the dosage of brain malondialdehyde (MDA) -a marker of lipid peroxidation, reduced glutathione GSH - the principal antioxidant enzyme of the body ,Superoxide dismutase(SOD) and Catalase (CAT).

Estimation of Protein Concentration

The total protein of brains homogenate was determined by the method described by Bradford (1976). Five (5) μl of the brain homogenate was introduced in microplate wells and 250 μl of Bradford reagent was added. After agitation, the absorbance of the mixture was read using a
microplate reader at 590 nm. The determination of the protein concentration was done using bovine serum albumin (BSA) as standard.

**Brain Reduced Glutathione Level**

Reduced glutathione (GSH) level was estimated in the brain supernatant according to the method of Ellman (1959). Twenty (20) μl of brain homogenates were mixed with 3 ml of Ellman reagent prepared in phosphate buffer (0.1 M pH 7.2) at room temperature. After 1 h, the absorbance of the mixture was read at 412 nm. The amount of glutathione was calculated with the formula of Beer Lambert using the extinction coefficient value of 13,600/M/cm (Fotio et al., 2009). Each assay was done in triplicate.

**Brain Malondialdehyde Level**

The brain malondialdehyde (MDA) level was measured in the supernatant using the thiobarbituric assay. One (1 ml) of brain's supernatant was added to 0.5 ml of trichloroacetic acid (20%) and 1 ml of thiobarbituric acid (0.67%). The mixture was heated in a water bath at 100°C for 60 min. After cooling, the mixture was centrifuged at 3000 rpm for 15 min. The absorbance of the supernatant was read at 530 nm. The amount of MDA was calculated with the formula of Beer Lambert using the extinction coefficient value of 1.56 × 10^5 M/cm. The concentration of MDA was inhibited by the rate of chromogen formation by 50%.

**Assay of Catalase Activity**

The activity of catalase in hippocampus was assayed following the method of (Aebi et al., 1984), using H_2O_2 as substrate. Briefly, reaction mixture in a final volume of 1.0 ml contained phosphate buffer (0.1 mM, pH 7.4), post mitochondrial fraction of sample (100 μl) and H_2O_2 (30 mM). The decrease in optical density was measured for 150 s at 240 nm using the spectrophotometer. The activity of the enzyme was calculated using the molar extinction coefficient 43.6 M/cm.

**Histopathological Studies**

After sacrifice, the brains were fixed in 10% formol saline for a week. Fifty (50) μm sagittal sections were made from the brain in the hippocampus region using the rat brain Atlas with the following coordinate (Anterior/Posterior = -2.0 mm, Medial/lateral = -1.5 mm, and dorsal/ventral. The brains sections were collected. The dehydration of brain section consisted in introducing brain section in ascending concentration of ethanol and then followed by immersion in xylene and then embedding in paraffin. Paraffin sections of the brain were de paraffinized and rehydrated through washes in descending concentration series of alcohol. Brain sections were then stained using the Hematoxylin & Eosin stain. After drying overnight, the brain sections were photographed and images were captured using a digital camera attached to a light microscope.

**Statistical Analysis**

Statistical analysis was done using the software Graph pad 6 for windows. The differences amongst groups were analyzed using One-Way Analysis of Variance (ANOVA). P-values ≤ 0.05 were considered significant.

**RESULTS**

**Phytochemical screening**

Qualitative estimation revealed that seed extracts of *B. coriacea* were enriched with alkaloids, phenolic compounds, tannins, phytosterols, flavonoids, saponins. The detailed summary of phytochemical screening of *B. coriacea* fractions is shown below (Table 1).
The results of spontaneous alternation show that there is a significant difference among all the treatment groups. Scopolamine reduced the rat spontaneous alternation. 14 days treatment with (all extracts) significantly reversed the effect of scopolamine and increased the spontaneous alternation percentage when compared to scopolamine-alone treated group. Donepezil reversed the effects of scopolamine at the percentage of 84% and the aqueous extract was highest at a percentage of 90%.

### Acute toxicity study:

#### Effects of Bucholzia Coriacea on Y-Maze

No mortality was observed following oral administration of *B. coriacea* (all fractions) even with the highest dose (2000 mg/kg). Moreover, no significant changes in body weight and behaviour were observed. Hence, *B. coriacea* could be safe up to the dose of 2000 mg/kg body weight of the animal.

<table>
<thead>
<tr>
<th></th>
<th>Saponins mg/100g</th>
<th>Alkaloids mg/100g</th>
<th>Reducing Sugar mg/100g</th>
<th>Cardiac glycoside mg/100g</th>
<th>Flavonoid mg/100g</th>
<th>Tannins mg/100g</th>
<th>Steroid mg/100g</th>
<th>Terpenoid mg/100g</th>
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<tr>
<td>Aqueous</td>
<td>35.87</td>
<td>29.38</td>
<td>34.17</td>
<td>31.13</td>
<td>31.06</td>
<td>20.61</td>
<td>23.99</td>
<td>21.58</td>
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<td>29.73</td>
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<td>N hexane</td>
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<td>28.27</td>
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<td>28.76</td>
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<td>Ethyl acetate</td>
<td>-</td>
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<td>26.54</td>
<td>27.04</td>
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<td>26.26</td>
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**Table 1: Phytochemical Screening of Bucholzia Coriacea seed extracts**

**Fig. 1: Effects of BC on Spontaneous Alternation of Scopolamine Treated Rats in the Y Maze**

An Official Publication of Enugu State University of Science & Technology   ISSN: (Print) 2315-9650   ISSN: (Online) 2502-0524

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The effect of the different extracts of *B. Coriacea* on spatial memory was assessed using the MWM test. Fig 2a represents the mean escape latency during three trials in day 1, 2 and 3 for each extract group. There were significant differences between scopolamine and treated groups (*P*<0.05) on day 3, which implies that the rats in all groups learnt water-maze performance during the training trial. There is also significant difference between the scopolamine group and the normal control group (# = *P*<0.05).

Rats were subjected to spatial memory performance over 4 consecutive days using a hidden platform, and a probe trial was conducted on the fourth day with no platform (Fig.2b). Post hoc analysis (Turkey) revealed that SCO injection significantly increased the escape latency (Fig.2a) compared with the control group (*P*<0.05). While, both *B. coriacea* and donepezil administrations significantly decreased the escape latency compared with the SCO-injected group (*P*<0.05). In the control group, latency times in the 2nd and 3rd days were significantly lower than the 1st day (*P*<0.05). However, SCO-treated group showed a non-significant change in the latency time in 2nd and 3rd days compared with the 1st day.

In the memory retention test (Fig.2b), animals in the control, BC, and donepezil-treated groups exhibited a significant increase in the number of crossings over a platform position than animals in SCO-treated group (*P*<0.05). Aqueous and hexane extracts of BC showed best improved performance over and above the standard drug.

Lipid peroxidation illustrates the damage into the cells. Scopolamine treatment increased Malonylaldehyde (MDA) levels, statistically significant when compared to control group (*P*<0.01). The various extracts of BC attenuated the MDA significantly (*P*<0.05). (Fig. 3a.)

Reduced Glutathione is an indicator of the ability of the tissues to naturalize the free radicals. The scopolamine treated rats showed that the levels of reduced glutathione was slightly decreased compared to the control rats but not statistically significant. However, administration of the various extracts prevented the effects of scopolamine on the reduced glutathione, which was significantly (*P*<0.05) increased in the aqueous and hexane extract treated rats comparable to donepezil (standard drug) (Fig. 3b.).

**B. Coriacea**

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The levels of catalase were significantly decreased in scopolamine treated group as compared to normal control group \( (p<0.01) \). The reduced levels of catalase increased significantly in the aqueous and hexane extracts of B. Coriacea groups as compared to scopolamine treated group; \( (*) = p<0.05, (**) = p<0.01 \). (Fig. 3c.)

These results demonstrated that the B. Coriacea exerts a strong antioxidant property in hippocampus. Values are means ± SEM (n=7 animals per group), \( *, P<0.05 \) and \( **, P<0.01 \) vs. SCO alone-treated group.

### Histopathological results

The hippocampus proper is formed by Cornu Ammonis. CA1 and CA2, a zone of small pyramidal cells, CA3 and CA4 formed of zone of large pyramidal cells. CA4 projects into concavity of dentate gyrus that is formed of small granule cells. Subiculum is outward continuation of CA1 region. Areas in between compact zones of cells comprise the molecular layer which consists of neuronal processes/(axons and dendrites), glial cells, and scattered nerve cells (Fig 4). In the CA3 region of hippocampus, control show large pyramidal cells (red arrow), with vesicular nuclei and normal glial cells (yellow arrow) while the scopolamine treated group showed marked shrinkage and darkening.
of large pyramidal cells of CA3 region with gliosis. The described histopathological changes were markedly attenuated in all treated group with donepezil and the various fractions of B. Coriacea.

Fig. 4: Histopathological changes in the CA3 of hippocampus in different treated groups (H&E X400).
A. Normal control group showing normal histological picture;
B. Scopolamine treated group showing marked degeneration of pyramidal cells (green arrow);
C. DON (5mg/kg) + scopolamine showing normal pyramidal cells (red arrow);
D. Hexane extract of BC (100 mg/kg) + scopolamine showing preservation of pyramidal cells (red arrow);
E. Ethanolic extract of BC (100 mg/kg) + scopolamine showing normal histological finding;
F. Ethyl acetate fraction of BC (100mg/kg) + scopolamine showing normal pyramidal cells
G. Aqueous extract (BC)100mg/kg + scopolamine showing close to normal histological finding

DENTATE GYRUS
The dentate gyrus of normal control group show layers of compact granular cells (black arrow) with dark nuclei while the molecular layer shows glial cells as well as large pyramidal cells. The scopolamine treated group show marked vacuolation, shrinkage and darkening of some granular cells (green arrow) with gliosis. The other treated groups show close to normal cyto-architecture of granular layer with restoration of granular cell layer close to the molecular layer with the exception of Ethyl acetate extract treated group that still had few degenerating cells compared to the scopolamine treated group. H & E 400. (Fig. 5)
PHOTOMICROGRAPH 2

A. Normal control group showing normal histological picture;
B. Scopolamine treated group showing marked degeneration and vacuolation of granular cells (green arrow);
C. DON (5mg/kg) + scopolamine showing normal granular cell layer but scanty towards the molecular layer (green arrow)
D. Hexane extract of BC (100 mg/kg) + scopolamine showing preservation of (red arrow)
E. Ethanolic extract of BC (100 mg/kg) + scopolamine showing normal histological finding;
F. Ethyl acetate fraction of BC (100mg/kg) + scopolamine still showing some degenerating granular cells
G. Aqueous extract (BC)100 mg/kg + scopolamine showing close to normal

Fig. 5: Histopathological changes in the dentate gyrus in different treated groups (H&E X400).

DISCUSSION

Cholinergic neurons present in the basal forebrain and hippocampus, with acetylcholine as a major neurotransmitter, are known to have important roles in learning and memory processes (Ellman et al. 1989; Soodi et al. 2014). Age-related dementia and memory deficit observed in AD, are correlated with the loss of cholinergic neurons in the basal forebrain and hippocampus (Terry et al., 2011). In addition, pharmacological blockage of cholinergic neurons in these areas causes impairment of memory and learning in experimental animals (Soodi et al. 2014). Cognitive impairment is one of the major health problems in normal aged life as well as in some neurological disease conditions like Alzheimer's. Several studies have employed scopolamine a known non selective
muscarinic receptor antagonist, to treat animals as a test model of cognitive function (Nadege et al. 2017). Since, no study had been conducted to evaluate the neuroprotective and cognitive enhancing potential of B. coriacea, the present study was conducted.

In this study, we evaluated the effect of the Buchholzia coriacea against scopolamine model of Alzheimers Disease (AD). Scopolamine is an alkaloid extracted from the Solanaceae Datura stramonium. It known to impair short-term, long term and spatial memory in animals and humans (Rabiei et al. 2015). Via its interference with acetylcholine in the brain, scopolamine can cause oxidative stress, impair the anti-oxidative defense system thus contributing & leading to cognitive impairment (Ishola et al. 2013; Rahnama et al. 2015). Thus, scopolamine-induced memory impairment is a valid model for the evaluation of anti–amnesic effects of new drugs. Diverse behavioral animal models are usually used for the evaluation and validation of new drugs against dementia (Rajendran et al. 2014). Clinical studies have reported with strong evidence that oxidative stress in involved in the pathogenesis of Alzheimer’s disease implying that these oxygen free radicals implicated in the age related decline in the cognitive performance may be responsible for the development of Alzheimer's disease (Gosalvez et al. 2013). In our study, there was increased levels of lipid peroxidation and decrease in the levels of GSH, superoxide dismutase (SOD) and catalase (CAT) in hippocampus of rats following treatment with scopolamine.

The phytochemical screening revealed that the seed fractions of B. coriacea were enriched with different secondary metabolites in their respective fractions.

To delineate the mechanism by which B. Coriacea exerts its Neuroprotective activity, B. Coriacea was administrated for 14 days consecutively 1 hour prior to scopolamine (1 mg/kg i.p.) injection. The MWM task and Y maze were used as behavioral task. The results obtained show that like donepezil, the various fractions of B. Coriacea significantly reduced the learning and retention deficits caused by repeated doses of scopolamine. B. Coriacea reduced the time to the invisible platform during acquisition and the latency time to the non-existing platform during retention phase. Our results with the MWM suggest that B. Coriacea improves spatial and long-term memory (Nadege et al. 2017). The results of MWM confirmed that treatment with B. Coriacea counteracted scopolamine induced learning and memory deficit thus B. Coriacea is Neuroprotective and a memory enhancer (Konar et al. 2011; Hritcu et al. 2015).

For the Y maze, Scopolamine reduced the rats spontaneous alternation. 14 days treatment with B. Coriacea with all extracts significantly reversed the effect of scopolamine and increased the spontaneous alternation percentage when compared to scopolamine-alone treated group. Donepezil reversed the effects of scopolamine at the percentage of 84% while the aqueous fraction was highest at a percentage of 90%.

The results of biochemical parameters show that 14 days administration of scopolamine increased the level of MDA, a measure of brain lipid peroxidation (Hritcu et al., 2015) and reduced the level of GSH (the main antioxidant enzyme of the body), Super Oxide Dismutase(SOD) and Catalase (Nagede et al., 2017). Our results are in accordance with literature that shows that administration of scopolamine in rodents can lead to increase of oxidative status in the brain (Konar, 2011; Ibrahim et al., 2013; Nadege et al. 2017). Treatment of rats with all the extracts B. Coriacea reversed the increase in oxidative stress induced by scopolamine, thus protecting animals against learning and memory loss. However, only the Ethyl acetate extract was able restore the activity of SOD while aqueous and hexane extracts significantly restored the activity of GSH.

Our histopathological studies demonstrated that 14 days administration of scopolamine resulted in neurodegenerative processes in the hippocampus when compared to the control group (Imam et al., 2012). This cell death in the CA3 and dentate gyrus was significantly prevented by a treatment with B. Coriacea (Imam et al., 2012; Salma et al., 2018). The dentate gyrus is the part of the brain where adult neurogenesis takes place, it is also implicated in hippocampal plasticity.
In addition to the fact that memory impairment induced by scopolamine is a result of an increase in AChE activity and brain oxidative status (Konar et al. 2011), studies have shown that scopolamine impairs neurogenesis in the brain in turn leading to cognitive deficits as in AD (Dae et al. 2010; Chen et al. 2014). By antagonizing the cell death in the dentate gyrus and CA3 induced by scopolamine, *B. coriacea* can be a good treatment for cognitive deficits and AD.

There are cumulative evidences in literature that scopolamine influences acquisition, consolidation and recall of information and that scopolamine is a cholinergic blocker (Konar et al. 2011; Rajendran et al. 2014). By counteracting the effect of scopolamine, *B. coriacea* can have the same mechanism of action, as donepezil which is a cholinergic enhancer widely used in the treatment of AD.

It has been scientifically validated that *B. coriacea* (wonderful kola) have analgesic, anti-depressant, anti-malaria, anti-anxiety, anti-diabetes, anti-microbial, anti-oxidants, anti-helminthes, anti-ulcer, anti-inflammatory, anti-hypercholesterolemic, anti-atherogenic, anti-trypanosomal, anti-diarrhea and fertility activities (Ezekiel and Onyecziri, 2009; Umeokoli et al. 2016; Izah et al. 2018). In the assay for anti-inflammatory activity, Umeokoli et al reported aqueous extract to be the most active fraction (Umeokoli et al. 2016) meanwhile, Okere and Ladeji (2016), reported that methanolic extract had more anti-inflammatory activity.

It is also regarded as brain food to promote memory.

To the best of our knowledge, our study is the first to show the neuroprotective and memory enhancing effects of *B. coriacea* as it ameliorates scopolamine-induced cholinergic dysfunction via decrease of oxidative stress markers, amelioration of neurodegeneration and improvement in Y maze and Morris water maze.

From our study, it can be concluded that the aqueous extract recorded better pharmacological activity than the ethanol, ethyl acetate and n-hexane extracts of *B. coriacea* seeds confirming the common use of aqueous decoctions of this plant seeds in South-Eastern Nigeria traditional medicine practice.

**Conflict of interest:** We declare no conflict of interest.

**ACKNOWLEDGEMENT**

Sincere gratitude goes to Dr Sanyo-olu Omolara and Dr Edidiong Akang for your immense intectual assistance during the course of this study.

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