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Neuroprotective activity of Ipomoea cairica leaf extract against cadmium chloride-induced biochemical changes in the brain of male Wistar rats

Omotayo B. Ilesanmi[1*], Temitope Temiloluwa Odewale[2], Oghenetega J. Avwioroko[3], Mohammed Alqarni[4,6], Ahmad J. Obaidullah[5,7], Francis O. Atanu[4], Toyin Binang[5] and Gaber El-Saber Batiha[8]

Abstract

Background: Exposure to cadmium is implicated in the etiology of some neurodegenerative diseases. Compounds isolated from *Ipomoea cairica* extract are neuroprotective. However, there is no reported neuroprotective activity of the crude extract of *I. cairica* (ICE). We investigated the neuroprotective activity of *I. cairica* extract against cadmium-induced biochemical changes in the brain of male Wistar rats. Thirty-six animals were divided into four groups of 9 animals per group: group I (Control); group II (3.5 mg/kg $CdCl_2$); group III (100 mg/kg ICE + $CdCl_2$); and group IV (250 mg/kg ICE + $CdCl_2$). Animals were pretreated with 100 and 250 mg/kg ICE before co-administration with cadmium chloride.

Results: $CdCl_2$ treatment caused a significant increase in acetylcholineesterase activity, lipid peroxidation, beta-amyloid aggregation, caspase 3 and 9, p53, and glutamate concentration. In addition, $CdCl_2$ caused a significant decrease in catalase activity, superoxide dismutase, glutathione-S-transferase, Na+/K+ ATPase, and glutamate dehydrogenase. ICE was able to reduce the neuronal damaging effect of $CdCl_2$ by acting as an antioxidant, antiapoptotic, anticholinesterase, and antiexcitotoxicity.

Conclusions: Our findings show that *Ipomoea cairica* leaf can be developed and included in the natural product in the prevention of neurodegenerative diseases.

Keywords: Cadmium, Neurotoxicity, Natural product, Oxidative stress, Beta-amyloid, Glutamate, *Ipomoea cairica*

Background

Cadmium (Cd) is one of the heavy metals human is exposed to as it is one of the major components of building materials. The presence of Cd in building materials and household appliances has made it one of the toxic heavy metals humans are exposed to. Though the regulatory agencies have put a stop to its inclusion in industrial uses, the existing products have found their way into developing countries such as Nigeria. The fact that Cd is classified as a carcinogenic metal has also increased its global awareness. The most common sources of Cd in the environment are polluted food and water, cigarette smoke inhalation, batteries, fertilizers, and insecticides (Al-Olayan et al. 2020; Min and Min 2016). The level of Cd toxicity in humans depends on the route of exposure, duration, and concentration. Various studies have also shown that the amount of Cd deposited in the body increases with age (Elinder and Järup 1996). The non-biodegradable nature of Cd further prolongs its stay

*Correspondence: ilesanmiob@fuotuoke.edu.ng
[1] Department of Biochemistry, Faculty of Science, Federal University Otuoke, Otuoke, Bayelsa State, Nigeria
Full list of author information is available at the end of the article

in the environment. In addition, the inability for animals and rats to excrete the metal further increases its bioaccumulation, thus enhancing its toxic effect (Şlencu et al. 2018; Nordberg et al. 2015). There is a growing concern about the role of Cd as a neurotoxicant; evidence has shown that Cd exposure can produce symptoms similar to what is observed in patients suffering from Parkinson's disease and Alzheimer's disease (Javorac et al. 2020; Branca et al. 2018; Wang and Du 2013; Agnihotri et al. 2015; Bocharova et al. 2005; Bush 2000; Ricchelli et al. 2005; Saturnino et al. 2014; Tamas et al. 2018). Cd was able to exert its neurotoxicity by its ability to cross the blood–brain barrier (BBB), where it accumulates and further increases its permeability to various regions of the brain (Kahtan 2020; Goncalves et al. 2012; Antonio et al. 2003). Some of the effects of Cd poison include memory impairment, loss of cognitive functions, and other disabilities. Though Cd possesses no redox status, its mechanism of neurotoxicity involves induction of oxidative stress through the initiation of oxidation, inhibition, and damage of several functional biomolecules. Oxidative activity of Cd includes inhibition of antioxidant systems, such as CAT and SOD (Shagirtha et al. 2017), leading to an increase in the formation of reactive oxygen species (ROS), such as superoxide anion and hydrogen peroxide. This ROS exacerbates the oxidative activity of Cd through an increase in formation of lipid peroxide, protein carbonyl, and DNA adduct. Apart from oxidative stress, Cd also causes alteration in the neurotransmitter system. Some studies have reported the inhibitory effect of the Cd on acetylcholineesterase activities and can also prevent the synaptic membrane response to Ach stimuli, a major defect observed in the brain of patient suffering from Alzheimer's disease (AD). The carcinogenic effect of Cd is also linked to the inhibition of the enzymes involved in the repair of defective DNA and interfering with p53 activity (Maodaa et al. 2016). Chandler et al. (2016) reported the role of Cd in the excitotoxicity activity of glutamate. They reported the inhibition of glutamate dehydrogenase and inhibiting the Na/K ATPase involved in the transport of glutamate across the glial cells.

The role of medicinal plants in managing health challenges is on the rise, and it is not reducing anytime soon. The renewed interest in medicinal plants can be linked to the general belief which has also been confirmed that they are far healthier than conventional drugs. Apart from this, they are a rich source of antioxidant, anti-inflammatory, and antiaging products. *Ipomoea cairica* is a plant that is often classified as a weed due to its invasive nature and natural habitats, such as dumpsites and abandoned areas. Its origin is unknown, although can be found in various parts of the world such as Asia and Africa. In Nigeria it is consumed as vegetables in the south--south region. Medicinally, it is used for treating jaundice, liver disorders, and aphrodisiac (Yanchon et al. 2021). Several reports have confirmed the antioxidant, anti-inflammatory, cardioprotective, and neuroprotective activities of the plant (Firdous and Koneri 2012; Banerjee and Firdous 2015; Ramachandran et al. 2019; Bag and Mumtaz 2013). Some active compound isolated from the plant includes matairesinol, vanillic acid, and lignin (Lin et al. 2008). Based on the limited scientific literature on the neuroprotective effect of crude extract of *Ipomoea cairica,* we decide to investigate the protective effect of *I. cairica* against Cd-induced neurotoxicity in male Wistar rats.

Methods

Extraction of plant materials (Ilesanmi et al. 2016)

Ipomoea cairica leaves were harvested from Nembe town, Bayelsa State, Nigeria, and identified by a Prof. Emmanuel I. Aigbokan in the department of Plant Biology and Biotechnology, faculty of Science, University of Benin, Edo State, Nigeria, and a voucher number UBH-1561 was issued by Dr Henry A. Akinnibosun. The leaves were air-dried under room temperature and ground into powdered form using a home-made blender. The powdered sample was weighed and soaked in 2.5 L of 80% methanol with regular stirring for even distribution for 48 h. The extracts were filtered using a Whatman filter paper. The filtrate was concentrated and lyophilized to obtain a pure sample free of methanol and water. The lyophilized sample was stored at 4 °C before the experiment.

Experimental design

Thirty-six (36) male Wistar rats weighing 170 ± 10 g were purchased from the Central Animal House, University of Benin, Edo State, Nigeria, were used for this experiment. The animals were housed in well-ventilated cages and provided water and food ad libitum. Animals were randomly divided into 4 groups of 9 rats per group as follows:

Group I: Control: administered vehicle (distilled water).
Group II: each rat was orally administered Cd chloride (3.5 mg/kg) for seven consecutive days.
Group III: each rat was orally administered 100 mg/kg of *Ipomoea cairica* leaf extract for 5 consecutive days before co-administration with $CdCl_2$.
Group IV: ICE (250 mg/kg) + Cd: each rat was orally administered 250 mg/kg of *Ipomoea cairica* leaf extract for 5 consecutive days before co-administration with $CdCl_2$.

N.B the dosage administered was extrapolated from the report of Ferreira et al. (2006)

Processing of the brain (Ilesanmi and Ikpesu 2021)

24 h after last administration, animals were sacrificed via cervical dislocation and the brain excised, rinsed, and homogenized in a phosphate buffer saline (0.1 M, pH 7.4) to obtain a 10% w/v homogenate. The homogenate was centrifuged at 15,000 rpm for 10 min with the temperature set at 4 °C to obtain a clear supernatant that was used for biochemical assays.

Biochemical assay

Estimation of oxidants

The level of oxidative stress was determined by measuring the amount of malondialdehyde (MDA) formed from lipid peroxidation (LPO) in the brain tissue according to the method of Varshney and Kale (1990).

Estimation of antioxidants in brain tissues

The concentration of glutathione (GSH) was measured according to Jollow et al. (1973). Catalase (CAT) activity was determined as described by Aebi (1974). The activity of superoxide dismutase (SOD) was measured as described by Misra and Fridovich (1972).

GST assay

The activity of GST was assessed as described by Habig et al. (1974).

p53

The concentration of p53 in rat brains was estimated using an ELISA kit, following the instructions from the kit manual. The level of p53 was expressed as pg/ml.

Acetylcholineesterase, Na^+/K^+ATPase, glutamate dehydrogenase, and glutamate

The activity of acetylcholineesterase and Na^+/K^+ ATPase was evaluated as described by Ilesanmi et al. (2017), while glutamate dehydrogenase and glutamate concentration in the brain were estimated according to the instruction from the kit manual.

Beta-amyloid, caspase 3 and 9

The amount of brain β-amyloid1-42 formed was determined according to the ELISA kit instruction manual supplied by RayBiotech Inc. (Norcross, GA, USA), and the activity of caspase 3 and 9 was determined according to the instruction manual from the ELISA kit supplied by Calbiochem.

Statistical analysis

All grouped data were statistically performed with Prism (GraphPad Prism, 6.01) software. Differences among groups were evaluated by one-way analysis of variance followed by Duncan's multiple range tests. All values were expressed as the mean ± standard deviation of nine animals per group.

Results

Effect of *Ipomoea cairica* leaf extract (ICE) on AchE and β-amyloid following Cd toxicity.

Treatment of animals with 35 mg/kg of Cd chloride caused a significant increase in AchE activity as compared to the control. Figure also shows that pretreatment with 100 and 250 mg/kg of ICE caused a significant reduction in the activity of AchE.

Figures 1and 2 show the effect of $CdCl_2$ (35 mg/kg) and ICE (100 and 250 mg/kg) on AchE activity and β-amyloid level.

Administration of $Cdcl_2$ caused a significant increase in the blood of β-amyloid as compared to the control ($P > 0.001$). However, pretreatment with 100 and 250 mg/kg of ICE was able to reduce the level of β-amyloid in a dose dependent manner.

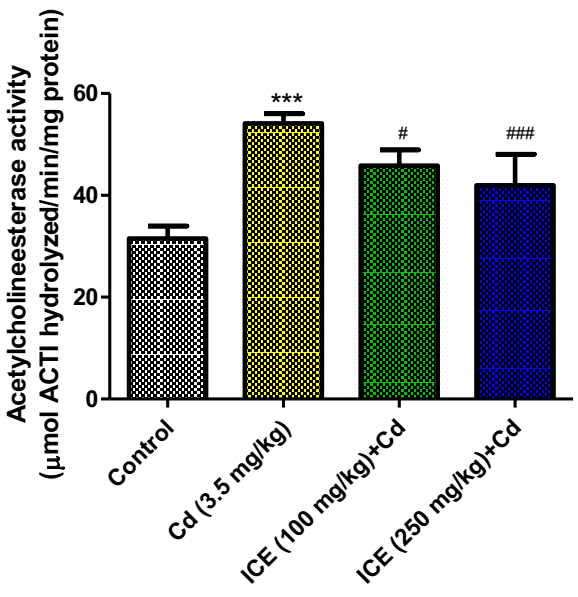

Fig. 1 Anticholinesterase (AChE) activity of *Ipomoea cairica* leaf extract (ICE) against cadmium-induced increase AChE activity in rat brain. Data are shown as mean ± standard deviation (SD) for 9 animals. Statistically significant differences: $^{***}P < 0.001$ = Control group vs Cd; $^{\#}P < 0.05$ = Cd vs 100 mg/kg ICE; $^{\#\#\#}P < 0.001$ = Cd vs 250 mg/kg

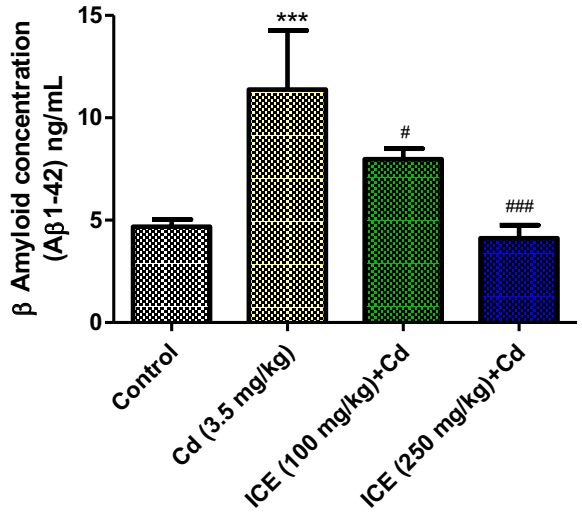

Fig. 2 Pretreatment of male Wistar rats with *Ipomoea cairica* leaf extract (ICE) prevents the accumulation of β amyloid induced by cadmium exposure in the brain. Data are shown as mean ± standard deviation (SD) for 9 animals. Statistically significant differences: *** P < 0.001 = Control group versus Cd; $^{\#}P < 0.05$ = Cd versus 100 mg/kg ICE; $^{\#\#\#}P < 0.001$ = Cd versus 250 mg/kg

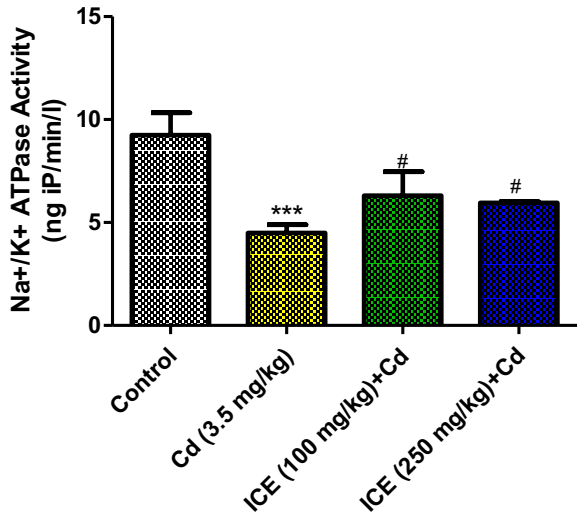

Fig. 3 Effect of *Ipomoea cairica* leaf extract (ICE) on Na^+/K^+ ATPase activity in the brain of male Wistar rats following cadmium exposure. Data are shown as mean ± standard deviation (SD) for 9 animals. Statistically significant differences: $^{***}P < 0.001$ = Control group versus Cd; $^{\#}P < 0.05$ = Cd versus treatment groups

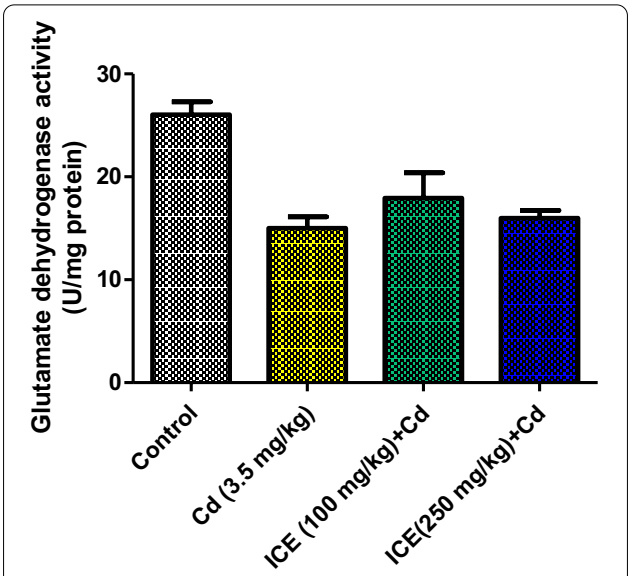

Fig. 4 Effect of *Ipomoea cairica* leaf extract (ICE) on glutamate dehydrogenase activity in the brain of male Wistar rats following cadmium exposure. Data are shown as mean ± standard deviation (SD) for 9 animals. Statistically significant differences: $^{***}P < 0.001$ = Control group versus Cd; $^{\#}P < 0.05$ = Cd versus 100 mg/kg ICE

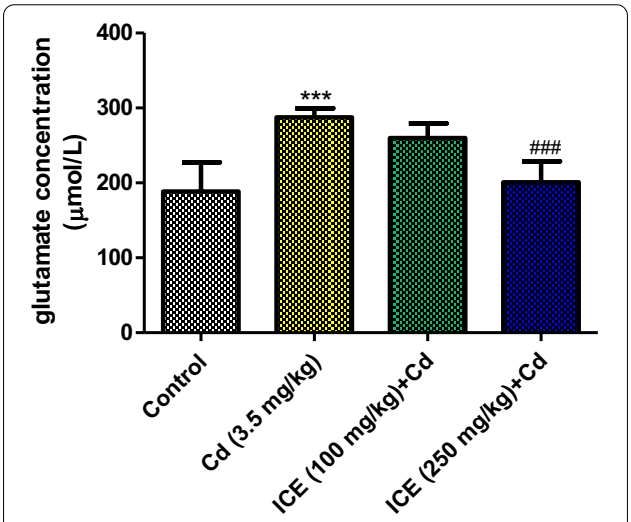

Fig. 5 Effect of *Ipomoea cairica* leaf extract (ICE) on glutamate content in the brain of male Wistar rats following cadmium exposure. Data are shown as mean ± standard deviation (SD) for 9 animals. Statistically significant differences: $^{***}P < 0.001$ = Control group versus Cd; $^{\#\#\#}P < 0.001$ = Cd versus 250 mg/kg

Effect of ICE on the activity of Na^+/K^+ ATPase and Glutamate dehydrogenase (GD) and concentration of glutamate following Cd exposure (Figs. 3, 4 and 5). Figures 3 and 4 show the effect of ICE and $CdCl_2$ on Na^+/K^+ ATPase and GD activity, while Fig. 5 shows the effect of ICE and $CdCl_2$ on glutamate concentration. Exposure of the animals to $CdCl_2$ causes a significant increase in the activity of Na^+/K^+ ATPase as compared to the control. Pretreatment of the animals

with 100 and 250 mg/kg of ICE caused a dose-dependent decrease in the activity of ATPase when compared with the untreated animals.

As shown in Fig. 4, exposure of the animals to $CdCl_2$ caused a significant decrease in the activity of GD as compared to control, and pretreatment with 100 mg/kg of ICE significantly ($P<0.05$) increases the activity of GD as compared to untreated group. However, pretreatment with high dose (250 mg/kg) of ICE had no significant effect on GD activity as compared with the untreated group ($P>0.05$).

Figure 5 shows the effect of $CdCl_2$ and ICE on concentration of glutamate in the brain of rats. $CdCl_2$ caused a significant increase in glutamate concentration as compared to the control ($P<0.001$). Pretreatment with ICE caused a dose-dependent decrease in glutamate concentration which was significant different ($P<0.05$) when compared to the untreated group.

Antioxidant activity of ICE against $CdCl_2$-induced oxidative stress

Figures 6, 7, 8, 9 show the effect of the pretreatment of animals with ICE and exposure to $CdCl_2$ on the level of MDA, GSH, and activity of catalase and SOD respectiv ely.

As observed in Fig. 6, $CdCl_2$ caused a significant increase in the concentration of MDA as compared to the control ($P<0.001$). Pretreatment with 100 mg/kg and 250 mg/kg caused a dose dependent decrease in the concentration of MDA as compared to the untreated group ($P<0.05$).

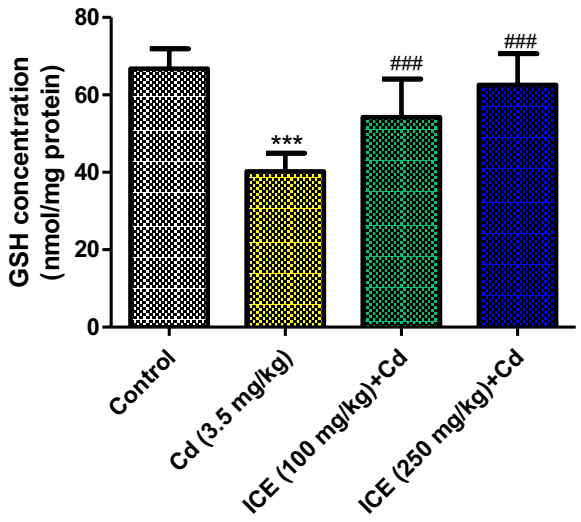

Fig. 7 The concentration of non-enzymatic antioxidant-reduced glutathione (GSH) in the brain tissue of male rats after pretreatment with *Ipomoea cairica* leaf extract (ICE), followed by exposure to cadmium (3.5 mg/kg) via intraperitoneal administration. Data are shown as mean ± standard deviation (SD) for 9 animals. Statistically significant differences: $^{***}P<0.001$ = Control group versus Cd; $^{###}P<0.001$ = Cd versus treatment groups

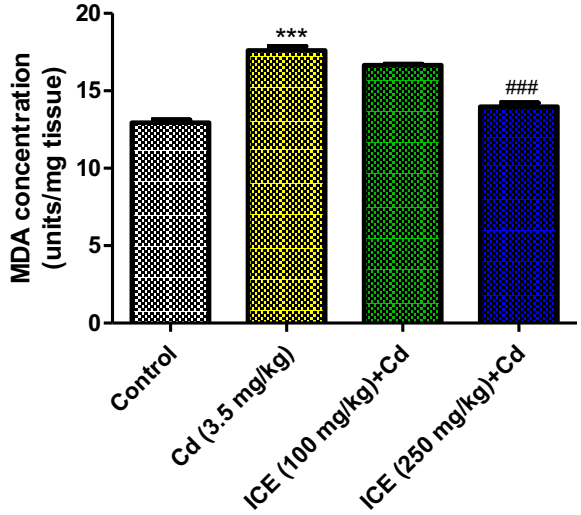

Fig. 6 The concentration of lipid peroxides product—malondialdehyde (MDA), in the brain tissue of male rats after pretreatment with *Ipomoea cairica* leaf extract (ICE) following exposure to cadmium (3.5 mg/kg) via intraperitoneal administration. Data are shown as mean ± standard deviation (SD) for 9 animals. Statistically significant differences: $^{***}P<0.001$ = Control group versus Cd; $^{###}P<0.001$ = Cd versus 250 mg/kg ICE

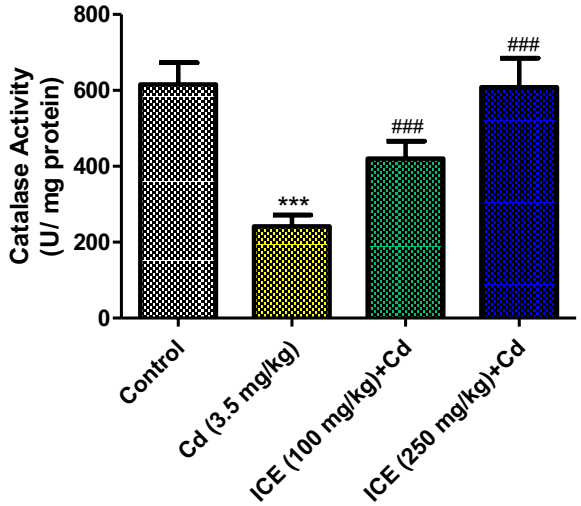

Fig. 8 The catalase activity in the brain tissue of male rats after pretreatment with *Ipomoea cairica* leaf extract (ICE) followed by exposure to cadmium (35 mg/kg) via intraperitoneal administration. Data are shown as mean ± standard deviation (SD) for 9 animals. Statistically significant differences: $^{***}P<0.001$ = Control group versus Cd; $^{###}P<0.001$ = Cd versus treatment groups (100- and 250 mg/kg ICE)

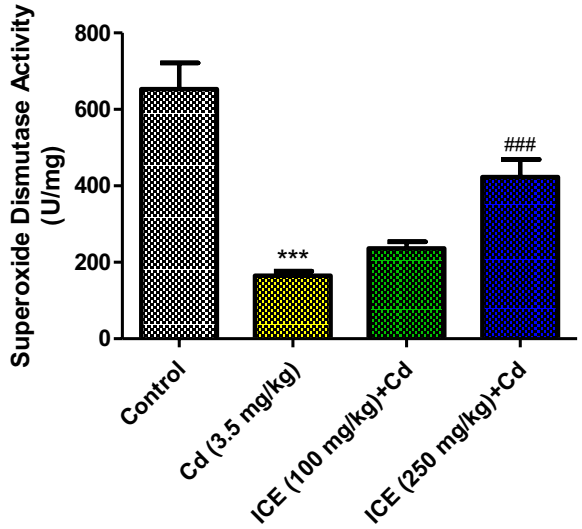

Fig. 9 The superoxide dismutase activity in the brain tissue of male Wistar rats after pretreatment with *Ipomoea cairica* leaf extract (ICE) followed by exposure to cadmium (3.5 mg/kg) via intraperitoneal administration. Data are shown as mean ± standard deviation (SD) for 9 animals. Statistically significant differences: ***$P < 0.001$ = Control group versus Cd; ###$P < 0.001$ = Cd versus 250 mg/kg

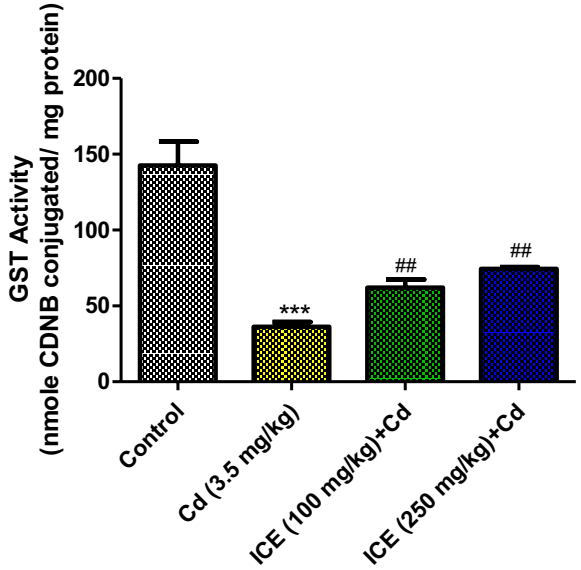

Fig. 10 The glutathione-S-transferase (GST) activity in the brain tissue of male rats after pretreatment with *Ipomoea cairica* leaf extract (ICE) before exposure to cadmium (3.5 mg/kg) via intraperitoneal administration. Data are shown as mean ± standard deviation (SD) for 9 animals. Statistically significant differences: ***$P < 0.001$ = Control group versus Cd; ##$P < 0.01$ = Cd versus treatment group (100- and 250 mg/kg ICE)

Figure 7 shows that $CdCl_2$ caused a significant depletion in the concentration of reduced glutathione as compared to the untreated group ($P < 0.001$).

Figures 8 and 9 show that $CdCl_2$ significantly suppresses the expression of CAT activity as compared to the control, and pretreatment with ICE at 100 and 250 mg/kg was able to prevent the suppression of CAT caused by $CdCl_2$ as observed in the significant increase in CAT activity as compared to the untreated group ($P < 0.001$).

The effect of $CdCl_2$ and ICE on SOD activity as presented in Fig. 9 showed that $CdCl_2$ caused a significant decrease in SOD activity as compared to the control ($P > 0.001$). Pretreatment with ICE at 100 and 250 mg/kg shows that the plant prevents Cd-induced decrease activity of SOD in a dose-dependent manner, as observed in the significant increase in SOD activity as compared to the untreated group.

Effect of $CdCl_2$ and ICE on glutathione-S-transferase (GST) activity

Figure 10 shows the activity of GST due to pretreatment with ICE and $CdCl_2$ exposure. $CdCl_2$ caused a significant decrease in the activity of GST as compared to control ($P < 0.001$); pretreatment with ICE (100 and 250 mg/kg) caused a significant increase in GST activity as compared to the untreated group ($P < 0.05$).

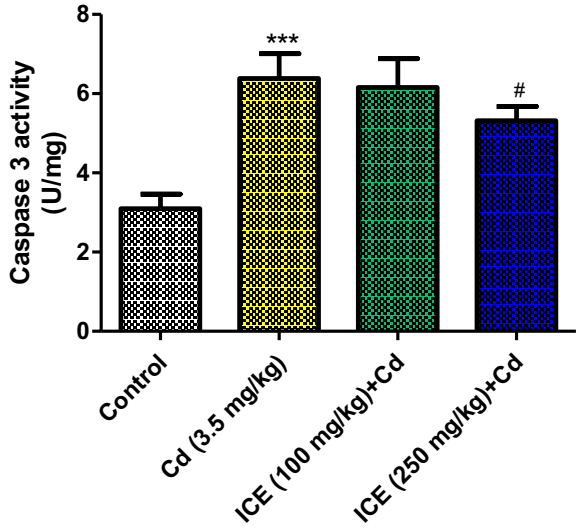

Fig. 11 Effects of pretreatment of *Ipomoea cairica* leaf extract (ICE) on Cd-induced increase on caspase-3 activity in the brain of male Wistar rats. Data are shown as mean ± standard deviation (SD) for 9 animals. Statistically significant differences: ***$P < 0.001$ = Control group versus Cd; #$P < 0.05$ = Cd versus 250 mg/kg ICE

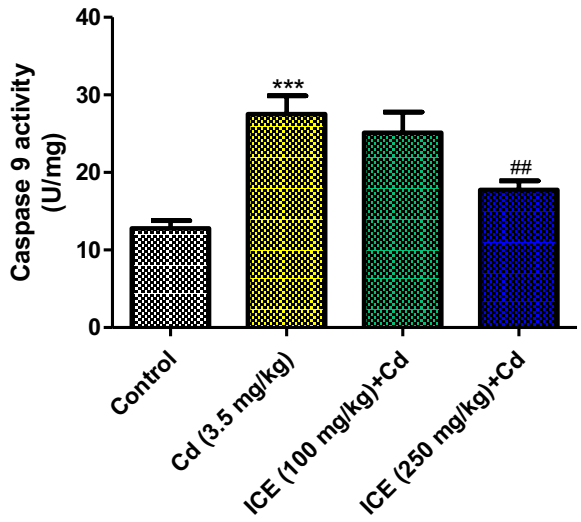

Fig. 12 Effects of pretreatment of *Ipomoea cairica* leaf extract (ICE) on Cd-induced increase on caspase-9 activity in the brain of male Wistar rats. Data are shown as mean ± standard deviation (SD) for 9 animals. Statistically significant differences: $^{***}P < 0.001$ = Control group versus Cd; $^{\#\#}P < 0.01$ = Cd versus 250 mg/kg

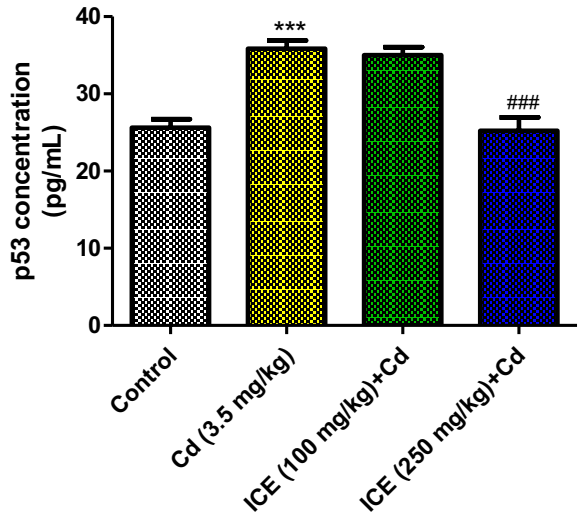

Fig. 13 Protective effect of *Ipomoea cairica* leaf extract (ICE) against cadmium-induced increased expression of p53 protein generation in rat brain. Data are shown as mean ± standard deviation (SD) for 9 animals. Statistically significant differences: $^{***}P < 0.001$ = Control group versus Cd; $^{\#\#\#}P < 0.001$ = Cd versus 250 mg/kg

Antiapoptotic activity of ICE against Cd-induced apoptosis

Figures 11, 12, and 13 show the effect of $CdCl_2$ and ICE on the activity of caspase 3, 9, and p53 level, respectively.

Figure 11 shows that $CdCl_2$ caused a significant increase in the activity of caspase-3 as compared to the control ($P < 0.001$). Pretreatment with 100 mg/kg of ICE could not prevent the Cd-induced expression caspase-3 activity; however, treatment with 250 mg/kg of ICE was able to significantly decrease the expression of caspase-3 ($P < 0.05$) when compared with the untreated group.

Figure 12 shows that $CdCl_2$ caused a significant increase in the activity of caspase-9 as compared to control ($P < 0.001$). Pretreatment with ICE caused a significant decrease in the activity of caspase-p as compared to the untreated group ($P < 0.05$).

Figure 13 shows that $CdCl_2$ caused a significant increase in the level of p53 as compared to the control. Pretreatment with 100 mg/kg of ICE could not increase the level of p53 induced by $CdCl_2$. However, treatment with 250 mg/kg was able to significantly decrease the level of p53 as compared to the untreated group ($P < 0.001$).

Discussion

Acetylcholine (ACh) is a neurotransmitter that plays important role in memory and cognitive function. Acetylcholineesterase (AchE) catalyzes the degradation of ACh into choline and acetate after it has performed its function. The study has shown that in most neurodegenerative diseases, the cholinergic system is often affected via decreasing activity of AChE. Exposure to heavy metals such as Cd has been linked to a decreased level of Ach through an induced increase in AchE activity (Bakulski et al. 2020; Goncalves et al. 2010; Del Pino et al. 2016; Francis et al. 1999*)*. Our result shows that the activity of AChE was elevated in the brain treated with Cd. The observation is supported by the result of other investigators on the role of Cd as an AchE-inducer (Al-Olayan et al. 2020). In the search of an efficient AchE inhibition in the treatment of ND linked to the activity of AchE, natural products are one of the most studied groups of compounds with the potential to inhibit AchE, they prolong the half-life of Ach in the brain (Khafaga et al. 2019; Iranshahy and Javadi 2019). Animals treated with ICE showed low activity of AchE and might prolong the half-life of AchE.

Aggregation of β-amyloid protein into β-plaques that is not easily degraded. These plaques are highly expressed in the brain of a patient suffering from neurodegenerative diseases such as AD (Chauhan et al. 2004; Ghahghaei et al. 2013). Cd is one of the heavy metals with the ability to increase β-amyloid synthesis through altering proteins such as α-secretin and amyloid precursor proteins in the metabolism of β-amyloid in the brain (Notarachille et al. 2014; Yuan et al. 2012). This pathology was observed in our experiment as the concentration of β-amyloid was greatly increased in the brain of rats exposed to Cd. There is a strong link between β-plagues and brain degeneration

as β-plaques have been reported to initiate apoptosis in the brain. Plant-rich antioxidant has been shown to prevent amyloidosis process in the brain (Singh et al. 2011; Ghahghaei et al. 2013; Asadi et al. 2015; Karuppagounder et al. 2009; Porquet et al. 2013). Our result shows that ICE was able to prevent the accumulation of beta-amyloid induced by Cd. The amyloidogenic properties of ICE might be due to various antioxidants phytochemicals present in it.

Alteration of the glutaminergic system is one of the mechanisms by which Cd exerts its excitotoxicity in the brain (Casalino et al. 1997; Chandler et al. 2016; Al-Olayan et al. 2020). Cd caused a significant decrease in the activity of NA^+/K^+ ATPase and GD, while the concentration of glutamate was elevated in the brain. NA^+K^+ ATPase is involved in the transportation of glutamate across the membrane (Ilesanmi et al. 2017, 2019), while GD is involved in the deamination of glutamate (Al-Olayan et al. 2020); when these two enzymes are inhibited, there will be an accumulation of glutamate in the brain causing degeneration of the brain. ICE shows the ability to prevent the neurotoxic effect of Cd by acting as an antiglutamate agent. In addition, compounds from ICE were effective against neurotoxicity of glutamate.

Cd is reported to upregulate the machinery involved in apoptotic processes (Djordjevic et al. 2019; Moon et al. 2019; Gharaji et al. 2019; Wallace et al. 2019). Caspase 3 and 9 and p53 are some of the apoptotic proteins that Cd exposure-induced, in various experimental models. Caspase-3 activation is often regarded as the final straw in the apoptotic process. p53 is a tumor suppressor protein that also plays an important role in apoptosis through the caspase processes. Cd has been shown to interfere with the induction, structure, and function of p53 (Șlencu et al. 2018). Our result also confirmed this statement as we observed an increase in the expression of p53 protein in rat's brain exposed to Cd. There is a strong interplay between caspase 3–9 and p53 in the mechanism by which various heavy metals exert their neurotoxicity. One of the important health benefits of medicinal plants is their antiaging properties, and they potentiate this property by inhibiting caspases activity (Pulido and Parrish 2003). These plants often slow down aging and cell death by acting as an antiapoptotic agent. The antiapoptotic effect of ICE was reflected in the low level of caspase 3, 9, and p53 in the rat brain.

The oxidative stress mechanism of toxicity has been confirmed by the result of various investigations (Joseph 2009; Rena et al. 2019). In addition, some of the above-reported observations on the neurotoxic effect of Cd can be a cause or effect of oxidative stress. β-amyloid and caspase increased generation of reactive species that damage brain cells (Rani et al. 2014; Patrick 2003; Liu et al. 2009). MDA is one of the major markers of oxidative stress (Branca et al. 2015; Sirin et al. 2015; Garcia-Blanco et al. 2017), with high concentration in the brain of Alzheimer's disease patient. Our result shows that the level of MDA is high in the brain of rats exposed to Cd, with resultant depletion in GSH levels. GSH plays an important role in scavenging and de-radicalization of reactive species to the harmless molecule that can be easily eliminated from the body (Eybl and Kotyzová 2010; Khan and Parvez 2015; Hernández et al. 2015). Apart from GSH, other antioxidants involved in the de-radicalization of reactive species include CAT, SOD, and GST. The activities of all these enzymes were highly reduced in the brain of the rat exposed to Cd. This corroborates the report of other work on the neurotoxicity of Cd (Chen et al. 2015; Al-Olayan et al. 2020). Interestingly, pretreatment with ICE was able to prevent the oxidative effect of Cd in the rat brain. The antioxidant effect of ICE has been reported by the various researchers (Raite and Lallianrawna 2013; Yanchon et al. 2021), while some compounds such as arctigenin and isolated from *Ipomoea cairica* have been reported to possess neuroprotective activity (Jang et al. 2002).

Conclusions

Our results shows that administration of 3.5 mg/kg of $CdCl_2$ to male Wistar rats causes biochemical changes observed in the brain of patients suffering from Alzheimer's diseases; this includes increased oxidative stress, low antioxidant activity, apoptosis, low acetylcholine, and formation of β amyloid. Pretreatment with *Ipomoea cairica* leaf extract was able to counter the neurotoxic effect of $CdCl_2$. The neuroprotective properties of I. cairica can be linked to the presence of active phytochemicals with confirmed antioxidant, antiapoptotic, anticholinesterase, and neuroprotective properties. These results reveal the potential use of I. cairica as an antidote against Cd poison. Further investigation will look at the neurobehavioral effect of the plants with respect to neurological disorder models in addition to the effect of the plant on some specific regions of the brain.

Abbreviations

ICE: *Ipomoea cairica* Leaf extract; Cd: Cadmium; ROS: Reactive oxygen species; Ach: Acetylcholine; AchE: Acetylcholineesterase; GD: Glutamate dehydrogenase; CAT: Catalase; GSH: Reduced glutathione; SOD: Superoxide dismutase; MDA: Malonedialdehyde; AD: Alzheimer's disease.

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Authors' contributions

OBI designed and carried out the experiment interpreted and analyzed the data. TTO, OJA, FOA, MA, AJO, TB, and GEB contributed in writing the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials
The datasets generated and analyzed during the current study are not publicly available as it is an ongoing project, but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
All the rats used for this experiment were healthy and treated according to the guidelines of the Helsinki Declaration of 1975 for the care and use of laboratory animals. The experimental design was approved by the ethical committee on animal research and treatment (ART) of the Federal University Otuoke, Nigeria. The approval code was ART2021008. In specific terms, the experiment was conducted in the animal house of the Department of Biochemistry, Faculty of Science, Federal University Otuoke, from February to June 2021.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Biochemistry, Faculty of Science, Federal University Otuoke, Otuoke, Bayelsa State, Nigeria. [2]Department of Biochemistry, Faculty of Life Science, University of Benin, Benin, Edo State, Nigeria. [3]Department of Biochemistry, Faculty of Basic Medical Sciences, Redeemer's University, Ede, Osun State, Nigeria. [4]Department of Biochemistry, Faculty of Natural Sciences, Kogi State University, P.O. Box 100, Anyigba, Nigeria. [5]Present Address: Lagoon School, Lagos, Nigeria. [6]Department of Pharmaceutical Chemistry, College of Pharmacy, Taif University, P.M.B 11099, Taif 21944, Saudi Arabia. [7]Department of Pharmaceutical Chemistry, College of Pharmacy, King Saud University, Riyadh, P.O. Box 2457, Riyadh 11451, Saudi Arabia. [8]Department of Pharmacology and Therapeutics, Faculty of Veterinary Medicine, Damanhour University, Damanhour 22511, AlBeheira, Egypt.

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