Research Article

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Scopolamine-Induced Memory Impairment in Mice: Neuroprotective Effects of Carissa edulis (Forssk.) Valh (Apocynaceae) Aqueous Extract.

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INTRODUCTION

Neurodegenerative illnesses impair nerve cell integrity, interfere with the nervous system's normal operation, and may, depending on the afflicted regions, have an impact on language, perception, cognition, memory, and movement during its evolution [1]. Globally, dementia is a significant public health issue, and its prevalence is rising among the elderly [2]. Alzheimer's disease (AD) is one type of dementia that is typified by elevated levels of amyloid beta (Aβ) and phosphorylated Tau protein, which are linked to changes in the central cholinergic system and an irreversible loss of cognitive function that worsens memory [3, 4]. There is currently no treatment for the illness or even a way to stop its advancement. But the majority of the treatment approaches already in use are symptomatic, halting the progression of the illness [5]. Acetylcholinesterase inhibitors and N-methyl-D-aspartate receptor antagonists are the primary therapy for the illness [3].

Unfortunately, because of their nonselective activity on a range of organ tissues both centrally and peripherally, these medications have been linked to a number of side effects, including nausea, vomiting, anorexia, and sleeplessness.

One potential source of AD medication in the future is medicinal plants. Generally speaking, Carissa edulis (C. edulis) was chosen because it is used to treat dementia in conventional medicine.

The plant C. edulis is widely dispersed throughout Africa and is used to treat a variety of conditions including oxidative stress, fever, headaches, malaria, and inflammatory illnesses including rheumatism. Numerous pharmacological studies have examined C. edulis, including in vitro antioxidant activity through scavenging of DPPH and ABTS radicals [10], anticonvulsant activity via various mechanisms, including voltage-gated sodium, calcium, and potassium or GABAergic pathway [11], and diuretic activity through increasing kidney blood flow and glomerular increased urine output due to filtration rate [12], antiviral activity against Herpes simplex virus (HSV) in vitro and in vivo studies [13], antiplasmodial activity against chloroquine-sensitive strains of Plasmodium falciparum parasite [14], and hepatoprotective effect against subchronic administration of dimethoate on guinea pigs [15] by normalizing and restoring the liver enzyme and the antioxidant markers. Even at high dose levels of 5000 mg/kg, C. edulis extracts have all been reported to be well tolerated in experimental animals [16–18]. The current study aims to evaluate the neuroprotective and memory enhancement effects of C. edulis on Scopolamine-induced memory impairment and oxidative stress in mice, with the goal of searching for safe and novel drugs against memory impairment associated to Alzheimer's disease.

MATERIAL AND METHODS

Plant Matter. The identification of the C. edulis leaves was verified at the National Herbarium Yaounde, Cameroon, where the voucher specimen was stored under the number 2965/SRFK. The leaves were collected in the Far North region of the country. To create a fine powder, the leaves were cleaned, allowed to dry in the shade, crushed, and then sieved.

Making an Aqueous Extract. After adding 10 grams of the powdered plant material and 60 milliliters of distilled water to a beaker, the mixture was allowed to boil for 20 minutes. Wattman paper no. 1 was used to filter the mixture once it had cooled. The resulting filtrate (C = 62:8 mg/ml) was given to the mice at a volume of 10 ml/kg after being diluted with distilled water at 1/10, 1/4, and 1/2. The C. edulis aqueous extract that was previously prepared as described above (35 ml) of the filtrate was evaporated in an oven at 80°C for 24 hours in order to obtain 2.2 g of dry extract, which was then used to calculate the amount of dry matter in the aqueous extract. The various doses per 10 ml/kg that were created in distilled water were 62.8, 157, 314, and 628 mg/kg.

creatures. 35 Mus musculus Swiss mice, weighing between 25 and 30 g at two months old, were taken from the Institute of

Medical Research and Medicinal Plants Studies' animal house in Yaounde, Cameroon. All of these creatures were housed in cages made of plexiglass, with a constant temperature of roughly 25°C and a light-dark cycle of 12 hours each. The animals were gradually denied food two days before to the studies in order to keep them between 80 and 85 percent of their body weight. Every experiment was conducted in compliance with the globally recognized guidelines for the use and care of laboratory animals.

Design Experiments. The idea is to administer scopolamine (1 mg/kg), a selective muscarinic acetylcholine receptor antagonist, intraperitoneally (i.p.) to mice in order to cause memory impairment, and then assess the behavioral and biochemical consequences on the mice. The animals were divided into seven groups, each consisting of five mice: distilled water was given to the control group; Scopolamine (1 mg/kg i.p.) was given to the Scopolamine group (Scopo); four test groups received C. edulis aqueous extract at varying doses (62.8, 157, 314, and 628 mg/kg) and then received an injection of Scopolamine (1 mg/kg i.p.); a positive control group received donepezil (5 mg/kg) and then received an injection of Scopolamine (1 mg/kg i.p.). The oral administration of donepezil and the aqueous extract of C. edulis was done half an hour prior to the injection of Scopolamine. For a span of seven days, every therapy was given every day. The International Journal of Alzheimer's Disease, Volume 2, Issue 9, Page 1, 2020 downloaded [09/07/2024] from Wiley Online Library at https://onlinelibrary.wiley.com/doi/10.1155/2020/6372059. Wiley Online Library's Terms and Conditions can be found at https://onlinelibrary.wiley.com/terms-and-conditions. Open Access articles are subject to the relevant Creative.

RESULTS

Impact of C. edulis on T-Maze Test-Induced Scopolamine-Induced Memory ImpairmentTime of Latency. Figure 1 illustrates the impact of the Carissa edulis aqueous extract on the latency time for the mice to access the preferred arm in the T-maze. The findings indicate that the Scopolamine group's latency time of entry into the preferred arm was significantly longer ($p < 0:001$) than that of the control group. When C. edulis and Donepezil are administered at different doses to the animals, the latency time decreases significantly ($p < 0:001$) in comparison to the Scopolamine group. It goes from 23:6±1:14 sec to 12:8±1:30 sec for mice receiving 628 mg/kg of C. edulis extract and 11:4±1:43 sec for mice receiving Donepezil, which is used as a positive control. These timings are similar to those of the control group that got time of 10:8±0:83 sec.

Movement of Locomotives in an Open Field. The mice were assessed for their locomotor activity in the open field following the T-maze test since they had been given scopolamine. When compared to the Scopolamine group, Table 1 demonstrates a substantial increase ($p < 0:001$) in locomotor activity based on the number of crossings in the mice receiving dosages of C. edulis aqueous extract and getting donepezil. When compared to the control group, the crossing number of the Scopolamine group (50:8±3:1) considerably decreased ($p < 0:001$). The same is true for rearing, where animals given a dose of 628 mg/kg C. edulis aqueous extract have increased activity ($p < 0:05$), while the Scopolamine group ($p < 0:001$) experiences a decrease in activity. The amount of time spent in the open field's center ($p < 0:001$). When the animals were given 628 mg/kg of C. edulis aqueous extract ($p < 0:01$) and Donepezil ($p < 0:001$) in comparison to the Scopolamine group, a longer period of time was seen. In charge 62.8 157 314 628 Scopo Donepezil 0 – 10 – 20 – 30 ### * C. edulis dosages (mg/kg) Figure 1: latency period to enter the chosen Tmaze arm. For n = 5, the mean ± SEM is shown for each bar. When C. edulis aqueous extract and donepezil are administered, the latency time decreases (###$p < 0:001$ vs. Scopo) and increases for the Scopolamine group (###$p < 0:001$ vs. control). one-way ANOVA and the Tukey multiple comparison test that come after. 4 International Journal of Alzheimer's Disease Scopo: Scopolamine Time lag (seconds) 9730, 2020, 1, Movement of Locomotives in an Open Field. The mice were assessed for their locomotor activity in the open field following the T-maze test since they had been given scopolamine.

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DISCUSSION

The goal of the current investigation is to determine whether

or not Carissa edulis can enhance memory impairment by acting on the cholinergic pathways. A notable role for medicinal plants is being played in the treatment of Alzheimer's disease and memory impairment. In this investigation, we assessed the impact of C. edulis on the Tmaze and new object recognition tests' effects on amnesic mice's memory function. As previously documented [26], scopolanine blocked the muscarinic cholinergic receptors in the brain, causing amnesia in the animals through decreased memory. In the current study, mice given continuous doses of scopolantine had longer latencies to enter the preferred arm, which decreased the amount of time spent in the preferred arm. Time spent in the preferred arm of the T-maze increases when C. edulis aqueous extract is administered because it reduces this latency time. As previously noted, the reduction in latency time suggested that memory had improved [27]. The notable rise in both the quantity of entries and the duration of time spent in the favored arm indicates s a memory that operates well [28, 29].

The findings indicate that the aqueous extract of C. edulis has antagonistic effects on the action of Scopolamine. This may be because the extract contains bioactive substances like coumarins, polyphenols, terpenes, tannins, flavonoids, cardiac glycosides, lignans, and sesquiterpenes that may improve memory loss by blocking the effects of Scopolamine. Numerous studies show that polyphenols have the antioxidant ability to permeate the blood-brain barrier and neutralize free radicals, protecting the brain and nervous system. Memory enhancement is one of polyphenols' primary roles [9]. Furthermore, the rise in the quantity of entries and the duration of time spent in the arms—both favored and discriminated—indicates an increase in the behavior of exploration and, consequently, in memory.

Memory functions heavily rely on the central cholinergic system [8]. Age-related cognitive deficits are caused by dysfunctional acetylcholinergic neurons [4, 6]. The available data align with the findings of Chen et al. [42], Budzynska et al. [43], and Park et al. [44], who documented that scopolanine causes significant cholinergic deficits and increases acetylcholinesterase activity in the hippocampus, hence exacerbating brain neurodegeneration. When compared to the Scopolamine group, treatment with the aqueous extract of C. edulis dramatically decreased the activity of acetylcholinesterase.

CONCLUSION

The goal of this study was to determine whether the aqueous extract of Carissa edulis, a muscarinic acetylcholine receptor antagonist, might prevent memory loss caused by the drug scopamine. Acetylcholinesterase activity was also elevated in response to cocaine-induced memory and learning deficits assessed in behavioral investigations using T-maze and object recognition tests. Administering C. edulis aqueous extract improved memory substantially, as evidenced by T-maze and novel object recognition tests. It also strengthened the antioxidant defense system, shielding neurons from oxidative stress and mitigating the memory loss caused by Scopolamine. This investigation was restricted to how C. edulis ameliorated the cognitive deficit brought on by scopolamine, thereby protecting the cholinergic system. Consequently, the impact of C. edulis on additional potential pathways implicated in the pathophysiology of AD.

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GAA edited the manuscript and oversaw the laboratory work. The study was developed, designed, and the final draft of the manuscript was revised by GST and ENB. The final draft of the manuscript was read, edited, and approved by all authors.

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