Aqueous extracts of two tropical ethnobotanicals (Tetrapleura tetraptera and Quassia undulata) improved spatial and non-spatial working memories in scopolamine-induced amnesic rats: Influence of neuronal cholinergic and antioxidant systems

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ARTICLE INFO

Keywords:
Scopolamine
Amnesia
Tetrapleura tetraptera
Quassia undulata

ABSTRACT

Background: Tetrapleura tetraptera (TT) and Quassia undulata (QU) are two predominant tropical ethnobotanicals with various medicinal values but are commonly used in folklore for the treatment of mental illness without justifiable mechanisms of action.

Aim of the study: To investigate the effects of aqueous extracts from TT fruits and QU leaves on the spatial and non-spatial working memory, antioxidant status and activities of neuronal marker enzymes of scopolamine-induced amnesic rats and thus, understand the possible mechanism of action of these plants.

Materials and Methods: Fifty-five albino rats were divided into eleven groups. Group I (normal rats) received normal saline (p.o.), Group II–V (normal rats) administered with 50 and 300 mg/kg of each extract group VI (induced rats) received 2 mg/kg of scopolamine (i.p.), groups VII–X (induced rats) pretreated with 50 and 300 mg/kg of TT and QU extracts (p.o) before scopolamine administration, group XI (induced rats) treated with 2.5 mg/kg of donepezil. The treatment lasted for 14 days and amnesia was induced by a single dose of 2 mg/kg of scopolamine on the last day. Spatial (Y-maze) and non-spatial (novel object recognition test) working memories of the rats were tested. Thereafter, the animals were sacrificed and homogenates of isolated brain samples were assayed for cholinesterase activity and malondialdehyde (MDA) content. The phenolic characterisation of the samples was also carried out using HPLC-DAD chromatography.

Results: Administration of 2 mg/kg of scopolamine brought about a decrease in spatial and non-spatial memory indices, increase in acetylcholinesterase and butyrylcholinesterase activities, as well as increased MDA content compared to the control. However, pretreatment with both extracts improved both spatial and non-spatial working memories and ameliorated the increased enzyme activities and MDA contents. Furthermore, the HPLC-DAD characterization of the extracts revealed the presence of p-coumaric acid, rutin, catechin, ellagic acid, quercetin, caffeic acid, chlorogenic acid and galic acid.

Conclusion: The ability of the extracts to improved cognitive function and ameliorate impairment in cholinergic enzyme activities and antioxidant status in scopolamine-induced amnesic rats could help justify the possible neuroprotective properties of TT and QU and also explain possible mechanism of action of these ethnobotanicals as obtained in folklore medical practices

1. Introduction

Cognitive enhancement is the ability to retain information for a specific time and still remembers it when needed [1]. Neurodegenerative diseases like Alzheimer’s disease (AD) among others are associated with impairments of cognitive function [2], and it’s associated with poor memory retention. Age, stress, emotions are conditions that may lead to memory loss, amnesia, anxiety, dementia, or to more ominous threats like schizophrenia and AD [1]. The National Institute of Health predicts that there will be more than 8.5 million AD patients by the year

**References**


2030 in the USA alone [2]. Global prevalence of AD is higher in Female than male [3].

AD is characterized by degeneration of memory, which is associated with functional decline and neurobehavioral disturbances [4,5]. It is a multifactorial disease in which many factors such as amyloid-beta deposition, tau phosphorylation, alteration of cholinergic transmission, oxidative stress, inflammation, monoamnergic disturbances, and apoptotic process contribute to this neurological disorder [6]. Numerous researches on the brains of AD and dementia patients have consistently reported abnormalities or damage in the central cholinergic pathways. In view of this, treatment of AD related dementia is usually by the use of acetylcholinesterase (AChE) inhibitors such as donepezil. Studies have shown that donepezil exerts neuroprotective properties [7–9]. Donepezil is a known drug for clinical treatment of scopolamine induced Alzheimer-type dementia [8,9]. It is a piperidine-based, noncompetitive, reversible inhibitor of AChE, which has high specificity for the central versus peripheral cholinergic system [10,11]. The use of donepezil comes with numerous side effects such as, nausea, insomnia and muscle cramps amongst others. Therefore, new therapeutic modalities with sufficient efficacy and better safety profiles have long been desired.

Scopolamine is a cholinergic antagonist which is known to interfere with acetylcholine transmission in the central nervous system. This drug has been used as reference for the induction of amnesia in animal models [6]. The most common characteristic of dementia is impairment of memory and learning and this could be induced chemically in experimental animals by administration of scopolamine. Effect of scopolamine on memory is accompanied with central cholinergic dysfunction [12–14]. Furthermore, scopolamine-induced amnesia is associated with decreased glucose oxidation, increase in brain oxidative and decrease of ATP levels in the brain [14]. Interest has grown in the development of novel animal models that could simulate human disease features and which could contribute to the increase in the knowledge about cellular mechanisms involved in these pathologies [14].

Phytochemicals present in plants have been shown to improve memory, general cognitive ability and learning [15]. Studies have highlighted the effects of phytochemicals as modulators of brain function [16]. Fruits, vegetables and plant-derived beverages are the main dietary sources of these phytochemicals [17]. Polyphenols are the major phytochemicals present in plants [18]. Studies have established that there is a relationship between ingestion of polyphenols and the prevention of AD [19]. Polyphenols are a large group of compounds which can be divided into many subgroups, including the flavonoids. Rutin and quercetin are the two most widely and abundantly present flavonoids present in herbs and plants [20]. Many plants are being used to treat cognitive disorders in folklore, and other memory related disorders e.g. amnesia. The use of plants (herbs) in treating diseases has since been part of man's folklore. In Nigeria, about 80% of the population live in rural areas and rely on herbal and traditional medicine for their health care needs [21]. Yoruba (Nigeria) traditional system of medicine offers a number of safe treatments from ethnobotanical plant for CNS related disorders including aging and memory loss [22]. The efficacies of TT and QU have been recognized as cognition enhancers for the treatment of mental illness in folk medicine [22]. TT (Schumm. & Thonn. Family: Mimosaceae.) Fruit, locally known as ‘prekese’ in Ghana and ‘aridan’ in South Western Nigeria is a medicinal plant, with 4 longitudinal wing like ridges, nearly 3 cm broad. Two sides of the wings are woody while, the other 2 are filled with soft, sugary pulp, oily and aromatic, common on the fringe of the West African rainforest belt [23]. It is used as spices and aroma. It is one of the molluscicidal medicinal plants of Nigeria. The fruit is useful in the management of leprosy, inflammation, convulsion and rheumatoid pains. The fruit contained varying amounts of nutrients such as protein, lipids and minerals [24]. QU (Guill. & Perr. Family: Simaroubaceae) is a perennial shrub that is distributed in an open grass land or wooded grassland in tropical and subtropical Africa, Asia, Australia and America. It is commonly called Akan-asse hotoro by the Ghanaians, and Oriji in Yorubas land (Nigeria) [23]. QU possesses antimarial activity due to the high concentration of quassiods present in it [25]. It also possess antimicrobial activities [26].

This study sought to characterize the bioactive constituents of the aqueous extracts from TT fruit and QU leaves; investigate the cognitive enhancing properties of the plants using Novel object recognition (NOR) and Y-Maze tests. The cholinesterase and antioxidant activities of the rats’ brain homogenate were also investigated in order to understand possible mechanism of action by which these ethnobotanicals are used in folklore for the management/treatment of neurological disorders.

2. Materials and methods

2.1. Chemicals and reagents

Scopolamine hydrobromide was purchased from Sigma–Aldrich Corp. (St. Louis, MO, USA). All other reagents used were of analytical grade and the water was glass distilled.

2.2. Sample collection

TT fruit and QU leaves were obtained from Akure, South West, Nigeria [7.2500’ N, 5.1950’ E] main market. The plants identification was carried out in the Department of Biology, Federal University of Technology, Akure, Nigeria by A. A. Shorungbe with voucher numbers BIO/FUTA/150 and BIO/FUTA/151 respectively and a voucher specimen was deposited at the herbarium of the Federal University of Technology, Akure.

2.3. Preparation of aqueous extract

The TT fruit and fresh leaves of QU were washed under running water and later air dried, after which the dried samples were pulverized and kept dry in an airtight container prior to the extraction. 10 g of the powdered sample was soaked in cold distilled water for 24 h placed in an orbital shaker. The mixture was then filtered through Whatman No. 1 filter paper and the filtrate centrifuged at 805 × g for 10 min. The clear supernantant collected was freeze dried and stored in small, capped plastic container at 4°C until required [27]. This was later reconstituted in distilled water to produce the administered doses (50 and 300 mg/kg)

2.4. Animal preparations and treatment

Fifty - five female albino rats weighed between 180–200 g were bought from the animals holding facility of the University of Ilorin, and in a good hygienic condition of 12 h alternating light and dark, controlled temperature, and adequate ventilation, free to feed and water ad libitum. The animals were divided randomly into eleven (11) groups of 5 animals (n = 5) each. Group I: Control rats that received normal saline, Group II–V: Normal rats treated with 50 and 300 mg/kg of each extract for a period of 14 days through oral administration, Group VI: induced rats that received 2 mg/kg of scopolamine via intraperitoneal (i.p.) alone, Group VII-X: induced rats but, pretreated with 50 and 300 mg/kg of each extract for a period of 14 days through oral administration, group XI: Induced rats treated with 2.5 mg/kg of donepezil. Scopolamine was i.p. (2 mg/kg) administered to all animals in the induced groups (VI–XI) on the 14th day after the training trial for NOR. The NOR testing trial was done 1 h after scopolamine administration, while the Y-maze was done 1 h later [13]. The choice of 2 mg/kg of scopolamine was based on previous studies using this dose to induce amnesic conditions in rats [28], while the choice of dose of extracts were based on our previous findings (data not shown) where oral administration of both extracts at ≤ 2000 mg/kg produced no acute
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