Original Research Article

COMPARATIVE MEMORY-ENHANCING ACTIVITY OF TWO CISSUS SPECIES: *Cissus arguta* HOOK.F. AND *Cissus quadrangularis* L. (VITACEAE)

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ABSTRACT

Memory dysfunction refers to the deterioration of cognition that affects the ability to reason, remember, make decisions, and communicate. Strategic Acetylcholinesterase enzyme inhibition helps in combating age-related neuronal degeneration that leads to memory loss. Some *Cissus* species have been reported for memory-enhancing activity, but there is still a dearth of research for this genus. Hence, the memory-enhancing activity of *Cissus arguta* and *Cissus quadrangularis* will be assessed. The plant samples (leaves and stems) were air-dried, pulverised, extracted to obtain methanolic extracts, concentrated in vacuo, and the extracts were subjected to in vitro acetylcholinesterase inhibitory activity using a modified Ellman's colorimetric assay method with eserine as the standard drug. The most active crude extract was then partitioned into n-hexane, dichloromethane, and methanol fractions and investigated for *in vitro* acetylcholinesterase inhibitory activity. All extracts had acetylcholinesterase inhibitory effect but the highest inhibition was observed in *Cissus arguta* leaf crude extract (IC_{50} = 0.23 ± 0.02 mg/mL), followed by *Cissus quadrangularis* stem extract (IC_{50} = 0.47 ± 0.02 mg/mL), *Cissus quadrangularis* leaf extract (IC_{50} = 0.85 ± 0.02 mg/mL) and *Cissus arguta* stem extract ((IC_{50} = 3.82 ± 0.23 mg/mL). The methanol fraction of *Cissus arguta* leaf extract showed promising acetylcholinesterase activity with an IC_{50} value of 0.06 ± 0.004 mg/mL. All values are comparable with the standard drug, eserine (IC_{50} = 0.04 ± 0.001 mg/mL). *Cissus arguta* and *Cissus quadrangularis* crude extracts possess memory-enhancing activity and are potential sources of drug candidates that can be harnessed in drug discovery to manage neurodegeneration and memory loss.

INTRODUCTION

Memory decline, commonly referred to as dementia are group of neurological disorders that gradually impair mental capabilities and are predominantly observed in adults [1]. The estimates of the prevalence of dementia globally are up to 7% of all individuals aged 65 years and above, and as high as 30% in those over the age of 85 [2-3], with an estimated prevalence of over 50 million cases worldwide and new cases occurring every three seconds [1]. The most frequently encountered forms are those linked to Alzheimer's disease (AD), which accounts for 60 to 70% of cases, followed by vascular dementia, dementia with Lewy bodies, and frontotemporal degeneration[1-4]. Alzheimer's disease is characterised by a reduction of acetylcholine level within synaptic junctions, alongside the accumulation of amyloid plaques and neurofibrillary tangles in cerebral tissues, which contributes to inflammation and nerve cell damage [5]. The neurotransmitter acetylcholine (ACh) is essential for an adequately functioning memory, and its deficiencies lead to the disruption of the

cholinergic system in Alzheimer's disease [5-6]. One of the primary therapeutic targets in managing this condition is the enzyme Acetylcholinesterase (AChE), which breaks down acetylcholine [6]. Medications employed to alleviate symptoms include Acetylcholinesterase (AChE) inhibitors, which inhibit the enzyme acetylcholinesterase and help to improve cognitive symptoms like confusion and memory loss, and N-methyl D-aspartate (NMDA) antagonists, which help to manage glutamate levels, a primary excitatory neurotransmitter in the human brain [7]. Severe side effects have been associated with synthetic drugs used in treating Alzheimer's disease; therefore, there is an urgent need for possible alternative treatments with fewer side effects for Alzheimer's disease and memory deficit [8]. Recently, medicinal plants have been widely accepted as a result of their fewer side effects compared to synthetic medicines and the need to meet the requirements of medicine for the increasing human population. In previous research, medicinal plants were reported to possess acetylcholinesterase inhibitory effects, which is effective against symptoms of memory decline [9-12].

Cissus plants belonging to the Vitaceae family hold much relevance due to its use in complementary medicines for managing pathological symptoms related to diabetes, infections, arthritis, menopause, obesity, pain, and cancer [13-14]. This genus is the largest in the Vitaceae family, with several phytochemical constituents, including ascorbic acid, alkaloids, terpenoids, saponins, flavonoids, sterols, quinones, phenolics, lignans, and tannins, which exhibit different therapeutic properties [15]. *Cissus arguta* Hook.f., a lesser-known member of the *Cissus* species, is a creeping plant native to the rainforests of southern Nigeria [16-17]. Ethnobotanically, it is used to treat severe fever, cough, chest pain, inflammation of the lymphatic nodes, blood vessel obstruction, rashes, boils, wounds, body aches, neck pain, as well as bone-related diseases and disorders [16-17]. Although *Cissus arguta* is mostly employed in traditional medicine, scientific exploration of this plant's potential remains limited. The acetylcholinesterase inhibitory property of this plant has not been evaluated yet. Reported pharmacological activities of the plant include anti-inflammatory, antifungal, antibacterial, and wound-healing properties, which have been attributed to the presence of phytochemicals such as flavonoids, tannins, alkaloids, glycosides, steroids, phenolic compounds, eugenols, and saponins in this plant, as reported in Literature [16-17].

Cissus quadrangularis L*.,* in comparison, is a glabrous, large climber or trailer native to West Africa, India, Sri Lanka, Malaysia, and Java (an island in Indonesia) [18]. Traditionally, its relevance is found in the treatment of diabetes, obesity, high cholesterol, bone fractures, allergies, cancer, stomach upset, painful menstrual periods, asthma, malaria, wounds, peptic ulcer disease, and weak bones (osteoporosis) [18]. Locally, its strong, fleshy, quadrangular stem is used to treat acid reflux, gastritis, eye disorders, piles, and anaemia [18]. *Cissus quadrangularis* contains phytochemicals such as phenols, tannins, alkaloids, phytosterol, saponins, glycosides, flavonoids, mucilage, β-sitosterol, terpenoids, and alkaloids [19-20]. The pharmacological activities include bone fracture healing, antimicrobial, antidiabetic, antioxidant, cholinergic, and anticancer activities [21-22]. The methanolic extract of *Cissus quadrangularis* has been reported to work on ulcer-related and cell-related diseases, for instance, indomethacin-induced gastric mucosal injury, as well as a beneficial effect on cardiovascular diseases [22]. The aqueous extract also shows acetylcholine-like activity *ex vivo* [22]. *Cissus quadrangularis* role in treating Alzheimer's disease has not been extensively established despite many reports. Hence, this study seeks to evaluate the acetylcholinesterase activity and make a comparison between the memory-enhancing activity of *Cissus arguta* and *Cissus quadrangularis* leaf and stem methanol extracts.

MATERIALS AND METHODS

Chemicals
Analytical-grade reagents used include acetylcholinesterase (EC 3.1.1.7), acetylthiocholine iodide (ATChI), 5,5'-dithio-bis-(2-nitrobenzoic acid) (DTNB), physostigmine (eserine), Phosphate buffer (pH 8.0, 0.1M), dichloromethane, n-hexane, and methanol.

Equipment and Materials
Precoated thin-layer chromatography (TLC) plates with silica gel G60.

Plant Collection
Cissus arguta and *Cissus quadrangularis* leaves and stems were collected from Amina Way and Ajibode, respectively, in Ibadan, Oyo State, Nigeria. *Cissus arguta* was identified and authenticated by Mr. T. K. Odewo at the Forest Herbarium Ibadan (FHI), (FRIN), and a voucher specimen (FHI 113879) was deposited at the Department of Pharmacognosy Herbarium, University of Ibadan. *Cissus quadrangularis* was identified by Mr. Olubunmi Mada, Herbarium Curator at the same institution.

Preliminary Phytochemical Screening
Preliminary screening of phytochemicals was carried out on the powdered samples of *Cissus arguta* (leaves and stems) and *Cissus quadrangularis* (leaves and stems) using standard methods [23-24] to evaluate the contents such as flavonoids, saponins, tannins, alkaloids, and anthraquinones.

Sample preparation
Pulverized plant samples were placed in 100% distilled methanol by maceration for 72 hours with regular stirring, after which the extracts were concentrated *in vacuo* at 40°C using a rotary evaporator [Rotavapor® R II, Buchi, Switzerland] to obtain crude methanol extracts. The most active memory-enhancing crude extract was partitioned into n-hexane, dichloromethane, and aqueous fractions. The required screening for acetylcholinesterase (AChE) inhibitory activities of both extracts (crude and fractions) followed afterwards.

Anticholinesterase Inhibitory Assay

Spectrophotometric methods were used to determine acetylcholinesterase inhibitory potentials of extracts, using acetylthiocholine iodide as the substrate, by the modified Ellman's method [21]. Stock solutions (5 mg/mL) of the crude extracts were diluted serially twofold using methanol to obtain these concentrations of 5, 2.5, 1.25, 0.625, 0.3125, and 0.15625 mg/mL. The fractions were also diluted serially from stock solutions (1 mg/mL) to achieve concentrations of 1, 0.5, 0.25, 0.125, 0.00625, and 0.03125 mg/mL. Eserine served as the positive control and standard memory-enhancing drug, and was diluted serially using a two-fold dilution to obtain final concentrations of 0.1, 0.05, 0.025, 0.0125, 0.000625, and 0.003125 mg/mL. In this method, 0.1 mL of each sample concentration was pipetted into labelled test tubes, followed by 2 mL of phosphate buffer (pH 8.0, 0.1M) and 0.1 mL of acetylcholinesterase enzyme. The mixtures were incubated at 37°C for 30 minutes. Afterwards, 0.1 mL of 10 mM Ellman's reagent (5, 5-dithio-bis-2-nitrobenzoic acid - DTNB) was added to all test tubes, followed by the addition of 0.1 mL of the substrate, acetylthiocholine iodide. The hydrolysis of acetylthiocholine iodide was determined spectrophotometrically at a wavelength of 412 nm by the formation of yellow 5-thio-2-nitrobenzoate anions resulting from the reaction of DTNB with acetylthiocholine, catalysed by the acetylcholinesterase enzyme. The assay was performed in triplicate, with methanol serving as the negative control. The % inhibition of each crude methanol extract was determined using the formula:

$$\frac{\Delta a - \Delta b}{\Delta a} \times 100$$

Where Δa = change in absorbance/minute of negative control, and Δb = change in absorbance/minute of plant extract/fractions.

Thin Layer Chromatography (TLC)

The TLC was carried out on crude extracts and their respective fractions, derived from the most active sample. The separation process utilized a solvent mixture of toluene and ethyl acetate in a 3.5:1.5 volume ratio. Each sample was applied to TLC plates that were pre-coated to a specific size, and the plates were then developed using a chosen solvent system. Visualization of the separated compounds was performed under UV illumination at wavelengths of 254 and 365nm.

Statistical analysis

Experimental data were presented as the mean and standard error, based on triplicate measurements from three separate trials. The half-maximal inhibitory concentration (IC$_{50}$) for each sample was determined by plotting concentration-response curves and applying non-linear regression analysis using GraphPad Prism software, version 8.1.2.

RESULTS

Table 1 shows the distribution of key phytochemicals across leaf and stem extracts of *Cissus arguta* and *Cissus quadrangularis*. Notably, *C. quadrangularis* stem extract exhibited the richest profile, with moderate presence of saponins, tannins, flavonoids, steroids, and anthraquinones, suggesting a potentially stronger pharmacological activity. Screening results indicated that saponins, tannins, flavonoids, steroids, and alkaloids were domiciled in the leaf extract of *Cissus arguta*, while anthraquinones were absent (Table 1). *Cissus arguta* stem extract possesses saponins, flavonoids, and alkaloids, whereas tannins, steroids, and anthraquinones were absent. Leaf extract of *Cissus quadrangularis* contains flavonoids, alkaloids, tannins, steroids, and anthraquinones, while saponins were absent. *Cissus quadrangularis* stem extracts contained saponins, flavonoids, alkaloids, tannins, steroids, and anthraquinones.

Effects of *Cissus arguta* and *Cissus quadrangularis* Extracts on Acetylcholinesterase Inhibition

Figure 1 compares the average percentage acetylcholinesterase inhibition of *Cissus arguta* (CAL) and *Cissus quadrangularis* (CQL) leaf extracts across concentrations. *Cissus arguta* leaf extract showed consistently higher inhibition, especially at 5 mg/mL, indicating stronger potential for memory enhancement. In this study, all the extracts exhibited inhibitory potential for acetylcholinesterase (AChE) in a dose-dependent manner. However, the leaf extract of *Cissus arguta* demonstrated the highest activity, showing average percentage inhibitions of 93.3% and 38.1% at 5 mg/mL and 0.15625 mg/mL concentrations, respectively. In comparison, the average percentage inhibition of *Cissus quadrangularis* leaf extract against acetylcholinesterase was observed to be 73.6% and 34.4% at 5 mg/mL and 0.15625 mg/mL, respectively.

Figure 2 presents the average percentage acetylcholinesterase inhibition by the stem extracts of *Cissus arguta* (CAS) and *Cissus quadrangularis* (CQS). The stem extract of *Cissus quadrangularis* demonstrated superior inhibition across most of the concentrations, suggesting greater therapeutic promise. The average percentage inhibition observed for *Cissus arguta* stem extract was 58.7% and 14.3% at the concentrations of 5 mg/mL and 0.15625 mg/mL, respectively. In comparison, *Cissus quadrangularis* stem extract showed average percentage inhibition of 81.5% and 39.9% at the concentrations of 5 mg/mL and 0.15625 mg/mL, respectively.

Figure 3 illustrates the average percentage acetylcholinesterase inhibitory activity of the standard memory-enhancing drug, Eserine. *Cissus arguta* leaf (CAL) and *Cissus quadrangularis* stem (CQS) extracts showed inhibition levels approaching that of Eserine, indicating strong potential as natural alternatives.

Table 1: Phytochemical Screening of *Cissus arguta* and *Cissus quadrangularis*

	Cissus arguta		*Cissus quadrangularis*	
Test	**Leaf**	**Stem**	**Leaf**	**Stem**
Saponins	+	++	-	++
Tannins	+	-	++	++
Flavonoids	++	+	++	++
Steroids	+	-	++	++
Alkaloids				
Dragendorff	++	+	++	++
Mayer	+	+	++	+
Wagner	+	+	++	++
Anthraquinones	-	-	+	++

Key: + = Present, **++** = Moderately Present, **-** = Absent.
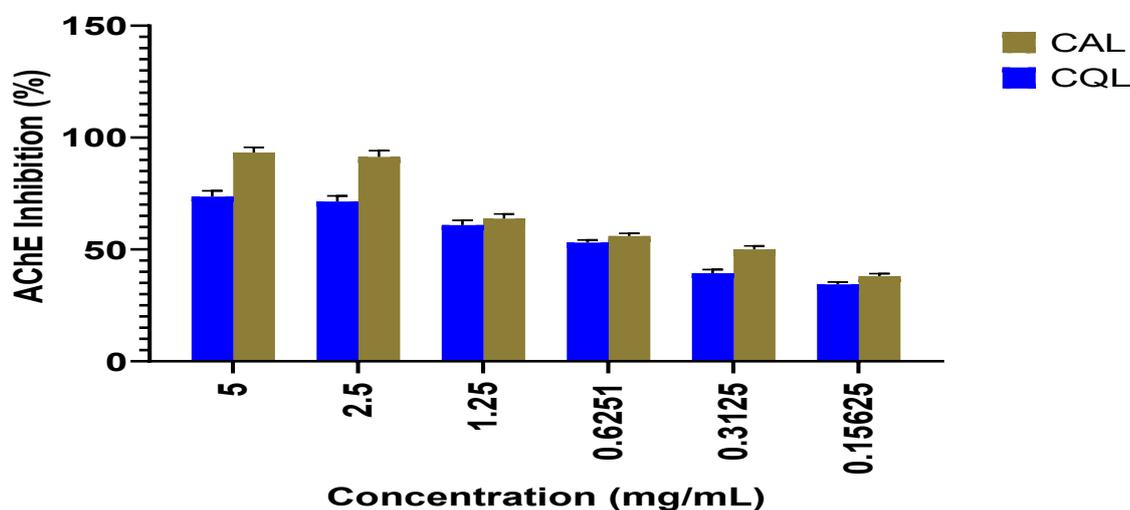

Figure 1: A chart comparing the Acetylcholinesterase Inhibitory Activity of crude extracts of *Cissus arguta* and *Cissus quadrangularis* leaves. KEY: CAL = *Cissus arguta* leaf, CQL = *Cissus quadrangularis* leaf
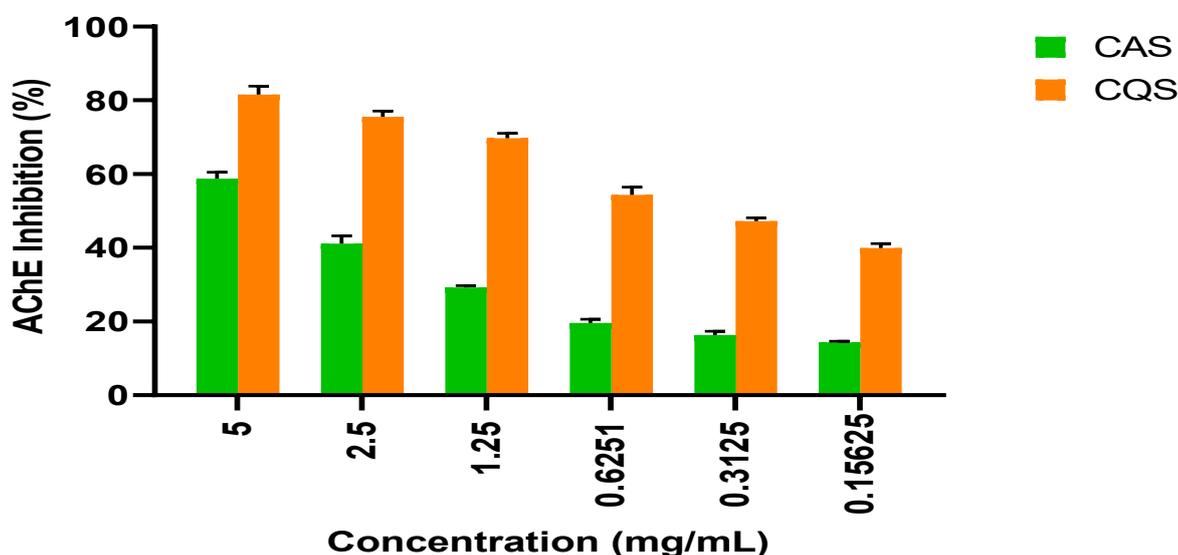
Figure 2: A chart comparing the Acetylcholinesterase Inhibitory Activity of crude extracts of *Cissus arguta* and *Cissus quadrangularis* stems
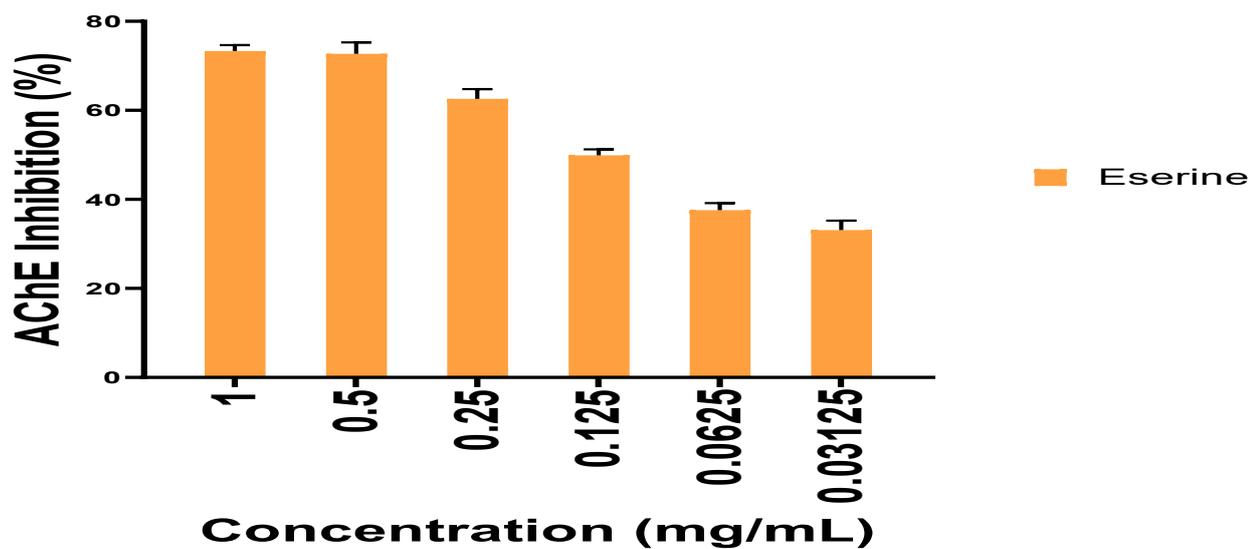

Figure 3: A chart showing the Acetylcholinesterase Inhibitory Activity of Eserine (Standard Memory-Enhancing Drug)
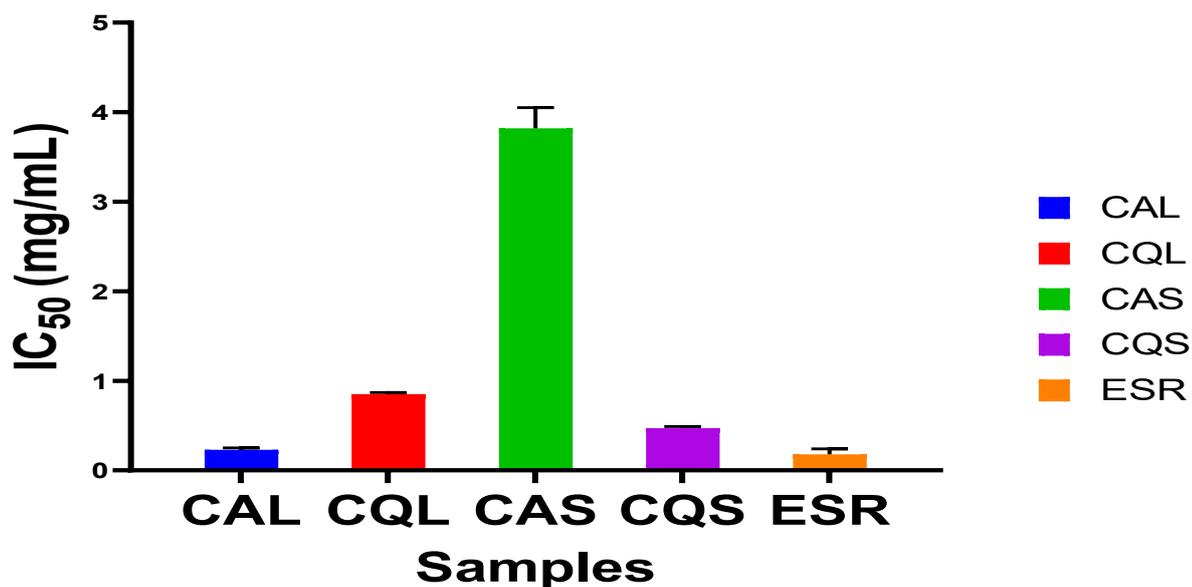

Figure 4: A chart showing the IC_{50} values (mg/mL) of crude extracts and the standard drug, Eserine. Key: CAL = *Cissus arguta* leaf, CQL = *Cissus quadrangularis* leaf, CAS = *Cissus arguta* stem, CQS = *Cissus quadrangularis* stem, ESR = Eserine.
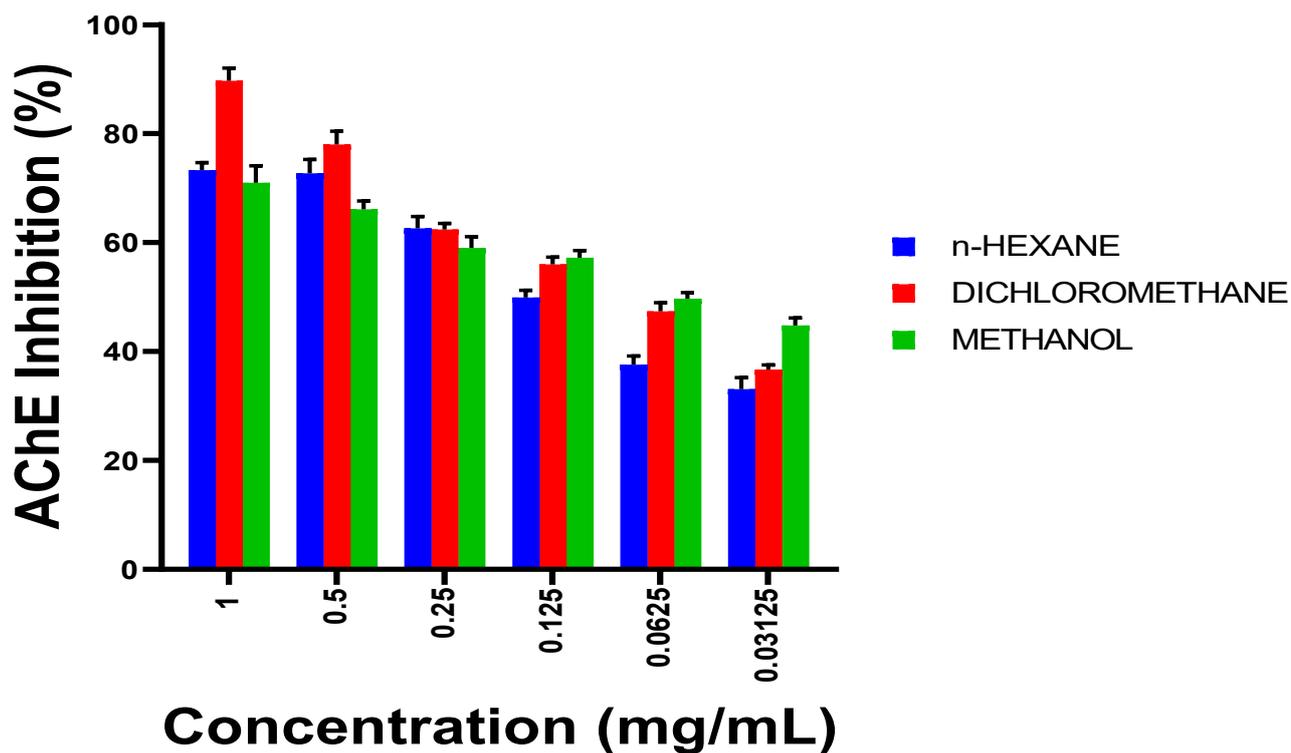
Figure 5: Acetylcholinesterase Inhibitory Activity of the fractions of *Cissus arguta* leaf extract
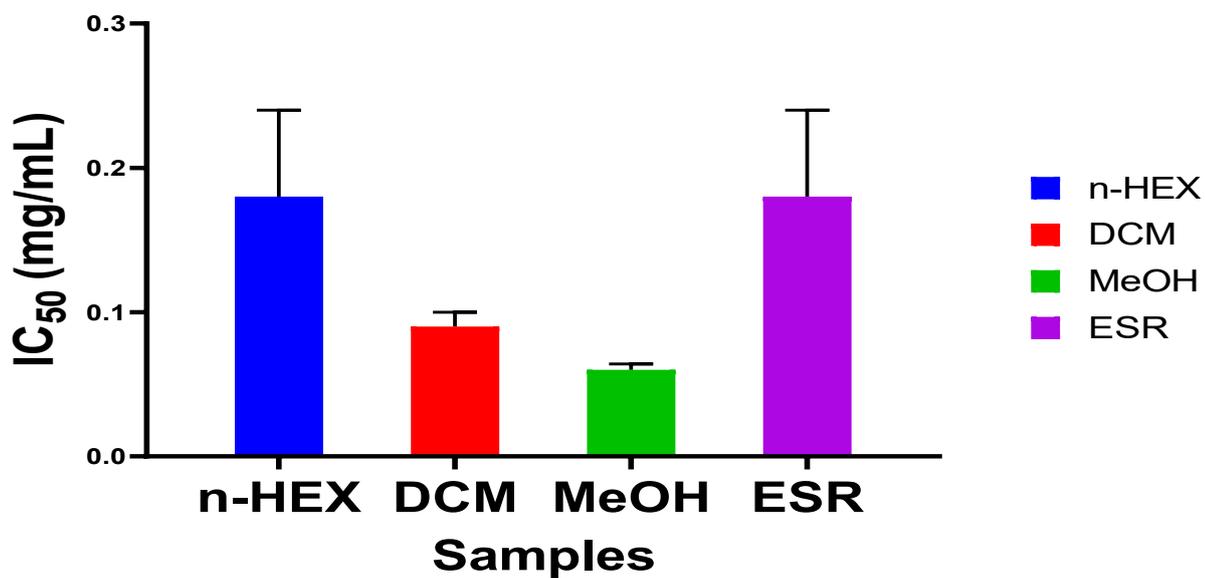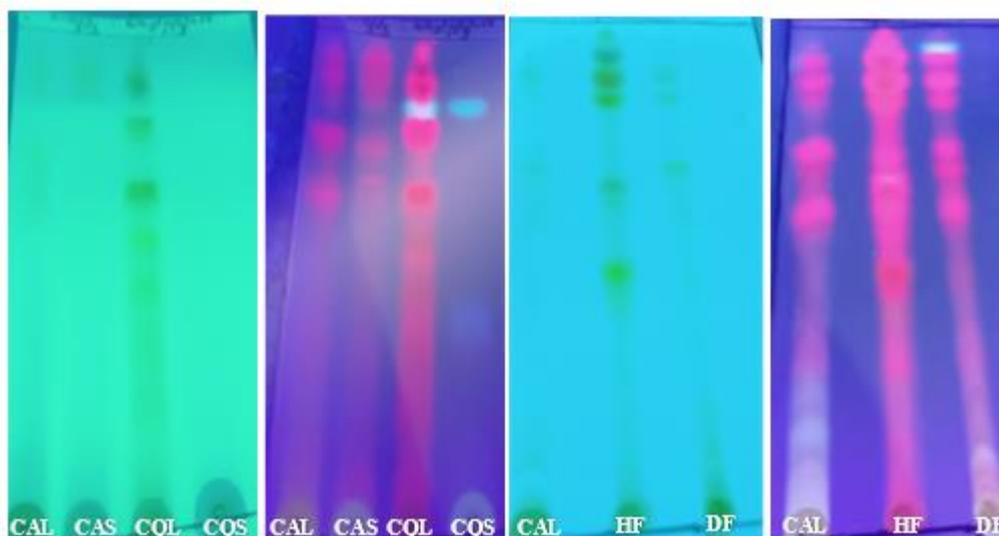

Figure 6: A chart showing the IC_{50} values (mg/mL) of fractions of *Cissus arguta* leaf extract and Eserine. Key: n-HEX = n-Hexane, DCM = Dichloromethane, MeOH = Methanol, ESR = Eserine.

Figure 7: TLC plates of Cissus arguta and Cissus quadrangularis leaf and stem crude extracts, and fractions of the leaf extract of Cissus arguta at 254 nm and 365 nm, respectively. Key: CAL - Cissus arguta leaf, CAS - Cissus arguta stem, CQL - Cissus quadrangularis leaf, CQS – Cissus quadrangularis stem, HF – Hexane fraction, DF – Dichloromethane fraction, Solvent system: Toluene: Ethyl acetate (3.5:1.5).

Figure 4 presents the IC_{50} values for *Cissus arguta* and *Cissus quadrangularis* leaf and stem extracts in comparison with those of Eserine, the standard memory-enhancing drug. Eserine had the lowest IC_{50} (0.04 ± 0.001 mg/mL), confirming its potency, followed by *Cissus arguta* leaf extract (IC_{50} = 0.23 ± 0.02 mg/mL), *Cissus quadrangularis* stem extract (IC_{50} = 0.47 ± 0.02 mg/mL), extracts of *Cissus quadrangularis* leaf (IC_{50} = 0.85 ± 0.02 mg/mL) and *Cissus arguta* stem extract (IC_{50} = 3.82 ± 0.23 mg/mL). The highest IC_{50} was observed in extracts of *Cissus arguta* stem, which suggests that it requires higher concentrations to achieve comparable inhibition with Eserine.

Figure 5 compares acetylcholinesterase inhibition across three solvent fractions - n-Hexane, Dichloromethane, and Methanol of the most active crude extract (*Cissus arguta* leaf), at varying concentrations. The various fractions also showed dose-dependent inhibition of acetylcholinesterase (AChE), most importantly, fractions of methanol, which consistently showed the highest inhibition of 71.0% and 44.8% at 1 mg/mL and 0.03125 mg/mL concentration, respectively. Aside from this, its IC_{50} value of 0.06 ± 0.004 mg/mL indicates its extracting power for bioactive compounds with memory-enhancing potential. These values are comparable with the standard drug, Eserine, with average percentage inhibition of 69.8% and 15.0% at 0.1 mg/mL and 0.003125 mg/mL, respectively, and an IC_{50} value of 0.04 ± 0.001 mg/mL.

Figure 6 compares the IC_{50} values of solvent fractions from *Cissus arguta* leaf extract and Eserine. The methanol fraction showed the lowest IC_{50}, indicating the highest potency, followed by dichloromethane and n-hexane fractions.

Thin Layer Chromatographic Analysis
Figure 7 displays the Thin Layer Chromatograph profiles of *Cissus arguta* and *Cissus quadrangularis* leaf and stem crude extracts and fractions under UV light. The Thin Layer Chromatographic Analysis (TLC) of *Cissus arguta* and *Cissus quadrangularis* leaf and stem extracts, as well as the fractions of *Cissus arguta* Leaf extract (n-hexane, dichloromethane, and aqueous), showed different spots. The distinct fluorescent bands across samples indicate diverse phytochemical compositions, with dichloromethane and methanol fractions showing richer compound separation, supporting their bioactivity in AChE inhibition. These phytochemicals are responsible for the biological activities of *Cissus arguta* and *Cissus quadrangularis*.

DISCUSSION
Cognitive decline leads to memory loss, difficulties with concentration, and challenges in understanding, remembering, following instructions, and solving problems [25]. Treatments for cognitive deficits often involve interventions for enhancing the level of acetylcholine by inhibiting acetylcholinesterase, the prevalent cholinesterase in the brain that induces the hydrolysis of acetylcholine to acetic acid and choline, leading to the mitigation of neurotransmitter effects at cholinergic synapses [26-27]. The focus of this research is based on the evaluation and comparison of the memory-enhancing activity of two *Cissus* species through their acetylcholinesterase inhibitory potentials. Using medicinal plants in enhancing the memory offers a natural and potentially safer alternative to conventional medicines. Previous literature has investigated the therapeutic properties of plants with medicinal value, many of which have been traditionally used for memory

enhancement. These plants contain bioactive compounds that help to improve cognition [28].

The results obtained from in figure 1 and 2 demonstrated that the leaf and stem extracts of *Cissus arguta* and *Cissus quadrangularis* showed dose-dependent acetylcholinesterase inhibitory activity at the tested concentrations. A similar result was also obtained for the standard drug (Eserine) in Figure 3. It was noted by de Torre et al. [29] that according to the inhibitory concentration at 50% (IC50) values recorded, the potency of the extracts against acetylcholinesterase could be evaluated.. The lower the IC_{50}, the higher the acetylcholinesterase inhibitory activity and vice versa. Dos Santos *et al*. [30], classified plant extracts as high (IC_{50} < 0.02 mg/mL), moderate (0.02 < IC_{50} < 0.2 mg/mL), and low (0.2 < IC_{50} < 1 mg/mL) potencies, concerning their acetylcholinesterase inhibitory activity. A comparative analysis (Figure 4) of the memory-enhancing activity of the two *Cissus* species showed that *Cissus arguta* leaf extract (IC_{50} = 0.23 ± 0.02 mg/mL) have a significantly higher acetylcholinesterase inhibitory activity than *Cissus quadrangularis* leaf extract (IC_{50} = 0.85 ± 0.02 mg/mL), while *Cissus quadrangularis* stem (IC_{50} = 0.47 ± 0.02 mg/mL) have a significantly higher acetylcholinesterase inhibitory activity than *Cissus arguta* stem extract (IC_{50} = 3.82 ± 0.23 mg/mL). The IC_{50} values (Figure 4) show that, in general, the acetylcholinesterase inhibitory activity of *Cissus arguta* methanolic leaf extract (the lowest and hence most effective IC_{50} value against acetylcholinesterase) is much higher than those of *Cissus arguta* stem, *Cissus quadrangularis* leaf, and *Cissus quadrangularis* stem. The fractions of *Cissus arguta* leaf, most active crude extract (Figures 5 and 6) were seen to have moderate potency, with the aqueous methanol fraction having the highest activity (lower IC_{50} value of 0.06 ± 0.04 mg/mL). This is comparable with that of eserine (Figure 6), the standard memory-enhancing drug (IC_{50} = 0.04 ± 0.001 mg/mL). This suggests that the active compounds responsible for the memory-enhancing property of *Cissus arguta* leaf extract are likely to be polar. Research on other plants like *Petiveria alliacea* also showed that the methanol fraction has the most promising inhibitory level against acetylcholinesterase at 86.5% [31]. Studies have shown that polar compounds such as tannins, alkaloids, and saponins, among others, possess antioxidant activity, thus neutralizing oxidative damage - a major symptom in Alzheimer's disease. [31-33].

Although some biological activities have already been reported for *Cissus arguta* and *Cissus quadrangularis*, but not on their acetylcholinesterase inhibitory activity. An *in vivo* anti-Alzheimer's study conducted by Sarvagod *et al*. [34] on *Cissus quadrangularis* ethanolic stem extract to assess memory recognition in Wistar albino rats with neurological disorders had earlier reported that the plant extract possesses significant anti-Alzheimer's and memory-enhancing activity. This activity was probably due to the presence of carotene, mainly β-carotene, a substance with free radical scavenging effect, thereby enhancing anti-Alzheimer activity. Other species of the Vitaceae family have also been seen as valuable sources of

anti-cholinesterase phytoconstituents. Root extracts of *Vitis amurensis* demonstrated notable inhibitory effects on acetylcholinesterase and butyrylcholinesterase using the Ellman's spectroscopic assay[35]. Vitisin A and Heyneanol A, which were compounds isolated and characterized from the root extract of *Vitis amurensis,* have been found to inhibit both acetylcholinesterase and butyrylcholinesterase. The extract demonstrated a dose-dependent inhibition of butyrylcholinesterase and showed greater effectiveness against this enzyme compared to galantamine, which served as the positive control [35]. Sofia *et al*. [36] also observed that several tropolone derivatives obtained from *Vitis vinifera* and other members of the Vitaceae family exhibited strong inhibitory effects on acetylcholinesterase. The cognitive-enhancing potential of *Vitis vinifera* fruit juice was evaluated in both normal and memory-impaired mice using spatial learning and recognition memory tests, suggesting its possible application in managing various forms of cognitive decline and supporting its nootropic properties [37]. Kakad *et al*. [38] investigated the influence of methanolic extract and its fractions from *Vitis vinifera* on learning and memory, attributing the effects to monoterpenes. Their study employed the Passive Shock Avoidance Test, Elevated Plus Maze (EPM), and Object Recognition Test, and found that raisins from *Vitis vinifera* improved memory across all three models. Additionally, some research has explored the neurological and anti-ageing effects of other Cissus species. For instance, *Cissus verticillata* has been studied for its antioxidant and neuroprotective properties using both in vitro and in vivo approaches [39,40], indicating promising memory-enhancing potential within the Cissus genus.. This evidence from other related species within the same family suggests a promising memory-enhancing activity. The findings from this current study align with existing literature, highlighting the potential of *Cissus arguta* and *Cissus quadrangularis* to inhibit the acetylcholinesterase enzyme, thereby improving cognitive functions. The observed acetylcholinesterase inhibitory effect of these two *Cissus* species can be attributed to bioactive compounds present in both plants. The phytochemical analysis conducted showed the presence of alkaloids, saponins, tannins, flavonoids, steroids, and anthraquinones (Figures 1 and 7). These compounds have been reported to help scavenge free radicals, thereby acting as antioxidants and memory-enhancers [41-45]. However, further research is needed on the plant extracts to isolate the active components responsible for their memory-enhancing effects and to assess the toxicity of these compounds to ensure their safe use as therapeutic agents.

CONCLUSION
This study evaluated and compared the memory-enhancing activity of two *Cissus* species. The leaf and stem extracts of *Cissus arguta* and *Cissus quadrangularis* showed promising memory-enhancing effects by inhibiting acetylcholinesterase. This is the first report indicating that the methanol extracts of both plants have acetylcholinesterase inhibitory properties. *Cissus arguta* leaf extract exhibited the highest potency

against acetylcholinesterase, followed by the extracts of *Cissus quadrangularis* stem, *Cissus quadrangularis* leaf, and *Cissus arguta* stem. This work provides a basis for further studies focused on developing new therapies from *Cissus arguta* and *Cissus quadrangularis* for neurodegenerative diseases like Alzheimer's.

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AUTHORS' CONTRIBUTION
TOA designed the work, EGM carried out the research, and drafted the manuscript; TOA supervised the study; and TOA and SAO revised the manuscript. All authors read, made comments, and agreed on the final manuscript.

CONFLICT OF INTEREST
All authors declare that there is no conflict of interest related to this article.

FUNDING

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