Unlocking the Therapeutic Potential: Comparative Enzyme Inhibition by Five Malaysian *Piper* Species

Syarifah Nadhirah Wan IDRUS[1]
Wan Mohd Nuzul Hakimi Wan SALLEH[1] (✉)
Norazrina Md RAMIN[1]
Faezatul Alwani Mohd RAHIM[1]
Nur Nabilah Mohd ZAINI[1]
Nurunajah Ab GHANI[2,3]
Abubakar Siddiq SALIHU[1,4]
Mohd Hafiz ARZMI[5]

Summary

The genus *Piper*, belonging to the Piperaceae family, includes over 2,000 species, many of which are widely recognized for their significant economic and medicinal importance. In recent years, research on *Piper* species has advanced, with numerous studies highlighting their intriguing pharmacological properties. The enzyme inhibitory effects of plant-derived compounds play a significant role in addressing various diseases, including neurodegenerative disorders, hyperpigmentation, and diabetes. This study evaluates the acetylcholinesterase (AChE), tyrosinase, and α-glucosidase inhibitory activities of ethanolic leaf extracts from five Malaysian *Piper* species: *Piper rostratum*, *P. frustratum*, *P. penangense*, *P. baccatum*, and *P. crassipes*. The extracts demonstrated varying degrees of enzyme inhibition, with *P. baccatum* exhibiting the strongest AChE inhibition (IC_{50} value of 21.5 μg·mL^{-1}), *P. frustratum* the highest tyrosinase inhibition (IC_{50} value of 12.6 μg·mL^{-1}), and *P. rostratum* the most potent α-glucosidase inhibition (IC_{50} value of 12.1 μg·mL^{-1}). These activities are attributed to the bioactive phytochemicals, including alkaloids, flavonoids, and phenolic compounds, known for their enzyme-inhibitory and antioxidant properties. This is the first study to report these specific activities for these *Piper* species, highlighting their potential as natural therapeutic agents and offering insights into their medicinal applications for neuroprotection, skin health, and diabetes management.

Key words

Piperaceae, *Piper*, acetylcholinesterase, antityrosinase, glucosidase

[1] Department of Chemistry, Faculty of Science and Mathematics, Universiti Pendidikan Sultan Idris, 35900 Tanjong Malim, Perak, Malaysia

[2] Atta-ur-Rahman Institute for Natural Product Discovery (AuRIns), Universiti Teknologi MARA, Puncak Alam Campus, Bandar Puncak Alam, Selangor, Malaysia

[3] Faculty of Applied Sciences, Universiti Teknologi MARA, Shah Alam, Selangor, Malaysia

[4] Department of Pure and Industrial Chemistry, Faculty of Natural and Applied Sciences, Umaru Musa Yar'adua University, Katsina, Nigeria

[5] Kulliyyah of Dentistry, International Islamic University Malaysia, Kuantan Campus, 25200 Kuantan, Pahang, Malaysia

✉ Corresponding author: wmnhakimi@fsmt.upsi.edu.my

Received: March 9, 2025 | Accepted: June 12, 2025 | Online first version published: June 22, 2025

Introduction

The enzyme inhibitory effect plays a critical role in regulating biological processes that contribute to the development of various diseases. By specifically targeting enzymes, these effects can modulate metabolic pathways, prevent disease progression, and improve health outcomes. The targeted enzyme inhibition forms the foundation of drug development and natural product-based therapies, emphasizing its significance in both therapeutic and industrial applications (Salleh et al., 2014). Acetylcholinesterase (AChE), an enzyme responsible for breaking down acetylcholine, is critical for nerve impulse transmission. Inhibiting AChE is a therapeutic approach for neurodegenerative disorders like Alzheimer's, as it increases acetylcholine levels in the brain. Numerous plant extracts exhibit AChE inhibitory activity due to their bioactive components such as alkaloids, flavonoids, and terpenoids (Walczak-Nowicka and Herbet, 2021). For example, *Ginkgo biloba* extract, recognized for its neuroprotective properties, contains flavonoids and terpenoids that inhibit AChE (Singh et al., 2019). Similarly, tyrosinase is a key enzyme in melanin biosynthesis and the browning of fruits and vegetables. Tyrosinase inhibitors are widely utilized in cosmetic and food industries to prevent hyperpigmentation and browning. Plant extracts rich in phenolic compounds, flavonoids, and tannins are common sources of tyrosinase inhibitors (Zolghadri et al., 2019). For instance, *Glycyrrhiza glabra* (licorice) extract, known for its high flavonoid and phenolic acid content, is a natural tyrosinase inhibitor widely used in skin-whitening products (Wahab et al., 2021). Additionally, glucosidases are enzymes that hydrolyze carbohydrates into glucose, influencing postprandial blood sugar levels. Inhibiting glucosidases has proven effective for managing diabetes, and plant extracts containing flavonoids, saponins, and phenolic compounds have shown promising activity in this regard (Kashtoh and Baek, 2022). For example, *Momordica charantia* (bitter melon) extract demonstrates antiglucosidase activity due to its triterpenes and flavonoids, which help regulate blood sugar levels (Richter et al., 2023). These examples underscore the therapeutic potential of plant extracts in addressing neurodegenerative diseases, hyperpigmentation, and diabetes through their acetylcholinesterase, antityrosinase, and antiglucosidase activities, respectively.

The Piperaceae family is a diverse group of flowering plants that includes around 1,000 species distributed across 13 genera, the most notable being *Piper*. The genus *Piper* is a diverse and economically significant, comprising over 1,000 species found primarily in tropical and subtropical regions (Azman et al., 2023). The most well-known species, *Piper nigrum* (black pepper), is widely cultivated for its pungent fruit, used as a spice in global cuisine. Other species in the genus, such as *Piper longum* (long pepper) and *Piper betle*, also have culinary and medicinal importance (Salleh et al., 2022a). *Piper* species are characterized by their aromatic, often heart-shaped leaves and small, unisexual flowers arranged in spike-like inflorescences. The plants produce bioactive compounds, with piperine being the most prominent, known for its characteristic spiciness and its numerous health benefits, including anti-inflammatory, antioxidant, antimicrobial, and pain-relieving properties (Salleh et al., 2022b). The genus's medicinal uses extend into modern pharmaceuticals, where compounds like piperine enhance the bioavailability of other drugs. Furthermore, *Piper* species are utilized in various cultural practices, such as betel chewing in Southeast Asia, with *Piper betle* leaves being chewed with areca nut for stimulant effects (Salleh, 2020). In addition to its culinary and medicinal value, *Piper* plays a significant role in the cosmetic industry, as its bioactive compounds have been incorporated into products for their therapeutic qualities (Salleh et al., 2021). Thus, the genus *Piper* holds considerable cultural, culinary, and pharmacological importance globally.

Piper rostratum Roxb. commonly found in tropical and subtropical regions of South and Southeast Asia, particularly in India, Myanmar, and other parts of the Indian subcontinent. It is a climbing shrub, generally found in forested areas, along the edges of forests. The plant is often a woody climber that twines around other vegetation for support. The leaves are large and have a distinctive aromatic smell (Suwanphakdee et al., 2018).

Piper frustratum (Miq.) Boerl. is native to tropical regions of Southeast Asia, particularly in countries like Malaysia and Indonesia. It is a woody climber or liana, typically growing in tropical forests and twining around other plants for support. The plant has large, heart-shaped leaves, while the flowers are small and arranged in typical spike-like inflorescences (Burkill, 1966).

Piper baccatum Blume, commonly known as '*rinu manuk*' in Indonesia, is a woody climber that thrives in the wet tropical biome. Key characteristics of *P. baccatum* include its conch-shaped or bilabiate floral bracts, thick, fleshy leaves that are glossy green when fresh and leathery when dry, and its sessile fruits, sometimes with a pseudostalk, which arise from the floral bract. This species is widely distributed across tropical regions, particularly in Asia, including countries such as India, Sri Lanka, Thailand, Malaysia, Singapore, Indonesia, and the Philippines (Suwanphakdee et al., 2020).

Piper penangense C.DC. is a climbing vine or woody shrub that thrives in the humid, warm conditions characteristic of the tropical biome. It is predominantly found in the tropical rainforests of Southeast Asia, with a particular concentration in the Malay Peninsula (Burkill, 1966).

Piper crassipes Korth ex Miq., commonly known as 'sireh murai' in Malaysia, is a climbing plant with swollen nodes. It is widely distributed across the tropics, particularly in Southeast Asia, including regions such as India, Myanmar, Thailand, Malaysia, and Singapore. The plant has leathery, heart-shaped leaves with short petioles, while its small white flowers form dense clusters that make up the inflorescence. The fruits are round, initially green, and turn orange-red as they ripen (Burkill, 1966).

Recently, the chemical composition of essential oils from *P. baccatum* (Salihu et al., 2024), *P. penangense* (Salleh et al., 2024a; Jantan et al., 1994), *P. crassipes* (Rezod et al., 2024), *P. rostratum* (Ramin et al., 2025), and *P. frustratum* (Idrus et al., 2025), has been reported, shedding light on the bioactive components present in these species. As part of ongoing research into the pharmacologically active compounds in Malaysian plants, a study was conducted to evaluate the acetylcholinesterase, antityrosinase, and α-glucosidase activities of ethanolic leaf extracts from five Malaysian *Piper* species: *P. rostratum*, *P. frustratum*, *P. ornatum*, *P. penangense*, and *P. crassipes*. To the best of our knowledge,

this is the first study to report these specific enzyme inhibitory activities for these *Piper* extracts, contributing valuable insights into their potential medicinal applications. The findings offer promising evidence of the therapeutic benefits of these plants, particularly in the management of neurodegenerative diseases, hyperpigmentation disorders, and diabetes.

Materials and Methods

Plant Materials

Five *Piper* species were collected in January 2023 from Behrang, Perak (3° 44' 51.612" N 101° 27' 19.9008" E) and Langgun Island, Langkawi (Latitude: 6°26'3.26" N 99°53'29.46" E). The specimens were identified by Shamsul Khamis, and the voucher specimens have been deposited at the UKMB Herbarium. The details of these species are provided in Table 1.

Plant Extraction

The dried and powdered leaves (50 g) of the aforementioned *Piper* species were subjected to cold extraction using ethanol as the solvent. The resulting extracts were filtered, and the solvent was removed under reduced pressure using a rotary evaporator (Eyela, Japan). The final extracts (w/w) were stored in a freezer until required for the experimental procedures.

Acetylcholinesterase Inhibitory Activity

The AChE inhibitory activity of the essential oil was initially measured by slightly modifying the spectrophotometric method (Jibril et al., 2020). Electric eel AChE was used, while acetylthiocholine iodide was employed as a substrate of the reaction, and DTNB acid was used for the measurement of the anticholinesterase activity. In brief, 140 µL of sodium phosphate buffer (pH 8.0), 20 µL of DTNB, 20 µL of extracts (conc. of 6.25-100 $\mu g \cdot mL^{-1}$), and 20 µL of AChE (0.22 $U \cdot mL^{-1}$) solution were added into a 96-well microplate and incubated for 15 min at 25 °C. The reaction was then initiated by adding 10 µL of acetylthiocholine iodide. The hydrolysis of acetylthiocholine iodide was monitored by the formation of the yellow 5-thio2-nitrobenzoate anion as a result of the reaction of DTNB with thiocholines at 412 nm using a 96-well microplate reader (Epoch Micro-Volume Spectrophotometer, USA). The percentage of inhibition (I%) of AChE was determined by comparing the reaction rates relative to the blank sample (EtOH in phosphate buffer, pH 8) using the formula:

$$I\% = [E - S/E] \times 100;$$

where E is the activity of the enzyme without the test sample and S is the activity of the enzyme with the test sample. Analyses were expressed as means ± SD of the triplicates, and galantamine at the same concentration as extract was used as a positive control.

Antityrosinase Inhibitory Activity

A modified version of the previously reported method was used to perform the tyrosinase inhibition assay (Salleh et al., 2024b). The extract was dissolved in dimethyl sulfoxide (DMSO) (conc. of 6.25-100 $\mu g \cdot mL^{-1}$). The reaction was carried out in a 96-well microplate and the absorbance at 475 nm was measured using an ELISA microplate reader (VersaMax, Molecular Devices, USA). Each well contained 40 µL of extract dissolved in DMSO, 80 µL of phosphate buffer (pH 6.8), 40 µL of tyrosinase enzyme, and 40 µL of L-DOPA. A control sample containing all components except L-DOPA was included for each reaction. The percentage of tyrosinase inhibition was calculated using the formula:

$$I\% = [A_{control} - A_{sample} / A_{control}] \times 100;$$

where $A_{control}$ represents the absorbance of the control reaction and A_{sample} represents the absorbance of the extract. Kojic acid was used as a positive control.

Table 1. List of *Piper* species

Name	Locality	Voucher no.	Medicinal uses
P. rostratum	Behrang, Perak	BB-12/23	It has been used to treat conditions such as digestive issues, respiratory disorders, and skin infections (Ramin et al., 2025).
P. frustratum	Behrang, Perak	BB-14/23	It has been used in folk medicine to treat a variety of conditions, including digestive disorders, respiratory issues, and infections (Idrus et al., 2025).
P. baccatum	Behrang, Perak	BB-10/23	A decoction of the roots has been used to treat venereal diseases, while the plant's juice is consumed as a remedy for coughs. The shredded leaves have been applied as a poultice on the neck. In Indonesia, the leaves and stems are used to treat fever and swelling, while the fruits are incorporated into tonics (Salihu et al., 2024).
P. penangense	Langgun Island	PT-60/22	No report
P. crassipes	Behrang, Perak	BB-11/23	The dried fruits have been used to treat conditions such as cough, sinusitis, poor digestion, and throat infections (Rezod et al., 2024).

α-Glucosidase Inhibitory Activity

The α-glucosidase inhibitory activity of the extracts was assessed according to the previous method with several modifications (Salleh and Ahmad, 2016). Firstly, α-glucosidase from yeast Maltase (2 Unit/mL) and p-nitrophenyl-α-D-glucopyranoside (PNPG) (1 mM) were prepared individually by dissolving in 50 mM phosphate buffer (pH 6.5). The reaction mixture, contained 10 µL of sample (conc. of 6.25-100 µg·mL^{-1}) in 130 µL of 30 mM phosphate buffer (pH 6.5) containing 5% DMSO and 10 µL of enzyme solution was incubated at 37 °C for 20 min in the dark. The reaction was initiated by pipetting 50 µL of PNPG and further incubated at 37 °C for 20 min in the dark. Lastly, 50 µL of 2 M glycine (pH 10) was added to each well to quench the reaction. The activity of α-glucosidase was quantified by measuring of p-nitrophenol released at 405 nm. The percentage of inhibition was calculated as follows:

$$I\% = [(A_{control} - [A_{sample} - A_{blank\ sample}]) / A_{control}] \times 100;$$

where A_{sample} is the absorbance of the test sample, A_{blank} sample is the absorbance of the mixture containing all reagents except enzyme and $A_{control}$ is the absorbance of the mixture containing all reagents except the test sample. An α-glucosidase inhibitor, quercetin with same concentrations was used as a positive control.

Statistical Analysis

Data obtained from the biological activities are expressed as mean ± SD of triplicate. The statistical analyses were carried out by employing one-way ANOVA. A statistical package (SPSS version 11.0) was used for the data analysis.

Results and Discussion

The acetylcholinesterase (AChE), tyrosinase, and α-glucosidase inhibitory activities of five *Piper* extracts, as indicated by their IC_{50} values, exhibit significant variability among the species tested, as summarized in Table 2. Additionally, the percentage inhibition at various concentrations is illustrated in Fig. 1.

Among the tested extracts, *P. baccatum* exhibited the strongest AChE inhibitory activity, with an IC_{50} value of 21.5 µg·mL^{-1}, followed by *P. crassipes* (26.5 µg·mL^{-1}) and *P. frustratum* (26.6 µg·mL^{-1}). Meanwhile, *P. penangense* and *P. rostratum* showed weaker inhibitory activities with IC_{50} values of 42.5 µg·mL^{-1} and 61.6 µg·mL^{-1}, respectively. The positive control, galantamine, demonstrated superior activity with an IC_{50} value of 2.5 µg·mL^{-1}, as expected for a standard compound known for its efficacy in inhibiting AChE. The strong activity of *P. baccatum* may be attributed to its phytochemical profile, particularly the presence of bioactive secondary metabolites such as alkaloids, amides, and flavonoids. These classes of compounds are well-documented for their ability to inhibit AChE (Khan et al., 2018; Kong et al., 2019). For instance, alkaloids such as piperidine and pyrrolidine derivatives, which are commonly found in the *Piper* genus, are potent inhibitors of cholinesterases (de Paula et al., 2009). Additionally, flavonoids and phenolic compounds may contribute synergistically to the observed activity through their antioxidant properties, which play a role in reducing oxidative stress, a key factor in neurodegenerative diseases like Alzheimer's (Minocha et al., 2022). The moderate activity of *P. frustratum* and *P. crassipes* suggests a similar presence of active constituents, though potentially in lower concentrations or with varying structural features that influence their inhibitory efficacy. On the other hand, the weaker activity observed for *P. penangense* and *P. rostratum* might be due to either a lower abundance of these bioactive compounds or the presence of antagonistic compounds that interfere with enzyme inhibition. When compared to previous studies on other *Piper* species, the results align with the established reputation of the genus for its AChE inhibitory properties.

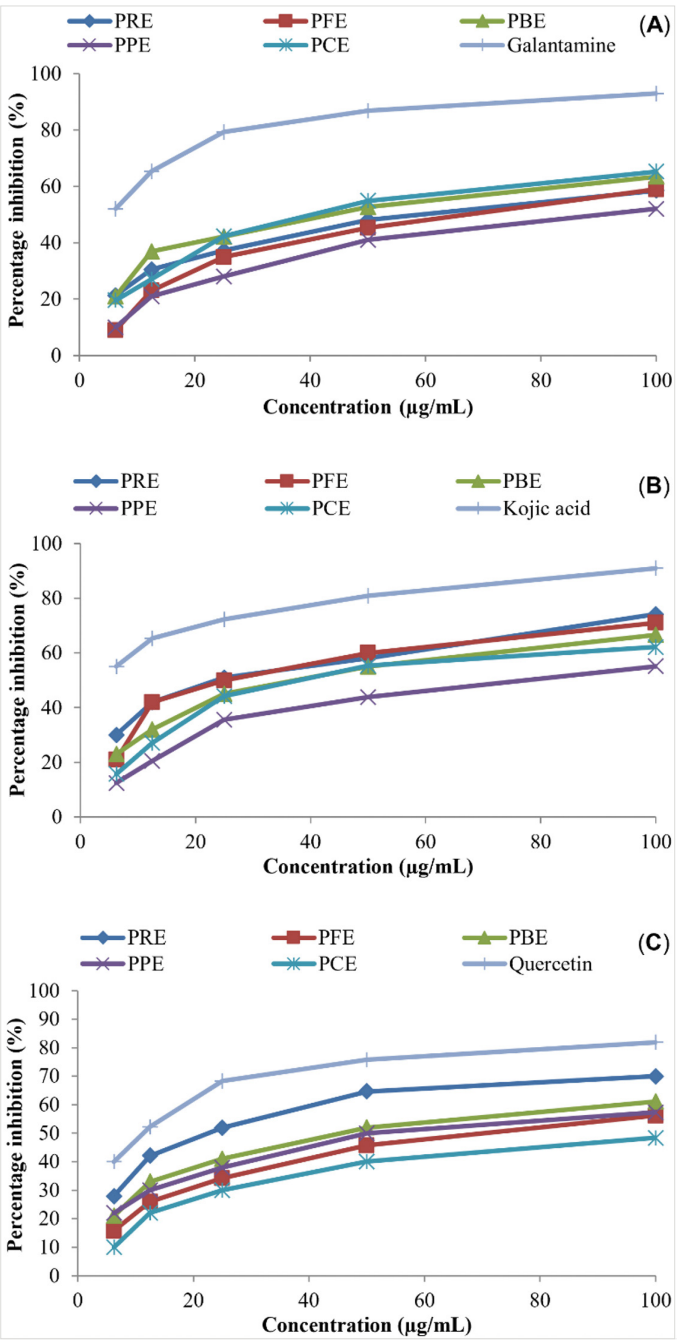

Figure 1. Percentage inhibitory activity of *Piper* extracts against acetylcholinesterase (A), tyrosinase (B), and α-glucosidase (C) at different concentrations

Table 2. Acetylcholinesterase, tyrosinase, and α-glucosidase inhibitory activities of *Piper* extracts

Extract	Yield (g)	IC_{50} (μg·mL^{-1})		
		AChE	Tyrosinase	α-Glucosidase
P. rostratum (PRE)	0.52	61.6 ± 0.14	33.3 ± 0.12	12.1 ± 0.15
P. frustratum (PFE)	0.68	26.6 ± 0.02	12.6 ± 0.04	36.9 ± 0.06
P. baccatum (PBE)	0.95	21.5 ± 0.03	27.0 ± 0.03	19.4 ± 0.11
P. penangense (PPE)	0.76	42.5 ± 0.05	24.2 ± 0.05	35.2± 0.03
P. crassipes (PCE)	0.72	26.5 ± 0.09	18.0 ± 0.03	26.4 ± 0.08
Standard				
Galantamine		2.5 ± 0.11	-	-
Kojic acid		-	5.5 ± 0.12	-
Quercetin		-	-	5.1 ± 0.05

For example, *P. nigrum* (black pepper) (Sharma et al., 2023) and *P. longum* (long pepper) (Khatami et al., 2020) have demonstrated notable AChE inhibition, often attributed to their rich alkaloid content, particularly piperine. The IC_{50} values reported for these species typically range between 10 and 30 μg·mL^{-1}, similar to the range observed for *P. baccatum* and *P. crassipes*. These findings further corroborate the hypothesis that the bioactive components responsible for AChE inhibition are conserved across the *Piper* genus, making it a promising group for neuroprotective studies. Despite the superior activity of galantamine, which acts as a benchmark for AChE inhibition, *Piper* extracts hold significant potential as natural, sustainable, and cost-effective alternatives. The complex phytochemical compositions of these extracts could provide multi-targeted effects, which might be advantageous in managing diseases like Alzheimer's. Unlike single-compound drugs, natural extracts often exhibit synergistic interactions among their constituents, enhancing overall bioactivity and reducing the likelihood of side effects (Sharifi-Rad et al., 2022).

For anti-tyrosinase activities, among the tested extracts, *P. frustratum* demonstrated the strongest tyrosinase inhibitory activity, with an IC_{50} value of 12.6 μg·mL^{-1}, followed by *P. crassipes* (18.0 μg·mL^{-1}). The IC_{50} values for *P. penangense*, *P. baccatum*, and *P. rostratum* were 24.2, 27.0 and 33.3 μg·mL^{-1}, respectively, indicating moderate to weak inhibitory activities. In comparison, kojic acid, the positive control, exhibited a significantly lower IC_{50} value of 5.5 μg·mL^{-1}, highlighting its potent tyrosinase inhibitory effect. The pronounced activity of *P. frustratum* could be attributed to its phytochemical profile, which likely includes a high concentration of bioactive phenolic compounds and flavonoids. These compounds are well-documented for their ability to inhibit tyrosinase activity by chelating the copper ions at the enzyme's active site or by interacting with its functional groups, thereby reducing its catalytic efficiency (Chang, 2009). The lower inhibitory activity observed for *P. rostratum* and *P. baccatum* could be due to differences in the abundance or bioavailability of active constituents. It is also possible that these species contain secondary metabolites that act as inhibitors of tyrosinase activity but with weaker binding affinities or stability compared to those in *P. frustratum* (El-Nashar et al., 2021). Furthermore, the relatively weak activity of these extracts might be influenced by the presence of antagonistic compounds that interfere with the enzyme-inhibitor interaction.

When compared with previous studies on other *Piper* species, these results align with the general finding that *Piper* plants possess significant tyrosinase inhibitory activities. For instance, studies on *P. nigrum* have reported IC_{50} values in the range of 10-20 μg·mL^{-1} (Khongkarat et al., 2024), which is comparable to the values observed for *P. frustratum* and *P. crassipes*. The tyrosinase inhibitory activity in these species has often been attributed to their high content of phenolic acids, flavonoids, and alkaloids like piperine (Zolghadri et al., 2019). Such compounds not only inhibit tyrosinase activity but also exhibit antioxidant properties, which can enhance their therapeutic potential by mitigating oxidative stress, a key factor in hyperpigmentation disorders (Cespedes et al., 2017). The exceptional inhibitory activity of kojic acid, which serves as a benchmark in this study, underscores the potential of developing *Piper* extracts as natural alternatives to synthetic inhibitors. Although *Piper* extracts exhibit higher IC_{50} values compared to kojic acid, they offer unique advantages, such as multi-functional activity and lower toxicity. Moreover, the combination of bioactive compounds in these extracts could lead to a broader spectrum of benefits, including anti-inflammatory and antioxidant effects, which are not typically provided by single-compound inhibitors like kojic acid (Zilles et al., 2022).

In the case of α-glucosidase inhibitory activities, *P. rostratum* exhibits the most potent inhibitory activity among the *Piper* extracts, with an IC_{50} value of 12.1 μg·mL^{-1}. This strong activity could be attributed to its unique phytochemical composition, possibly rich in bioactive alkaloids, flavonoids, or phenolic compounds, which are known to inhibit α-glucosidase effectively (Assefa et al., 2019). Previous studies on related *Piper* species, such as *P. nigrum* (Magaña-Barajas et al., 2021) and *P. betle* (Ahmed et al., 2022), have identified compounds like piperine, chavicine, and hydroxychavicol, which have demonstrated antidiabetic and α-glucosidase inhibitory effects. It is plausible that similar bioactive molecules in *P. rostratum* contribute to its efficacy. Meanwhile, *P. baccatum* and *P. crassipes* follow with IC_{50} values of 19.4 and 26.4 μg·mL^{-1}, respectively. These moderate activities suggest the presence of active secondary metabolites, albeit at potentially lower concentrations or with lower binding affinities compared to *P. rostratum*. Studies on *Piper* species have shown that differences in inhibitory potency often correlate with the abundance and diversity of their phytochemicals, influenced by environmental factors, extraction methods, and plant parts used. Furthermore, *P. penangense* and *P. frustratum* exhibit weaker inhibitory activities with IC_{50} values of 35.2 and 36.9 μg·mL^{-1}, respectively. Despite their relatively high IC_{50} values, these species may still possess therapeutic potential, especially when used in combination with other bioactive compounds. Their lower activities might result from the predominance of less potent or non-specific inhibitors or from the lack of certain synergistic compounds that enhance enzyme inhibition (Lee et al., 2016). Comparing these results with quercetin highlights the exceptional potency of this flavonoid, a known antioxidant and α-glucosidase inhibitor. Quercetin's strong activity reinforces the critical role of flavonoids in α-glucosidase

inhibition, suggesting that enhancing flavonoid content in *Piper* extracts could improve their efficacy (Li et al., 2009). Previous research on *Piper* species has consistently emphasized their medicinal potential, particularly in managing metabolic disorders like diabetes. For instance, *P. guineense* extracts have shown significant α-glucosidase and α-amylase inhibitory activities, attributed to piperine's ability to interact with the enzyme's active site (Oboh et al., 2013). Similarly, studies on *P. longum* have reported potent antidiabetic properties due to its alkaloid-rich profile (Pullela et al., 2006). These findings resonate with the observed activities in *P. rostratum* and *P. baccatum*, suggesting that the bioactive profiles of these *Piper* species may share structural or functional similarities with those of previously studied species. Moreover, variations in inhibitory activity among the tested extracts might reflect interspecies differences in phytochemical composition. Factors such as geographic origin, environmental conditions, and genetic diversity significantly influence the biosynthesis of secondary metabolites in *Piper* species (Bazargani et al., 2021).

Conclusions

The findings of this study underscore the significant potential of *Piper* species as natural sources of bioactive compounds with diverse therapeutic applications. The strong acetylcholinesterase (AChE) inhibitory activity of *P. baccatum*, the remarkable anti-tyrosinase activity of *P. frustratum* and notable α-glucosidase activity of *P. rostratum* highlight the genus's pharmacological versatility. Future studies should focus on isolating and characterizing the bioactive constituents from highly active species. Comparative phytochemical profiling across *Piper* species can reveal the structural and functional attributes that enhance biological activity. In silico molecular docking studies can provide valuable insights into the interactions between these compounds and target enzymes, while in vivo studies are essential for validating their efficacy and safety in biological systems. Overall, the integration of phytochemical research with pharmacological testing offers a promising pathway for the development of *Piper*-derived therapies. These natural alternatives not only hold potential for managing neurodegenerative diseases and hyperpigmentation disorders but also align with the growing demand for sustainable and multifunctional therapeutic agents.

Acknowledgment

This research was supported by the Geran Penyelidikan Universiti (Kecemerlangan@UPSI) under grant number 2025-0012-103-01, funded by Universiti Pendidikan Sultan Idris.

CRediT Authorship Contribution Statement

Syarifah Nadhirah Wan Idrus, Norazrina Md Ramin, Faezatul Alwani Mohd Rahim and Nur Nabilah Mohd Zaini: Conceptualization, investigation, performed the experiments and original draft preparation. **Wan Mohd Nuzul Hakimi Wan Salleh and Nurunajah Ab Ghani:** Funding, supervision and manuscript editing. **Abubakar Siddiq Salihu:** Field collection. **Mohd Hafiz Arzmi:** Data analysis on bioactivities.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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