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Phenolic Composition and Enzyme Inhibitory Activity of Sabah Stingless Bee Honey

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Stingless bee honey (SBH) is recognised for its unique nutritional and bioactive profile, which varies with its botanical origin. This study evaluated the enzyme inhibitory activities targeted on cardioprotective potential of SBH from eight distinct floral sources in Sabah (Malaysia), using *in vitro* assays. The phenolic profile of the honey samples was also determined. Inhibition assays were conducted for angiotensin-converting enzyme (ACE), α-amylase, and pancreatic lipase to evaluate antihypertensive, antihyperglycaemic, and antihyperlipidemic effects, respectively. Anti-hypercholesterolemic potential was assessed by determining inhibitory activity against 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase and cholesterol esterase. SBH from Singapore rhododendron exhibited the highest total phenolic content (105.21 mg GAE/g) and significant ACE inhibitory activity (74.62% at honey concentration of 10 mg/mL) and cholesterol esterase inhibitory activity (IC_{50} of 11.80 mg/mL). In contrast, multifloral SBH had the highest total flavonoid content (35.53 mg QUE/g honey), while coconut SBH exhibited the strongest HMG-CoA reductase inhibitory activity (65.05%). Principal component analysis revealed that SBH was differentiable between botanical origins at 62.26% total variance, and phenolic compounds were the primary factor contributing to the discrimination. Caffeic acid and kaempferol were associated to the ACE inhibitory activity. These findings suggest that the enzyme inhibitory activities of SBHs related to cardioprotective potential are significantly influenced by the floral source, offering new possibilities for the targeted development of functional foods based on SBH.

Keywords: antihyperglycemic potential, antihyperlipidemic potential, antihypertensive potential, bioactive compounds, botanical origins

INTRODUCTION

Stingless bee honey (SBH), produced by bees from the Meliponini tribe, is a natural product derived from nectar or sap collection that is enzymatically modified and stored within the colony [Pimentel *et al*., 2022]. Compared with honey from *Apis mellifera*, SBH typically has a higher moisture, ash, and free acidity, along with lower pH and diastase index, and exhibits distinctive organoleptic properties [Alvarez-Suarez *et al*., 2018]. Beyond its long-standing traditional use, the growing scientific evidence supports the nutraceutical use of SBH as a dietary supplement, functional food, and medicinal food. The benefits of SBH are primarily attributed to its bioactive compounds such as flavonoids, phenolic acids, and carotenoids accompanied with nutrients such as free amino acids, vitamins (especially vitamin C and B_9), and minerals (including K, Na, Mg, and Ca) [Alvarez-Suarez *et al*., 2018; Biluca *et al*., 2016, 2019; 2020]. The bioactive compounds of SBHs have been linked to antioxidant [Chuah *et al*., 2023], antimicrobial [Dallagnol *et al*., 2022], anti-inflammatory [Biluca

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et al., 2020], antidiabetic [Ali *et al*., 2020], antihypertensive [Farida *et al*., 2023], neuroprotective [Zulkifli *et al*., 2022], and chemopreventive effects [Yazan *et al*., 2016].

Cardiovascular diseases (CVDs) continue to represent a significant public health challenge. An estimated 19.8 million deaths were attributed to CVDs in the recent years representing about one-third of all global deaths [WHO, 2025]. This burden is also evident nationally, in Malaysia, where ischaemic heart disease remained the principal cause of medically certified deaths in 2024, accounting for 17,421 deaths (13.0%) [Department of Statistics Malaysia, 2025]. Cardiovascular disease risk is driven by factors such as hypertension, diabetes, dyslipidaemia, obesity, sedentary lifestyle, tobacco and alcohol use, and stress, alongside genetic predisposition [Sharifi-Rad *et al*., 2020]. Among them, high blood pressure, high cholesterol level, diabetes, and current smoking are considered standard modifiable cardiovascular risk factors and remain the primary focus of CVD prevention strategies [Tang *et al*., 2025]. Given the sustained and increasing burden of CVD worldwide, the identification of safe, food-based strategies that support cardiometabolic risk reduction remains of high interest.

The cardiovascular disease risk can be reduced by targeting key endogenous enzymes that regulate blood pressure, glycaemic control, lipid handling, and cholesterol synthesis. For example, one established therapeutic approach for controlling postprandial hyperglycaemia in type-2 diabetes is to inhibit α-amylase and α-glucosidase, the enzymes responsible for intestinal starch breakdown and glucose release [Vadivelan *et al*., 2019]. Similarly, inhibition of angiotensin-I-converting enzyme (ACE) facilitates blood pressure regulation and is a key target in the treatment of hypertension [Alcocer *et al*., 2023]. The inhibition of pancreatic lipase and cholesterol esterase prevents the breakdown of dietary fats and cholesterol esters into absorbable free fatty acids, monoacylglycerols, and free cholesterol, providing a novel strategy for managing hyperlipidaemia and obesity [Jiang *et al*., 2023]. Additionally, inhibition of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase, a rate-limiting enzyme in cholesterol biosynthesis, plays a crucial role in regulating cholesterol metabolism and synthesis [Zhou *et al*., 2024]. Although pharmacological inhibitors targeting these enzymes are effective in clinical management, they may be associated with adverse effects or tolerability issues in some individuals [Penson *et al*., 2022]. Therefore, food-derived enzyme inhibitors are being actively investigated as complementary strategies [Farida *et al*., 2023; Habib *et al*., 2021].

The chemical composition of SBH varies with botanical source of the nectar, bee species, and harvest season, as well as honey processing and storage [Gebreyes *et al*., 2025]. Since phenolic composition depends strongly on nectar origin, SBH from different floral sources can differ substantially in phenolic profiles and, consequently, in biological activities [Shamsudin *et al*., 2019a]. Studies on the influence of various factors on these parameters provide complex datasets, the interpretation of which is facilitated by chemometric methods. These methods enable pattern identification, sample classification based on origin, and the selection of potential markers. Methods including principal component analysis (PCA), hierarchical cluster analysis (HCA), k-nearest neighbours (k-NN), artificial neural networks (ANN), uniform manifold approximation and projection (UMAP), and partial least squares-discriminant analysis (PLS-DA) are commonly applied to evaluate chromatographic fingerprints and improve discrimination within complex datasets [Lopes *et al*., 2025; Mello dos Santos *et al*., 2025]. For example, a study reported botanical origin-dependent antioxidant patterns in Sabah SBH and identified flavonoid derivatives as key markers for acacia SBH using multivariate modelling [Chuah *et al*., 2023]. Another study applied PCA to differentiate Malaysian SBH using organic acid profiles consistent with floral origin [Shamsudin *et al*., 2019b].

Despite the progress in chemometric-based discrimination of honey by floral origin, evidence on the phenolic composition and *in vitro* enzyme inhibitory activities associated with the cardioprotective potential of Sabah SBHs remains limited. Given Sabah's rich floral diversity, understanding how botanical origin influences phenolic composition and potential cardioprotective properties of SBHs is important. Therefore, this study aimed to determine the *in vitro* inhibitory activity of Sabah SBHs against ACE, α-amylase, pancreatic lipase, HMG-CoA reductase, and cholesterol esterase, and their relationship with the phenolic composition.

MATERIALS AND METHODS

Honey samples

Stingless bee honey produced by *Heterotrigona itama* was sampled from meliponiculture farms at three locations (Telipok, Menggatal, and Kiulu) in Sabah, Malaysia, from September to December 2022. Eight types of honey with different botanical origins were collected, including those derived from acacia (*Acacia mangium* Willd.), coconut (*Cocos nucifera* L.), rubber tree (*Hevea brasiliensis* Müll.Arg.), durian (*Durio zibethinus* L.), coral vine (*Antigonon leptopus* Hook. & Arn.), rose myrtle (*Rhodomyrtus tomentosa* (Aiton) Hassk.), Singapore rhododendron (*Melastoma malabathricum* L.), and multifloral. For each floral source, honey was collected from several colonies to improve the representativeness of the samples. The honey samples labelled according to floral source were transferred into airtight plastic containers, protected from light, and transported at 4°C to the laboratory. Then, the SBH samples were stored at −20°C until further analysed.

Total phenolic content determination

The total phenolic content (TPC) was determined using the method with a Folin-Ciocalteu phenol reagent described by Singleton *et al*. [1999]. A 5-g portion of each honey was dissolved in distilled water to a final volume of 50 mL. Then, the solution was filtered through Whatman No. 1 filter paper. A 96-well microplate was used to conduct the reaction. Into each well, 12.5 µL of the honey (0.1 g/mL) and 12.5 µL of the Folin-Ciocalteu phenol reagent were pipetted, and, after plate shaking, the mixture was left for 5 min at room temperature. Then, 125 µL of 7% sodium carbonate was added, and the mixture was

kept for another 90 min at 25°C. The absorbance was measured at 750 nm against a blank containing all the reaction agents, excluding the sample, using Multiskan Sky microplate reader (Thermo Scientific, Waltham, MA, USA). The standard calibration curve was prepared using gallic acid solutions with concentrations ranging from 10 to 120 mg/mL. The TPC was expressed as mg of gallic acid equivalent (GAE) *per* 100 g of honey. Each sample and standard were analysed in triplicate.

Total flavonoid content determination

The total flavonoid content (TFC) was determined using the aluminium chloride colorimetric method following a microplate-based procedure developed by Herald *et al*. [2012], with modifications. Into each well, 100 µL of distilled water, 10 µL of a sodium nitrite solution (50 g/L) and 10 µL of the honey solution (1 mg/mL) or a standard solution (quercetin solution in the concentration range of 10–100 mg/mL) were pipetted, and the mixture was left for 5 min. Then, 15 µL of an aluminium chloride solution (100 g/L) was added and left for an additional 6 min. Finally, after adding 50 µL of a sodium hydroxide solution (40 g/L) and 50 µL of distilled water, the plate was shaken for 30 s, and the absorbance was measured at 515 nm against distilled water. TFC was expressed as mg of quercetin equivalent (QUE) *per* 100 g of honey. The samples and standard were run in triplicate.

Phenolic composition determination

Sample extraction

The extracts of SBHs were obtained by the dispersive liquid-liquid microextraction as described by Campone *et al*. [2014]. In this extraction method, 10 g of SBHs was dissolved in acidified water at pH 2 to a final volume of 100 mL. The solution was passed through polytetrafluoroethylene (PTFE) filters with a 0.45 µm pore size. A 10-mL aliquot of the filtered SBH solution was placed in a conical flask. Then, 3 g of ammonium sulphate were added and after dissolving the salt, the pH of the solution was adjusted to pH 2 with 1 M HCl. Subsequently, 450 µL of chloroform and 750 µL of acetone were pipetted into the acidified aqueous mixture, and the conical flask was then vigorously shaken by hand for 10 s until persistent turbidity was obtained. Next, following centrifugation at 2,879×*g* for 5 mins using an ALC PK 120 centrifuge (Thermo Electron Corporation, Needham, MA, USA), the lower phase was collected into a 2-mL Eppendorf tube and dried under a low-flow nitrogen stream. The dried residue was dissolved in 100 µL of a mixture of methanol and water (1:4, *v/v*) and passed through 0.45-mm nylon syringe filter prior to the chromatographic separation.

Phenolic compound analysis

The analysis of the phenolic profile was carried out using the Agilent 1200 Series high-performance liquid chromatography (HPLC) system with a diode array detector (Agilent Technologies, Inc., Santa Clara, CA, USA) equipped with a reversed-phase C-18 column (Kromasil, 250 × 4.6 mm, 5 µm; Nouryon, Bohus, Sweden) as described by Chen *et al.* [2021]. The column temperature was maintained at 28°C. The mobile phase, consisting of 5% (*v/v*) formic acid (solution A) and methanol (solution B), was used at a constant flow rate of 0.7 mL/min. The gradient elution mode was achieved with a 10% to 65% solvent B over 50 min, followed by a 65% to 100% solvent B over 5 min, an isocratic 100% solvent B hold for 5 min, and re-equilibration of the column to its initial solvent conditions. The detection wavelengths were set at 280 nm and 340 nm. The phenolic compounds were identified based on their retention times and the shape of the spectra of standards (chlorogenic acid, (+)-catechin, caffeic acid, *p*-coumaric acid, rosmarinic acid, rutin, quercetin, and kaempferol) purchased from Sigma-Aldrich Chemical Co. (St. Louis, MO, USA). Quantification was carried out by comparing the peak areas obtained during sample separation with the peak areas of the standards. Results were expressed as µg *per* 100 g of honey.

Angiotensin-converting enzyme inhibition assay

The ACE inhibitory activity of honeys was assessed according to the method described by Nagai & Nagashima [2006]. Briefly, SBH and captopril (positive control, Sigma-Aldrich Chemical Co., St. Louis, MO, USA) were dissolved in deionised water at a concentration of 10 mg/mL. Then, 25 µL of these solutions were mixed with 75 µL of 0.1 M sodium borate buffer (pH 8.3) containing 5.83 mM hippuryl-L-histidyl-L-leucine (HHL) as a substrate and 1.0 M NaCl. Control without inhibitors was prepared in parallel. Mixtures were pre-incubated at 37°C for 5 min, and afterwards 25 µL of 0.1 M sodium borate buffer (pH 8.3) with 1 mU of angiotensin I-converting enzyme (Sigma-Aldrich) and 1.0 M NaCl were added. Reactions were carried out at 37°C for 60 min and then terminated by adding 125 µL of 1.0 M HCl. Hippuric acid released during the reaction was extracted using ethyl acetate; 750 µL of the solvent was added to the mixture, which was vigorously mixed for 15 s and centrifuged at 2,879×*g* for 3 min. A 500-µL aliquot of the upper layer was collected and ethyl acetate was evaporated at 40°C for 2 h. The residue was dissolved in 500 µL of deionised water, and absorbance of the solution was measured at 228 nm using a microplate reader (Fluoroskan Ascent, Thermo Fisher Scientific, Bremen, Germany). ACE inhibitory activity was calculated as a percentage using Equation (1):

$$\text{Inhibition (\%)} = [(A_{control} - A_{sample})/A_{control}] \times 100 \quad (1)$$

where: $A_{control}$ is absorbance of the control sample (without inhibitor) and A_{sample} is absorbance of the test sample (with inhibitor).

α-Amylase inhibition assay

The method described by Habib *et al*. [2021] was used to determine α-amylase inhibitory activity of SBH. To this end, 50 µL of SBH and acarbose (positive control) solutions with different concentrations (5, 10, 15, 20, and 25 mg/mL) were pipetted into each microplate well. Then, 50 µL of 0.02 M sodium phosphate buffer (pH 6.9) with 6 mM NaCl and 13 U/mL α-amylase (Sigma-Aldrich) were added. The mixture was left for 10 min at

25°C. Then, 50 µL of a 1% potato starch solution were added as the substrate. After further 10-min sample retention at 25°C, 1 mL of a 1% dinitrosalicylic acid (DNS) solution was added, and the mixture was heated for 10 min at 100°C to develop the colour. After cooling to room temperature (25°C), the absorbance was measured at 540 nm using a microplate reader (Fluoroskan Ascent, Thermo Fisher Scientific). The control sample without inhibitors and the blank containing the SBH without the enzyme were prepared in parallel. The absorbance of the blank was extracted from the absorbance of the reaction mixture with the SBH solution and enzyme. The α-amylase inhibitory activity was calculated as a percentage using Equation (1). Then, the half-maximal inhibitory concentration (IC_{50}), defined as the concentration of SBH or acarbose required to inhibit 50% of α-amylase activity, was determined from the concentration–response curve plotted with the tested SBH and acarbose concentrations.

Pancreatic lipase inhibition assay

The *in vitro* pancreatic lipase inhibition assay was performed as described by Zhang *et al*. [2020], with slight modifications. Aliquots (50 µL) of the SBH solution or orlistat (positive control, Sigma-Aldrich Chemical Co., St. Louis, MO, USA) at concentrations of 5, 10, 15, 20, and 25 mg/mL were pipetted into wells of a 96-well microplate, followed by 50 µL of a porcine pancreatic lipase (Sigma-Aldrich) solution prepared by dissolving the enzyme (1 mg/mL) in 13 mM Tris-HCl buffer (pH 8.0) with 1.3 mM $CaCl_2$, and 150 mM NaCl and centrifuging at 3,200×g for 15 min at 25°C. The mixtures were pre-incubated at 37°C for 10 min. Subsequently, 50 µL of a *p*-nitrophenyl butyrate solution (2 mg/mL in assay buffer) was added as substrate, and the reaction was carried out at 37°C for 20 min. A control reaction without inhibitors was performed in parallel. The amount of *p*-nitrophenol, colour agent released during the reaction was monitored by measuring absorbance at 405 nm using a microplate reader (Fluoroskan Ascent, Thermo Fisher Scientific). The percentage of pancreatic lipase inhibition was calculated using Equation (1). The IC_{50}, defined as the concentration of SBH or orlistat required to inhibit 50% of pancreatic lipase activity, was determined from the concentration–response curve generated with the tested SBH or orlistat concentrations.

Cholesterol esterase inhibition assay

The cholesterol esterase inhibitory activity of SBHs was determined based on the method described by Zhang *et al.* [2020] with minor modifications. The analysis was conducted using 96-well plates and measured with a microplate reader (Fluoroskan Ascent, Thermo Fisher Scientific). Aliquots of 50 mL of SBH and orlistat solutions with different concentrations (5, 10, 15, 20, and 25 mg/mL) and 50 mL of a *p*-nitrophenyl butyrate solution (1 mg/mL in 100 mM sodium phosphate buffer, pH 7.0, with 100 mM NaCl and 5.16 mM sodium taurocholate) were incubated at 37°C for 10 min. Then, 50 mL of a cholesterol esterase (Sigma-Aldrich) solution (0.163 U/mL in 0.1 M sodium phosphate buffer, pH 7.0) was added to the mixture, followed by incubation at 37°C for 20 min. The absorbance of the mixture was measured at 405 nm. The cholesterol esterase inhibitory activity was calculated as a percentage of activity sample without inhibitor using Equation (1). The IC_{50}, defined as the concentration of SBH or orlistat required to inhibit 50% of cholesterol esterase activity, was determined from the concentration–response curve plotted with the tested SBH or orlistat concentrations.

3-Hydroxy-3-methylglutaryl-coenzyme A reductase inhibition assay

The inhibitory activity of SBH against HMG-CoA reductase was determined *in vitro* using an HMG-CoA reductase assay kit (CS1090; Sigma-Aldrich), which is based on a spectrophotometric measurement of reduced nicotinamide adenine dinucleotide phosphate (NADPH) consumption. The kit contained pravastatin as the reference inhibitor, assay buffer, NADPH, HMG-CoA as the substrate, and HMG-CoA reductase (0.50–0.70 nM). The samples and pravastatin were prepared at a concentration of 10 mg/mL, while distilled water was used as the negative control. For each assay, 1 µL of the SBH solution, pravastatin solution, or distilled water was added to the wells of a UV-compatible 96-well microplate. The assay buffer was then added according to the manufacturer's protocol, followed by 4 µL of an NADPH solution, 12 µL of an HMG-CoA solution, and 2 µL of an HMG-CoA reductase solution. The final reaction volume was adjusted to 200 µL. The reaction mixtures were incubated at 37°C, and the absorbance at 340 nm was measured using a microplate reader (Fluoroskan Ascent, Thermo Fisher Scientific). Enzyme specific activity expressed in unit/mg protein was calculated based on absorbance change over time (ΔA, in 1/min) using Equation (2) for reaction mixtures with inhibitor and control without inhibitor:

$$\text{Specific activity} = \frac{\Delta A \times V_{total}}{12.24 \times V_{enzyme} \times 0.6 \times LP} \quad (2)$$

where: V_{total} is the total volume (mL), V_{enzyme} is the volume of an enzyme solution added to the mixture (mL), LP is light path (0.55), 12.44 is a doubled extinction coefficient of NADPH, because two molecules of NADPH are used in the reaction (1/(mM×cm)), and 0.6 is enzyme concentration (mg protein/mL).

HMG-CoA reductase inhibitory activity was expressed as a percentage. The percentage inhibition was calculated according to Equation (3):

$$\text{Inhibition (\%)} = \frac{C - S}{C} \times 100 \quad (3)$$

where: C is control specific activity (unit/mg protein) and S is sample specific activity (unit/mg protein)

Statistical analysis

All data were expressed as mean and standard deviation. Statistical analyses were conducted using XLSTAT 2021 (Addinsoft, Paris, France). Differences among the means were evaluated by one-way analysis of variance (ANOVA), followed by Tukey's post hoc

test, with statistical significance set at $p<0.05$. Pearson's correlation coefficient (r) was used to assess the relationships between total phenolic content, total flavonoid content, and enzyme inhibitory activities, with significance determined at $p<0.05$. Principal component analysis (PCA) was subsequently applied to assess patterns and relationships within the dataset and to visualise the distribution of the samples based on the measured variables. Honey samples were considered objects, and phenolic compounds and enzyme inhibitory activities were considered variables. Data variability was investigated based on the first two principal components (PC). The number of PCs to be selected was determined using the Kaiser criterion, where only eigenvalues greater than one are considered significant. The Bartlett's test was used to check the correlation between variables and to test the null hypothesis, with a $p<0.05$ indicating that the variables are adequate. Hierarchical cluster analysis (HCA) was performed to evaluate the similarities and dissimilarities among the SBH samples. Clustering was conducted using the Euclidean distance (ED) as the dissimilarity measure and Ward's method as the linkage criterion.

RESULTS AND DISCUSSION

Total phenolic content

Phenolic compounds are the key contributors to the health-promoting properties of SBH, and their levels vary depending on the floral origin [Biluca *et al.*, 2020; Shamsudin *et al.*, 2022]. In the present study, the total phenolic content (TPC) of the eight SBH samples ranged from 45.31 to 105.21 mg GAE/100 g (**Table 1**). SBH from the Singapore rhododendron origin showed the highest TPC at 105.21 mg GAE/100 g, followed by acacia and coconut honeys. In contrast, rose myrtle and durian honeys showed the lowest TPC, indicating considerable variation among the honeys from different botanical origins. These differences were statistically significant ($p<0.05$), confirming that the floral source had a strong influence on the phenolic content of SBH. The TPC observed in this study fell within the range commonly reported for SBH [Gebreyes *et al.*, 2025; Ng *et al.*, 2021]. Badrulhisham *et al.* [2020] recorded TPC ranging from 40.11 to 179.04 mg GAE/100 g for Malaysian SBH, which was comparable to our findings. However, the TPC of the Brazilian SBH from different floral sources ranged from 6.21 to 15.79 mg GAE/100 g [Dias *et al.*, 2025], which was significantly lower than the results obtained in the current study. Thus, these findings suggest that both geographical and botanical origins shape the total phenolic content of SBH.

Most of the monofloral samples, including acacia, coconut, rose myrtle, and Singapore rhododendron honeys, had higher TPC as compared to the multifloral honey (**Table 1**). This pattern aligned with the results reported by Ali *et al.* [2020], where the total phenolic content of monofloral SBH was higher, *i.e.*, for mangrove (141.74 mg GAE/100 g), coconut (101.41 mg GAE/100 g), and acacia (99.74 mg GAE/100g) honeys, compared to the multifloral and multifruit samples (83.08 and 77.52 mg GAE/100 g, respectively). Monofloral SBHs had higher TPC, likely due to the dominance of a single nectar source particularly rich in phenolic compounds.

Table 1. The total phenolic content (TPC) and total flavonoid content (TFC) of stingless bee honeys from different floral sources.

Honey	TPC (mg GAE/100 g)	TFC (mg QUE/100 g)
Acacia	96.68±0.55^{b}	34.40±0.23^{c}
Coconut	87.30±0.43^{c}	35.10±0.22^{b}
Rubber tree	65.30±0.39^{f}	13.40±0.17^{f}
Durian	56.31±0.35^{g}	24.57±0.27^{e}
Coral vine	75.30±0.50^{d}	25.44±0.23^{d}
Rose myrtle	45.31±0.33^{h}	12.20±0.15^{g}
Singapore rhododendron	105.21±0.62^{a}	43.22±0.29^{a}
Multifloral	70.30±0.47^{e}	35.53±0.25^{b}

Values are reported as mean ± standard deviation (n=3). Different lowercase letters (a–h) within the same column indicate significant differences ($p<0.05$). GAE, gallic acid equivalent; QUE, quercetin equivalent.

Total flavonoid content

Flavonoids are a major class of phenolic compounds that occur naturally in plants and plant-derived products. In this study, the total flavonoid content (TFC) ranged from 13.44 to 43.22 mg QUE/100 g (**Table 1**). Similarly to the trend observed for TPC, the honey from Singapore rhododendron had the highest TFC (43.22 mg QUE/100 g). In contrast, honeys from rubber tree and rose myrtle exhibited the lowest TFC. When comparing monofloral samples with the multifloral honey, the TFC showed an interesting pattern. Although Singapore rhododendron honey clearly dominated in the total flavonoid content, acacia and coconut honeys, in contrast to TPC, exhibited TFC comparable to that of the multifloral sample, suggesting that not all monofloral sources provide high flavonoid levels. The total flavonoid content found in SBHs in our study was higher than the results reported by Shamsudin *et al.* [2019a], who documented TFC of 2.38 to 9.31 mg QUE/100 g in Malaysian SBHs. This difference may be attributed to factors such as geographic location (west and east Malaysia) and plant diversity.

Phenolic compound composition

In this study, a total of nine phenolic compounds were identified in stingless bee honey, including five phenolic acids and four flavonoids: gallic acid, chlorogenic acid, caffeic acid, *p*-coumaric acid, rosmarinic acid, (+)-catechin, rutin, quercetin, and kaempferol. An example of the HPLC separation of these compounds of a multifloral honey is shown in **Figure 1**, while the quantitative profile of identified phenolics in all analysed honeys is shown in **Table 2**. Rosmarinic acid was the major phenolic compound in all the SBHs. Among the samples, SBH from Singapore rhododendron contained the highest level of rosmarinic acid (734.81 µg/100 g), as well as rutin (600.13 µg/100 g), caffecic acid

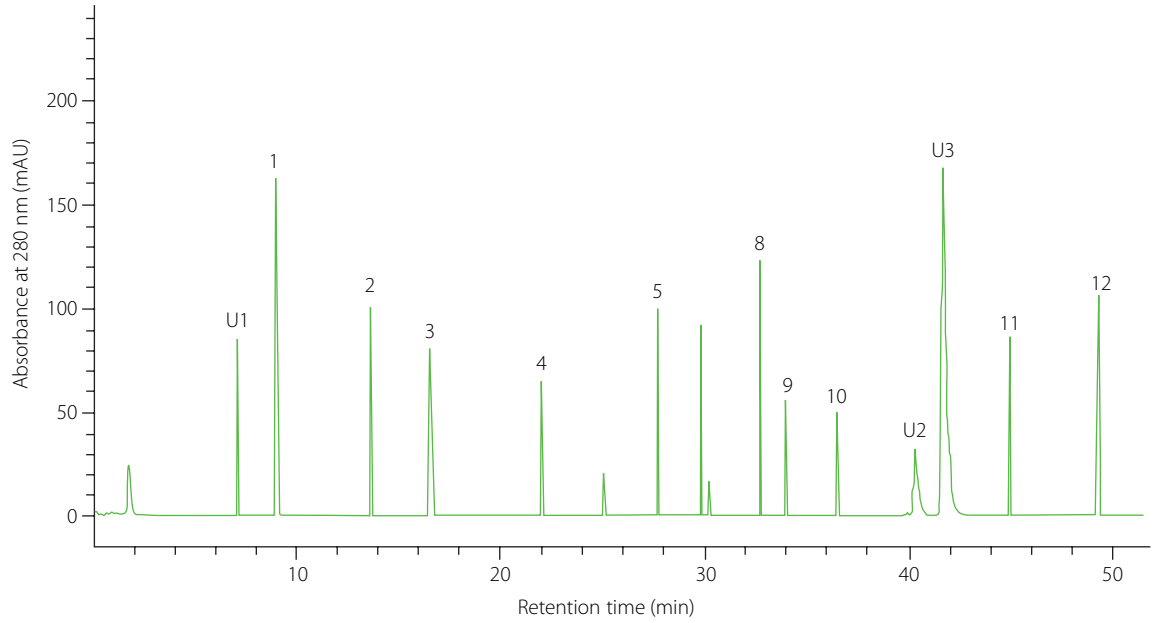


Figure 1. HPLC chromatogram of multifloral stingless bee honey. 1, Gallic acid; 2, chlorogenic acid; 3, (+)-catechin; 4, caffeic acid; 5, *p*-coumaric acid; 9, rosmarinic acid; 10, rutin; 11, quercetin; 12, kaempferol; U1–U3, unknown phenolic compounds.

(102.71 µg/100 g), and *p*-coumaric acid (122.02 µg/100 g), where the rutin content was six times higher than the content found in acacia honey. The latter was the richest in chlorogenic acid (408.19 µg/100 g) and quercetin (312.83 µg/100 g). The content of (+)-catechin was the highest in acacia and rubber tree honeys. In turn, the content of rosmarinic acid in multifloral honey was comparable to that of acacia honey; however, its kaempferol content (342.04 µg/100 g) was the highest among all samples. It was more than three times higher than that of coconut honey (100.44 µg/100 g). Additionally, three unknown phenolic compounds (U1, U2, and U3) were detected in the multifloral SBH, as shown in the chromatogram (**Figure 1**). These phenolic profiles suggest that multifloral foraging of bees can yield a more complex phenolic composition compared to the monofloral.

Compared to the previous studies performed on Malaysian SBH, a different set of phenolic compounds were reported. Ismail *et al.* [2016] identified 15 phenolic compounds in honey using HPLC-DAD, with ellagic acid and benzoic acid reported as the predominant compounds. However, a study by Majid *et al.* [2020] on SBH from Johor identified six phenolic compounds, which were chlorogenic acid, *p*-coumaric acid, catechin, protocatechuic acid, epicatechin, and rutin. Chen *et al.* [2021] identified rosmarinic acid, chlorogenic acid, quercetin, kaempferol, and rutin, with rosmarinic acid and quercetin being the most abundant phenolic compounds in Sabah SBH. Our findings are consistent with the phenolic profile presented in the aforementioned study, despite differences found in the contents of individual compounds. Notably, benzoic acid, a primary compound found in acacia SBH as reported by Shamsudin *et al.* [2022], was not detected in this study, suggesting that regional and seasonal variations can strongly influence phenolic composition. Overall, the results demonstrate that botanical origin plays an important role in shaping the distinct dominant phenolic fingerprint of monofloral honeys. In contrast, multifloral honey displayed greater compositional diversity.

Angiotensin-converting enzyme inhibitory activity

A key regulatory step in the renin–angiotensin system is catalysed by ACE, which converts angiotensin I to angiotensin II [Balla *et al.*, 2021]. ACE inhibitory drugs (*e.g.*, captopril) are used to block this conversion, leading to a lower blood pressure. In our study, all eight SBH samples demonstrated *in vitro* measurable ACE inhibitory activity at 10 mg/mL, with inhibition values ranging from 10.92% to 74.62% (**Figure 2A**). Among them, Singapore rhododendron honey exhibited the strongest inhibitory effect (74.62%), approaching the activity of the standard ACE inhibitor, captopril at 10 mg/mL (80.02%). This inhibitory level was nearly seven times higher than that of rose myrtle honey, which showed the weakest activity (10.92%). The second strongest inhibition was observed for coconut honey (65.51%), which was slightly ($p<0.05$) higher than those determined for acacia and rubber tree honeys. Notably, durian and multifloral honeys displayed markedly lower ACE inhibitory activity (34.20–33.59%), representing less than half the inhibition observed for Singapore rhododendron honey. These variations clearly indicate that ACE inhibitory activity of SBH was strongly influenced by its botanical origin. It seems the samples with a higher total phenolic content (**Table 1**) showed more potent ACE inhibition; the Singapore rhododendron and coconut honeys, which had the highest TPC showed the strongest ACE inhibitory effects. Al Shukor *et al.* [2013] found that many individual phenolics exhibited high ACE inhibitory activity, and in the case of phenolic acids and flavonoids, they acted through the interaction of their hydroxyl groups with the zinc ion of the ACE active site, thereby inhibiting

Table 2. Content of individual phenolic compounds in stingless bee honeys from different floral sources (µg/100 g honey).

Honey	Gallic acid	Chlorogenic acid	(+)-Catechin	Caffeic acid	*p*-Coumaric acid	Rosmarinic acid	Rutin	Quercetin	Kaempeferol
Acacia	162.8±0.2^{c}	408.2±3.6^{a}	68.2±5.6^{ab}	36.8±0.2^{f}	37.0±0.9^{g}	628.4±1.8^{b}	96.2±2.7^{g}	312.8±6.9^{a}	138.6±2.1^{e}
Coconut	168.6±5.0^{c}	167.7±1.0^{e}	58.8±2.3^{bc}	44.7±0.1^{e}	47.7±0.6^{f}	457.0±13.3^{c}	357.4±10.3^{c}	131.5±1.2^{e}	100.4±0.7^{f}
Rubber tree	201.6±3.6^{b}	206.2±1.5^{d}	79.6±1.2^{a}	63.2±0.1^{a}	59.6±0.9^{e}	419.7±6.2^{cd}	134.5±1.2^{de}	157.9±5.6^{d}	192.0±9.5^{b}
Durian	272.0±2.9^{a}	288.9±3.1^{b}	54.0±4.3^{c}	59.4±0.4^{d}	36.3±0.3^{g}	376.5±23.8^{d}	107.5±13.2^{ef}	229.1±0.5^{c}	159.4±5.4^{cd}
Coral vine	122.8±2.4^{e}	147.3±0.3^{e}	61.2±1.6^{bc}	69.5±0.8^{c}	68.2±0.2^{d}	477.1±7.2^{c}	146.4±0.7^{d}	125.9±1.2^{e}	138.3±4.3^{e}
Rose myrtle	129.6±1.5^{e}	205.4±11.4^{d}	55.4±3.8^{bc}	70.7±2.4^{c}	88.4±0.2^{c}	478.3±8.1^{c}	239.0±0.6^{d}	230.7±3.0^{c}	142.8±1.8^{de}
Singapore rhododendron	159.3±1.3^{c}	256.3±11.5^{c}	53.1±4.3^{c}	79.0±1.6^{b}	95.3±2.1^{b}	734.8±1.6^{a}	600.1±12.7^{a}	236.0±0.8^{c}	170.3±2.5^{c}
Multifloral	145.3±3.3^{d}	280.7±10.6^{b}	49.1±2.8^{c}	102.7±0.5^{a}	122.0±3.8^{a}	651.3±38.4^{b}	545.1±12.8^{b}	277.6±0.5^{b}	342.0±1.5^{a}

Values are reported as mean ± standard deviation (n=3). Different lowercase letters (a–g) within the same column indicate significant differences (p<0.05).

enzyme activity. Moreover, this interaction is stabilised by other interactions with amino acids [Al Shukor *et al.*, 2013]. Collectively, the Singapore rhododendron honey was the most potent natural ACE inhibitor among the samples, which suggests that certain SBH types, especially those rich in phenolic compounds, may serve as promising natural antihypertensive agents.

α-Amylase inhibitory activity

α-Amylase facilitates the breakdown of starches and complex carbohydrates into smaller oligosaccharides, thereby playing a central role in digestion. Its inhibition can prevent postprandial blood glucose spikes, which represents a promising therapeutic strategy for the management of type 2 diabetes and obesity [Vadivelan *et al.*, 2019]. All SBH samples demonstrated concentration-dependent α-amylase inhibition between 5 and 25 mg/mL. At 25 mg/mL, the inhibition followed the order of honeys: multifloral (75.29%) > durian (73.14%) > rubber tree (72.21%) > rose myrtle (63.99%) > acacia (58.88%) > coconut (53.56%) > Singapore rhododendron (33.60%) > coral vine (36.55%), while the standard acarbose reached 78.58% inhibition. The IC_{50} values of the samples, shown in **Figure 3A**, further support the inhibition patterns displayed. Multifloral SBH exhibited the lowest IC_{50} (12.93 mg/mL), indicating the strongest α-amylase inhibitory activity, and was more potent than acarbose (IC_{50} of 15.36 mg/mL), which in turn showed comparable activity ($p \geq 0.05$) to Singapore rhododendron honey (15.80 mg/mL). In contrast, coral vine honey exhibited the weakest inhibition, with an IC_{50} of 26.42 mg/mL, being nearly twice as high as that of the multifloral honey. The enhanced α-amylase inhibitory activity of multifloral honey was likely related to its high flavonoid content, particularly quercetin (277.57 µg/100 g) and kaempferol (342.04 µg/100 g) (**Table 2**). These values were among the highest across all samples, with quercetin in multifloral honey being two times higher than in coral vine honey. Previous studies have indicated that flavonoids, such as quercetin and luteolin, are known as α-amylase inhibitors by binding to the active site or modifying enzyme conformation, thus reducing starch hydrolysis [Zhao *et al.*, 2021]. The α-amylase inhibitory activity of honeys analysed in our study was high compared to the results obtained by Ali *et al.* [2020] for flavonoid-rich SBHs from acacia, mangrove, coconut, starfruit, and multifloral sources, which exhibited inhibitory activity ranging from 36.77% to 72.14% at a concentration of 100 µg/mL. Taken together, our findings suggest that multifloral SBH exhibits high α-amylase inhibitory activity and may have potential relevance in carbohydrate digestion regulation. However, further studies are needed to confirm its effects on the postprandial glucose control.

Pancreatic lipase inhibitory activity

Pancreatic lipase catalyses the hydrolysis of dietary triglycerides, facilitating fat absorption. Inhibiting this enzyme reduces triglyceride uptake and can help prevent obesity and obesity-related diseases [Ketprayoon *et al.*, 2021; Liu *et al.*, 2020]. In this study, eight SBH samples were assessed for lipase inhibitory

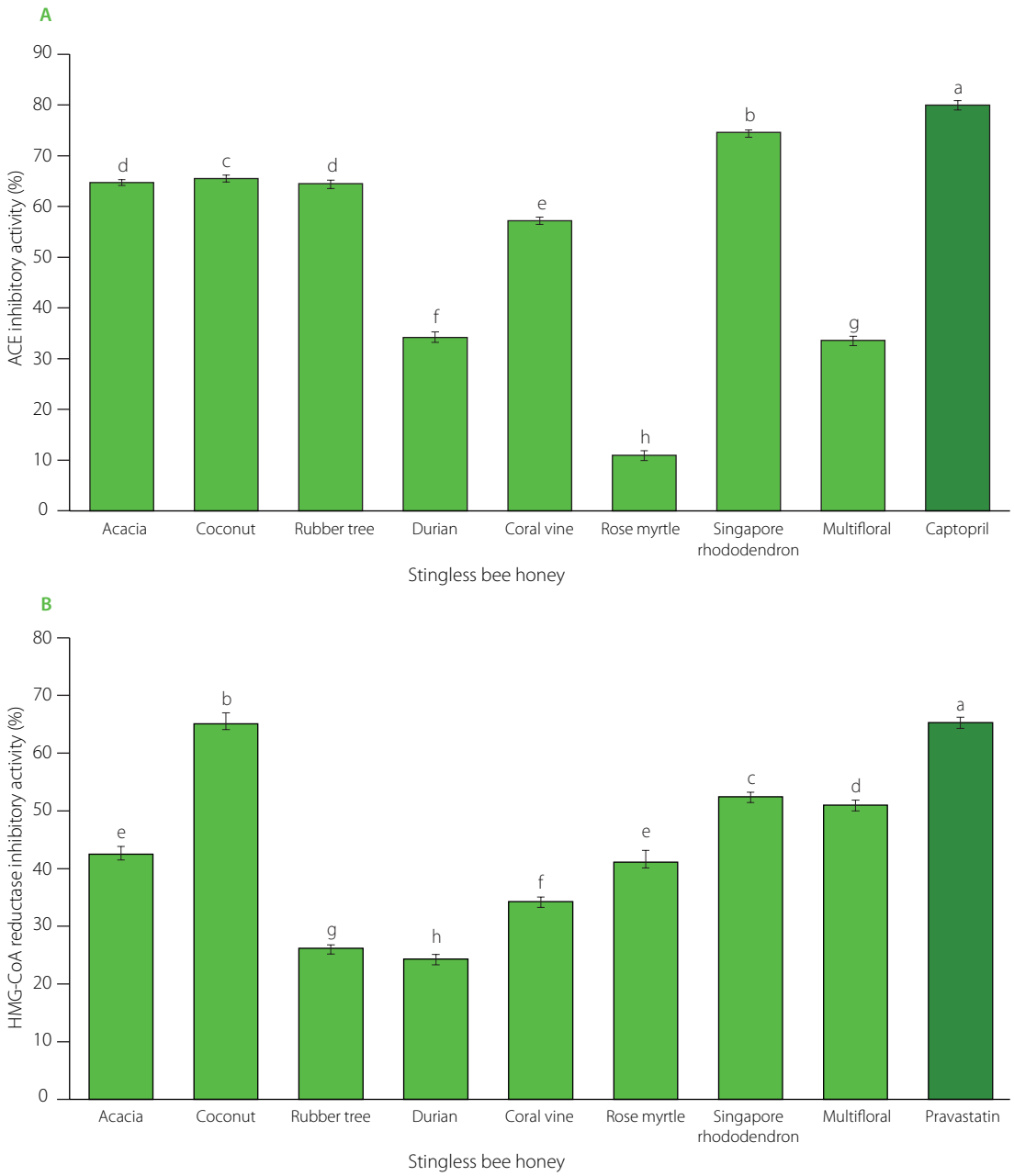


Figure 2. Angiotensin converting enzyme (ACE) inhibitory activity (**A**) and 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitory activity (**B**) of stingless bee honeys from different floral sources at 10 mg/mL. Values are reported as mean and standard deviation (n=3). Different superscript letters indicate the significant differences at p<0.05.

activity alongside orlistat as the positive control. At 25 mg/mL, inhibition ranged from 33.97% to 68.85%, compared to 75.01% determined for orlistat. The multifloral honey showed the lowest IC_{50} value (12.02 mg/mL), followed closely by rubber tree honey (12.57 mg/mL) (**Figure 3B**). Coconut honey displayed moderate inhibition, while coral vine honey exhibited the highest IC_{50}, indicating the lowest pancreatic lipase inhibitory activity among the samples tested. Orlistat exhibited an IC_{50} of 10.30 mg/mL.

The pancreatic lipase inhibitory activity observed in the SBH samples is due to their bioactive compounds. Previous studies have demonstrated that certain bioactive compounds, such as β-lactone derivatives (orlistat, vibralactone), heterocyclic compounds (oxadiazol-2-ones, benzimidazoles, carbazoles, thiazolidinediones, rhodanines), and peptides, inhibit pancreatic lipase by forming covalent or hydrogen bonds with the catalytic serine residue (Ser152) in the active site of the enzyme [Kumar & Chauhan, 2021]. Phenolic compounds, particularly flavonoids from

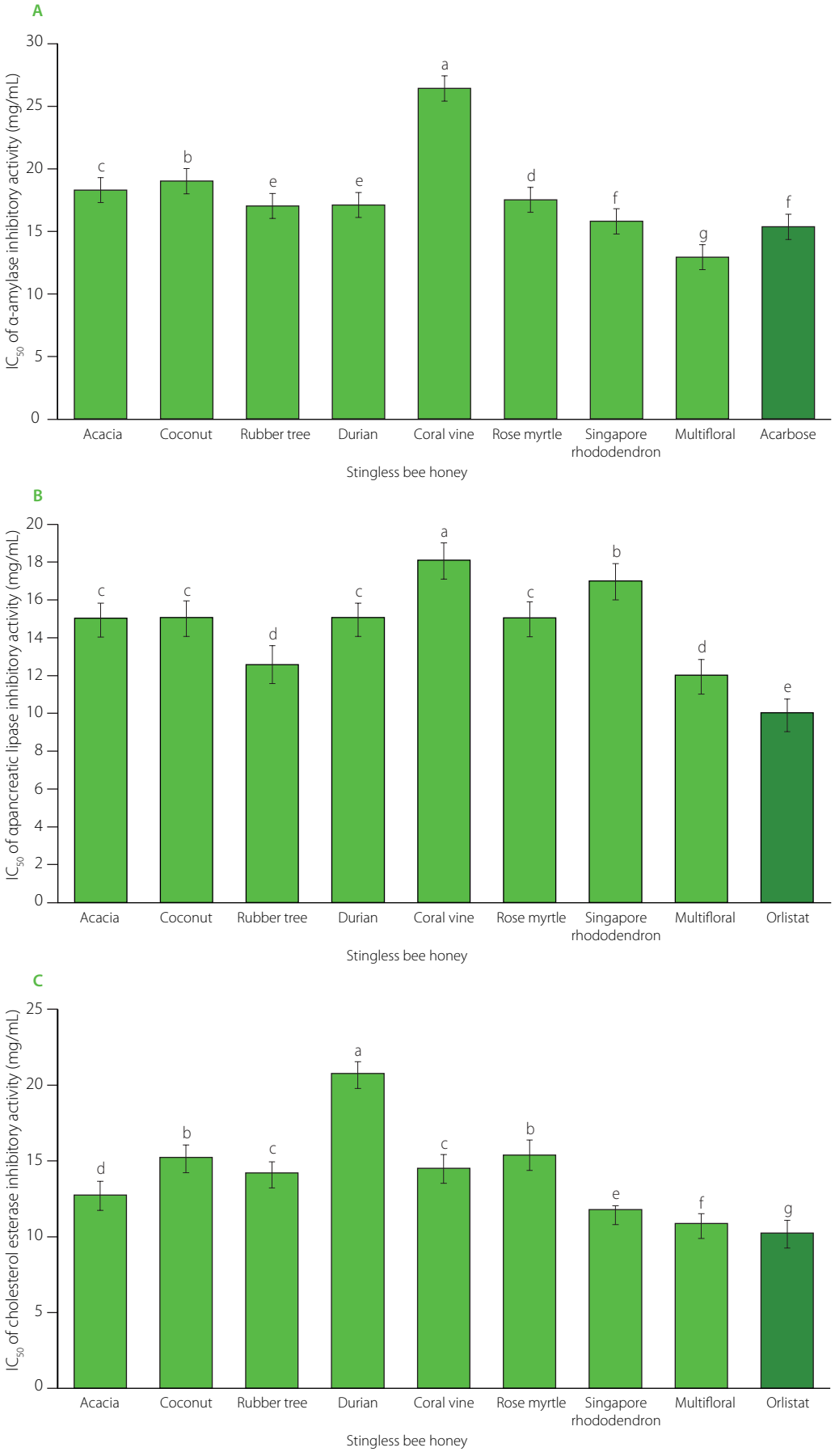


Figure 3. The IC_{50} for α-amylase (**A**), pancreatic lipase (**B**), and cholesterol esterase (**C**) inhibitory activities of stingless bee honeys from different floral sources. Values are reported as mean and standard deviation (n=3). Different superscript letters indicate the significant differences at $p<0.05$.

various natural sources, are also recognised as lipase inhibitors [He *et al*., 2023; Liu *et al*., 2020]. Therefore, the potent inhibitory activity of the multifloral sample could be attributed to its high individual flavonoid content (**Table 2**). Overall, the results suggest that selected SBHs may serve as a promising natural source of pancreatic lipase inhibitors, potentially beneficial for the modulation of dietary fat absorption and the management of obesity-related metabolic conditions.

Cholesterol esterase inhibitory activity

Alongside pancreatic lipase, cholesterol esterase (CEase) is an essential enzyme in intestinal lipid digestion and absorption, making it a potential target for regulating lipid metabolism [He *et al*., 2023]. All SBH samples exhibited measurable cholesterol esterase inhibitory activity (**Figure 3C**). At 25 mg/mL, Singapore rhododendron honey showed the strongest inhibitory effect (65.05%), comparable to the positive control orlistat (67.76%). In contrast, durian honey displayed the weakest activity (29.51%). Other samples demonstrated moderate inhibition ranging from 54% to 63%. The IC_{50} values further highlighted that the multifloral honey exhibited the lowest IC_{50} (10.88 mg/mL), followed closely by Singapore rhododendron honey (11.80 mg/mL), both approaching the potency of the standard orlistat (10.25 mg/mL). By contrast, durian honey showed the highest IC_{50} (20.77 mg/mL), requiring nearly twice the concentration of multifloral honey to achieve the same degree of inhibition. The variation in inhibitory activity among the SBH samples was likely related to differences in their phenolic compound profiles.

Plant phenolics have been widely recognised for their role in inhibiting CEase and regulating cholesterol metabolism [Eilam *et al*., 2022; He *et al*., 2023]. Past research has shown that *Camellia nitidissima* Chi flower extract rich in phenolic compounds, such as epicatechin, procyanidins, rutin, and other quercetin glycosides, inhibited CEase activity [Zhang *et al*., 2020]. Therefore, the high inhibitory activity of the multifloral sample may be probably due to its high levels of rutin and quercetin (**Table 2**).

3-Hydroxy-3-methylglutaryl-coenzyme A reductase inhibitory activity

HMG-CoA reductase is the rate-limiting enzyme in cholesterol biosynthesis and catalyzes the conversion of HMG-CoA to mevalonate using NADPH. Statins lower cholesterol levels by inhibiting this enzyme, making it an important target for managing hypercholesterolemia [Santos-Sánchez *et al*., 2024]. All SBH samples demonstrated the ability to inhibit HMG-CoA reductase and their inhibitory activity ranged from 24.36% to 65.06% (**Figure 2B**). Coconut honey exhibited the strongest inhibition against HMG-CoA reductase, which was comparable to the positive control pravastatin (65.27%). The Singapore rhododendron and multifloral honeys had two times higher inhibitory activity as compared to the durian honey. The strong HMG CoA reductase inhibition observed for these honeys (coconut, Singapore rhododendron, and multifloral) corresponded closely with their high TFC. Notably, the kaempferol content in the multifloral sample was more than three times higher than that of coconut honey. Similarly, the content of quercetin, a well-established HMG-CoA reductase inhibitor [Riyad *et al*., 2023], in the Singapore rhododendron honey (235.95 µg/100 g) was nearly twice that of coconut honey (131.47 µg/100 g). Yet, the coconut honey remained the most potent HMG-CoA reductase inhibitor, suggesting that synergistic interactions among multiple bioactive compounds, rather than single-compound dominance, contribute to the overall inhibitory effect.

The HMG-CoA reductase inhibition may occur *via* a dual-action mechanism that involves both direct enzymatic inhibition and transcriptional downregulation of HMG-CoA reductase mevalonate [Ding *et al*., 2026; Riyad *et al*., 2023; Santos-Sánchez *et al*., 2024]. A study by Riyad *et al*. [2023] reported that quercetin had a high binding affinity (–8.4 kcal/mol) for HMG-CoA reductase, forming multiple stable hydrogen bonds with key amino acid residues, such as Ser637 and Lys606, which potentially obstructed the catalytic activity of the enzyme *via in silico* docking. Direct interactions of compounds such as *p*-coumaric acid and chlorogenic acid exert a regulatory effect at the genetic level by significantly suppressing HMG-CoA reductase mRNA expression [Ding *et al*., 2026; Riyad *et al*., 2023]. This transcriptional modulation is frequently mediated through the SREBP2 pathway, the central regulator of cholesterol homeostasis, leading to reduced cholesterol biosynthesis in hepatocytes [Ding *et al*., 2026].

Aside from phenolics, peptides present in SBH may further contribute to HMG-CoA reductase inhibition. A previous study reported that certain food-derived peptides could bind to the HMG-CoA reductase, interfering with the conversion of HMG-CoA to mevalonate [Santos-Sánchez *et al*., 2024]. Given that SBH is rich in small peptides and free amino acids [Biluca *et al*., 2019], such compounds may act synergistically with phenolics to enhance overall inhibition. Thus, the strong HMG-CoA reductase inhibitory activities of the coconut, Singapore rhododendron, and multifloral honeys, which were comparable to the pharmacological statins, highlight their potential value as natural cholesterol-lowering agents.

Pearson's correlations

Pearson's correlation analysis showed several significant relationships between the enzyme inhibitory activities, TPC and TFC (**Table 3**). The α-amylase inhibitory activity was positively, significantly correlated with pancreatic lipase inhibitory activity (r=0.751), while pancreatic lipase inhibitory activity also showed a strong positive correlation with cholesterol esterase inhibitory activity (r=0.753). In contrast, pancreatic lipase inhibitory activity was significantly and negatively correlated with ACE inhibitory activity (r=–0.578), indicating that SBH samples with higher pancreatic lipase inhibitory activity generally exhibited lower ACE inhibitory activity.

The total phenolic content was strongly correlated with the total flavonoid content (r=0.841). In turn, ACE inhibitory activity was positively correlated with both TPC (r=0.538) and TFC (r=0.504), suggesting a possible contribution of phenolic

Table 3. Coefficients of Pearson's correlations between total phenolic content (TPC), total flavonoid content (TFC), and enzyme inhibitory activities of stingless bee honeys from different floral sources.

Parameter	PL	CEase	ACE	HMG-CoA	TPC	TFC
α-Amylase	0.751**	0.421*	–0.348	0.139	0.211	–0.010
PL	1	0.753**	–0.578**	0.143	0.097	–0.114
CEase		1	–0.108	0.566**	0.128	–0.008
ACE			1	0.311	0.538**	0.504*
HMG-CoA				1	0.177	0.393
TPC					1	0.841**

α–Amylase, α-amylase inhibitory activity; PL, pancreatic lipase inhibitory activity; CEase, cholesterol esterase inhibitory activity; ACE, angiotensin converting enzyme inhibitory activity; HMG-CoA, 3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitory activity. *Correlation is significant at $p<0.05$; **correlation is significant at $p<0.01$.

compounds to ACE inhibition. However, no significant correlations were found between TPC or TFC and α-amylase, pancreatic lipase, cholesterol esterase, or HMG CoA inhibitory activities ($p\geq0.05$), indicating that the inhibitory activities of these enzymes were not directly associated with the total phenolic or flavonoid content of the SBH samples. This could be explained by variations in hydroxylation patterns in phenolic structure, glycosylation, molecular size, and hydrophobicity, which may influence the binding affinity of phenolic compounds toward different enzyme active sites, which affect the inhibitory activities [Ding *et al*., 2026; Riyad *et al*., 2023; Santos-Sánchez *et al*., 2024; Zhang *et al*., 2020]. Additionally, the individual phenolic compounds identified in SBH in the current study, such as gallic acid, chlorogenic acid, catechin, rutin, quercetin, and kaempferol, may exhibit distinct inhibitory mechanisms against the target enzyme. These findings suggest that the biological activities of SBH are affected by complex interactions among bioactive compounds rather than by total phenolic or flavonoid content alone.

Interrelationship of the *in vitro* enzyme inhibitory activities and phenolic composition

A principal component analysis (PCA) was employed to explore the interrelationship between the phenolic composition and the enzyme inhibitory activities. The original variables (individual phenolic compound contents, and ACE, pancreatic lipase, α-amylase, HMG-CoA reductase, and cholesterol esterase inhibitory activities) were reduced into a smaller number of underlying variables known as principal components (PC) [Kherif & Latypova, 2020]. This approach helps to reveal the relationship among the various variables and to use high-correlation clusters to form major components.

Two principal components were extracted, where PC1 accounted for 39.66% of the total variance, and PC2 explained an additional 22.60%, cumulatively describing 62.26% of the dataset structure (**Figure 4A**). The loading distribution revealed a distinct clustering pattern. C caffeic acid, kaempferol, *p*-coumaric acid, rutin, rosmarinic acid, and quercetin, together with ACE and HMG-CoA reductase inhibitory activities, loaded strongly on the right side of PC1, indicating a coordinated contribution to antihypertensive and cholesterol-lowering activities. This interpretation is biologically consistent with the previous evidence where kaempferol has been shown to reduce ACE activity and suppress angiotensin II upregulation [Maneesai *et al*., 2024]. *p*-Coumaric acid and quercetin are known inhibitors of HMG-CoA reductase and cholesterol-lowering agents [Ding *et al*., 2026; Riyad *et al*., 2023]. Singapore rhododendron and multifloral honeys were loaded on PC1 (**Figure 4A**). This supports the observation that these honeys showed stronger ACE and HMG-CoA inhibitory activities. In contrast, the inhibitory activity against α-amylase, pancreatic lipase, and cholesterol esterase was positioned on the left side of the PC1, along with chlorogenic acid, (+)-catechin, and gallic acid contents. This group of variables corresponds to acacia, rose myrtle, coconut, coral vine, durian, and rubber tree SBHs. Among them, honeys from acacia, rose myrtle, and coconut showed the strongest association with antihyperglycemic and antihyperlipidemic potential.

The results obtained from the hierarchical cluster analysis (HCA) are presented as a dendrogram (**Figure 4B**), which reveals three well-defined clusters. Cluster A is composed of Singapore rhododendron and multifloral honeys. These samples were associated with ACE and HMG-CoA inhibitory activity, as well as with the contents of kaempferol and caffeic acid. The second cluster (B) consists of acacia, coconut, and rose myrtle honeys due to their significant contributions to the inhibition of α-amylase, pancreatic lipase, and cholesterol esterase activities. Cluster C is grouped with rubber tree, durian, and coral vine honeys. These findings align with the results of the PCA. Interestingly, the HCA revealed a clustering due to sampling locations. Cluster A comprised samples from Kiulu, Cluster B included those from Telipok, and Cluster C consisted of samples from Kota Kinabalu. Although this pattern reflects a geographical grouping, it is likely incidental and not the primary driver of variability. Botanical origin remains the dominant factor shaping phenolic composition and bioactivity.

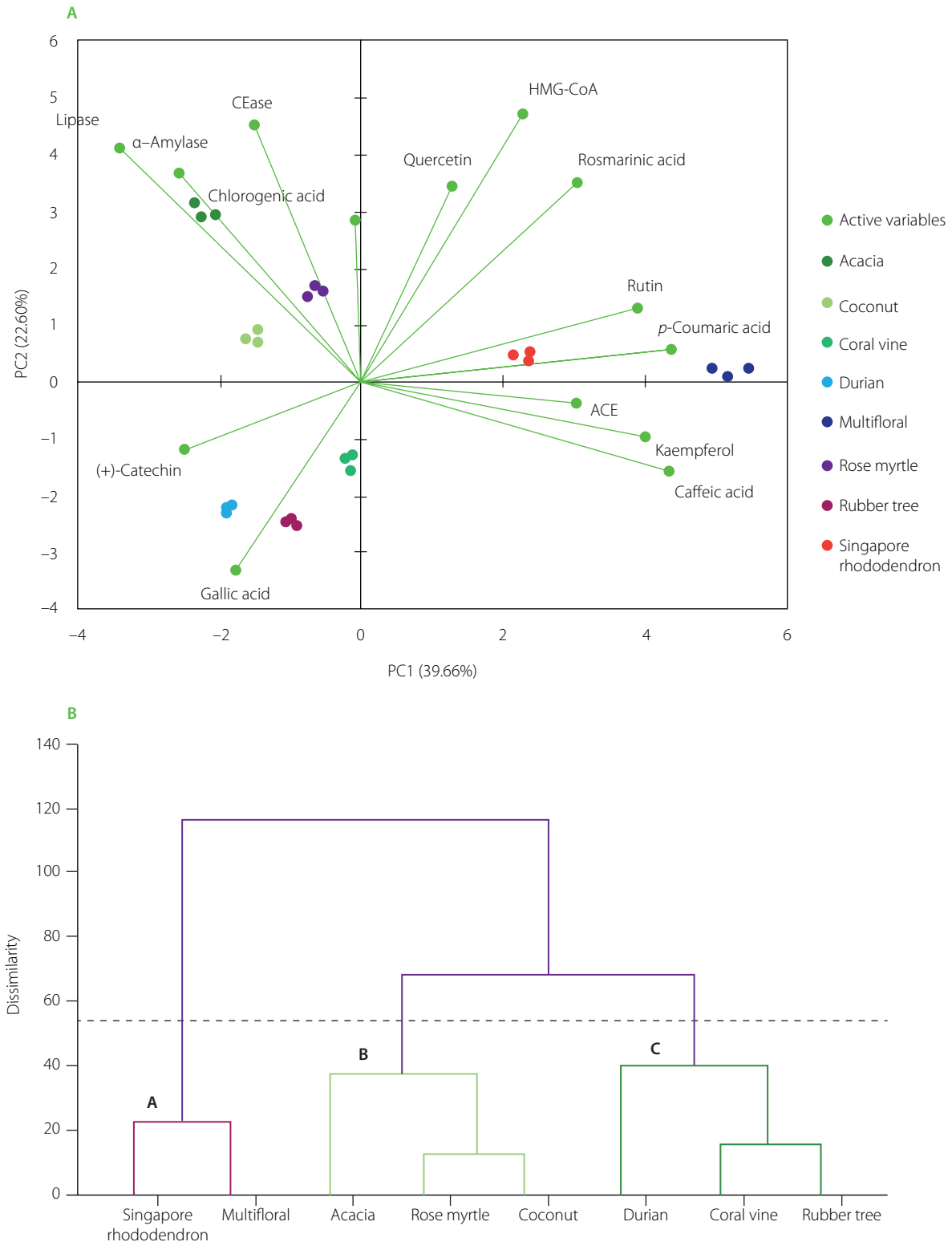


Figure 4. Plot of principal component analysis (PCA) showing the distribution of honeys and the loading vectors of the measured variables (**A**) and dendrogram of hierarchical cluster analysis (HCA) grouping stingless bee honeys based on their botanical origins (**B**). α–Amylase, α-amylase inhibitory activity; PL, pancreatic lipase inhibitory activity; CEase, cholesterol esterase inhibitory activity; ACE, angiotensin converting enzyme inhibitory activity; HMG-CoA, 3-hydroxy-3--methylglutaryl-coenzyme A reductase inhibitory activity.

CONCLUSIONS

This study demonstrated that SBHs exhibit inhibitory activity against several enzymes, including ACE, α-amylase, pancreatic lipase, HMG-CoA reductase, and cholesterol esterase, which implies their potential cardioprotective effects. The observed differences in enzyme inhibitory activities among SBH samples were associated with differences in their phenolic composition and botanical origins. Honeys high in flavonols (kaempferol,

quercetin) and hydroxycinnamic acids (caffeic acid, *p*-coumaric acid, chlorgenic acid) showed stronger enzyme inhibition. Among the samples analysed, SBH from Singapore rhododendron displayed the highest total phenolic content and exhibited strong enzyme inhibitory activities as compared to other samples. This study underpins the feasibility of developing functional foods and nutraceuticals based on SBH. Future research should investigate the possible synergistic effects of phenolics and amino acids on their enzyme inhibition that reflect their cardioprotective potential.

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CONFLICT OF INTERESTS

The authors declare that they have no conflict of interest.

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