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In Vitro Inhibition of Cardiometabolic Health-Related Enzymes by Monofloral Stingless Bee Honey

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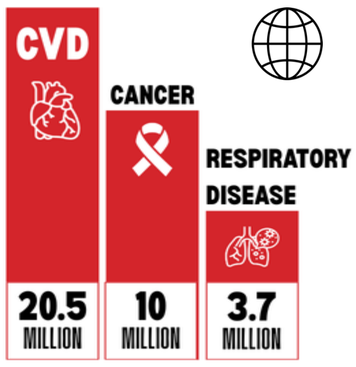
INTRODUCTION & AIM

Cardiovascular Disease (CVD)

Current Situation



Modifiable Risk Factor of CVD

- Hypertension
- Obesity
- High cholesterol
- High blood sugar
- Sedentary lifestyle
- Smoking
- Unhealthy eating
- Alcohol consumption

(World Heart Report, 2025).

Prevention strategies is based on the enzyme inhibition activities

ACE inhibition activity
- Reduces conversion of angiotensin I → angiotensin II
- Lowers vasoconstriction and blood pressure

→ antihypertensive

HMG-CoA reductase inhibition activity
- Reduces endogenous cholesterol synthesis
- Lowers LDL-cholesterol production

Cholesterol esterase inhibition activity
- Reduces hydrolysis of dietary cholesterol esters
- Limits cholesterol absorption into enterocytes

→ anti hypercholesterolemic

Pancreatic lipase inhibition activity
- Reduces lipid hydrolysis and dietary fat absorption
- Helps lower postprandial triglyceride levels

α-amylase & α-glucosidase inhibition activities
- Slow carbohydrate digestion
- Reduce glucose spikes and insulin demand

→ antiobesity

(Zhang et al., 2022, Rauf et al.,2022).

Stingless bee honey could be one of the natural inhibitors

Sustainable
- Requires minimal land and resources
- Provides highly efficient pollination,
- Naturally adapted to tropical regions,
- Enhances rural livelihoods

Health Promoting Properties
- Antioxidant properties
- Anti-inflamatory properties
- Antidiabetes properties
- Antihypertensive properties
- Anti-cancer properties
- Neuroprotective properties

Factor influencing the properties of SBH
- Geographical origins
- Botanical origins
- Bee species
- Harvesting season
- Storage condition

(Chuah et al., 2023; Shaheran et al., 2025; Wu et al., 2022; Zulkifli et al., 2023)

Objectives

1. To determine the phenolic compounds and amino acids of Sabah stingless bee honey from different botanical origins.
2. To determine the cardioprotective potential of Sabah stingless bee honey through *in vitro* assays.
3. To discriminate Sabah stingless bee honey based on its botanical origins using chemometric analysis.

METHOD

Melissopalynology

Nutrient profile determination
1. Phenolic acid profile
2. Amino acid profile

Cardioprotective inhibition activities (*in vitro*)
1. ACE inhibition activity
2. α-amylase inhibition activity
3. α-glucosidase inhibition activity
4. Pancreatic lipase inhibition activity
5. Cholesterol esterase inhibition activity
6. HMG-CoA reductase inhibition activity

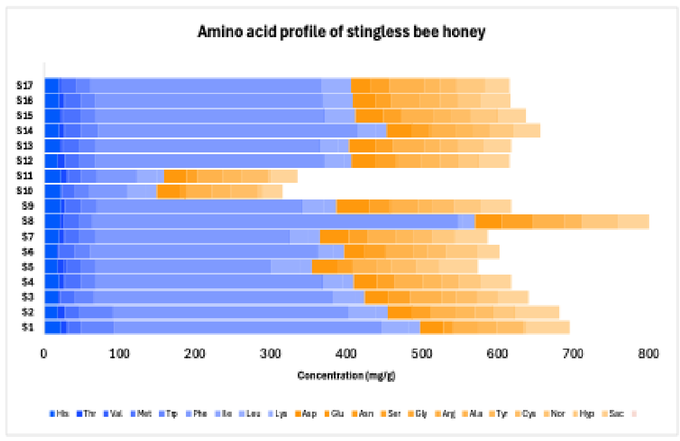
(Zheng et al. 2020, Ng et al.,2021, 3)

RESULTS & DISCUSSION

Phenolic Acid Composition

- 8 phenolic acids, 5 flavonoids
- Flavonoids dominated (x2 more than phenolic acids)
- Principle compounds (Rosmarinic acid, Kaempferol, Myricetin)

Amino Acid Composition



- **Phe, Met** and **Leu** are the **dominant EAA** across all honey samples
- **Phe** is the main **EAA** – precursor **to build proteins** and **to produce key neurotransmitters**
- ↑**Pro & Phe** indicate **good honey maturity** and **neuroprotective properties**
- The **EAA/total AA ratio** is **~39%** → **S1** & **S8** showing the highest EAA density → indicating better nutritional amino acid quality

Cardioprotective activities (*in vitro*)

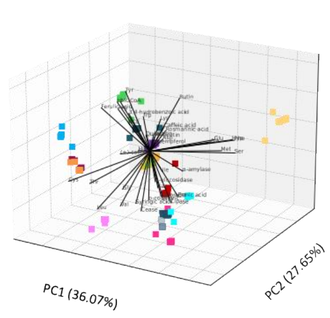
ACE Inhibition Activities
- ACE inhibition varies widely by botanical origin
- **Elderberry; S8 (74.3%)** and **Gloden Shower Tree; S9 (71.2%)** show strong ACE inhibition close to Captopril.

HMGCoA Inhibition Activities
- All SBH samples shown **>50% of inhibition**
- SBH samples from **Gloden Shower Tree (S9)**, **Rubber Tree (S14)** , **Elderberry (S8)** demonstrated HMG-CoA inhibition comparable to Pravastatin.

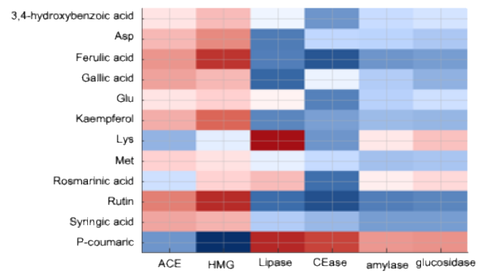
Cholesterol Esterase Inhibition Activities
- All sample shown dose-dependent inhibition
- **Acacia (S1), Gloden Shower Tree (S9), Rubber Tree (S13)** demonstrated inhibition comparable to Simvastatin.

Pancreatic Lipase Inhibition Activities
- All samples show dose-dependent inhibition from 20 - 100 mg/mL
- **Elderberry (S8) → IC_{50} = 51.73 mg/mL**
- **Sticky Niger (S17) → IC_{50} = 54.53 mg/mL**

α-Amylase & α-Glucosidase Inhibition
- All SBH samples inhibited both carbohydrate-digesting enzymes
- **Acacia origins SBH (S1&S2), Elderberry (S8) & Gloden Shower Tree (S9)** → high inhibition on both enzyme → indicating promising natural anti-hyperglycemic potential.



- PC1 separates amino-acid–rich samples
- PC2 separates gallic acid, rutin and rosmarinic acid rich sample
- Samples cluster clearly by geographical and botanical origins, indicating both factors strongly shape their cardioprotective properties



Compounds that drive stronger enzyme inhibition (VIP>1)
- Gallic acid –ACE and HMG-CoA inhibition
- Gallic acid & Rutin – lipid-digesting enzyme inhibition
- Glutamic acid & Lysine – major contributors for lipase and cholesterol esterase

CONCLUSION

- All SBH samples demonstrated inhibition across ACE, HMG-CoA reductase, cholesterol esterase, pancreatic lipase, α-amylase, and α-glucosidase.
- Samples from **Elderberry (S8)** consistently showed the strongest inhibitory activities, comparable to standard drugs.
- These findings suggest that SBH have promising **multi-target cardiometabolic benefits** and **potential as a natural functional ingredient**.

FUTURE WORK / REFERENCES

1. Isolate and characterize the bioactive peptides and phenolic compounds responsible for these inhibitory effects
2. Explore their mechanisms *in vitro* and *in vivo*

List of references