LIPID AND BLOOD PRESSURE LOWERING POTENTIAL OF *MIKANIA MICRANTHA* THROUGH ENZYMATIC INHIBITION

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INTRODUCTION

Mikania micrantha Kunth (Asteraceae) or locally known as "Selaput tunggul" is a perennial creeping vine that widely used by local practitioners for treatment or prevention of various diseases. In Malaysia, *M. micrantha* is consumed as a juice (by boiling in hot water) as an alternative to reduce cholesterol, high blood pressure, and glucose.

Hyperlipidemia is defined as increased blood cholesterol, triglycerides or both, while hypertension is defined as persistent elevation of systolic (> 140 mmHg) and diastolic (> 80 mmHg) blood pressures [1]. A combination of different strategies is used to treat and manage hyperlipidemia and hypertension. One of them is through inhibition of the key enzymes responsible for hyperlipidemia and hypertension.

Aim: To examine the potential of various extracts of the leaves and stems of *M. micrantha* to inhibit enzymes relevant to hyperlipidemia *i.e.,* pancreatic lipase (PL), lipoprotein lipase (LPL), 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGR) and hypertension *i.e.,* angiotensin-I converting enzyme (ACE).

METHODOLOGY

Sample Preparation
The leaves and stems of *M. micrantha* were separated, washed, dried, and ground to produce fine powder.

Sample Extraction
The leaves and stems of *M. micrantha* were extracted with hot water, cold water, 70% ethanol and ethyl acetate.

Determination of Enzymatic Inhibition
The inhibition activities of *M. micrantha* extracts were determined spectrophotometrically using PL, LPL, HMGR, and ACE inhibition assays.

Table 1 – Enzymatic inhibition assays

Inhibition assays	Pancreatic lipase (PL)	Measure the hydrolysis of *p*-nitrophenyl butyrate (*p*-NPB) to *p*-nitrophenol at 405 nm [2,3]
	Lipoprotein lipase (LPL)	
	HMG-CoA reductase (HMGR)	Measure rate of NADPH consumed at 340 nm [4]
	Angiotensin-I converting enzyme (ACE)	Measure release of hippuric acid (HA) from synthetic substrate Hippuryl-His-Leu (HHL) at 410 nm [5]

RESULTS

Pancreatic Lipase Inhibition

Table 2 – IC_{50} values for pancreatic lipase (PL) inhibitory activity of *M. micrantha* extracts

Extraction solvents	IC_{50} (µg/mL)	
	Leaves	Stems
Hot water	4.56 ± 0.07^{ab}	42.37 ± 4.63^{d}
Cold water	28.97 ± 4.22^{cd}	16.93 ± 1.99^{bc}
70% ethanol	8.02 ± 1.56^{ab}	**4.49 ± 2.50^{ab}**
Ethyl acetate	18.00 ± 3.78^{bc}	16.73 ± 0.70^{bc}
Orlistat	0.31 ± 0.01^{a}	

Lipoprotein Lipase Inhibition

Table 3 – IC_{50} values for lipoprotein lipase (LPL) inhibitory activity of *M. micrantha* extracts

Extraction solvents	IC_{50} (µg/mL)	
	Leaves	Stems
Hot water	4.59 ± 0.87^{a}	8.04 ± 2.75^{a}
Cold water	2.34 ± 1.88^{a}	2.70 ± 1.79^{a}
70% ethanol	**1.42 ± 0.48^{a}**	4.26 ± 1.23^{a}
Ethyl acetate	7.35 ± 2.68^{a}	5.69 ± 2.46^{a}
Orlistat	1.98 ± 1.22^{a}	

Results are expressed as the means ± SEM (n=3). Means with different letters are significant at $p < 0.05$. Orlistat is a positive control. The concentration of extracts and orlistat used were 0 – 100 µg/mL. IC_{50} is the concentration of extracts (µg/mL) required to inhibit PL and LPL activity by 50%. A low IC_{50} indicates the highest PL and LPL inhibitory activity.

HMG-CoA Reductase Inhibition

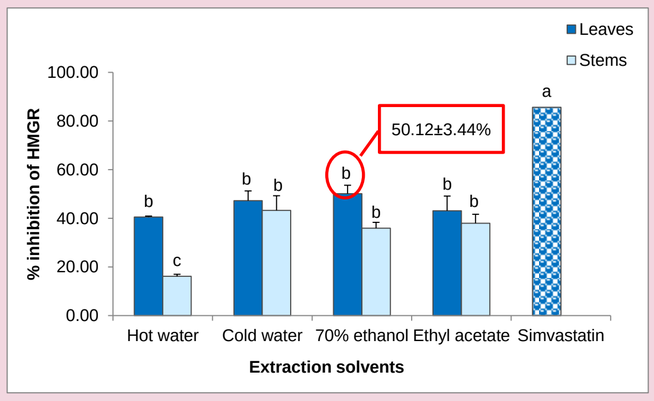

Fig. 1 - HMGR inhibitory activity of *M. micrantha* extracts. Data are shown as the means ± SEM (n=3). Bars with different letters are significant at $p < 0.05$. Concentration of extracts used was 1000 µg/mL. Simvastatin is a positive control at 100 µM (419 µg/mL)

ACE Inhibition

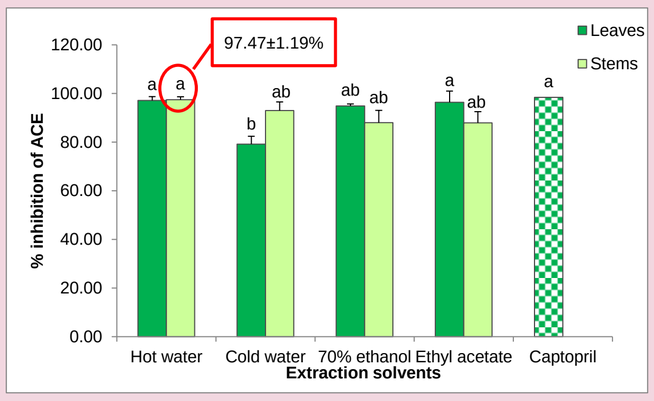

Fig. 2 - ACE inhibitory activity of *M. micrantha* extracts. Data are shown as the means ± SEM (n=3). Bars with different letters are significant at $p < 0.05$. Concentration of extracts and captopril used was 1000 µg/mL

DISCUSSION

- The ethanol stems, hot water leaves and ethanol leaves extract exhibited the highest PL inhibitory activity.
- The ethanol leaves extract demonstrated the highest LPL and HMGR activities.
- Hot water stems extract showed the highest ACE inhibitory activity but least inhibitory activity against PL, LPL, and HMG-CoA reductase.
- Presence of alkaloids, terpenoids, tannins, cardiac glycosides, and luteolin in 70% ethanol extract of *M. micrantha* could be the potential PL, LPL and HMGR inhibitors [6-7].

CONCLUSION

All extracts exhibited remarkable inhibitory activities against pancreatic lipase, lipoprotein lipase, HMG-CoA reductase, and angiotensin-I converting enzyme *in vitro*.

This study revealed the potential of *M. micrantha* extracts as anti-hyperlipidemic and anti-hypertensive agents.

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