Mikania micrantha Extract Ameliorates Hypercholesterolemia by Inhibiting HMG-CoA Reductase and Acetyl- CoA Acetyltransferase 2 in High Cholesterol-Fed Rats

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Introduction

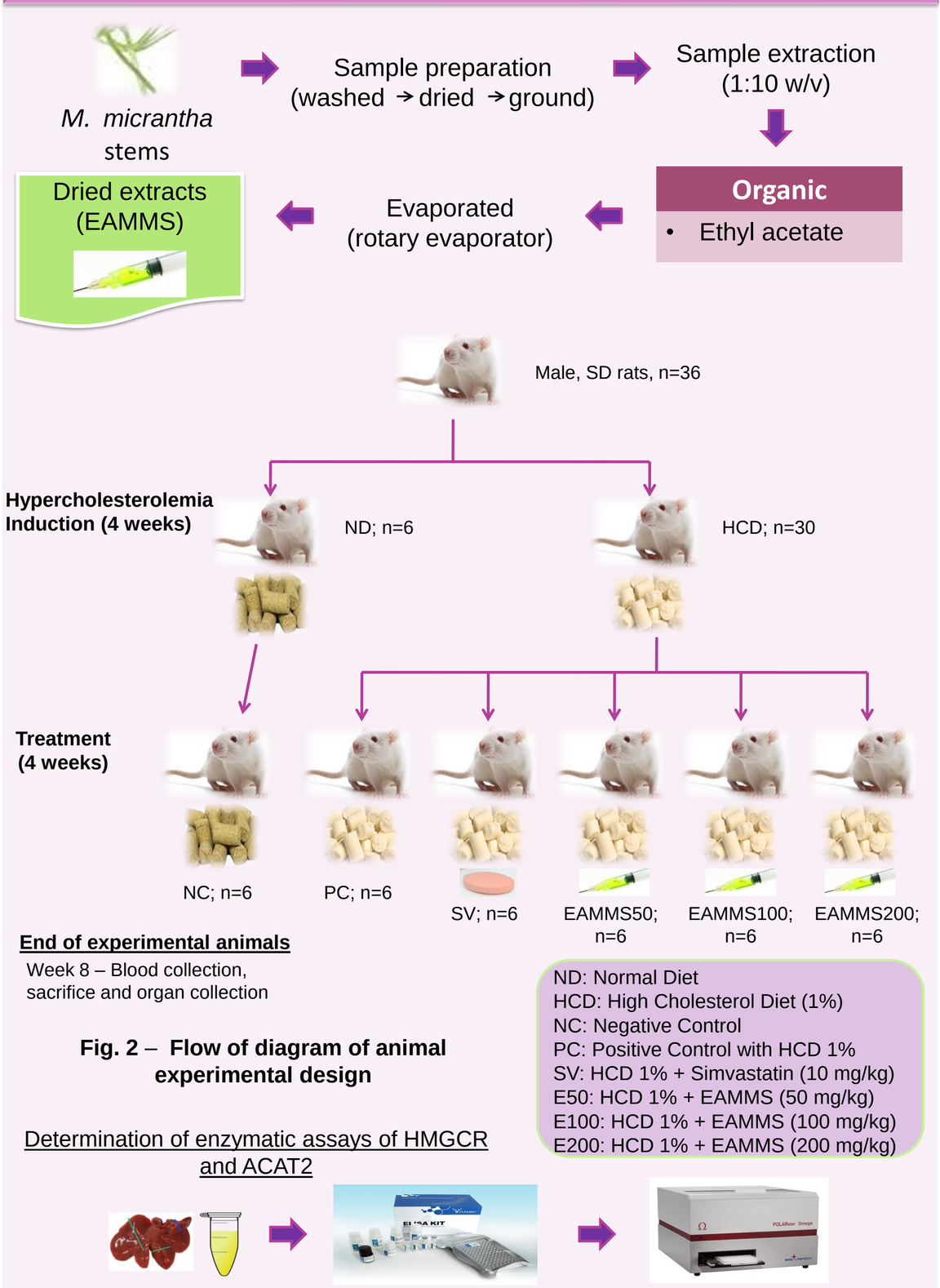
Mikania micrantha Kunth or known by the locals as Selaput tunggul is a traditional medicinal plant from the family Asteraceae. It is native to the tropical Central and South America, where it has been used traditionally by local practitioners for treatment or prevention of various ailments[1]. In Malaysia, *M. micrantha* is consumed as a juice to treat diabetes, hypertension and hypercholesterolemia[1,2]. The present of various secondary metabolites including terpenoids, phenolics, alkaloids, flavonoids, and vitamins showed this plant to have high potential for its anti-hypercholesterolemic and other medicinal properties such as antioxidant[3], anti-diabetic[4], anti-cancer[5], anti-inflammatory[6], antiproliferative[7] and antibacterial[1] activities.

Fig. 1 – ***Mikania micrantha* Kunth (Selaput tunggul)**

Objective

- To determine the potential anti-hypercholesterolemic activity of *Mikania micrantha* stems (EAMMS) extract in high-cholesterol-fed rats
- To determine the effects of EAMMS extract on enzymatic activities [HMG-CoA reductase (HMGCR) and acetyl-CoA acetyltransferase 2 (ACAT2)] in the liver of high-cholesterol-fed rats.

Methodology



End of experimental animals

Week 8 – Blood collection, sacrifice and organ collection

Fig. 2 – Flow of diagram of animal experimental design

ND: Normal Diet
HCD: High Cholesterol Diet (1%)
NC: Negative Control
PC: Positive Control with HCD 1%
SV: HCD 1% + Simvastatin (10 mg/kg)
E50: HCD 1% + EAMMS (50 mg/kg)
E100: HCD 1% + EAMMS (100 mg/kg)
E200: HCD 1% + EAMMS (200 mg/kg)

Determination of enzymatic assays of HMGCR and ACAT2

Results

Table 1 - Biochemical profiles of hypercholesterolemia induced rats treated with different concentrations of EAMMS extracts at week 8

Group	TC (mmol/L)	TG (mmol/L)	LDL-C (mmol/L)	HDL-C (mmol/L)	AST (U/L)	ALT (U/L)
NC	1.18±0.14^{a}	0.56±0.11^{a}	0.24±0.10^{a}	1.27±0.09^{a}	127.16±1.78^{a}	71.00±1.99^{a}
PC	3.16±0.39^{b}	0.73±0.17^{b}	2.64±0.39^{b}	1.65±0.36^{a}	222.00±6.06^{b}	226.00±7.21^{b}
SV	1.45±0.13^{a}	0.41±0.21^{a}	1.09±0.27^{c}	1.59±0.17^{a}	264.33±4.72^{c}	191.00±7.01^{c}
EAMMS 50	1.61±0.18^{a}	0.48±0.14^{a}	1.09±0.28^{c}	1.60±0.25^{a}	162.83±7.36^{ab}	134.00±4.95^{ac}
EAMMS 100	1.53±0.11^{a}	0.46±0.29^{a}	1.12±0.19^{c}	1.61±0.09^{a}	207.83±3.07^{ab}	194.00±4.83^{ac}
EAMMS 200	1.65±0.38^{a}	0.46±0.33^{a}	1.02±0.26^{c}	1.79±0.55^{a}	148.50±4.01^{ab}	182.00±6.36^{ac}

Superscripts with different letters in a column indicate statistically different at $p<0.05$ by Tukey's multiple comparison test. TC- Total cholesterol; TG- Triglyceride; LDL-C- Low density lipoprotein cholesterol; HDL-C- High density lipoprotein cholesterol; AST- Aspartate aminotransferase; ALT- Alanine aminotransferase.

Table 2 - Effect of EAMMS extracts on levels of HMGCR and ACAT2 enzymes in experimental rats at week 8

Group	HMGCR (pg/mL)	ACAT2 (pg/mL)
NC	202.10±6.68^{a}	264.07±1.01^{a}
PC	271.50±11.94^{b}	529.46±4.50^{b}
SV	245.88±15.94^{c}	349.07±2.40^{c}
EAMMS50	258.54±13.70^{c}	405.87±0.76^{c}
EAMMS100	254.22±8.64^{c}	497.96±1.33^{c}
EAMMS200	255.33±21.33^{c}	454.42±3.33^{c}

Superscripts with different letters in a column indicate statistically different at $p<0.05$ by Tukey's multiple comparison test. HMGCR- HMG-CoA reductase; ACAT2- acetyl-CoA acetyltransferase 2

Discussions

1. Terpenoids (Sesquiterpene lactones) such as acetyl β-amyrin, lupeol, stigmasterol and stigmateryl-β-D-glucopyranoside were the major phenolic compounds identified in the EAMMS[7,8].
2. Structure similarity of stigmasterol with cholesterol makes plant sterol as one of the best substance in reducing cholesterol level in the blood[9]. Plant sterol also convert bile acids into secondary bile acids, thereby reducing the intestinal cholesterol[9].
3. EAMMS has an antioxidant activity owing to the presence of its flavanoids, alkane hydrocarbons, phenols and phytosterols[3], thus these bioactive compounds may helps to suppress the HMGCR activity and reduce cholesterol biosynthesis in the mevalonate pathway[10].
4. The presence of chlorogenic acid was found to reduce the activity of HMGCR and ACAT of lipid metabolism in rats[11]. Phytosterols such as stigmasterol and sitosterol showed significantly reduced mRNA expression of ACAT2 activity in rodents[12]

Conclusions

Mikania micrantha stems (EAMMS) extract had cholesterol-lowering properties and could be used as an alternative treatment for hypercholesterolemia.

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Acknowledgements

This research was funded by Putra-IPM Grant (UPM). Special thanks to all members of the Nutrition Laboratory, Faculty of Medicine and Health Sciences, UPM, Serdang, Selangor, Malaysia.