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Short Communication

EVALUATION OF ANTIDIABETIC AND ANTI HYPERLIPIDEMIC ACTIVITIES OF *MACARANGA TANARIUS* IN RATS FEED WITH HIGH GLUCOSE-FRUCTOSE DIET

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ABSTRACT

Objective: *Macaranga tanarius* showed a potent α–glucosidase inhibitors that may benefit diabetes treatment. The hexane-ethanol fraction of methanol extract of *Macaranga tanarius* was investigated for antidiabetic, and anti hiperlidemia activity in rats feed with high glucose-fructose diet.

Methods: After induced with high glucose-fructose diet for 42 d, the rats were treated with the hexane-ethanol fraction of methanol extract of *Macaranga tanarius* at doses of 34.2, 78.5, 137 mg/kg per oral once in a day for 5 d and high glucose-fructose diet consecutively. Fasting blood glucose, cholesterol, triglyceride, HDL and LDL concentration were evaluated at the next day after treatment.

Results: The 5 d administration of hexane-ethanol fraction of methanol extract of *Macaranga tanarius* did not produce any significant difference in any of the assigned parameters between the diet and all dose groups.

Conclusion: The hexane-ethanol fraction of methanol extract of *Macaranga tanarius*at all level has not antidiabetic and anti hiperlidemia activity in rats feet with high glucose-fructose diet.

Keywords: *Macaranga tanarius*, antidiabetic, Antihiperlipedmia, Glucose-fructose.

It is known that many diabetics have hypercholesterolemia and hypertriglyceridemia. At present, the importance of looking not only for possible glucose-lowering drugs but also lipid lowering drugs to be given as adjuvant therapy in the treatment of diabetic patients [1].

Macarangatanarius (*Euphorbiaceae*) is a very fast-growing species and well known as an ant-plant defended by ants against herbivores [2]. It has been reported that isolated compounds of *Macarangatanarius* had cytotoxic, antioxidant activities as well as inhibitory activity against a cycloxygenase-2 test system and 2,2-diphenyl-picrylhydrazyl (DPPH) radical scavenging activity [3-5]. *Invitro* study showed that the isolated ellagitannin and chebulagic acid of *Macarangatanarius* inhibited α-glucosidase and intestinal maltase that may benefit diabetes treatment [6]. Based on Marvin Sketch software, ellagitanin and chebulagic acid of *Macaranga tanarius* have a similar lipophilic character as hexane-ethanol 50:50. Therefore, it is crucial to evaluate the antidiabetic and anti-hyperlipidemia activities of a hexane-ethanol fraction of methanol extract of *Macarangatanarius* against high glucose-fructose diet in rats.

The fresh leaves of *Macarangatanarius* were collected from Sleman Yogyakarta Indonesia and were identified and authenticated using descriptive literature. A voucher specimen was deposited in the Laboratory of Pharmaceutical Biology, Pharmacy Faculty, Sanata Dharma University, and Yogyakarta, Indonesia. Dried leaves of *Macarangatanarius* were extracted with 50% aqueous methanol for 24h at room temperature. The crude extract was extracted with hexane-ethanol 50:50 for 24 h at room temperature. The resulting suspension was filtered and was evaporated by vaccum rotary evaporator at 50 ^{o}C to yield a solid residue of a hexane-ethanol fraction of methanol extract of *Macarangatanarius* (HEMM) (yield 3.51%).

Adult male Wistar rats (180-250g) were used in this study. The animals were obtained from the Imono Laboratory of Pharmacy Faculty of Sanata Dharma University, Indonesia. The animals were maintained under standard laboratory condition. They were housed in standard cages (five animals per cage) at a temperature of 22^{o}±2^{o}C and 12:12h light-dark cycle. The animals were provided with pelleted diet and water ad libitum. The experimental protocol and procedures used in this study were approved by The Medical and Health Research Ethics Committee (MHREC) Faculty of Medicine Gadjah Mada University Indonesia. Healthy rats were weighed and randomly divided into 5 groups of 5 animals in each. Group 1 was treated with normal diet (BR2) for 47 d. Group 2-5received high glucose-fructose for 42 d. After induction for 42d, group 2 received CMC as the vehicle and high glucose-fructose for 5 d, whereas group 3-5 received HEMM at doses of 34.2, 78.5, 137 mg/kg per oral once in a day for 5 d and high glucose-fructose diet consecutively. Blood for biochemical analysis from all groups was obtained by sinus orbitals after 24 h administration. Parameters of blood biochemical such as fasting blood glucose, cholesterol, triglyceride, HDL, LDL were measured. Results were analyses by one-way analysis of variance (ANOVA) and followed by Tukey HSD test for multiple comparisons of clinical pathology parameters. The significant difference was considered at $P<0.05$.

In order to establish a scientific basic for the utilization hexane-ethanol fraction of methanol extract of *Macarangatanarius* (HEMM) in the treatment of diabetes, it was decided to evaluate the antidiabetic and anti-hyperlipidemia in high glucose-fructose feed in rats. Fructose-feed in animal models are frequently induce insulin resistance, impaired glucose tolerance, hyperinsulinemia, hyper-tension and hyperlipidemia [7-10]

Our present study showed that the high glucose-fructose feed possesses definite hypertriglyceridemic and hyperglycemic after 42 d of treatment as revealed in the table (1). The levels of triglyceride and fasting blood glucose were found significantly increased in high feed glucose-fructose diet rats for 42 d when compared with the normal diet ($P<0.05$). The HDL levels of high feed glucose and fructose diet decreased significantly as compared to the normal diet. No significant increase on cholesterol levels was observed between high feed glucose-fructose diet as compared to normal diet. LDL levels did not significantly affected by high feed glucose-fructose diet when compared to normal diet. Hypertriglyceridemia and low plasma concentration of HDL comprise the typical dyslipidemia of insulin resistant state and type 2 diabetes. The interaction between HDL that is triglyceride-enriched and hepatic lipase action plays an important role in the enhanced catabolism of HDL in insulin resistant and hypertriglyceridemic states [11]. Huang *et al.* reported that the adverse effect of fructose on hepatic lipid metabolism, even by low concentration of fructose. Fructose leads to increased de

novo hepatic fatty acid synthesis and release of triglycerides in comparison to glucose [12]. Glucose and fructose transporter, GLUT8, is reported for hepatocyte fructose transport and fructose-induced macrosteatosis [13].

Previous studies have shown that serum triglyceride levels were increased to rates of feeding fructose diet for 3 and 8 w. However after 8 w of feeding, the blood glucose levels were increased significantly compared to a control diet [14].

Table 1: Effectofhexane-ethanol fraction of methanol extract of *Macarangatanarius* (HEMM) on cholesterol, triglyceride, HDL, LDL and blood glucose in rats feeds with high glucose-fructose (GF) diets

Treatment	Cholesterol (mmol/l)	Trigliyceride (mmol/l)	HDL (mmol/l)	LDL (mmol/l)	FastingBlood Glucose (mmol/l)
Normal diet	1.71±0.08	1.05±0.04	1.63±0.04	0.22±0.03	3.53±0.31
GF+CMC	2.11±0.15	2.31±0.20[a]	0.88±0.05[a]	0.32±0.03	5.49±0.21[a]
GF+HEMM 34.2 mg/kg	1.86±0.12	2.03±0.04[a]	0.88±0.03[a]	0.27±0.02	5.29±0.19[a]
GF+HEMM 68.5 mg/kg	1.87±0.03	2.26±0.20[a]	0.89±0.03[a]	0.30±0.02	6.50±0.19[a]
GF+HEMM 137 mg/kg	1.63±0.13[b]	2.65±0.15[a]	0.78±0.05[a]	0.30±0.03	5.55±0.24[a]

Values are mean±S. E. M., n = 5 animals per group, a: P<0.05 compared with the normal diet, b: P<0.05 compared with the GF+CMC

There was no significant reduction of the levels of triglyceride and fasting blood glucose in the rats administered 34.2, 78.5, 137 mg/kg of HEMM. In addition, the HDL level was not elevated significantly after HEMM administration. The preliminary phytochemical screening of isolated compounds of *Macarangatanarius* supports its inhibitory effect on α-glucosidase and intestinal maltase [6]. In addition, another report mentioned that methanol-water extract of *Macarangatanarius* at dose 0.43; 1.28 and 3.84 mg/kg was effective in improving oral glucose tolerance [15].

However, administration of HEMM 34.2, 78.5, 137 mg/kg for 5 d to rats feed with glucose-fructose diet did not bring the levels of fasting glucose, triglyceride, and HDL into the normal range. This clearly indicates that HEMM has not antidiabetic and anti-hyperlipidemia activities. The time period of administration likely to be responsible for these results. The overall results of the present study indicate the hexane-ethanol fraction of methanol extract of *Macarangatanarius* (HEMM) at three dose levels (34.2; 78.5; 137 mg/kg) for 5 d has not antidiabetic and anti-hyperlipidemia activity in rats feet with high glucose-fructose diet.

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CONFLICT OF INTERESTS

The author(s) declared no conflicts of interest with respect to the authorship and/or publication.

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