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Research Article

PREVENTIVE EFFECT ON OBESITY OF MANGOSTEEN (*GARCINIA MANGOSTANA* L.) PERICARP ETHANOLIC EXTRACT BY REDUCTION OF FATTY ACID SYNTHASE LEVEL IN MONOSODIUM GLUTAMATE AND HIGH-CALORIE DIET-INDUCED MALE WISTAR RATS

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ABSTRACT

Objective: This study evaluated the preventive effect of mangosteen pericarp ethanolic extract (MPEE) on obesity by measuring body weight changes and fatty acid synthase (FAS) concentration in the adipose tissue and serum of monosodium glutamate and high-calorie diet-induced male Wistar rats.

Methods: The content of MPEE was determined by high-performance liquid chromatography (HPLC) analysis, using α-mangostin and xanthone as the marker compounds. The experimental study with rats was conducted for 9 weeks, with rats divided into 5 treatment groups which were normal (standard diet), control (high-calorie diet), dose 1 (MPEE 200 mg/kg b.w., high-calorie diet), dose 2 (MPEE 500 mg/kg b.w., high-calorie diet), and orlistat (orlistat 21.6 mg/kg b.w., high-calorie diet) groups. The FAS concentration was measured by enzyme-linked immunosorbent assay (ELISA) method.

Results: MPEE contained 29.13% of α-mangostin based on HPLC analysis and no xanthone detected. The dose 1 (MPEE 200 mg/kg b.w., high-calorie diet) and dose 2 (MPEE 500 mg/kg b.w., high-calorie diet) groups showed less body weight gain than the control, normal, and orlistat group with dose 2 showed the lowest body weight gain. Dose 1 and dose 2 groups also had significantly lower FAS concentration in either adipose tissue or serum compared to the control group.

Conclusion: MPEE have great potential as a therapeutic agent in preventing obesity, by suppressing major body weight gain and reducing FAS concentration.

Keywords: Mangosteen, α-mangostin, Anti-obesity, Fatty acid synthase, High-performance liquid chromatography.

INTRODUCTION

The global concern about obesity has been increasing significantly over the years, as the number of obese individuals expands remarkably both in developing and developed countries [1,2]. By 2013, the number of overweight and obese individuals escalated to 2.1 billion from 857 million in 1980 throughout the world. Obesity is already well-known contributed to the health impairment and several diseases such as work disability, sleep apnea, cardiovascular disease, cancer, type 2 diabetes mellitus, and osteoarthritis [3]. It was estimated that 3.4 million deaths in the year 2010 were caused by overweight and obesity [4]. Unabated, the upturn trend of obesity could lead to the decrease of life quality in the future. Therefore, the preventive methods and treatments for obesity are urgently needed [3,4].

Obesity is resulted from an imbalance between energy intake and expenditure, characterized by an increase in the size and also in some individuals, the number of fat cells [1]. The regulation of energy intake and expenditure is monitored by the hypothalamus, which responds to peripheral status signals by releasing neuropeptides including neuropeptide Y (NPY) [5]. Recent reports have shown that several fatty acid synthase (FAS, EC 2.3.1.85) inhibitors were able to down-regulate fasting-induced expression of NPY, inhibited food intake, and reduced weight in obese and lean mice [6]. FAS is a dimer multifunctional enzyme, catalyzing the synthesis of long-chain fatty acid from acetyl-CoA (Ac-CoA), malonyl-CoA (Mal-CoA), and nicotinamide adenine dinucleotide phosphate hydrogen (NADPH) in animals and therefore is a prospective therapeutic target for obesity [7].

To date, there are a number of available anti-obesity drugs on the market such as orlistat (Xenical) and sibutramine (Reductil), but the use of these drugs has implicated in several side effects, some of which are mood changes and gastrointestinal or cardiovascular complications [8]. Thus, natural products have been suggested as better alternative therapies [8]. Plants are rich sources of numerous biologically active compounds that have great therapeutic effects [9]. Mangosteen (*Garcinia mangostana* L.), presumably originated from Southeast Asia, is one of the plants that popularly known for its medicinal properties [10]. The pericarp of mangosteen has been used for many years as a traditional medicine to treat several health problems such as abdominal pain, diarrhea, dysentery, wound infections, suppuration, and chronic ulcers [9]. The major active substance isolated from mangosteen pericarps is α-mangostin and it has been demonstrated to have antioxidant, antibacterial, anti-inflammatory, antitumor, and renoprotective activities [11].

Previous *in vitro* study revealed that mangosteen pericarp ethanolic extract (MPEE) contained phytochemical bioactive contents that possess anti-obesity potential through inhibition of pancreatic lipase and α-amylase [12]. Thus, in this *in vivo* study, we further evaluated the potential and mechanism of MPEE on preventing the obesity, by measuring the FAS level in monosodium glutamate (MSG) and high-calorie diet-induced Wistar rats. The MSG was used since it can increase the food intake and stimulate the appetite of rats [13].

METHODS

MPEE preparation

Mangosteen (*G. mangostana* L.) pericarps were collected from Indonesian farms in Cicantayan, Sukabumi, Bandung, West Java, Indonesia. The plants were identified by a staff from Herbarium in the Department of Biology, School of Life Science and Technology, Bandung Institute of Technology, Bandung, West Java, Indonesia. The mangosteen pericarps were dried, ground, and extracted using reflux method in water and 50% ethanol. The 50% ethanol extract then freeze-dried to get the dried powder of MPEE [14].

High-performance liquid chromatography (HPLC) analysis of MPEE

The analysis of chemical profiling of MPEE was done using HPLC. The marker compounds used are α-mangostin and xanthone. The HPLC system consisted of HPLC Pump Hitachi L-6200, Reverse Phase Column C-18 (Phenosphere ODS-2, Phenomenex, 4.6 mm × 250 mm), and Hitachi L-4000 UV detector. The mobile phase used was acetonitrile 70% and delivered isocratically with a flow rate of 1.0 ml/minutes. The samples were dissolved in methanol as solvent (1000 µg/ml) and filtered through a 0.22 µm syringe and injected with a volume of 20 µl. The UV absorbance was measured at 244 nm. The percentage of α-mangostin in the extract was calculated based on the peak area [15].

Experimental design

The study was conducted at the Laboratory of Experimental Animals, School of Pharmacy, Bandung Institute of Technology, Bandung, Indonesia and Biomolecular and Biomedical Research Center, Aretha Medika Utama, Bandung, Indonesia. The methods related to the use of animals in this study have been approved by the Ethical Commission, School of Pharmacy, Bandung Institute of Technology with ethical approval number 05/KEPHP-ITB/05-2015.

A total of 25 male Wistar rats with the age of 4 weeks, with weight in the range of 90-110 g were used. All rats were kept under standard environment for laboratory animals. Before the treatment, they were acclimatized for 7 days by giving normal food and water. Subsequently, the rats were divided randomly into five groups, namely, normal, control, dose 1, dose 2, and orlistat group. The normal group was given sodium carboxymethyl cellulose (CMC-Na) 0.5% (0.05 g/kg) solution; the control group was not given any treatment; the dose 1 group was given MPEE (200 mg/kg b.w.); the dose 2 group was given MPEE (500 mg/kg b.w.); and the orlistat group was given orlistat (Xenical) (21.67 mg/kg b.w.). For the first 5 days, all groups except the normal group were received MSG 2 mg/kg b.w. through subcutaneous injection together with high-calorie diet to induce the obese condition, whereas the normal group was received standard diet. For 9 weeks, the normal group was continuously received standard diet while the other groups received high-calorie diet without MSG. The composition of the standard and high-calorie diet was in accordance with Adnyana *et al.* (2014) study [16] with slight modification, as it can be seen in Table 1. The rats were maintained daily and checked for the body weight changes. 24 hrs after the last day of the experiment, all rats were sacrificed using carbon dioxide. Following the euthanasia procedure the serum, perirenal, and perianal fat were immediately isolated and stored in a freezer at the temperature of −20°C.

FAS measurements in adipose tissues and serum

FAS level from adipose tissue and serum was measured using Rat FASN (FAS) ELISA kit (Elabscience, E-EL-R0395) per manufacturer instructions. To prepare the serum samples, the serum was incubated to clot for 2 hrs at room temperature before centrifugation for 15 minutes at 1000 × *g*. The supernatant was collected and used immediately or stored at −80°C. To prepare the adipose tissue homogenates, around 100 mg of adipose tissue from rats were minced into small pieces and homogenized in 900 µl of cold phosphate-buffered saline (0.01 M, pH 7.4). The suspension then was sonicated and centrifuged for 5 minutes at 5000 × *g*. The supernatant was collected and used immediately or stored at −80°C. For the ELISA assay, 100 µl of standard or samples were introduced to a well plate, incubated for 90 minutes at 37°C. The liquid then removed, and 100 µl of biotinylated detection Ab was added. The plate was incubated for 1 hrs at 37°C, after that it washed for 3 times. Afterward, 100 µl of horseradish peroxidase conjugate was added to each well, incubated for 30 minutes at 37°C. The plate was washed again for 5 times, and 90 µl of substrate reagent was added followed by incubation for 15 minutes at 37°C in the dark. Finally, 50 µl of stop solution was added to stop the reaction, and the absorbance was read at 450 nm using a microplate reader.

Table 1: Composition of experimental diets

Component	Standard diet (g/kg)	High-calorie diet (g/kg)
Rice flour	-	300
Cornstarch	250	200
Fish flour	160	100
Bean flour	140	100
Wheat flour	340	150
Fat	70	200
Vitamin B complex	Ad Libitum	Ad Libitum

Data analysis

The results were analyzed using the Statistical Package for the Social Sciences version 16 program by applying the analysis of Variance (ANOVA). The *post-hoc* least significant difference was used, with p value below 0.05 was considered as statistically significant. The data were expressed as the mean±standard deviation.

RESULTS

HPLC analysis of MPEE

Based on the Fig. 1, it can be seen that α-mangostin had a retention time at 10.92 minutes and xanthone at 5.42 minutes. The MPEE had a peak at 10.90 minutes which allegedly is the culmination of the α-mangostin compound, but the xanthone peak was not found. Therefore, only concentration of α-mangostin in MPEE was calculated. The concentration of α-mangostin in 1000 µg/ml MPEE was found to be 291.29 µg/ml. Thus, α-mangostin content in MPEE amounted to 29.13% (w/w).

Changes in body weight

The body weight gain in the control group which was fed high-calorie diet alone was the highest after 9 week of the experiment, with more than 100% of increase from initial weight. All of the treatment groups, which are dose 1 (MPEE 200 mg/kg b.w.), dose 2 (MPEE 500 mg/kg b.w.), and orlistat (orlistat 21.6 mg/kg b.w.) group, were found to have lower body weight gain than the control group and even the normal group, indicating the treatment successfully prevented obese condition for the rats. The dose 2 group which was given MPEE 500 mg/kg b.w. and high-calorie diet had the lowest body weight gain, with only 35% of increase from initial weight.

FAS levels in adipose tissues and serum

The concentration of FAS in the adipose tissue and serum was measured quantitatively using ELISA, and the result can be seen in Figs. 2 and 3. Based on Fig. 3, the FAS concentration in adipose tissue of rats in the control group was the highest, even though it was not significantly different from the normal and orlistat group. In contrast, the dose 1 (MPEE 200 mg/kg b.w.) and dose 2 (MPEE 500 mg/kg b.w.) group found to had significantly lower FAS concentration than the control group, indicated that MPEE was able to reduce the FAS level in high-calorie diet rats. The similar condition also achieved in the quantification of FAS concentration in the serum of the experimental rats, with only dose 1 (MPEE 200 mg/kg b.w.) and dose 2 (MPEE 500 mg/kg b.w.)

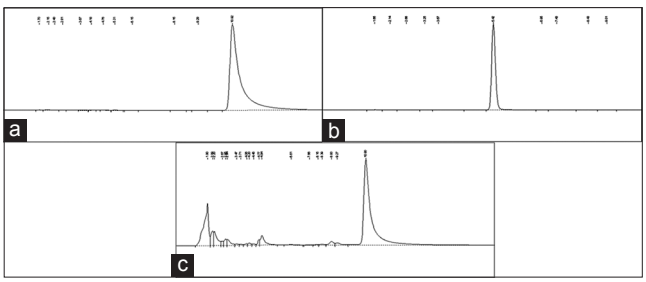

Fig. 1: Chromatography results on high-performance liquid chromatography analysis of (a) α-mangostin compound, (b) xanthone compound, and (c) mangosteen pericarp ethanolic extract

group to had significantly lower FAS concentration than the control group (Fig. 4).

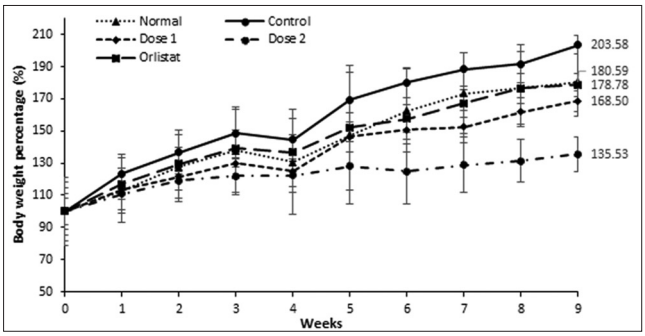

Fig. 2: The percentage of body weight of rats in normal, control, dose 1 (mangosteen pericarp ethanolic extract [MPEE] 200 mg/kg b.w.), dose 2 (MPEE 500 mg/kg b.w.), orlistat (orlistat 21.67 mg/kg b.w.) group for 9-week period, the results are mean±standard deviation (n=5)

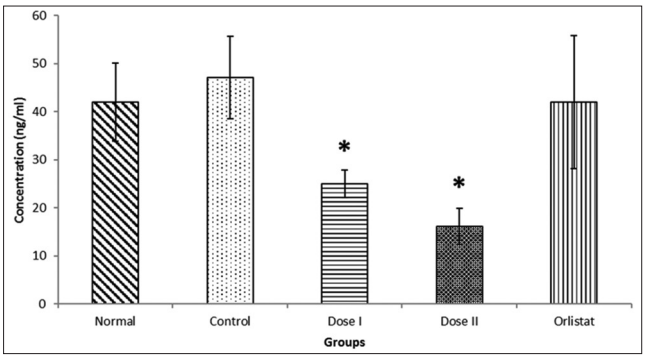

Fig. 3: Fatty acid synthase concentration in the adipose tissue of male Wistar rats in normal group (standard diet), control group (high-calorie diet), dose 1 group (high-calorie diet and mangosteen pericarp ethanolic extract [MPEE] 200 mg/kg b.w.), dose 2 group (high-calorie diet and MPEE 500 mg/kg b.w.), and orlistat group (high-calorie diet and orlistat 21.6 mg/kg b.w.). The results are means±standard deviation (n=5), with * marks indicate significant differences compared to the control group, using one-way ANOVA least significant difference *post-hoc* test and p<0.05 considered as significant

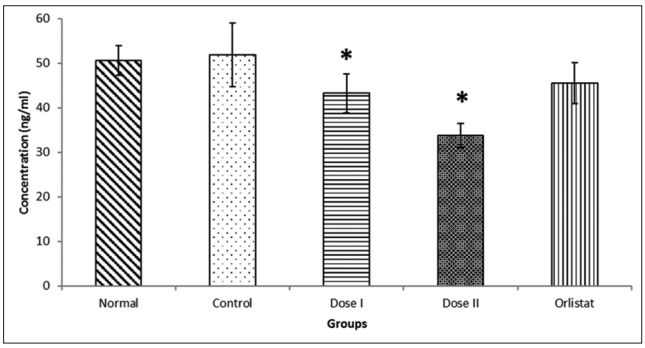

Fig. 4: Fatty acid synthase concentration in the serum of male Wistar rats in normal group (standard diet), control group (high-calorie diet), dose 1 group (high-calorie diet and mangosteen pericarp ethanolic extract [MPEE] 200 mg/kg b.w.), dose 2 group (high-calorie diet and MPEE 500 mg/kg b.w.), and orlistat group (high-calorie diet and orlistat 21.6 mg/kg b.w.). The results are means±standard deviation (n=5), with * marks indicate significant differences compared to the control group, using one-way ANOVA least significant difference *post-hoc* test and p<0.05 considered as significant

DISCUSSION

Mangosteen has been reported to have several medicinal properties, as it contained a variety of secondary metabolites that have numerous pharmacological activities [17]. In this study, we demonstrated that MPEE has a potential to prevent the obesity in male Wistar rats.

The HPLC revealed that MPEE had a notable α-mangostin content, which was 29.13% (w/w). The α-mangostin content in the MPEE used this study was higher than Nakatani *et al.* (2002) findings, which reported that 40% ethanol extract of mangosteen contained 10% α-mangostin and 100% ethanol extract of mangosteen contained 13% α-mangostin [18]. Another study also reported lower α-mangosteen content, which was 10.5% [15]. According to Widowati *et al.* (2014) study, α-mangostin is the major xanthone component in the MPEE, as the concentration of other xanthones such as γ-mangostin, garcinone-C, and garcinone-D was significantly low compared to the α-mangostin concentration in the extract [15].

Based on the percentage of body weight results in Fig. 3, it showed that the control group has the highest body weight gain. At the 9th week, the control group has over than 20% difference of body weight percentage than the normal group, indicated the obese condition was achieved [16]. The control group consisted of rats fed by high-calorie diet without any treatment, with MSG induced at first 5 d of the experiment after acclimatization. The result suggested that the MSG and high-calorie diet succeed in creating the obese condition for the rats. MSG was able to destruct the ventromedial hypothalamic and arcuate nuclei in newborn rats, leading to the development of obesity due to the lack of control over absorption and energy expenditure [13]. The MSG also reported to increased food intake and induced metabolic disorders associated with oxidative stress [19]. The groups which were given high-calorie diet and MPEE showed remarkably lower weight gain than the control group, moreover lower than normal and orlistat group. Orlistat has been known as a pharmacological agent used for promoting weight loss in obese individuals, by inhibiting the gastric and pancreatic lipase which important for the digestion of long-chain triglycerides and reduces fat absorption [20]. These results demonstrated that MPEE has a great ability to prevent obesity. The ability of MPEE to lowering the body weight gain might be related to its beneficial properties toward the lipid profile. A study conducted by Adiputro *et al.* (2013) revealed that the ethanolic extract of mangosteen pericarp reduced total cholesterol, triglyceride, and low-density lipoprotein levels along with increased high-density lipoprotein levels in rats fed high-lipid diet [17]. The α-mangostin content in the mangosteen also could play a role in inhibiting major body weight gain. The α-mangostin reported to had reduced lipid accumulation with decreased peroxisome proliferator-activated receptor gamma (PPARγ) expression along with stimulated the glucose uptake and free fatty acid release from 3T3-L1 adipocytes via GLUT4 and leptin expression [21]. PPARγ is a nuclear transcription factor that contributes to activate adipocyte-specific gene expression and differentiation, as well as controlling energy accumulation in the form of adipose tissue mass which strongly correlated with obesity development [22].

The preventive effect of obesity by MPEE also could relate to the FAS level reduction as seen in Figs. 3 and 4 in this study. Both MPEE treatment in dose 1 (high-calorie diet, MPEE 200 mg/kg b.w.) and dose 2 (high-calorie diet, MPEE 500 mg/kg b.w.) groups showed significantly lower level of FAS compared to the control group which given high-calorie diet and no treatment, in either rats adipose tissue or serum. Interestingly, the FAS level in both of adipose tissue and serum of the rats in the normal group (standard diet) and orlistat group (high-calorie diet, orlistat 21.6 mg/kg b.w.) did not differ significantly than those of in the control group. FAS is a key metabolic enzyme that functions in the *de novo* synthesis of long-chain saturated fatty acids from Ac-CoA and Mal-CoA in the presence of reducing substrate nicotinamide adenine dinucleotide phosphate [23]. Excessive accumulation of fatty acid in the body will lead to lipotoxicity, fatty liver and insulin resistance or other obesity-related diseases [24]. Inhibition of FAS activity by FAS inhibitors has been proposed to cause the reduction of body weight and food intake

of obese mice in several studies [5,6,25]. Therefore, the reduction of FAS concentration in this study might as well become one of the mechanisms to prevent and/or treat the obesity [26]. The anti-obesity of MPEE could strongly be related to its bioactive compound, α-mangostin. Li *et al.* (2014) study demonstrated that α-mangostin was able to effectively down-regulate FAS expression and inhibited intracellular FAS activity, resulting in suppression of intracellular fatty acid accumulation [27]. Some studies also reported the properties of phenolic constituents from *G. mangostana* in inhibiting FAS activity [11,23], supported the potential use of mangosteen as a therapeutic agent for obesity.

CONCLUSION

In conclusion, MPEE has a beneficial effect toward obesity showed by preventing major body weight gain and reducing FAS concentration in MSG and high-calorie diet-induced male Wistar rats. The MPEE with the concentration of 500 mg/kg b.w. caused the lowest body weight gain percentage as well as the lowest FAS concentration in adipose tissue and serum of experimental rats after 9 w of treatment. The anti-obesity properties of MPEE might strongly relate to its α-mangostin content, which was 29.13% based on HPLC assay. Further clinical studies should be pursued to ensure the safety of MPEE utilization as a therapeutic agent for obesity.

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REFERENCES

1. Bray GA. Obesity: The disease. J Med Chem 2006;49(14):4001-7.
2. Kelly T, Yang W, Chen CS, Reynolds K, He J. Global burden of obesity in 2005 and projections to 2030. Int J Obes (Lond) 2008;32(9):1431-7.
3. Seidell JC, Halberstadt J. The global burden of obesity and the challenges of prevention. Ann Nutr Metab 2015;66 Suppl 2:7-12.
4. Ng M, Fleming T, Robinson M, Thomson B, Graetz N, Margono C, *et al.* Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: A systematic analysis for the global burden of disease study 2013. Lancet 2014;384(9945):766-81.
5. Shimokawa T, Kumar MV, Lane MD. Effect of a fatty acid synthase inhibitor on food intake and expression of hypothalamic neuropeptides. Proc Natl Acad Sci U S A 2002;99(1):66-71.
6. Loftus TM, Jaworsky DE, Frehywot GL, Townsend CA, Ronnett GV, Lane MD, *et al.* Reduced food intake and body weight in mice treated with fatty acid synthase inhibitors. Science 2000;288(5475):2379-81.
7. Wu D, Ma X, Tian W. Pomegranate husk extract, punicalagin and ellagic acid inhibit fatty acid synthase and adipogenesis of 3T3-L1 adipocyte. J Funct Foods 2013;5:633-41.
8. Liu QY, Wang YT, Lin LG. New insights into the anti-obesity activity of xanthones from *Garcinia mangostana*. Food Funct 2015;6(2):383-93.
9. Cui J, Hu W, Cai Z, Liu Y, Li S, Tao W, *et al.* New medicinal properties of mangostins: Analgesic activity and pharmacological characterization of active ingredients from the fruit hull of *Garcinia mangostana* L. Pharmacol Biochem Behav 2010;95(2):166-72.
10. Akao Y, Nakagawa Y, Iinuma M, Nozawa Y. Anti-cancer effects of xanthones from pericarps of mangosteen. Int J Mol Sci 2008;9(3):355-70.
11. Quan X, Wang Y, Ma X, Liang Y, Tian W, Ma Q, *et al.* α -Mangostin induces apoptosis and suppresses differentiation of 3T3-L1 cells via inhibiting fatty acid synthase. PLoS One 2012;7(3):e33376.
12. Adnyana IK, Abuzaid AS, Iskandar EY, Kurniati NF. Pancreatic lipase and α-amylase inhibitory potential of mangosteen (*Garcinia mangostana* Linn.) pericarp extract. Int J Med Res Health Sci 2016;5(1):23-8.
13. Von Diemen V, Trindade EN, Trindade MR. Experimental model to induce obesity in rat]. Acta Cir Bras 2006;21(6):425-9.
14. Shibata MA, Iinuma M, Morimoto J, Kurose H, Akamatsu K, Okuno Y, *et al.* a-Mangostin extracted from the pericarp of the mangosteen (*Garcinia mangostana* Linn) reduces tumor growth and lymph node metastasis in an immunocompetent xenograft model of metastatic mammary cancer carrying a p53 mutation. BMC Med 2011;9:69.
15. Widowati W, Darsono L, Suherman J, Yelliantty Y, Maesaroh M. High performance liquid chromatography (HPLC) analysis, antioxidant, antiaggregation of mangosteen peel extract (*Garcinia mangostana* L.). Int J Biosci Biochem Bioinformatics 2014;4(6):458-66.
16. Adnyana IK, Elin YS, Ary Y, Finna S. Anti-obesity effect of the pomegranate leaves ethanol extract (*Punica granatum* L.) in high-fat diet induced mice. Int J Pharm Sci 2014;6(4):626-31.
17. Adiputro DL, Widodo MA, Romdoni R, Sargowo D. Extract of mangosteen increases high density lipoprotein levels in rats fed high lipid. Univ Med 2013;32(1):37-43.
18. Nakatani K, Atsumi M, Arakawa T, Oosawa K, Shimura S, Nakahata N, *et al.* Inhibitions of histamine release and prostaglandin E2 synthesis by mangosteen, a Thai medicinal plant. Biol Pharm Bull 2002;25(9):1137-41.
19. Diniz YS, Faine LA, Galhardi CM, Rodrigues HG, Ebaid GX, Burneiko RC, *et al.* Monosodium glutamate in standard and high-fiber diets: Metabolic syndrome and oxidative stress in rats. Nutrition 2005;21(6):749-55.
20. Mahmoud RH, Elnour WA. Comparative evaluation of the efficacy of ginger and orlistat on obesity management, pancreatic lipase and liver peroxisomal catalase enzyme in male albino rats. Eur Rev Med Pharmacol Sci 2013;17(1):75-83.
21. Taher M, Mohamed Amiroudine MZ, Tengku Zakaria TM, Susanti D, Ichwan SJ, Kaderi MA, *et al*. α-Mangostin improves glucose uptake and inhibits adipocytes differentiation in 3T3-L1 cells via PPARγ, GLUT4, and leptin expressions. Evid Based Complement Alternat Med 2015;2015:740238.
22. Stern JS, Peerson J, Mishra AT, Sadasiva Rao MV, Rajeswari KP. Efficacy and tolerability of a novel herbal formulation for weight management. Obesity (Silver Spring) 2013;21(5):921-7.
23. Jiang HZ, Quan XF, Tian WX, Hu JM, Wang PC, Huang SZ, *et al.* Fatty acid synthase inhibitors of phenolic constituents isolated from *Garcinia mangostana*. Bioorg Med Chem Lett 2010;20(20):6045-7.
24. Vázquez-Vela ME, Torres N, Tovar AR. White adipose tissue as endocrine organ and its role in obesity. Arch Med Res 2008;39(8):715-28.
25. Wolfgang MJ, Lane MD. Hypothalamic malonyl-CoA and CPT1c in the treatment of obesity. FEBS J 2011;278(4):552-8.
26. Asyifah MR, Lu K, Ting HL, Zhang D. Hidden potential of tropical fruit waste components as a useful source of remedy for obesity. J Agric Food Chem 2014;62(19):3505-16.
27. Li P, Tian W, Ma X. Alpha-mangostin inhibits intracellular fatty acid synthase and induces apoptosis in breast cancer cells. Mol Cancer 2014;13:138.