ORIGINAL ARTICLE

Short-term Effects of *Garcinia cambogia* on Blood Glucose and Body Weight in Streptozosin-induced Diabetic Rats

Hari Hendarto[1], Alissa Rifa[2], Nounik Cheri Dwita[3], Intan Nurjannah[1], Flori R. Sari[3], Femmy Nurul Akbar[1]

[1] Internal Medicine Department, Faculty of Medicine, Univesitas Islam Negeri Syarif Hidayatullah Jakarta, Ciputat, Timur, Banten, Indonesia. 15412
[2] Faculty of Medicine, Univesitas Islam Negeri Syarif Hidayatullah Jakarta, Ciputat, Timur, Banten, Indonesia. 15412
[3] Pharmacology Department, Faculty of Medicine, Universitas Islam Negeri Syarif Hidayatullah Jakarta, Ciputat Timur, Banten, Indonesia. 15412

ABSTRACT

Introduction: Diabetes Mellitus is chronic metabolic disorders characterized by persistent high blood glucose due to impaired insulin secretion or insulin resistance. *Garcinia cambogia* or Malabar tamarind is a tropical fruit, widely grown in South Asia and Southeast Asia including Indonesia. It is used for food condiment and flavouring and also popular as weight-loss supplement. *Garcinia cambogia* contains high amount Hydroxy-citric acid (HCA), an active component have shown increased hepatic glycogen synthesis and increased serotonin release in the brain that leading an appetite-suppression effect, which finally decrease body weight. HCA has also been reported could also increase of alpha amylase and intestinal alpha-glucosidase that leading reduction carbohydrate metabolism, however further benefit in diabetes has not been yet elucidated. The aim to this study was to determine the effects of *Garcinia cambogia* 400 mg/kg body weight (BW) on blood glucose and body weight in streptozotocin-induced diabetic rat after 28 days of decoction. **Methods:** This experimental study was done in acute diabetic rats using 50 mg/kg BW streptozotocin injection. *Garcinia cambogia* extract were given daily at 400 mg/kg BW for 28 days. Body weight and blood glucose were analysed according to protocol. **Results:** This study showed significant reduction of blood glucose ($p<0.05$), however body weight did not differ significantly after 28 days of decoction. **Conclusion:** *Garcinia cambogia* 400 mg/kg BW gave short term effects to reduce blood glucose in diabetic rat after 28 days of decoction. Therefore, *Garcinia cambogia* may give beneficial effect on diabetic treatment.

Keywords: *Garcinia cambogia*, Body Weight, Blood Glucose, Diabetic Rats

Corresponding Author:
Hari Hendarto, PhD
Email: hari.hendarto@uinjkt.ac.id
Tel: +62 82261656561

INTRODUCTION

Diabetes Mellitus is chronic metabolic disease characterized by persistent hyperglycemia or high blood glucose, due to impaired insulin secretion or insulin resistance (1,2). There are 422 million people with diabetes worldwide according to the World Health Organization (WHO) and number of people with these diseases is predicted to double by 2030. Half of them spread across Asia, especially India, China, Pakistan, and Indonesia (1,2).

While the treatment of diabetes has made significant progress in the past three decades, result of medical treatment in patient is still far from perfect. Some treatment involves medicinal use of plants or herbal are suggested. Most plants contain terpenoids, alkaloids, glycosides carotenoids, flavonoids showed anti-hyperglycaemic effects. The effects anti-hyperglycaemic from herbals due to their potential are to build up the performance of pancreatic tissue to increase insulin secretions or reduce glucose absorption in intestinal.

Indonesia as a mega biodiversity country is endowed with a rich natural resource as a national asset that need to be explored. Traditional herbal plants is used as an alternative or additional therapy since its relatively cheap and usually easy to find around residential areas. *Garcinia cambogia* is a tropical fruit widely grown in Indonesia that originated from India and resembled a mini pumpkin used in the kitchen as condiment and flavour enhancer in daily cooking for centuries, especially Malay cuisine.

Hydroxycitric acid (HCA), which is an active component in *Garcinia cambogia* were found to have the benefit to increase rates of hepatic glycogen synthesis, to supress food intake and decrease body weight gain (3). HCA has also been reported to increase serotonin release in the brain that lead an appetite-suppression effect and commonly consumed to help lose weight (4,5,6).

HCA has also been reported could increase intestinal alpha-glucosidase and alpha amylase that leading carbohydrate metabolism reduction and decrease blood sugar levels (5,7)

One of animal studies using female rats of the Charles River CD strain have confirmed that consumption of HCA, one of active compound from *Garcinia cambogia*, significantly reduce appetite which subsequently reduce food intake in rats and the body weight (8). Additionally, the effects of HCA on diabetes have not yet been elucidated mainly because the clinical studies have not proven the dose and duration HCA-based medicine. Rasha et al study have proven that 100 mg/kg bodyweight (BW) and 200 mg/kg BW of *Garcinia cambogia* extract could decrease blood glucose level, while Mahmoud et al study showed significant decreased in body weight and lipid profile (9,10). However, a lack of evidence on the role of *Garcinia cambogia* as an anti-diabetic agent is still need to be clarified (11).

Therefore the aim to this study was determine the effects of *Garcinia cambogia* 400 mg/kg BW on body weight and blood glucose in streptozotocin-induced diabetic rat after 28 days of decoction.

MATERIALS AND METHODS

Research Design

The design of this study was experimental research using normal and diabetic rats with the *Garcinia cambogia* (C) extract as the treatment intervention. This study used four groups of rats including normal rats without treatment as diabetic negative control (N), normal rats with treatment (NC), diabetic rats without treatment as diabetic positive control (D) and diabetic rats with treatment (DC). Minimum number of mice in each group were estimated in accordance with the Federer method. In this study, minimum number of mice in each group are four.

Diabetic Rat Model

Male Sprague Dawley rats with the weight of 150 to 160 g were intraperitoneally injected with single dose of 50 mg/kg BW streptozotocin (STZ) dissolved in citrate buffer (pH 4) according to the previous guideline acute diabetic rats' protocol (12). Five days after the injection, blood glucose (BG) level was analysed with the Medi-safe glucose strip and rats with BG ≥ 300 mg/dL were considered as diabetes. Rats were randomly divided into four groups; 1. diabetic rats without treatment (D, n=6), 2. diabetic rats received 400 mg/kgBW *Garcinia cambogia* extract (DC, n = 5, due to sudden death of 1 rat), 3. normal rats (N, n= 6) and 4. normal rats received 400 mg/kgBW *Garcinia cambogia* extract (NC, n = 6).

First day treatment was started after 5 days injection of STZ. During the treatment phase, rats were maintained with careful supervision, received food and water, and weighed regularly. All animals were managed under the ethical guidelines for animal experiment. This study was approved by Ethical Approval number Un. 01/F10/KP.01.1/KE. SP/06.05.006/2017.

Garcinia cambogia extract

Garcinia cambogia fruit was extracted in the Bogor Agriculture Institute according to their procedure of extraction. First the leaves of *Garcinia cambogia* were put through a blender. After that, they were sieved then all that remains are fine ground leaves. The ground leaves were mixed by 70% ethanol with the ratio 10 mg of ground leaves in 100 ml of 70% ethanol. The mixture was added into a hot plate stirrer for 5 hours, then went through a micro filter to become a liquid version of *Garcinia cambogia* extract. The liquid then was evaporated to make dry or solid extract (13). The dry extract powder was mixed with aquadest when given to both diabetic and normal rats for 28 days by oral gavage. This extract was certified by Bogor Agricultural Institute number of 6295/IPH.3/KS/XI/2015.

Blood glucose measurement

The non-fasting blood glucose was measured day 1 or first day of extract treatment and day 28 or last day of extract treatment using Medi-safe blood glucose strips as instructed by the protocol Terumo, Inc.,Tokyo.

Toxicity studies

According to Taher et al and Shubasree et al studies, no acute toxicity was found when injecting below 2000 mg/kg of Garcinia mangostana pericarp extract in the rats. The dose selected for this study was 1/5 of the maximum dose (14,15). Previous study showed impaired liver function in the administration of HCA, causing elevation in ALT and AST plasma levels. Taher has been reported hepatotoxicity and other studies also showed similar results (14,15,16,17).

Statistical analysis

Data were analyzed as means and standard deviation (SD). Mann Whitney analysis was performed to make comparison among groups. Statistical significances were defined as probability value ($p < 0.05$).

RESULTS

Animal diabetic model

Animal diabetic model is confirmed five days after the STZ peritoneal injection. First day of the study, blood glucose (BG) was significantly higher in the diabetes group compared to the normal rat group ($p<0.01$), however, no significant difference BG was observed in the diabetes without treatment (D) group and diabetes with extract (DC) group, suggesting an equal baseline for both diabetic groups.

Garcinia cambogia effect on body weight

Figure 1 represented body weight of the rats after 28

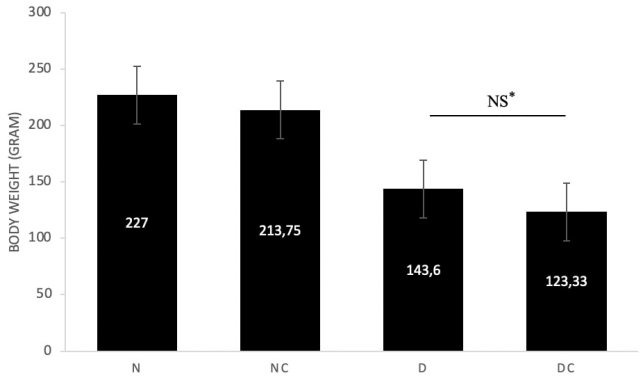

Figure 1: The Effects of Daily Decoction of Garcinia Cambogia Extract after 28 days on Body Weight

Day 28 = Day 28 of extract treatment. N = Normal; NC = Normal with 400 mg/kg BW Garcinia cambogia ; D = Diabetes; DC = Diabetes with Garcinia cambogia treatment, NS* = Not Significant (p>0.05).

days. It showed that diabetic rats tend to have lower body weight and also showed that the rats given *Garcinia cambogia* tends to have a lower bodyweight when compared to its counterpart (NC VS N, DC VS D). But Mann Whitney test showed there were no significant difference of body weight between the D and DC group after 28 days (p>0.5).

Garcinia cambogia effect on BG

Figure 2 represented blood glucose level among groups after 28 days decoction. The blood glucose level remained significantly high above 400 mg/dL in the D group compared to the N group. Daily decoction of 400 mg/kg BW *Garcinia cambogia* extract did not alter blood glucose level in the N group so that no significant difference of blood glucose level observed between the N and the NC group (p<0.05). Conversely, daily decoction in diabetic rat (DC) could gradually reduce BG level to 388.67±172.44 mg/dl after 28 days decoction. It also showed that the rats with extract tends to have a lower blood glucose level. Mann Whitney test showed significant decreased blood glucose in diabetic rat with *Garcinia cambogia* extract (DC) compared to diabetic without *Garcinia cambogia* extract (D) (p<0.05) as also showed in Figure 2.

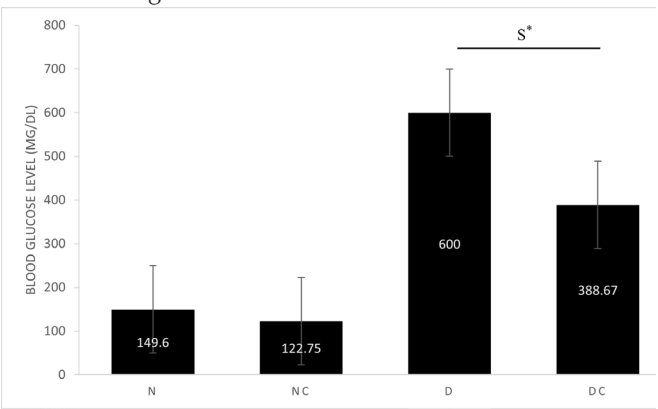

Figure 2:The Effects of Daily Decoction of Garcinia Cambogia Extract after 28 days on Blood Glucose Level

Day 28 = Day 28 of extract treatment. N = Normal; NC = Normal with 400 mg/kg BW Garcinia cambogia, D = Diabetes; DC = Diabetes with Garcinia cambogia treatment, S* = significant (p<0.05).

DISCUSSION

The salient finding of this study were: (1) Significant hyperglycemia was observed in diabetic rat 5 days after the injection of 50 mg/kg BW STZ and the hyperglycemia remained high up to day 28 confirming diabetic model (2) Daily decoction of *Garcinia cambogia* 400 mg/kg BW gradually decreased blood glucose with significant result was achieved after 28 days.

Garcinia cambogia has been widely reported as a weight-reduction agent. Its main component was hydroxycitric acid (HCA), which can be found in its fruit rind (up to its 30 percent by weight). Despite of *Garcinia cambogia* role as a rich source for hydroxycitric acid, it also possesses an antioxidant activity (18,19). Recent evidence has further shown that administration of *Garcinia cambogia* not only reduced the body weight but also blood glucose in diabetes (20).

This study showed that daily decoction of *Garcinia cambogia* extract for 28 days significantly reduce blood glucose in diabetic rats. This improvement possibly mediated at least in part through the antioxidant role of *Garcinia cambogia*.

But this study showed non-significant decrease in body weight with *Garcinia cambogia* extract treatment, although Mahmoud et al study showed a statistically significant decrease in body weight on 400 mg/kg of *Garcinia cambogia* extract (10). But meta-analysis by Onakpoya et al also stated that HCA in *Garcinia cambogia* extract may cause weight loss, but not statistically significant (5).

This study also showed that there were significantly decrease in blood glucose levels after 28 days of 400 mg/kg daily administration of the *Garcinia cambogia* extract in diabetic rat. This result was similar with Taher et al study that showed while given 400 mg Garcinia mangostana extract daily can cause a significant drop in blood glucose levels after 28 days (14). Rasha et al also stated that there are statistically significant reduce in blood glucose level when they administered only 200 mg/kg daily extract of the *Garcinia cambogia* (9).

CONCLUSION

In conclusion, *Garcinia cambogia* 400 mg/kg BW gave short term effects on blood glucose reduction in diabetic rat after 28 days of decoction, despite without body weight reduction effects. *Garcinia cambogia* may give beneficial effect on diabetic treatment. Further exploration on dose and duration are fully required.

ACKNOWLEDGEMENT

The author are grateful to those who dedicated their time and participation to this study.

REFERENCES

1. World Health Organization (WHO). Diabetes. https://www.who.int/health-topics/diabetes#tab=tab, 1 November,15 ,2021
2. Korytkowski MT, Forman DE. Management of Atherosclerotic Cardiovascular Disease Risk Factors in the Older Adult Patient With Diabetes. Diabetes Care.2017;40(4):476-84.
3. Heymsfield SB, Allison DB, Vasselli JR, Pietrobelli A, Greenfield D, Nunez C. *Garcinia cambogia* (hydroxycitric acid) as a potential antiobesity agent: a randomized controlled trial. JAMA. 1998;280(18):1596-600.
4. Fassina P, Scherer Adami F, Terezinha Zani V, Kasper Machado IC, Garavaglia J, Quevedo Grave MT, Ramos R, Morelo Dal Bosco S. The Effect Of *Garcinia cambogia* As Coadjuvant In The Weight Loss Process. Nutr Hosp. 2015;32(6):2400-8. Oxidative stress and diabetic cardiomyopathy: a brief review. Cardiovasc Toxicol. 2001;1(3):181-93.
5. Onakpoya I, Hung SH, Perry R, Wider B, and Ernst E. The Use of Garcinia Extract (Hydroxycitric Acid) as a Weight loss Supplement: A Systematic Review and Meta-Analysis of Randomised Clinical Trials . 2011. Peninsula Medical School, University of Exeter, Devon EX2 4NT, UK. Volume 2011, Article ID 509038. doi:10.1155/2011/509038
6. Chuah LO, Ho WY, Beh BK, Yeap SK. Updates on Antiobesity Effect of Garcinia Origin (-)-HCA. Evid Based Complement Alternat Med. 2013;2013:751658.
7. Sugimoto Y, Kimura I, Yamada J, Watanabe Y, Takeuchi N, Horisaka K. Effects of serotonin on blood glucose and insulin levels of glucose- and streptozotocin-treated mice. Jpn J Pharmacol. 1990;54(1):93-6.
8. Sullivan AC, Triscari J, Hamilton JG. Effect of (–)-hydroxycitrate upon the accumulation of lipid in the rat: I. Lipogenesis. Lipids. 1974;9:121-8.
9. Rasha HM, Salha, Thanai and Zahar. The Biological Importance Of *Garcinia cambogia*. 2013. Saudi Arabia.
10. Ghada S Mahmoud and Ayman S Amer. Effect of Natural Extract of Hydroxycitric Acid On Lipid Profile, Liver, And Testes of Adult Male Rats. Assiut University, Egypt. 2013. AAMJ, Vol. 11, N. 1, January, 2013
11. Menezes RCR, Schumacher JC, Bertoletti ACC, Faccioli LS, Freitas JB, Rosa da Mata I, et al. *Garcinia cambogia* and diabetes mellitus : a lack of evidence. Int Phys Med Rehab J. 2021;6(3):67-8.
12. Sari FR, Anwar S, Alfan D, Hendarto H, Adhiyanto C, Uzair AY, et al. Daily intake of liquid sweetener from Stevia rebaudiana extract improves chronic diabetes mellitus in the streptozotocin-induced rat. Eco Env Cons. 2019;25(3):1424-28
13. Ministry of Health of the Republic of Indonesia. General Standard Parameters of Medicinal Plant Extracts "Parameter Standar Umum Ekstrak Tumbuhan Obat". Directorate General of Drug and Food Control. 2000 Jakarta, Indonesia
14. Taher M, Syafiq MF, Zakaria, Susanti D, Zakaria ZA. Hypoglycaemic activity of ethanolic extract of Garcinia mangostana Linn. in normoglycaemic and streptozotocin-induced diabetic rats. 2016 May 21;16:135. doi: 10.1186/s12906-016-1118-9
15. Subhasree N,Kamella A, Kaliappan I, Agrawal A, Dubey GP. Antidiabetic and antihyperlipidemic activities of a novel polyherbal formulation in high fat diet/streptozotocin induced diabetic rat model. Indian J Pharmacol. 2015 Sep-Oct; 47(5): 509–513. doi: 10.4103/0253-7613.165200
16. Jones FJ , Andrews AH (2007). Acute liver injury associated with the herbal supplement hydroxycut in a soldier deployed to Iraq. Am J Gastroenterol, 102(10), 2357-8.
17. Shim M, Saab S (2009). Severe hepatotoxicity due to Hydroxycut: a case report. Dig Dis Sci, 54(2), 406-408.
18. Setyowati FM, Wardah. Diversity of medicinal plant by Talang Mamak tribe in surrounding of Bukit Tiga Puluh National Park, Riau. Biodiversitas. 2007;8(3). 228-32.
19. Jena BS, Jayaprakasha GK, Singh RP, Sakariah KK. Chemistry and biochemistry of (-)- hydroxycitric acid from Garcinia. J Agric Food Chem. 2002;50(1):10-22.
20. Maia-Landim A, Ramнrez JM, Lancho C, Poblador MS, Lancho JL. Long-term effects of *Garcinia cambogia*/Glucomannan on weight loss in people with obesity, PLIN4, FTO and Trp64Arg polymorphisms. BMC Complement Altern Med. 2018;18(1):26.