

Potential roles of *Garcinia* family as antimetabolic syndrome

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ABSTRACT

The incidence rate is directly proportional to the incidence of obesity or overweight and Type 2 diabetes mellitus. *Garcinia* is a plant that has been proven empirically, preclinically, and clinically to have activities for the avoidance and treatment of metabolic syndrome and on the pathogenesis and pathophysiology caused by the disease. The aim of this study is to create a discussion and summarize information regarding the activity or usefulness of the *Garcinia* plant. This review article was based on the published journals obtained from Google Scholar, Scopus, and PubMed databases using the keywords *Garcinia* obesity, *Garcinia* overweight, and *Garcinia* metabolic syndrome. *Garcinia* had many activities related to metabolic syndrome because it was able to reduce body fat mass, blood sugar level, body weight, total cholesterol, and triglyceride level. These activities were mediated by numerous apparatuses of feat together with a reserve of fatty acid synthase, α -amylase, α -glucosidase, and several other enzymes and pathways associated with the metabolic syndrome. *Garcinia* plant was able to be used as a candidate for a new herbal that had a good effect in treating metabolic syndrome in future.

Key words: Body fat mass, *Garcinia*, insulin resistance, metabolic syndrome, obesity

INTRODUCTION

The incidence of metabolic syndrome is directly proportional to the incidence of obesity/overweight and Type 2 diabetes mellitus (T2DM).^[1] Obesity is a dangerous aspect leading to several dangerous illnesses, such as diabetes, hypertension, heart syndrome, and stroke.^[2,3] The patients with obesity and overweight have 3.6 times the risk of having coronary artery disease,^[4] 85% of hypertension was associated with

body mass index (BMI) from 25 kg/m²-29.9 kg/m², and 90% of patients with T2DM have a BMI more than 25 kg/m².^[5]

Nowadays, obesity and overweight are treated by synthetic drugs, which are known to have a lot of side effects and can decrease the quality of life.^[6] Considering those limitations, the treatment has been developed using herbal medicines because of their excellent bioactivity and pharmacological properties including anti-obesity and overweight.^[7] In addition, herbal medicines have lower side effects than synthetic drugs due to their multicomponent.^[8]

Garcinia is one herbal medicine that has been used empirically for treating degenerative diseases such as obesity,^[9] diabetic mellitus,^[10] and arthritis.^[11] *Garcinia* is known with different names according to its place, namely, *Garcinia atroviridis*, *Garcinia cola*, *Garcinia cambogia*,

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and *Garcinia indica*. *G. atroviridis* is more common on the mainland of Peninsular Malaysia, including Indonesia.^[12] *G. cambogia* has been studied as anti-obesity since 20 years ago.^[13] Whereas *G. atroviridis* and *G. cola* were effective against obese females with a BMI of 25 kg/m² in Thailand.^[14] The intervention group received hydroxycitric acid (HCA) from *G. atroviridis* taken before the meals, 3 × 1.15 g/day in 200 ml of water. The results showed that the intervention group experienced a weight loss of 2.8 kg ($P = 0.05$).^[15]

Based on the potential and excellent effects of *Garcinia* herbs, there are numerous published journals of *Garcinia* herbs in treating obesity and overweight, which will be more useful if made in one article review. Taken together, the authors believed that this review is concerned with the discussion and summarized the effectivity of *Garcinia* herbs in treating obesity, overweight, and other metabolic syndrome-related diseases.

PHARMACOLOGICAL ACTIVITY OF GARCINIA AGAINST METABOLIC SYNDROME

The pharmacological content of *Garcinia* has been shown in Table 1. Garcinol as an antioxidant was able to reduce the BW of mice induced by high-fat diet. In addition, fat, triglycerides (TG), activated protein kinase,^[16] and cholesterol were decreased. On the other hand, *Akkermansia* has increased. *Akkermansia* could prevent fat absorption to reduce the levels of TG, cholesterol, and body fat.^[17]

The bioactive content of *Garcinia mangostana* are α -mangostin, mangosenone F, and γ -mangostin [Figure 1]. *G. mangostana* extract reduced serum urea levels in renal failure of streptozotocin-induced T2DM rats.^[18]

G. cambogia pharmacologically contains HCA, tartaric acid, citric acid, malic acid, and HCA lactone [Figure 2]. The efficacy

Table 1. Garcinia's effects on Weight Loss and Some Metabolic Syndrome Markers

No	Nutraceutical	Effects	Ref.
1	<i>Garcinia cambogia</i> <i>Camellia sintesis</i> unroasted <i>Coffea Arabica</i> and <i>Lagerstroemiaspeciosa</i>	BW↓Body fat↓	[17]
2	Extract of <i>Garcinia Cambogia</i> (HCA-SX)	Appetite↓Weight↓TG↓Glucose↓Insulin↓Insulin resistance↓CRP↓MDA↓IL-6 ↓	[65]
3	Extract of <i>Garcinia atroviridis</i>	AgNPs suppressed expression of the CD4 ⁺ IL17R ^{high} population. MAPK Pathway did not change in control and AgNP. This <i>Garcinia</i> does't cause inflammatory effects.	[66]
4	<i>Garcinia atroviridis</i>	Group 1 get 1 HCA sachet (@1,15 gram) before eats, 3 times a day for 8 weeks. Fat loss occurs in the skin of the triceps ($p < 0.05$).	[67]
5	<i>Garcinia cambogia</i>	Insulin after meals Glycogen synthesis was greater than placebo. GLUT4↓under the placebo group. mRNA ^[68] /CD36 increased over placebo. HCA increased energy in fat oxidation.	[69]
6	<i>Garcinia indica</i> Poly-isoprenylated isolated	BW of the HFD rat↓SGPT↓total cholesterol↓TG↓AMPK↓Fat mRNA↓Fat/body↓akkermansia↓	[70]
7	Extract of <i>Sphaeranthus indicus</i> flowers and, <i>Garcinia mangostana</i> fruits	BW↓of 1.6% BMI 2.7%, waist circumference 4.6% on 2, 4, in 8 weeks. Cholesterol↓compared to placebo ($p = 0.016$), TG↓ ($p = 0.012$). PPAR- γ , ADRP, CD36 and triglycerides was↓Adiponectin↓	[56]
8	<i>Garcinia mangostana</i>	GMPE could reduce plasma creatinine levels and improved the proximal tubule of the kidney in STZ-induced DM rats.	[63]
9	Ethanol extract of <i>Garcinia hanburyi</i>	Pro-inflammatory agent↓	[71]
10	Ethanol extract of <i>Garcinia brasiliensis</i>	PPR- γ ↑ IL-10↓LPL↓FAS↓TNF- α ↓ BG↓Alanine aminotransferase↓	[72]
11	Extract of <i>Garcinia cambogia</i> 10% hot and cold	Total lipids↓TG↓cholesterol↓LDL↓BG↓Albumin↓Ureum↓ALT↓AST↓and HDL↓	[73]
12	Combination green tea (<i>Camellia sinensis</i>) & <i>G. Atroviridis</i> extracts	Cholesterol ↓ TG ↓ LDL ↓ BG ↓ SGOT↓ ↓-amylase↓ ↓-glucose↓	[73]

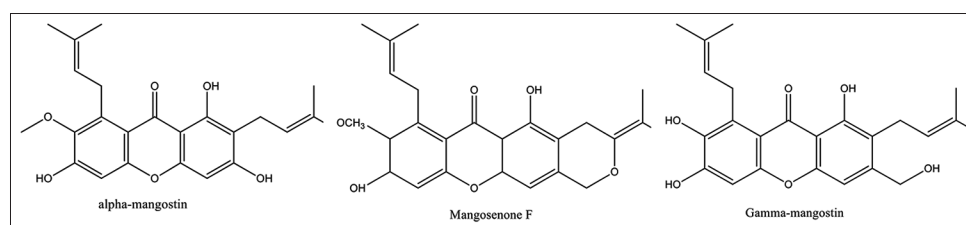


Figure 1: Chemical structure of *Garcinia mangostana* fruit

of *G. cambogia*, either alone or mixed with other *Garcinias* such as *G. camellia*, had the property of reducing body weight, body fat, appetite, TG, blood sugar, insulin after meals, C-reactive protein (CRP), malondialdehyde, glucose transporter Type 4 (GLUT-4), interleukin (IL)-6, TG, low-density lipoprotein (LDL), urea, alanine transaminase (ALT), and aspartate transaminase (AST).^[9-11,19] The results of several studies indicated that *G. atroviridis* suppressed the expression of CD4+ IL17R as a pro-inflammatory gene.^[20] *G. atroviridis* could also remove fat under the skin of the triceps for 8 weeks of *G. atroviridis* administration.^[21]

Garcinia brasiliensis was able to increase peroxisome proliferator-activated receptors γ (PPR- γ), which could inhibit beta-catenin. PPR- γ was bound to the catenin bond domain, namely, pyruvate dehydrogenase kinase, which inhibited the pyruvate dehydrogenase complex in the mitochondria.^[22]

PATHOGENESIS AND PATHOPHYSIOLOGY OF METABOLIC SYNDROME

There are four pathogeneses of metabolic syndrome. The first, insulin resistance that is one of the pathological conditions in metabolic syndrome.^[23] The second, free fatty acids that are secreted through the encounter of c-AMP during lipolysis. This process is instigated by catecholamines for the period of fasting. This pathway can inhibit insulin's antilipolytic properties that lead to advanced lipolysis.^[24] The third, metabolic syndrome that also involves mitochondrial malfunction, increase of fat, and disruption of the antioxidant structure.^[25] The last, pathophysiology-related vascular diseases and immune system that considerably escalates the danger of T2DM and atherosclerotic syndrome.^[26] Metabolic syndrome is closely related to fat accumulation in tissues that can

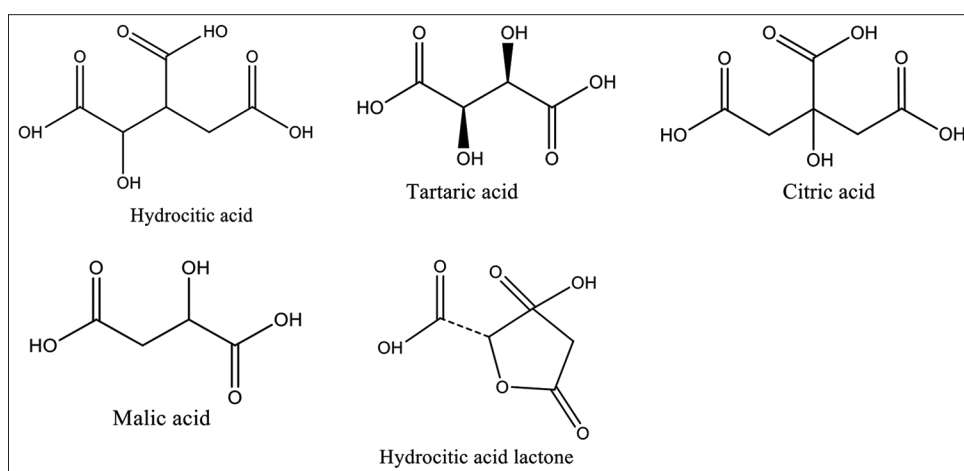


Figure 2: Chemical of *Garcinia cambogia*

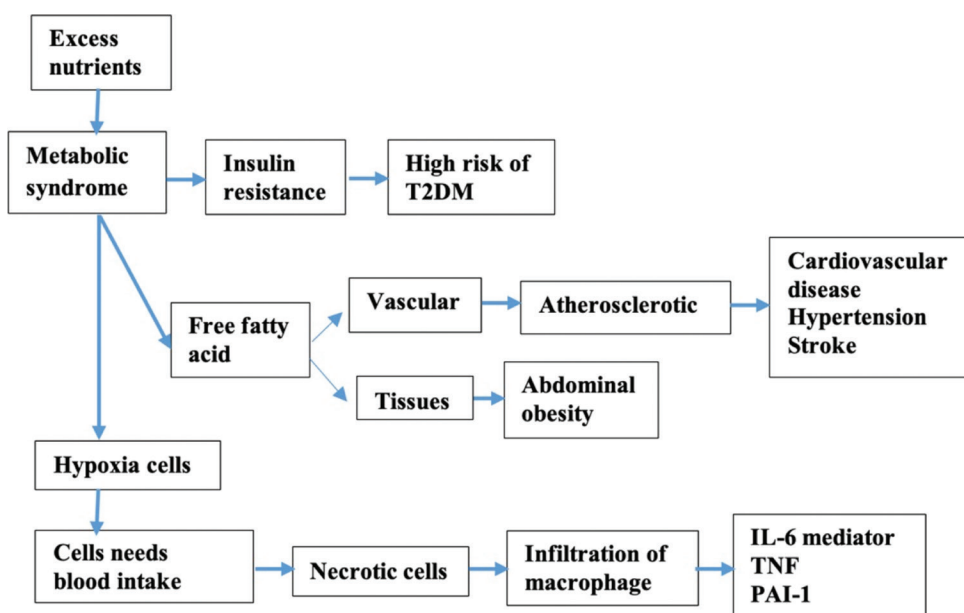


Figure 3: Metabolic syndrome's pathophysiology

lead to abdominal obesity.^[27] Adipose tissue experiences hyperplasia and hypertrophy in response to excess nutrients. Therefore, cells need blood intake due to induced hypoxia as shown in Figure 3.^[28] Hypoxia leads to necrotic cells with macrophage infiltration.^[29] Metabolic syndrome is caused by the accumulation of visceral adipose tissue (VAT), which leads to critical VAT threshold (CVATT). CVATT clues metabolic syndromes such as insulin resistance.^[30] In VAT accumulation, insulin sensitivity is required. If CVATT occurs, insulin resistance will occur, resulting in the disruption of fat deposits such as in the liver, heart, kidneys, and pancreas.^[31]

GARCINIA HERBS

Garcinia described in this review is included in kingdom *Plantae*, family *Clusiaceae*, and genus *Garcinia*.

Bioactivity and pharmacological properties-related metabolic syndrome of *Garcinia* plants

The activities are a function of the secondary metabolite compounds of *Garcinia* variants including xanthone derivative compounds, carboxylic acid, HCA, γ -lactone,

atroviride, atroviridone, atrovirone, benzophenone, phenolic acid, gambogic acid, isomorellin, isoforbesone, morellic acid, desoxygambogenin, hanburin, and flavonoid compounds.^[32]

The activity of *Garcinia* had been proven pharmacologically to have many bioactivities and pharmacological properties as shown in Figure 3.^[33] Its effectiveness in the treatment of obesity had scores of 1.6% in weight loss, 2.7% in reducing BMI, and 4.6% in reducing waist circumference. The decrease in cholesterol level was 26.7 mg/dL and in TG was 56 mg/dL.^[34] *Garcinia* could induce changes in the body's metabolism. Several studies proved that taking *Garcinia* could reduce body fat composition.^[21,35-37]

Based on Figure 4, the effects of various *Garcinia* herbs could be seen to have similar bioactivity and pharmacological properties related to metabolic syndrome disorder. *Garcinia* herbs had several mechanisms of action reducing body weight such as through increasing FAS, activating the scavenger receptor CD36, and regulating PPR- γ , which could decrease lipid level, cholesterol production, and triglyceride level. Besides, *Garcinia* herbs

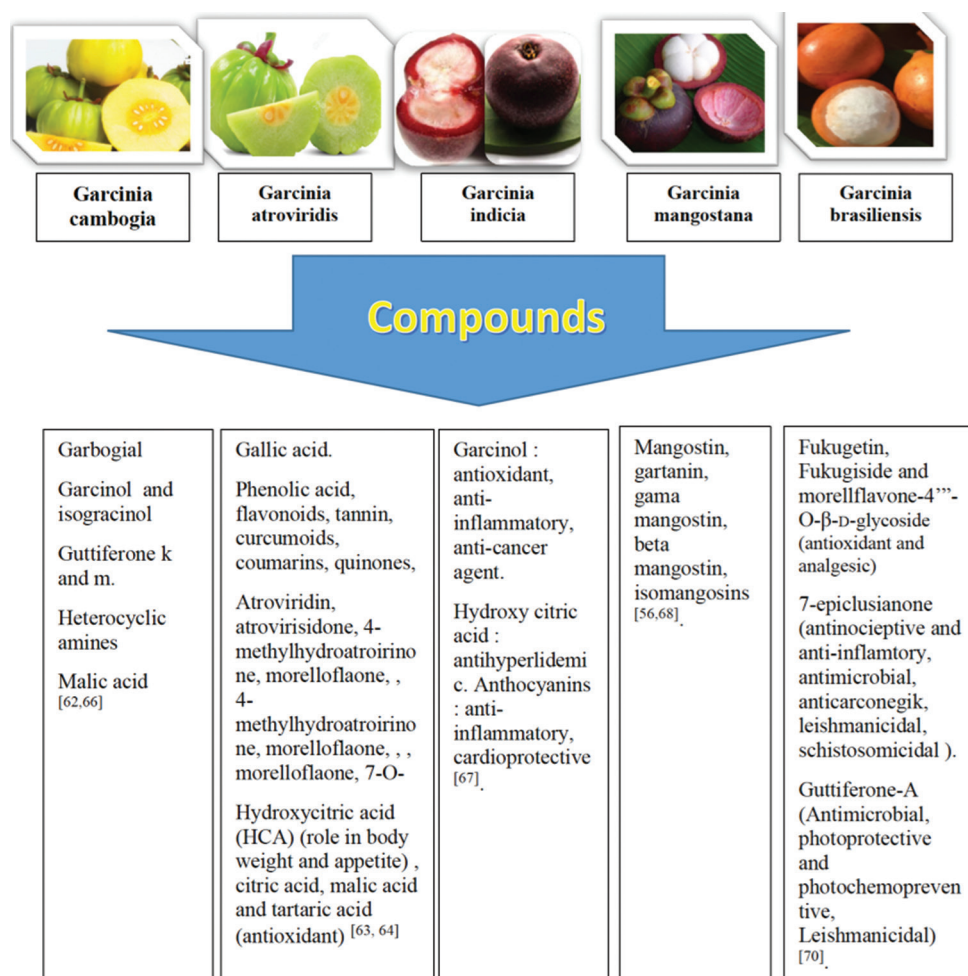


Figure 4: Various *Garcinia* and their bioactive contents

had an effect as an antidiabetic agent to reduce GLUT-4, increase glycogenesis, and regulate LPL. These actions decreased insulin resistance and could reduce the blood glucose level. The effectivity of *Garcinia* herbs in treating metabolic syndrome disorders also had been proven by several studies related to the immune system, which had mentioned that *Garcinia* herbs could reduce IL-1, IL-6, IL10, and tumor necrosis factor- α (TNF- α). The immune system in metabolic syndrome disorder was usually increased by hypoxia-induced hypertrophy/hyperplasia of adipose tissue, which could lead to necrotic cells with macrophage infiltration. In this case, a decrease of the immune system thereby indicated that the *Garcinia* herbs had a potential effect on the clinical manifestation of metabolic syndrome. Furthermore, studies showed that the *Garcinia* herbs could also reduce the alanine aminotransferase, AST, and ALT levels, which indicated hepatic healing. Moreover, the effect of *Garcinia* might reduce the CRP, an excellent indicator for determining the high/low risk of cardiovascular disease.^[12]

Roles of *Garcinia* herbs in metabolic syndrome

Garcinia could induce changes in the body's metabolism. Several studies proved that taking *Garcinia* could reduce body fat composition, obesity, and overweight.

There were several hypothesis mechanisms for the underlying pathophysiology of metabolic syndrome, and the most widely accepted of these was insulin resistance with fatty acid flux. Other potential mechanisms included low-grade chronic inflammation and oxidative stress.^[38,39] Metabolic syndrome began with an excess nutrient intake which caused clinical symptoms of metabolic disorders [Figure 3]. These metabolic disorders included insulin resistance, free fatty acid accumulation, hypoxic cells, dyslipidemia (increased TG, decreased high-density lipoprotein [HDL] levels), central obesity, hypertension, impaired blood sugar tolerance, diabetes mellitus, and high atherosclerotic tendencies.^[40] Metabolic syndrome could increase the risk of insulin resistance leading to T2DM disease. The accumulation of free fatty acids also occurred as a result of the metabolic syndrome, which could cause disturbances in blood vessels and tissues. Metabolic disorders in blood vessels could be in the form of atherosclerosis, which had a risk of heart disease, stroke, and hypertension. Disorders caused by metabolic syndrome began with cell hypoxia, cells needing oxygen supply, cell death, and macrophage infiltration in the form of IL-6 mediators, TNF, and PAI-1.^[41]

There were several herbal therapies that could improve metabolic syndrome and affect hormones, lipid profile, blood glucose, and inflammatory factors.^[42] The lipid profiles improved by herbal medicines contained total cholesterol, LDL, HDL TG,^[43] and HDL. The best reduction in TG and total cholesterol was applied *G. cambogia*

with an effective dose of 2,400 mg/day. HDL increased significantly by consuming *G. cambogia* in the actual dosage of 3,000 mg/day.^[44] This proof about the good substance of these herbs for the treatment of metabolic syndrome made *Garcinia* a candidate for new drugs with good effectiveness in future.

CONCLUSION

The results of the review showed that various types of *Garcinia*, which were *G. cambogia*, *G. atroviridis*, *G. indica*, *Garcinia brasiliensis*, *G. mangostana*, and *Garcinia handburyi* had bioactivity and pharmacological properties for the treatment of metabolic syndrome including anti-obesity and antihyperlipidemia that worked through various mechanisms and multiple pathways.

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Conflicts of interest

There are no conflicts of interest.

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