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Efficacy and Mechanism of Action of *Aloe Vera, Cinnamomum Zeylanicum, Curcuma Longa, Garcinia Cambogia,* and *Garcinia Mangostana* Extracts in Lowering Body Weight in Obesity: A Literature Review

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The habits of today's society, which are influenced by economic growth and globalization have brought new lifestyles, especially those related to diet, resulting in minimal physical activity accompanied by a high calorie intake. This energy imbalance can lead to the metabolic syndrome, including obesity, which is still a burden on the world today. Some plants in Indonesia are believed to help lose weight, such as Aloe vera, Cinnamomum zeylanicum, Curcuma longa, Garcinia cambogia, and Garcinia mangostana. This literature review was conducted to determine the effects of Aloe vera, Cinnamomum zeylanicum, Curcuma longa, Garcinia cambogia, and Garcinia mangostana on weight loss and preventing obesity. The review of twelve relevant articles concluded that Aloe vera, Cinnamomum zeylanicum, Curcuma longa, Garcinia cambogia, and Garcinia mangostana have the potential to prevent and treat obesity but further research is required.

Keywords: Aloe Vera; Cinnamomum Zeylanicum; Curcuma Longa; Garcinia Cambogia; Garcinia Mangostana; Obesity; Weight Loss.

Economic growth and globalization impact people's lifestyles, leading to changes in eating habits and consumption of sugary drinks, thereby an increase in the consumption of sugar, fat, and protein. Furthermore, if accompanied low physical activity, the risk of obesity increases.[1] Indeed, the incidence of the metabolic syndrome has increased globally over the last two decades,[2,3] with more than one billion people being overweight and obese.[3,4] Consequently, obesity is considered as a pandemic[3,4] and a major health problem facing both developed and developing countries.[5]

Modernization and the transition of consumptive lifestyles experienced by people in developing countries have led to a tendency for an increased rate of the incidence of obesity.[4,5] Furthermore, an unstable economy and low level of education increase the risk of obesity, so populations in developing countries are currently very vulnerable to obesity.[4,5]

Obesity increases the risk for comorbidities such as type 2 diabetes mellitus, cardiovascular disease and cancer, indirectly affecting the quality of life of obese people.[1,4] It is also associated with dysregulated adipocyte differentiation, which is influenced by an unbalanced metabolic flux, in which the amount of energy stored is greater than the energy used,[1] as well as several other genetic, endocrine and neurological factors.[6] Long term unbalanced metabolic activity increases the likelihood of comorbidities,[2] thus the chronic condition of weight gain caused by the accumulation of fat in adipose tissue can have a negative impact on health.[7]

Indonesia has second largest biodiversity in the world, with about 80% of the global medicinal plants found in its tropical forests of Indonesia,[8,9] such as *Aloe vera*, *Cinnamomum zeylanicum*, *Curcuma longa*, *Garcinia cambogia*, and *Garcinia mangostana*.[8,10] This literature review was conducted to determine the effect and mechanism of action of these plants in weight loss and preventing obesity.

METHOD

The literature search was performed in PubMed using the following Medical Subject Heading (MesH) keywords, obesity, weight loss, body mass index, *Aloe vera*, *Cinnamomum zeylanicum*, *Curcuma longa*, *Garcinia cambogia*, and *Garcinia mangostana*. The inclusion criteria were original articles written in English of clinical trials and in vivo studies which investigated the effects of *Aloe vera*, *Cinnamomum zeylanicum*, *Curcuma longa*, *Garcinia cambogia*, and *Garcinia mangostana* on obesity and overweight in the last 10 years (2011-2020). The exclusion criteria were scientific articles that were not available or could not be accessed in full text and duplicate articles. The search retreived 256 articles which were screened per the inclusion and exclusion criteria, of which, twelve articles were selected for review (Figure 1).

RESULTS AND DISCUSSION

The results of the studies reviewed are presented in Table 1.

Aloe vera

Aloe vera belongs to the Liliaceae family and is commonly used in Indonesia. It is also widely used in the manufacture of food products, beverages, pharmaceuticals and cosmetics. Choi *et al.* (2013) found a more signifcant weight loss in the group receiving *Aloe vera* supplementation compared to the placebo group, possibly due to the optimal and specific metabolic effect exerted by *Aloe vera* supplementation on reducing body fat mass and increasing lean body mass (LBM). This increase in LBM shows that *Aloe vera* gel can optimize metabolism rather than just losing weight. *Aloe vera* gel also reduced body fat and increased the activation of AMP-activated muscle protein kinase, which is important in lipid metabolism.[11] A previous research study of obese mice given phytosterols from the *Aloe vera* plant showed an improvement in the triglyceride levels and fat accumulation in the mouse liver. The study concluded that the phytosterols contained in *Aloe vera* can change the expression of the PPAR gene in mice that were previously obese. Phytosterols can suppress PPARã activity, thereby inhibiting the activation of adipocytokines including adiponectin.[12]

Cinnamomum zeylanicum

Cinnamon belongs to the Lauraceae family and is a small tree native to Sri Lanka, East Asia, Southeast Asia, and parts of Central Asia[16,17] which can grow to more than ten meters with characteristic oval-shaped leaves and a hairy texture.[17] Cinnamon extracts contain many active substances such as flavonoids, phenols, alkaloids, quinones, steroids, saponins, tannins, procyanidins, and cathecins.[17] According to Jain *et al.* (2017), the main compounds in cinnamon include cinnamaldehyde, cinnamic acid, eugenol and coumarin, which play an important role in the hydrolysis of fat molecules and increase glycogen synthesis in the liver. Borzoei *et al.* (2018) showed that cinnamon supplementation significantly reduced total cholesterol and body weight in

the intervention group compared to the control group (p<0.05). Serum triglycerides and BMI were also significantly decreased in the cinnamon supplementation group compared to the control (p=0.001 and p=0.002, respectively), with no significant changes in serum adiponectin in either group.[13] The study concluded that cinnamon extract can effectively reduce body weight and body mass index, as well as improve serum lipid parameters in obese and overweight patients.[14] According to Whitfield *et al.* (2016), a mixture of cinnamon extract with Kanuka honey reduced body weight, total cholesterol, and LDL more significantly than blood glucose and other parameters of type 2 diabetes mellitus.[15] Other studies have also found that cinnamon extract can increase protein kinase A signaling, the expression of several thermogenic genes, and phosphorylation of HSL-PLIN1 in primary adipocytes. Cinnamon extract also triggers thermogenesis and heat metabolism in mouse and

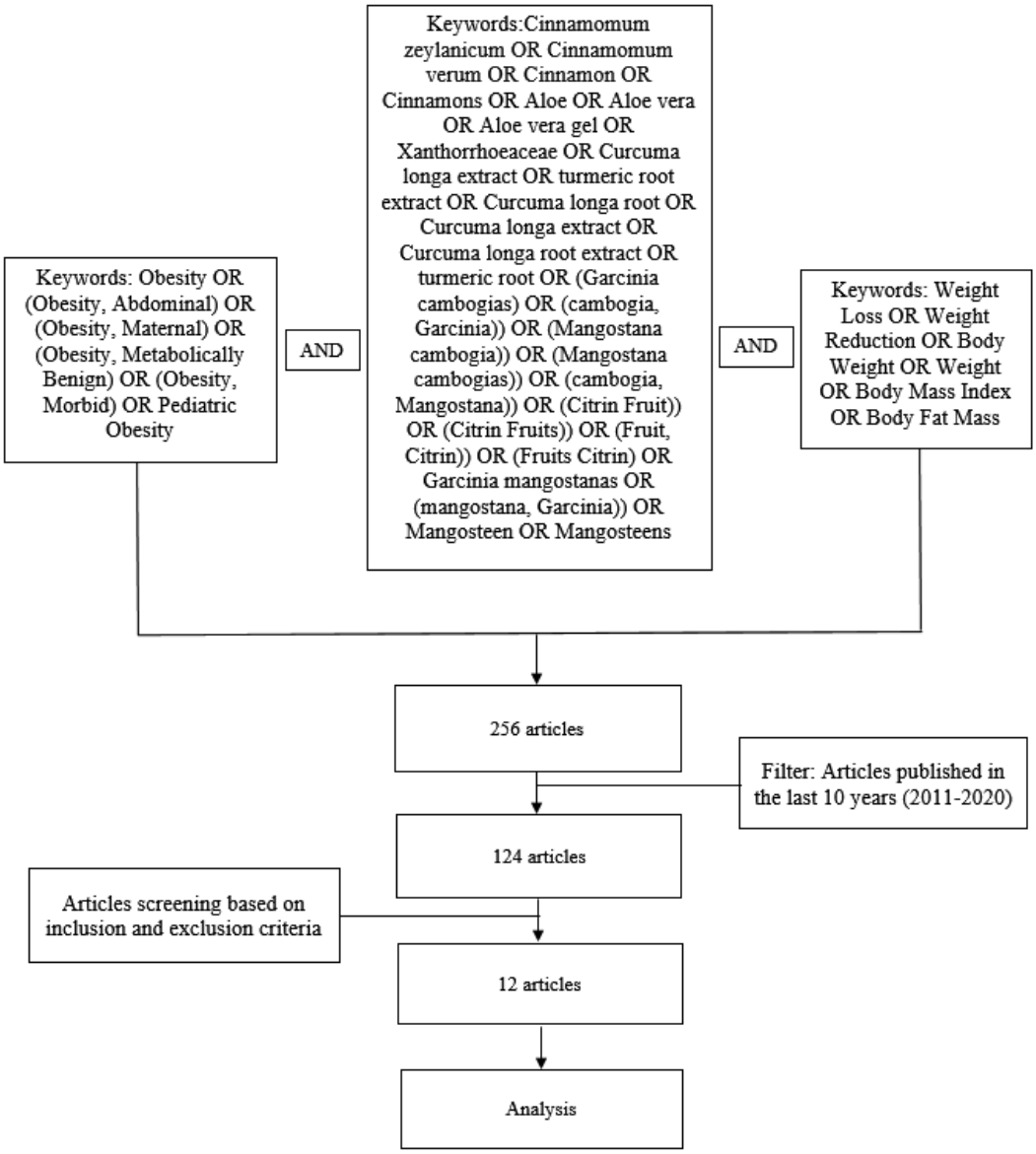

Fig. 1. Flowchart of literature study

human subcutaneous adipocytes. These explain how cinnamon has an anti-obesity effect and improves the quality of the body's metabolism.[16]

Turmeric *(Curcuma longa)*

Curcuma longa is a perennial plant characterized by yellow flowers and broad leaves which belongs to the Zingiberaceae family and grows in tropical countries.[21,22] The main active substance contained in *Curcuma longa* is curcumin, a lipophilic polyphenolic with an aromatic ring and one or more hydroxyl groups.[16,21] Curcumin has beneficial effects on metabolism, potentially anti-obesity and anti-inflammatory properties.[16] In an animal study conducted by Leray *et al.* (2011), there was no information on body weight and body mass index, with no significant changes observed in other obesity parameters.[18] Saraf-Bank *et al.* (2019) reported that turmeric supplementation had a more significant effect on reducing body weight, body mass index, waist circumference, and triglycerides in the intervention group than in the placebo group.[19] Nieman *et al.* (2012) detected no significant differences in biomarkers of inflammation, oxidative stress, and other parameters related to obesity in the subjects after 4 weeks of supplementation with a mixture of 112 mg curcumin extract and 10 mg capsaicin. However, it is known that these two chemicals have high anti-oxidant effects and the results may be influenced by the high doses used in this study.[20] Curcumin can suppress mitogen activated protein kinase (MAPK) which plays an important role in differentiation of preadipocytes into adipocytes and activation of the adipocyte differentiation signaling

Table 1. Efficacy and mechanism of action of *Aloe vera*, *Cinnamomum zeylanicum*, *Curcuma longa*, *Garcinia cambogia*, and *Garcinia mangostana* on obesity treatment and body weight reduction

Author	Research Method	Subjects	Results								
			Body weight	BMI	WC	Serum TG	Total cholesterol	LDL	Fat mass (%)	Active compo	Mechanism of action
1. *Aloe vera*											
Choi *et al.*, 2013	Double blind RCT	n=136 subjects, divided into intervention group (n=68) and placebo group (n=68)	↓	↓	-	-	-	-	-	Phytosterol	Phytosterol → PPARγ expression ↓ → adipocytokine activation ↓ → adiponektin ↓
2. *Cinnamomum zeylanicum*											
Borzoei *et al.*, 2018	Double blind RCT	84 subjects with overweight or PCOS, divided into intervention group (n=42) and placebo group (n=42)	↓	↓	-	↓	-	-	-	Cinnam-aldehyde, cinnamic acid, flavonoid, phenol	Flavanoid → thermogenic gene expression ↑ → thermogenesis ↑ → subcutaneous adipocyte metabolism ↑
Jain *et al.*, 2017	Double blind RCT	116 subjects with metabolic syndrome, divided into intervention group (n=58) and placebo group (n=58)	↓	-	↓	-	↓	↓	-		
Whitfield *et al.*, 2015	Cross over RCT	12 subjects	↓	-	-	-	↓	↓	-		
3. *Curcuma longa*											
Leray *et al.*, 2011	Cross over study	Obese cats	-	-	↓	↓	-	-	-	Curcumin	Curcumin → MAPK activity ↓ → adipocyte differentiation ↓ → lipid accumulation ↓ Curcumin → inflammatory mediators ↓ → systemic inflammation ↓ → improved lipid metabolism
Saraf-Bank *et al.*, 2019	Randomized placebo-controlled clinical trial	60 female subjects (13-18 years old), divided into intervention and placebo group	↓	↓	↓	-	-	-	-		
Nieman *et al.*, 2012	Randomized placebo-controlled crossover study	62 female subjects with overweight and obesity, divided into 3 groups: group supplemented with capsaicin, curcumin, and placebo	-	-	-	-	-	-	-		

4. *Garcinia cambogia*											
Kim *et al.*, 2011	RCT	68 overweight subjects (BMI: 23-29 m/kg^2), divided into intervention and placebo groups	-	-	-	-	-	-	-	HCA	HCA → competitive inhibitor of ATP-citrate lyase → inhibition of conversion of citrate into oxaloacetate and acetyl-coA → lypogenic activity ↓
Vasques *et al.*, 2013	Double blind RCT	60 female subjects with BMI≥25 kg/m^2 (25-60 years old), divided into intervention and placebo	-	-	-	↓	-	-	-		
5. *Garcinia mangostana*											
Kudiganti *et al.*, 2016	Double blind RCT	60 subjects (average of BMI=28.3 kg/m^2), divided into intervention group (n=30) and placebo group (n=30)	↓	↓	-	-	↓	↓	-	Xanthone, alpha-mangostin, gamma-mangostin, dan HCA	Xanthone → PPARγ expression ↓ → aktivation of adipocytokine ↓ → adiponektin expression ↓ Alpha-mangostin, gamma-mangostin → adipogenesis ↓ and inflammation ↓ HCA → competitive inhibitor for ATP-citrate lyase → inhibition of the conversion of citrate into oxaloacetate and acetyl-coA → lypogenic metabolism ↓
Stern *et al.*, 2013	Double blind RCT	100 subjects (BMI 30-40 kg/m^2), divided into intervention group (n=50) and placebo group (n=50)	↓	↓	↓	-	-	-	-		
Watanabe *et al.*, 2018	RCT	22 subjects (BMI ≥ 30 kg/m^2 and bodyweight < 135 kg), divided into extract supplementation + behavioral intervention (n=11) and behavioral intervention only (n=11)	↓	↓	↓	-	-	-	↓		

BMI: body mass index; WC: waist circumference; PCOS: polycystic ovary syndrome; HCA: hydroxycitric acid;

cascade. When MAPK is suppressed, adipocyte differentiation is inhibited preventing the formation of large adipocytes and fat accumulation. Curcumin also plays a pivotal role in reducing inflammatory mediators, leptin, and blocking leptin receptors in adipose tissue, thereby suppressing systemic inflammation due to obesity.[21]

Garcinia cambogia

Garcinia cambogia grows in Southeast Asia and is native to Indonesia. The genus Garcinia is belongs to the family Clusiaceae, with more than 300 species of trees and shrubs, and has a green fruit.[25] According to Kim *et al.* (2011), there was no significant difference in body weight and body mass index in the group supplemented with *Garcinia cambogia* compared to the placebo group.[23] Vasques *et al.* (2014) reported that *Garcinia cambogia* can be an alternative to control and lose weight by affecting the peripheral metabolic profile. *Garcinia cambogia* extract contains hydroxycitric acid (HCA), a competitive inhibitor of ATP-citrate lyase, an enzyme that catalyzes the breakdown of citrate into oxaloacetate and acetyl-CoA, thereby inhibiting endogenous lypogenic activity.[24] Previous animal studies have shown that HCA promotes the oxidation of fatty acids and improves the lipid profile.[24] Also, HCA in *Garcinia cambogia* can reduce fat production and appetite.[26] The active substance possessed by Garcinia cambogia predominantly works in liver and brain tissues. Animal studies also revealed that HCA inhibits adenosine triphosphate citrate lyase, which breaks down citrate into acetyl coenzyme A (acetyl-CoA) and oxaloacetate in the citric acid cycle in the liver. Acetyl-CoA is required for fatty acid synthesis and lipogenesis. HCA causes decreased acetyl-CoA production, thereby reducing fatty acid synthesis and lipogenesis. In addition, acetyl-CoA is a precursor of malonyl-CoA, which inhibits carnitine palmitoyltransferase I (CPT 1), one of the most important enzymes in lipid oxidation. The limited production of malonyl-CoA, decreased inhibition of CPT 1 and increased lipid oxidation reduce the fat mass, although it must be followed by aerobic physical activity.[25]

Mangosteen plant *(Garcinia mangostana)*

Kudiganti *et al.* (2016) and Stern *et al.* (2013) reported that *Garcinia mangostana* extract inhibits de novo lipogenesis and increases fat burning through beta-oxidation, as well as inhibiting adipogenic differentiation and increasing lipid breakdown in mature fat cells. As well as anti-obesity effects, *Garcinia mangostana* extract can also maintain lipid profiles in the normal range in overweight subjects.[27] Watanabe *et al.* (2018) observed no significant differences between the group given mangosteen peel extract and the placebo group but both groups experienced weight loss. This study stated that mangosteen has the potential to help manage obesity and its comorbidities but had several limitations. The absence of a significant difference between the two groups may be due to small sample, some participants having other abnormal conditions such as insulin resistance, the short study duration, and only one gender was included in the study.[28] The main active substances contained in the mangosteen plant are xanthones and the predominant xanthones contained in the mangosteen fruit are alpha-mangostin and gamma-mangostin.[16] Xanthones show antiadipogenic effects and suppress PPARã activity, while alpha-mangostin and gamma-mangostin suppress adipogenesis and inhibit inflammatory receptors, cyclic adenosine monophosphate (cAMP) phosphodiesterase, activity of cyclo-oxygenase-1 (COX-1) and COX-2, and the conversion of arachidonic acid to prostaglandin E2. These anti-inflammatory effects stabilize the condition of lipid metabolism in obese people.[29] In addition to xanthones, another active component in mangosteen fruit is HCA, which is essential in providing anti-obesity effects. HCA can inhibit weight gain by suppressing adenosine triphosphate (ATP)-citrate lyase, an enzyme that plays a role in catalyzing citrate to oxaloacetate and acetyl-CoA, thereby inhibiting fat synthesis.[30]

CONCLUSION

In conclusion, extracts of *Aloe vera*, *Cinnammum zeylanicum*, *Curcuma longa*, *Garcinia cambogia*, and *Garcinia mangostana* have the potential to be used for weight management but further research is necessary to determine their mechanisms of action.

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Conflict of Interest

The authors declare no conflict of interests in this work.

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