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REVIEW

A systematic review of the anti-obesity and weight lowering effect of ginger (*Zingiber officinale Roscoe*) and its mechanisms of action

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Recently, the beneficial effects of ginger on obesity is taken into consideration. Albeit, it seems that the anti-obesity effect of ginger and its mechanism of action has not yet been reviewed. Therefore, the aim of this study was to systematically review the effect of *Zingiber officinale Roscoe* on obesity management. Databases including PubMed, Scopus, Google scholar, and Science Direct were searched from 1995 until May 2017 using the definitive keywords. Searching was limited to articles with English language. All of the relevant human and animal studies and also in vitro studies were included. Review articles, abstract in congress, and also other varieties of ginger were excluded. Eligibility of included articles were evaluated by 3 reviewers, which also extracted data. Articles were critically assessed individually for possible risk of bias. Twenty-seven articles (6 in vitro, 17 animal, and 4 human studies) were reviewed. Most of the experimental studies supported the weight lowering effect of ginger extract or powder in obese animal models, whereas the results of the available limited clinical studies showed no changes or slight changes of anthropometric measurements and body composition in subjects with obesity. Ginger could modulate obesity through various potential mechanisms including increasing thermogenesis, increasing lipolysis, suppression of lipogenesis, inhibition of intestinal fat absorption, and controlling appetite. This review article provides some convincing evidence to support the efficacy of ginger in obesity management and demonstrates the importance of future clinical trials.

KEYWORDS

appetite, body fat, ginger, obesity, overweight, *Zingiber officinale*

1 | INTRODUCTION

The global epidemic of obesity is a major contributor to the increasing prevalence of chronic diseases like Type 2 diabetes mellitus, hypertension, cardiovascular diseases, and some types of cancer (Racette, Deusinger, & Deusinger, 2003; Smith, 2012). The World Health Organization has reported that more than 1.6 billion adults (≥15 years) are with overweight and at least 400 million adults are affected by obesity (Baalwa, Byarugaba, Kabagambe, & Otim, 2010).

The prior intervention for obesity management is dietary modification and increasing physical activity. However, pharmacologic

Abbreviations: 5-HT:, 5-hydroxytryptamine; BMI:, body mass index; C/EBP-α:, CCAAT/enhancer-binding protein alpha; cAMP:, cyclic-adenosine monophosphate; CKD:, chronic kidney disease; FAS:, fatty acid synthase; FBS:, fasting blood sugar; GEO:, ginger essential oil; HFD:, high fat diet; HOMA-IR:, homeostatic model assessment-insulin resistance; HSL:, hormone sensitive lipase; JNK:, c-Jun-NH2-terminal kinase; NAFLD:, non-alcoholic fatty liver disease; NE:, norepinephrine; PPARγ:, peroxisome proliferator-activated receptor gamma; PPARδ (β):, peroxisome proliferator-activated receptor sigma/beta; QUICKI:, quantitative insulin sensitivity check index; RCT:, randomized clinical trial; T2DM:, Type 2 diabetes mellitus; TRPV1:, transient receptor potential vanilloid Type 1; UCP-1:, uncoupling Protein 1

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treatment such as sibutramine, orlistat, phentermine, diethylpropion, and fluoxetin are used in some circumstances (Bray & Ryan, 2012). Despite short-term benefits of the anti-obesity drugs, the potential for drug abuse, weight gain after their withdrawal, and some other side effects along with their high costs are of important barriers to use (Ioannides-Demos, Proietto, Tonkin, & McNeil, 2006).

Medicinal plants have long been used around the world to treat a lot of diseases and also to reduce body weight and obesity related complications (Bray & Ryan, 2012). There are promising reports of different anti-obesogenic phytochemicals (Bahmani et al., 2016; Farhat, Drummond, & Al-Dujaili, 2017; Ríos-Hoyo & Gutiérrez-Salmeán, 2016; Stohs & Badmaev, 2016).

Ginger (*Zingiber officinale Roscoe*, family Zingiberaceae) is one of the most widely used spices and medicinal plants. Ginger contains volatile oils (1% to 3%) including terpenoids such as zingiberene and pungent components such as gingerol, shogaol, and zingerone. Among them, the gingerols and shogaols are considered as the major bioactive constituents of fresh and dried ginger, respectively (Ali, Blunden, Tanira, & Nemmar, 2008; Mahmoud & Elnour, 2013; Nammi, Sreemantula, & Roufogalis, 2009).

In traditional medicine, ginger powder is prescribed for some ailments such as vomiting, indigestion, joint and muscular pain, and cold (Ali et al., 2008). Moreover, its various pharmacological effects have been reported including antiemetic (Palatty, Haniadka, Valder, Arora, & Baliga, 2013), anti-inflammatory and antioxidant (Grzanna, Lindmark, & Frondoza, 2005; Mashhadi et al., 2013), glucose and lipid lowering (Li, Tran, Duke, & Roufogalis, 2012; Mahluji et al., 2013), and anticancer effects (Pereira, Haniadka, Chacko, Palatty, & Baliga, 2011; Thamlikitkul, Srimuninnimit, Akewanlop, et al., 2017).

The beneficial effects of *Zingiber officinale* regarding the obesity management including its prevention and treatment has also been recently considered, and there are some promising results from experimental studies (Ahn & Oh, 2012; Goyal & Kadnur, 2006; Lai, Lee, Lin, et al., 2016; Li et al., 2014; Mahmoud & Elnour, 2013; Malik & Sharmaa, 2011; Nammi et al., 2009; Okamoto, Irii, Tahara, et al., 2011; Pulbutr, Thunchomnang, Lawa, Mangkhalathon, & Saenubol, 2011; Saravanan, Ponmurugan, Deepa, & Senthilkumar, 2014).

However, scientific researches in humans and clinical trials are very limited (Atashak, Peeri, Azarbayjani, Stannard, & Mosalman, 2011; Ebrahimzadeh Attari, Asghari Jafarabadi, Zemestani, & Ostadrahimi, 2015; Ebrahimzadeh Attari, Ostadrahimi, Asghari Jafarabadi, Mehralizadeh, & Mahluji, 2016 and Mansour et al., 2012). It is hypothesized that the rhizomes of ginger and its extract could influence many key features of the obesity through different mechanisms such as increasing thermogenesis and energy expenditure, increasing the lipolysis, inhibition of the intestinal absorption of dietary fat, and controlling the appetite (Ebrahimzadeh Attari et al., 2015). Although there are some review articles on different medicinal properties of ginger, it seems that the weight lowering and anti-obesity effect of ginger has not yet been reviewed. Therefore, the present study was aimed to systematically review the effect of *Zingiber officinale Roscoe* on obesity management (e.g., anthropometric measurements, body composition, and appetite) in healthy obese/overweight human subjects and animal models.

2 | METHODS

2.1 | Articles' selection

We searched databases of PubMed, Scopus, Google scholar, and Science Direct from 1995 until May 2017. The search terms were "*Zingiber officinale Roscoe*" or "ginger" and "overweight" or "obesity" or "body fat" or "appetite." Searching was limited to articles with English language. All of the relevant human and animal studies and also in vitro studies were included. The references of those articles were also checked to find possible new studies. Review articles, abstract in congress, and articles about the effects of ginger mixed with other plants and also the wild type of ginger (*Zingiber mioga*) or bitter ginger (*Zingiber zerumbet*) were excluded. In addition, articles about the effects of ginger in other disease were also excluded. To reduce duplication data, searching was conducted by one person (V. E.), and then, three reviewers (V. E., A. M., S. M.) studied the articles and extracted data independently, and any irrelevant paper was excluded. Generally, there was agreement among reviewers' decision, and some differences were resolved by the 4th reviewer (Z. J.). Based on the defined keywords and the above mentioned inclusion criteria, 27 articles were selected and reviewed (6 in vitro, 17 animal, and 4 human studies). Figure 1 shows the flowchart of screening and selecting articles. Characteristics of eligible studies have been summarized in Tables 1–3.

2.2 | Risk of bias assessment

All of the eligible articles were critically assessed individually for possible risk of bias. The risk of bias was judged, using the Cochrane Collaboration's tool (Higgins, Altman, Gøtzsche, et al., 2011), for randomized clinical trials and SYRCLE's risk of bias tool (Hooijmans et al., 2014) for animal studies. In vitro studies were also assessed based on Checklist for Reporting in vitro Studies guideline (Krithikadatta, Gopikrishna, & Datta, 2014). The SYRCLE's risk of bias tool is based on the Cochrane tool and has been adjusted for aspects of bias that play a specific role in animal intervention. Both of tools have six domains as shown in Figure 2. Accordingly, each domain was assessed as having a low, unclear, or high risk of bias.

3 | RESULTS AND DISCUSSION

3.1 | Methodological quality and risk of bias

Risk of bias was assessed for clinical trials, animal studies, and in vitro studies. An unclear risk of selection bias (due to lack of information on the method of randomization n = 25 and concealment, n = 27), performance bias (due to lack of information on blinding of participants and personnel, n = 25), and detection bias (blinding of outcome assessment, n = 26) was observed. The risk of bias for the included studies was low for reporting bias and attrition bias (Figure 2).

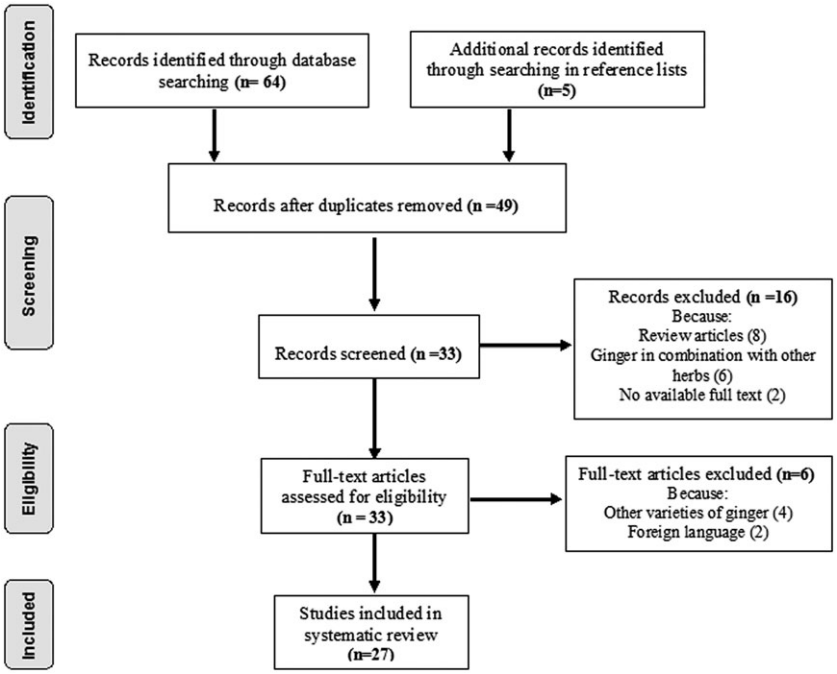


FIGURE 1 Flowchart of screening and choosing eligible articles

3.2 | Effects of ginger on obesity management and its potential mechanisms

The related studies were classified into two groups: human and animal/in vitro studies.

3.2.1 | Human studies

To the best of our knowledge, the effect of ginger supplementation on healthy obese/overweight subjects was reported just in four studies. In the study of Atashak et al. (2011) with low sample size (n = 8 in each group), ginger consumption versus placebo (1 g/day) for 10 weeks did not cause any significant changes on anthropometric parameters and body composition in men with obesity.

Recently, we conducted a double blind randomized controlled trial in 80 healthy women with obesity (Ebrahimzadeh Attari et al., 2016). According to our findings, ginger supplementation (2 g/day ginger powder) for 12 weeks caused a slight but significant decrease of the body weight, body mass index, waist, and hip circumferences as compared to the placebo, whereas there was no significant difference in changes of body composition between groups. Moreover, the other finding of our study was a significant reduction of total appetite score in ginger versus placebo group, whereas there were no significant differences between groups in energy and macronutrients intake (Ebrahimzadeh Attari et al., 2015). In agreement, Mansour et al. (2012) showed that drinking a single dose of ginger beverage (containing 2 g ginger powder) before a standard breakfast decreased the appetite and increased the satiety and fullness in overweight men (n = 10), compared to the control group.

Moreover, there are a few studies that examined the effect of ginger on weight changes (as a secondary objective) in obese/overweight patients with diabetes, chronic kidney disease, or non-alcoholic fatty liver disease (Imani et al., 2015; Mozaffari-Khosravi, Talaei, Jalali, Najarzadeh, & Mozayan, 2014; Rahimlou, Yari, Hekmatdoost, Alavian, & Keshavarz, 2016).

Mozaffari-Khosravi et al. (2014) demonstrated that supplementation with ginger powder (3 g for 8 weeks) in Type 2 diabetes mellitus patients had no significant effect on body weight compared to the placebo. Moreover, Imani et al. (2015) reported that 1-gram ginger powder intake for 10 weeks in peritoneal dialysis patients had no significant effect on body weight compared to the placebo. In a recent study, Rahimlou et al. (2016) examined the effect of 2 g/day ginger powder supplementation or the identical placebo for 12 weeks in 44 patients with non-alcoholic fatty liver disease. According to the results, anthropometric measures, including weight, body mass index, waist and hip circumference, and waist-to-hip ratio decreased significantly in both groups without any significant differences between groups. However, hip circumference reduced significantly more in the ginger group.

3.2.2 | Animal studies

The weight lowering effect of *Zingiber officinale* is supported by findings from different in vitro and animal studies as shown in Tables 1 and 2. The effects of ginger extracts or its active components were examined in those animal models either to prevent or treat obesity. Recently, Suk, Kwon, Lee, et al., 2017 reported that administration of gingerenone A for 15 weeks to high fat diet (HFD)-fed mice caused significant decrease of weight gain and adipocyte size versus HFD control group. Lai et al. (2016) showed that oral feeding of ginger essential oil significantly decreased weight gain and hepatic lipid accumulation in HFD-fed mice. Moreover, in obesity treatment arm, studies on HFD induced obese rats showed significant decrease of body weight and fat by administration of 6-gingerol (Brahma Naidu, Uddandrao, Ravindar Naik, et al., 2016; Saravanan et al., 2014) and also ginger aqueous extract (Ismail, 2014; Nazish, Ansari, Arora, & Ahmad, 2016; Shalaby & Saifan, 2014).

Results of in vitro studies also indicated that treatment of 3T3-L1 preadipocytes with bioactive components of ginger such as 6-shogaol,

TABLE 1 Characteristic of in vitro studies regarding the effect of *Zingiber officinale* on obesity related parameters

Author/date	Subjects	Treatment	Dosage	Duration	Results	Reference
Suk et al. (2016)	3T3-L1 preadipocytes	6-shogaol or 6-gingerol	10, 20, and 40 μM	3 days	(1) 6-Shogaol at 40 μM dose inhibited adipogenesis and decreases expression of various adipogenic/lipogenic marker proteins more potentially than 6-gingerol (2) 6-Shogaol and not 6-gingerol increased lipolysis in mature adipocytes	57
Li and Zhou (2015)	3T3-L1 preadipocytes	6-gingerol	5, 10, and 15 μg/ml	7 days	(1) Inhibition of the adipogenic differentiation via activation of the Wnt/β-catenin signaling pathway (2) ↓Expression of adipogenic transcription factors such as PPARγ and C/EBP-α	31
Tzeng and Liu (2013)	3T3-L1 preadipocytes	6-gingerol	5, 10, and 15 μg/ml	8 days	Inhibition of the adipogenic differentiation through downregulation of PPARγ and C/EBP-α and the subsequent inhibition of FAS and aP2 expression	60
Ahn and Oh (2012)	3T3-L1 preadipocytes	Galanolactone isolated from *Zingiber officinale* extract	50 and 100 μM	8 days	(1) Suppressed adipocyte differentiation and lipid droplet accumulation in a dose-dependent manner (2) ↓Expression of adipogenic transcription factors and adipogenic marker genes	2
Pulbutr et al. (2011)	Adipocytes isolated from normal pellet diet (NPD)-fed rats and high fat diet (HFD)-fed rats	Zingerone	10, 100, and 1,000 μM	—	Zingerone only at the concentration of 100 μM increased isoprenaline (0.l μM)-induced lipolysis in adipocytes of NPD and HFD. In addition, it was increased the basal lipolysis in adipocytes derived from the NPD-fed rats	48
Isa et al. (2008)	3T3-L1 preadipocytes	6-shogaol or 6-gingerol	10 and 25 μM	1 hr	(1) Inhibition of the TNFα-mediated downregulation of adiponectin expression 2) PPARγ agonistic effect by 6-shogaol and its transactivation (3) Inhibition of TNFα- induced c-Jun-NH2-terminal kinase signaling activation (JNK) by 6-gingerol	24

Note. PPARγ = peroxisome proliferator-activated receptor gamma; C/EBP-α = CCAAT/enhancer-binding protein alpha; FAS = fatty acid synthase.

TABLE 2 Characteristic of animal studies regarding the effect of *Zingiber officinale* on obesity related parameters

Author/date	Subjects	Intervention	Dosage	Duration	Results[a]	Reference
Sampath, Rashid, Sang, and Ahmedna (2017)	HFD fed mice	[6]-gingerol	25 and 75 mg/kg	17 weeks	↓Liver weight, plasma glucose, alanine aminotransferase, aspartate aminotransferase, AGEs and insulin levels vs. HFD control group	52
Suk et al. (2017)	HFD fed mice	Gingerenone A	10 and 50 mg/kg	15 weeks	↓Weight gain and adipocyte size, ↓circulating free fatty acid levels, and regulates fatty acid metabolism and mitochondrial biogenesis via activation of AMPK in adipose tissue vs. HFD control group	57
Lai et al. (2016)	HFD fed mice	Ginger essential oil (GEO)	12.5, 62.5, and 125 mg/kg	12 weeks	↓Weight gain, ↓serum free fatty acid, triglyceride and total cholesterol, ↓hepatic lipid accumulation	30
Brahma Naidu et al. (2016)	HFD induced obese rats	[6]-gingerol	75 mg kg	30 days	↓Body weight, plasma glucose, insulin levels, and insulin resistance ↓activity of lipid marker enzymes (HMG-CoA reductase, FAS, PPARγ, and SREBP1c) and inflammatory markers	8
Nazish et al. (2016)	HFD induced obese rats	Aqueous *Zingiber officinale* extract.	20 mg/kg body weight (b.w)	42 days	↓Body weight and serum insulin, leptin, and lipids levels vs. HFD control group ↑ high density lipoprotein (HDL-C)	44
Misawa et al. (2015)	HFD fed mice	Ginger ethanol extract	0.3% of diet weight	18 weeks	↓Weight gain, ↓fat accumulation, ↑energy expenditure	41
Saravanan et al. (2014)	HFD induced obese rats	[6]-gingerol	25, 50, 75 mg/kg b.w	10 weeks	↓Body weight, ↓adipose tissue, ↓serum leptin, glucose, insulin, and lipid profile vs. control group especially in 75 mg/kg/day dose of gingerol	53
Li et al. (2014)	High-fat high-carbohydrate diet-fed rats	Ginger extract	100, 200 mg/kg b.w	10 weeks	↓Weight gain, slightly and non sig. And a marked reduction in blood glucose in the high-dose ginger extract (200 mg/kg) vs. control group	33
Shalaby and Saifan (2014)	HFD induced obese rats	Ginger aqueous extract	200, 400 mg/kg b.w	6 weeks	↓Body weight, ↓adipose tissue, ↓serum leptin, glucose, lipid profile, and liver enzymes vs. control group	54
Ismail (2014)	HFD induced obese rats	Ginger aqueous extract	100, 200 mg/kg b.w	6 weeks	↓Body weight, ↓adipose tissue, ↓serum leptin, glucose, and lipid profile vs. control group	25
Mahmoud and Elnour (2013)	HFD fed rats	Ginger powder	5% of diet weight	4 weeks	↓Weight gain and ↓ serum lipid profile vs. control group	36
Wadikar and Premavalli (2011)	Rats on a normal diet	Ginger juice	12 ml ginger juice 12%	10 days	↑Food consumption, ↑ weight gain, and ↓serum leptin level	61
Okamoto et al. (2011)	HFD fed rats	[6]-gingerol or aza-[6]-gingerol (A6G)	0.06% of diet weight	12 weeks	↓Weight gain, ↓fat accumulation and ↓serum glucose, insulin, and leptin vs. control group	45
Malik and Sharmaa (2011)	HFD fed rats and HFD induced obese rats	Lyophilized ginger juice	0.25, 0.5, 1 mg/kg b.w	8 weeks	↓Weight gain, ↓adipose tissue and ↓serum glucose, and lipid profile vs. control group	37
Beattie, Nicol, Gordon, et al. (2011)	HFD fed mice	[6]-gingerol	0.05% of diet weight	6 weeks	↓Weight gain, ↓adipose tissue and ↓serum triglyceride ↑ HDL-C, and ↑expression of fatty acids' beta-oxidation enzymes such as acetyl-coenzyme A acyltransferase 1 and enoyl CoA hydratase vs. control group	7
Nammi et al. (2009)	HFD fed rats	Ethanolic extract of ginger	100, 200, and 400 mg/kg b.w	6 weeks	↓Weight gain and ↓ serum glucose, insulin, and lipid profile vs. control group especially in 75 mg/kg/day dose of gingerol lipid profile vs. control group	43
Goyal and Kadnur (2006)	Goldthioglucose induced obese rats	Methanol and ethyl acetate extracts of ginger	250 mg/kg b.w	8 weeks	↓Body weight, ↓serum glucose, insulin, and lipid profile vs. control group	16

Note. HFD = high fat diet; FAS = fatty acid synthase; PPARγ = peroxisome proliferator-activated receptor gamma.

[a]All the changes were statistically significant unless otherwise noted.

TABLE 3 Characteristic of human studies regarding the effect of *Zingiber officinale* on obesity related parameters

Author/date	Subjects	Intervention	Dosage	Duration	Results[a]	Reference
Ebrahimzadeh Attari et al. (2015, 2016)	Women with obesity (*n* = 40 per group)	Ginger powder	2 g/day	12 weeks	↓BMI, ↓ anthropometric measurements, ↓serum insulin, HOMA-IR index, ↑ QUICKI indexes as compared to the placebo	12, 13
Mansour et al. (2012)	Men with overweight (*n* = 10 per group)	Ginger powder	2 g dissolved in a hot water beverage	A single dose	↓Hunger, ↓ prospective food intake, ↑fullness vs. placebo group	38
Atashak et al. (2011)	Men with obesity (*n* = 8 per group)	Ginger powder	1 g/day	10 weeks	Non-significant changes of anthropometric indices and body composition in ginger alone vs. placebo group	4

Note. BMI = body mass index; HOMA-IR = homeostatic model assessment-insulin resistance; QUICKI = quantitative insulin sensitivity check index.

[a]All the changes were statistically significant unless otherwise noted.

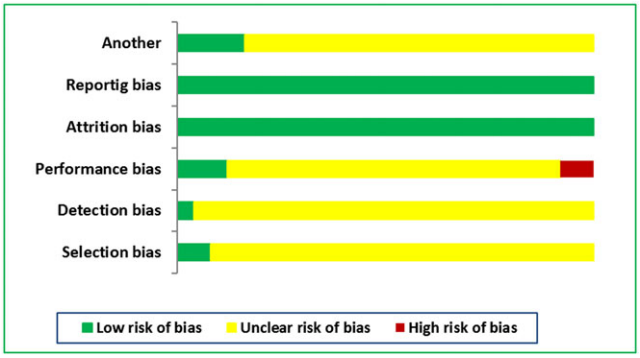


FIGURE 2 Risk of bias assessment across the studies (*n* = 27) [Colour figure can be viewed at wileyonlinelibrary.com]

6-gingerol, or galanolactone suppressed adipocyte differentiation and decreased the expression of adipogenic transcription factors such as peroxisome proliferator-activated receptor gamma (PPAR-γ) and CCAAT/enhancer-binding protein alpha (Ahn & Oh, 2012; Li & Zhou, 2015; Suk, Seo, Yu, et al., 2016; Tzeng & Liu, 2013) and also increased lipolysis in adipocytes (Pulbutr et al., 2011; Suk et al., 2016).

3.3 | Mechanisms of action

The exact mechanisms of the anti-obesity action of ginger are not fully known. However, some default mechanisms through which *Zingiber officinale* could influence body weight and body composition are described below and also summarized in Figure 3. It seems that the pungent components of ginger (gingerols, shogaol, and other polyphenols) are mostly responsible for its various pharmacological effects including the weight lowering effect (Mahmoud & Elnour, 2013; Nammi et al., 2009)

1. **Increasing thermogenesis and energy expenditure**: It was reported that ginger components have some catecholamine-releasing action that affect the beta adrenergic receptors and activate the sympathetic nerve system and then increase the expression and synthesis of uncoupling protein 1 and thermogenesis (Fujisawa, Nadamoto, & Fushiki, 2005; Iwasaki, Morita, Iwasawa, et al., 2006; Mansour et al., 2012; Pulbutr et al., 2011).
2. **Increasing lipolysis**: Ginger consumption can increase the activity of hormone sensitive lipase enzyme by activating sympathetic nerve system and therefore increase the lipolysis of white adipose tissue (Ahn & Oh, 2012; Iwasaki et al., 2006; Pulbutr et al., 2011).
3. **Suppression of lipogenesis and lipid accumulation**: It was reported that the active components of ginger could have the agonistic activity toward peroxisome proliferator-activated receptor sigma/beta and increased peroxisome proliferator-activated receptor delta-dependent gene expression and decrease lipid deposition in the skeletal muscle and adipose tissue (Chung, Kim, Chung, et al., 2009; Misawa et al., 2015). Ginger compounds may also decrease the expression of some enzymes involved in the lipogenesis, for example, fatty acid synthase and acetyl CoA carboxylase (Okamoto et al., 2011).
4. **Suppression of adipogenesis**: It was reported that treatment with active components of ginger reduced the adipogenesis in adipocytes (3T3-L1), maybe by decreasing the expression of PPARγ-associated genes (Ahn & Oh, 2012; Tzeng & Liu, 2013). However, there are some controversy toward the agonistic (Ahn & Oh, 2012; Tzeng & Liu, 2013) or antagonistic effects (Chung et al., 2009; de Las, Valero-Muñoz, Martín-Fernández, et al., 2017; Isa, Miyakawa, Yanagisawa, et al., 2008) of ginger on PPARγ.
5. **Inhibition of intestinal absorption of dietary fat**: It was reported that ginger could suppress the pancreatic lipase enzyme and decrease intestinal absorption of dietary fat that was comparable with the orlistat effect in animal model (Mahmoud & Elnour, 2013).
6. **Controlling appetite**: It seems that ginger supplementation may decrease the appetite (Ebrahimzadeh Attari et al., 2015; Mansour et al., 2012); albeit, there is not a full agreement toward this idea (Abd Allah, Makboul, & Mohamed, 2016; Wadikar & Premavalli, 2011). Two conflicting hypotheses regarding ginger's mechanism of action on appetite have been reported. Generally, ginger has modulatory effect on 5-hydroxytryptamine (5-HT; serotonin). It was reported that the main constitutes of ginger could control the appetite, maybe through binding to 5-HT_{2c} receptors in the central nervous system (Goyal & Kadnur, 2006; Mansour et al., 2012; Palatty et al., 2013). However, according to the other

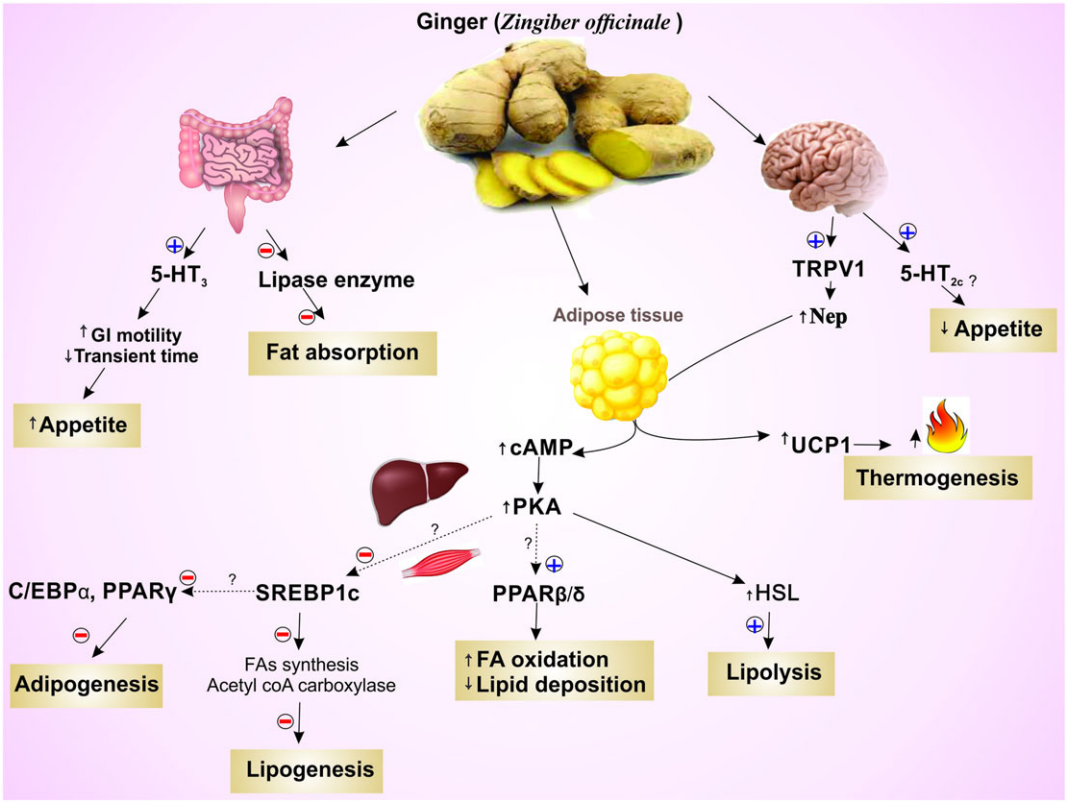


FIGURE 3 Some default mechanisms of the weight lowering effect of ginger. Active components of ginger seem to have agonistic effect on transient receptor potential vanilloid Type 1 (TRPV1) as one of the temperature sensors and cause the activation of sympathetic nerve system and release of norepinephrine (NE). The sympathomimetic effect of ginger has some important effects in adipose tissue such as increasing the expression of uncoupling protein-1 (UCP-1) and thermogenesis along with the high production of cAMP that increases the hormone sensitive lipase (HSL) activity and lipolysis. Moreover, the active components of ginger have the agonistic activity toward peroxisome proliferator-activated receptor sigma/beta [PPARδ (β)] and decrease the expression of some enzymes involved in the lipogenesis, for example, fatty acid synthase and acetyl CoA carboxylase in the skeletal muscle, liver, and adipose tissue, maybe through rising cAMP and intermediates. One of the other ginger's mechanisms of action may be the reduction of adipogenesis through decreasing the expression of peroxisome proliferator-activated receptor gamma (PPARγ). Ginger can also suppress intestinal absorption of dietary fat by decreasing lipase enzyme. In addition, ginger has modulatory effects on 5-hydroxy tryptamine (5-HT; serotonin) and its receptors. Ginger can decrease the appetite, maybe through binding to 5-HT_{2c} receptors in the central nervous system. On the other hand, ginger may act as an appetizer through intestinal 5-HT_3 receptors [Colour figure can be viewed at wileyonlinelibrary.com]

hypothesis, ginger may act as an appetizer through a modulatory effect on intestinal 5-HT receptors (may be 5-HT_3) that increases gastrointestinal tract peristalsis and decrease the food transit time (Abd Allah et al., 2016; Hu, Rayner, Wu, et al., 2011; Jin et al., 2014; Lua, Salihah, & Mazlan, 2015; Micklefield et al., 1999; Wu, Rayner, Chuah, et al., 2008) and although by decreasing leptin levels (Ismail, 2014; Okamoto et al., 2011; Saravanan et al., 2014; Shalaby & Saifan, 2014; Wadikar & Premavalli, 2011).

3.4 | Limitations

Although systematic reviews are at the top in the hierarchy of the clinical evidence (Izzo, Hoon-Kim, Radhakrishnan, & Williamson, 2016), there are some limitations toward them. In the present study, the first limitation is the few number of related clinical trials, whereas the number of experimental studies is increasing and most of them have almost similar research methodology. Moreover, according to risk of bias assessment, all of the experimental studies had unclear risk of bias on randomization, allocation concealment, and blinding methods due to lack of reporting. Because the clinical studies are often justified based on the results of animal studies, a recent systematic review indicated the need for randomization, allocation concealment, and blinding outcome assessment of animal studies to decrease the risk of bias (Hirst, Howick, Aronson, et al., 2014).

4 | CONCLUSION

The health-promoting properties of ginger as a complementary treatment in different diseases are well known. During this review article, it was also tried to provide convincing evidence regarding the efficacy of ginger in obesity management and its mechanisms of action. Overall, there is an agreement on the efficient weight lowering effect of *Zingiber officinale* in animal models of obesity, whereas the results of the available limited clinical studies showed no changes or slight changes of anthropometric measurements and body composition in subjects with obesity. However, it should be noticed that most of the animal studies used ginger extract or its bioactive compounds in high doses instead of ginger powder. Generally, given the lack of enough

clinical data in this area, more randomized controlled clinical trials are needed to make a definitive conclusion.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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