



Anti-obesity activity of *Cymbopogon citratus* (lemongrass): A systematic review

[Actividad antiobesidad de *Cymbopogon citratus* (hierba limón): Una revisión sistemática]

Musthika Wida Mashitah^{1,2*}, Nashi Widodo³, Nur Permatasari⁴, Achmad Rudijanto⁵

¹Department of Nursing, Faculty of Health Sciences, Institute of Technology, Science and Health Dr. Soepraoen Hospital, Malang, 65147, Indonesia.

²Doctoral Program in Medical Science, Faculty of Medicine, Universitas Brawijaya, Malang, 65145, Indonesia.

³Department of Biology, Faculty of Mathematics and Natural Science, Universitas Brawijaya, Malang, 65145, Indonesia.

⁴Department of Pharmacology, Faculty of Medicine, Universitas Brawijaya, Malang, 65145, Indonesia.

⁵Division of Endocrinology and Metabolic Disease, Department of Internal Medicine, Faculty of Medicine, Universitas Brawijaya/Dr. Saiful Anwar Hospital, Malang, 65145, Indonesia.

*E-mail: ns.musthika@itsk-soepraoen.ac.id

Abstract

Context: Obesity represents a significant global health challenge. The limited efficacy and possible side effects of available anti-obesity agents highlight the need to find new, effective, and safe agents. Lemongrass (*Cymbopogon citratus*) is an aromatic herbal plant traditionally used as an anti-obesity agent, but previous review studies did not explain the mechanism in detail.

Aims: To evaluate the anti-obesity activity of *C. citratus* *in vitro*, *in vivo*, and in humans.

Methods: Full-text relevant articles published between 2003 and 2023 were searched through Google Scholar, PubMed, and Scopus. The American Dietetic Association (ADA) quality criteria checklist was used to assess the risk of bias. Data were systematically analysed and presented in tables and flowcharts.

Results: Eighteen articles met the inclusion criteria. The anti-obesity activity of *C. citratus* could come from various parts of the plant (leaves, stalks, roots, or whole plant). Its hydroalcoholic-based extract was rich in polyphenols, which had anti-obesity activity through inhibiting digestive enzymes, appetite suppression, modulation of lipid metabolism, and adipogenesis inhibition. Its essential oil and citral had anti-obesity activity through energy expenditure stimulation, lipid metabolism modulation, and adipogenesis inhibition. Dietary fibre from *C. citratus* had anti-obesity activity by inhibiting digestive enzymes and modulating lipid metabolism.

Conclusions: The anti-obesity activity of *C. citratus* could come from its polyphenol content, essential oil, or fibre through the same or different mechanisms, namely inhibition of digestive enzymes, suppression of appetite, modulation of lipid metabolism, inhibition of adipogenesis, and stimulation of energy expenditure.

Keywords: anti-obesity; *Cymbopogon citratus*; lemongrass.

Resumen

Contexto: La obesidad representa un importante desafío para la salud mundial. La eficacia limitada y los posibles efectos secundarios de los agentes contra la obesidad disponibles resaltan la necesidad de encontrar agentes nuevos, eficaces y seguros. La hierba limón (*Cymbopogon citratus*) es una planta herbaria aromática utilizada tradicionalmente como agente contra la obesidad, pero estudios de revisión anteriores no explicaron el mecanismo en detalle.

Objetivos: Evaluar la actividad antiobesidad de *C. citratus* *in vitro*, *in vivo* y en humanos.

Métodos: Se buscaron artículos relevantes de texto completo publicados entre 2003 y 2023 a través de Google Scholar, PubMed y Scopus. Se utilizó la lista de verificación de criterios de calidad de la Asociación Dietética Americana (ADA) para evaluar el riesgo de sesgo. Los datos fueron analizados sistemáticamente y presentados en tablas y diagramas de flujo.

Resultados: Dieciocho artículos cumplieron los criterios de inclusión. La actividad antiobesidad de *C. citratus* podría provenir de varias partes de la planta (hojas, tallos, raíces o planta entera). Su extracto de base hidroalcohólica era rico en polifenoles, que tenían actividad antiobesidad mediante la inhibición de las enzimas digestivas, la supresión del apetito, la modulación del metabolismo de los lípidos y la inhibición de la adipogénesis. Su aceite esencial y citral tenían actividad antiobesidad mediante la estimulación del gasto energético, la modulación del metabolismo de los lípidos y la inhibición de la adipogénesis. La fibra dietética procedente de *C. citratus* tenía actividad antiobesidad al inhibir las enzimas digestivas y modular el metabolismo de los lípidos.

Conclusiones: La actividad antiobesidad de *C. citratus* podría proceder de su contenido en polifenoles, aceite esencial o fibra a través de los mismos o diferentes mecanismos, a saber, inhibición de las enzimas digestivas, supresión del apetito, modulación del metabolismo lipídico, inhibición de la adipogénesis y estimulación del gasto energético.

Palabras Clave: antiobesidad; *Cymbopogon citratus*; hierba limón.

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AUTHOR INFO

ORCID:

[0000-0001-8711-5318](https://orcid.org/0000-0001-8711-5318) (MWM)

[0000-0002-1126-498X](https://orcid.org/0000-0002-1126-498X) (NW)

[0000-0002-1630-1380](https://orcid.org/0000-0002-1630-1380) (NP)

[0000-0003-3380-3208](https://orcid.org/0000-0003-3380-3208) (AR)

INTRODUCTION

Obesity represents a critical global health challenge, posing substantial risks to human health. The prevalence of obesity worldwide has increased in the last 50 years, reaching pandemic levels (Blüher, 2019). In 2016, more than 1.9 billion (39%) adults (≥ 18 years) in the world were overweight, and 650 million (13%) were obese. Overweight and obesity are major risk factors for chronic diseases such as cardiovascular disease, diabetes, musculoskeletal disorders, and some cancers. More than 4 million people died every year from being overweight and obese in 2017 (WHO, 2021).

Obesity is excessive fat accumulation due to energy imbalance, where energy intake exceeds energy expenditure (WHO, 2021). When energy intake chronically exceeds energy expenditure, almost all excess energy is stored as triglycerides in white adipose tissue (WAT). An increase in adipocyte mass can occur due to hypertrophy and hyperplasia of adipocytes, which subsequently causes adipocyte dysfunction, including insulin resistance, production of adipokines, free fatty acids, and inflammatory mediators (Ferranti and Mozaffarian, 2008; Jakab et al., 2021; Spiegelman and Flier, 1996).

Current management of obesity includes lifestyle modification (dietary interventions and physical activity), medication, and bariatric surgery. Lifestyle modification is recommended as a cornerstone of obesity management, but many patients do not achieve long-term benefits due to difficulties with compliance. Pharmacotherapy plays a minor role because of the side effects that can be caused; it is considered given to patients with a body mass index (BMI) ≥ 30 kg/m² and a BMI ≥ 27 kg/m² with comorbidities such as type 2 diabetes mellitus. Bariatric surgery is indicated for severe obesity or with comorbidities and results in substantial and sustained weight loss with resolution of diabetes mellitus. Still, costs are high, and the risk of serious complications is small. The balance of benefits against risks of these methods needs to be considered for therapeutic decisions (Gadde et al., 2018; Zhang et al., 2014).

In general, pharmacotherapy is aimed at increasing satiety and decreasing hunger (suppressing appetite), inhibiting fat absorption, or increasing catabolism (stimulating thermogenesis and fat mobilisation) (Gjermeni et al., 2021; Gurevich-Panigrahi et al., 2009; Zhang et al., 2014). The appetite suppressant is divided into noradrenergic, serotonergic, and mixed agents (Gurevich-Panigrahi et al., 2009). Currently, there are six main anti-obesity drugs approved by the Food and Drug Administration (FDA), namely phen-

termine/topiramate, naltrexone/bupropion, setmelanotide, liraglutide and semaglutide, and orlistat. Phentermine is a sympathomimetic that stimulates noradrenaline and suppresses appetite (anorexigenic mechanism). Topiramate is an antiepileptic, which is also used for migraine therapy. Naltrexone is an opiate antagonist that blocks the autoinhibitory opioid-mediated proopiomelanocortin (POMC) receptor and bupropion selectively inhibits the reuptake of dopamine and noradrenaline thereby reducing food intake and increasing energy release. Setmelanotide is a melanocortin-4 receptor (MC4R) agonist that acts on the paraventricular nucleus of the hypothalamus and the lateral hypothalamic area to suppress appetite. Liraglutide and semaglutide are glucagon-like peptide-1 (GLP1) receptor agonists with incretin effects interfering with glucose homeostasis, food intake, and satiety. Orlistat inhibits pancreatic and gastric lipase, reducing fat absorption (Gjermeni et al., 2021; Lin and Li, 2021).

The limited efficacy, possible side effects, and drug interactions of available anti-obesity agents highlight the need to find new effective and safe anti-obesity agents (Lin and Li, 2021). Many nutraceutical and botanical dietary supplements are used to modulate body weight and its associated complications because they provide many benefits with few or no side effects (Bertuccioli et al., 2021). Phytopharmaceutical compounds and preparations, based on their natural origin, easy availability, cost-effectiveness, and beneficial traditional use based on accumulated experience, have been extensively explored to reduce the global burden of obesity (Borah et al., 2021). In addition to identifying and quantifying potential bioactive compounds and proving their efficacy at the cellular and molecular level (Sandner et al., 2020).

Lemongrass [*Cymbopogon citratus* (DC.) Stapf, *Poaceae*] is an aromatic herbal plant widely used in tropical countries and commonly used as a cooking ingredient (Ajayi et al., 2016; Olorunnisola et al., 2014). In Asia, South America, and Africa, *C. citratus* leaves are traditionally used for tea, infusion, or decoction. The essential active substances in *C. citratus* are phenolics (flavonoids, phenols, tannins), alkaloids, terpenoids (essential oils), saponins, minerals, and vitamins (Ekpenyong et al., 2015; Oladeji et al., 2019). Citral is the most abundant essential oil (65-85%) and a pharmacologically and physiologically important component of *C. citratus* (Ekpenyong et al., 2014). Other essential oils are myrcene, geraniol, nerol, citronellol (cymbopogonol and cymbopogone), and limonene. The leaves contain essential bioactive compounds that provide anti-obesity, anti-bacterial, anti-fungal, anti-nociceptive, antioxidants, anti-diarrheal, and anti-

inflammatory effects (Merchaoui et al., 2018; Oladeji et al., 2019).

The previous reviews about *C. citratus* focused on its general pharmacological activities and stated one of them as anti-obesity but did not explain in detail the mechanism of its anti-obesity activity (Ekpenyong et al., 2015; Kiani et al., 2022; Oladeji et al., 2019; Olorunnisola et al., 2014; Tibenda et al., 2022). Other previous review studies about medicinal plants for the treatment of obesity stated that *C. citratus* was included but also did not explain the details of its anti-obesity mechanism (Cercato et al., 2015; de Freitas Junior and de Almeida, 2017). Therefore, this review aims to be the first systematic review investigating the anti-obesity activity of *C. citratus* and its phytochemicals from previously published studies *in vitro*, *in vivo*, and in humans.

MATERIAL AND METHODS

Information sources

The reviewers searched articles and extracted data from studies that met the criteria. Studies were retrieved on Google Scholar, PubMed, and Scopus with the keywords: "*Cymbopogon citratus*" OR "lemongrass" OR "citral" AND "anti-obesity" OR "hypolipidemic" OR "adipocyte". Boolean operators (OR and AND) are used to refine search results. Articles published between 2003-2023 were included, and to minimise retrieval of irrelevant articles, these keywords and MeSH terms were searched within the "Title/Abstract" category.

Eligibility criteria

Study eligible for the current review was original research with (i) the population for *in vivo* studies was normal animal, obesity, or hyperlipidaemia models; for *in vitro* studies was a culture of adipocytes, lipids, or enzymes involved in lipid metabolism; for in human studies was obese or hyperlipidaemia patients, (ii) intervened by *C. citratus*, (iii) as compared to those without, (iv) observing the outcome if there was an anti-obesity effect. The specific inclusion criteria were (i) studies that used a randomised controlled trial design, (ii) administered *C. citratus* and its phytochemicals from various parts of the plant and various preparations, (iii) showed anti-obesity activity as the outcome, anti-obesity activity was focused on its relation to lipid metabolism. Research with irrelevant topics and incomplete manuscripts would be excluded from this review. Studies using models of obesity or hyperlipidaemia accompanied by other metabolic syndromes, such as diabetes and cardiovascular disease, were excluded. *C. citratus* extract and its phytochemicals in combination with ex-

tracts/phytochemicals from different plants were not included.

Search strategy

Two reviewers independently searched the databases and identified literature through other sources in Rayyan (<http://rayyan.qcri.org>), a web-based platform for accelerating the initial screening of abstracts and titles that incorporates a high level of usability as it filters duplicates (Ouzzani et al., 2016). Searches were exported from the database to Rayyan in "txt" and "ris" formats. The reviewers independently screen the retrieved abstracts according to the specified criteria. Specifically, the population, type of intervention, and outcomes assessed will be assessed during the selection process. Any disagreements were resolved through consensus among the other authors.

Selection process

All included studies underwent a three-stage assessment to collect the necessary data. The first stage of the selection process is collecting general information about the year of publication, the country, and the period during which the research was conducted. In the second stage, each article was assessed regarding the research design: (i) the plant part of *C. citratus* used or its phytochemicals and preparations, (ii) for *in vivo* studies, the experimental animal model used (normal, obesity model, or hyperlipidaemia), how the method induction, and its comparison, (iii) for *in vitro* studies, whether the research object is adipocyte culture cells, lipids, or enzymes involved in lipid metabolism, (iv) for in human studies, the research subjects used and the comparison, (v) the duration of the intervention. In the final stage, the reviewer documented the anti-obesity effects observed in each study.

The data collection process and the items

All reviewers will gather data from the included studies. The results will be organised by identifiers, including author(s), year of publication, and country where the research was conducted. The subsequent data set will include detailed characteristics of each study, including the plant part of *C. citratus* used or its phytochemicals, preparation, dose or concentration, research objectives, population, and duration of intervention. Results from the intervention and control groups will be extracted and categorised based on observed anti-obesity effects, organised into groups reflecting different anti-obesity mechanisms or activities such as inhibition of digestive enzymes, appetite suppression, inhibition of adipocyte differentiation, or regulation of lipid metabolism. Conclusions will be formulated based on the findings documented in the manuscript and validated by the reviewing team.

Study risk of bias assessment

The included studies' quality and risk of bias were assessed using the American Dietetic Association (ADA) quality criteria checklist, which includes separate sections for primary research on human subjects and *in vitro* and *in vivo* research on non-human subjects. Each section contains 14 questions (Academy of Nutrition and Dietetics). Two reviewers independently conducted this assessment and discussed their findings with other reviewers before advancing to the subsequent review phase. Eligible research received a positive (+) value, indicating that the study adequately addressed issues of inclusion/exclusion, bias, generalizability, and data collection and analysis. Studies were rated negatively (-) if they failed to address and neutrally (Φ) if they were neither particularly strong nor weak in these areas (ADA, 2008).

Effect measures, synthesis methods, reporting bias assessment

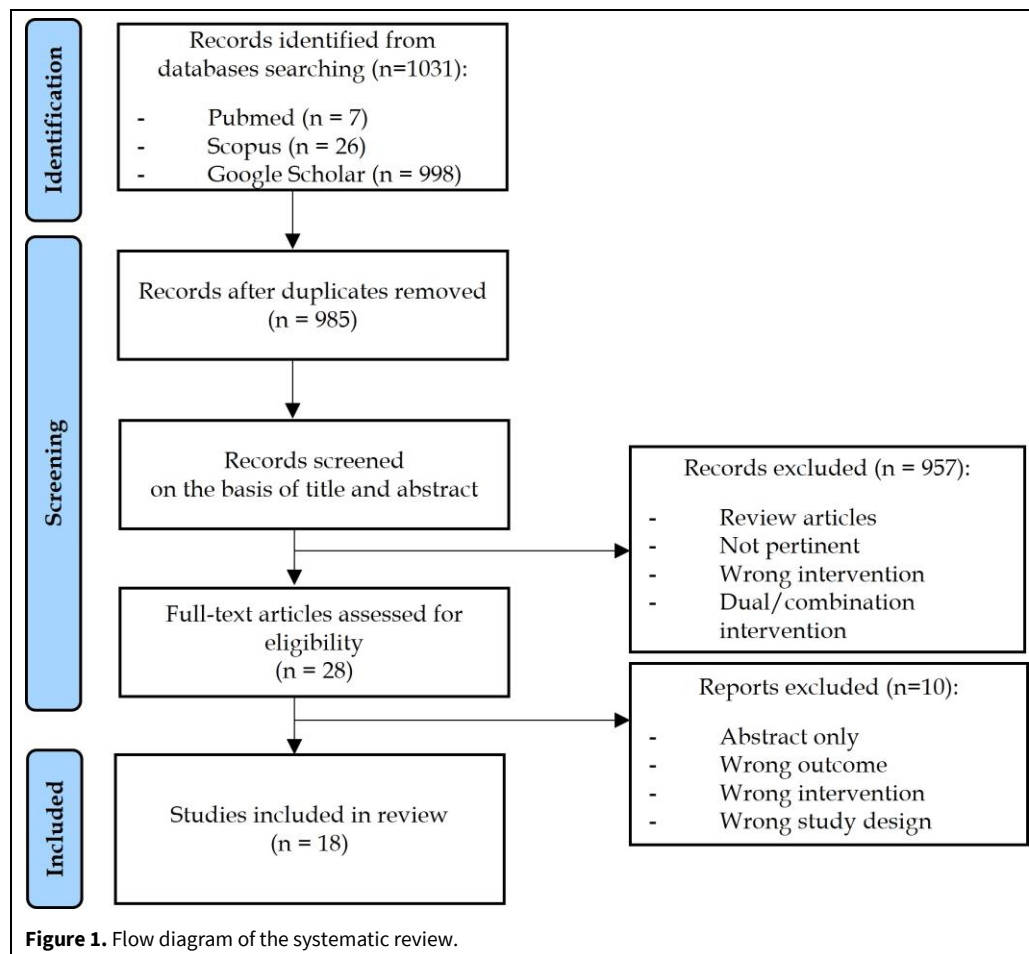
Online data processing tools, like Google sheets, will be used to tabulate the data. This tool was chosen for its unique feature of real-time collaboration. This

process allows all reviewers to access and correct data synthesis results simultaneously, significantly reducing the chances of errors in our collaborative data synthesis.

RESULTS

Study selection

A total of 1031 studies were initially retrieved through databases, specifically PubMed (n = 7), Scopus (n = 26), and Google Scholar (n = 998). After duplicates were removed, 985 studies remained. Initially, screening was based on titles and abstracts, followed by a full-text review. Articles were included or excluded based on specific criteria, and reasons for exclusion were documented, e.g., review article, not pertinent, wrong intervention, or dual/combination intervention. Of these, 957 studies were excluded, leaving 28 for detailed full-text screening. After further exclusions, 10 articles were excluded based on the exclusion criteria, e.g., abstract only, wrong outcome, wrong intervention, or wrong study design. Thus, 18 final articles were selected for inclusion in this systematic review (Fig. 1).



Study characteristics

The characteristics of the studies reviewed are summarised in Table 1. Of the 18 articles, there were 11 *in vivo* studies, 5 *in vitro* studies, 1 was a human study, and 1 combined *in vivo* and *in vitro* methods. The studies reviewed varied in the parts of the *C. citratus* plant used, the extraction types, and the active compound used. For *in vivo* studies, Somparn et al. (2018) utilised a whole plant water extract, Betancourt et al. (2015) utilised a hydroalcoholic extract from aerial parts, Adeneye and Agbaje (2007) and Dimgba et al. (2017) used an aqueous extract from leaves, Agbafor and Akubugwo (2007) employed an ethanol extract from leaves, Furtado et al. (2011) utilised a hydroalcoholic extract from leaves, and Abbas et al. (2019) developed an aqueous extract from roots. Villalobos et al. (2021) used total dietary fibre fermentation, and Abdelrahman and Omar (2023) used *C. citratus* powder; however, the specific parts of the plant used were not specified in either study. Costa et al. (2011) used essential oils from leaves, Kumar et al. (2011) used essential oils without specifying the plant part, and Modak and Mukhopadhaya (2011) used citral. Adeneye and Agbaje (2007), Dimgba et al. (2017), and Somparn et al. (2018) used normal experimental animals, while other studies used models of obesity or hyperlipidaemia.

In an *in vitro* study, Da Ressurreição et al. (2022) used aqueous leaf extract on micellar to study the solubility of cholesterol. Jo et al. (2019) used ethanol extract (part of the plant used was not stated), Ngamdokmai et al. (2021) used essential oil from stalk and citral, Sri Devi and Ashokkumar (2018) used citral, while Sprenger et al. (2022) used citral and its isomers, and all studies used 3T3-L1 cells. A human study by Waheed et al. (2019) used *C. citratus* leaf powder on hyperlipidaemia non-smoker male patients.

Risk of bias in studies

Quality assessment was carried out using the ADA quality checklist (ADA, 2008). No articles were excluded based on the assessment results. All of the 18 studies reviewed had positive ratings (Table 2).

Results of individual studies

Effect of Cymbopogon citratus on weight loss

In several *in vivo* studies reviewed, it was proven that leaves aqueous extract (Adeneye and Agbaje, 2007; Dimgba et al., 2017) starting at a dose of 125 mg/kg/day, leaves ethanol extract (Agbafor and Akubugwo, 2007) starting at a dose of 100 mg/kg/day, powder 7.5% (Abdelrahman and Omar, 2023), essential oil (Costa et al., 2011) at a dose of 100

mg/kg/day, and citral (Modak and Mukhopadhaya, 2011) starting at a dose of 10 mg/kg/day from *C. citratus* decreased body weight in normal mice (Adeneye and Agbaje, 2007; Dimgba et al., 2017) and hyperlipidaemia or obese models (Abdelrahman and Omar, 2023; Agbafor and Akubugwo, 2007; da Costa et al., 2015; Modak and Mukhopadhaya, 2011).

Effect of Cymbopogon citratus on suppressing appetite

In the study by Dimgba et al. (2017), aqueous leaves extracted from *C. citratus* suppressed appetite in normal Wistar rats. The amount of food consumed by a treated group with *C. citratus* (150, 300, and 600 mg/kg) significantly decreased dose-dependent across treatment periods (21 days).

Effect of Cymbopogon citratus on lipid metabolism

In vivo research reviewed in this study showed that leaves ethanol extract (Agbafor and Akubugwo, 2007), aerial hydroalcoholic extract (Betancourt et al., 2015), leaves hydroalcoholic extract (Furtado et al., 2011), root aqueous extract (Abbas et al., 2019), total dietary fibre (Villalobos et al., 2021), powder (Abdelrahman and Omar, 2023), and essential oil (Costa et al., 2011; Kumar et al., 2011) from *C. citratus* decreased total cholesterol in the hyperlipidaemia model. Leaves aqueous extract (Adeneye and Agbaje, 2007) and whole plant water extract (Somparn et al., 2018) of *C. citratus* also decreased total cholesterol in normal rats. *C. citratus* whole plant water extract reduced the expression of the catalysator of endogenous cholesterol synthesis (HMGR) in normal rats (Somparn et al., 2018). An *in vitro* study by Da Ressurreição et al. (2022) showed that aqueous extracts of *C. citratus* leaves and their polyphenols (flavonoids, tannin, luteolin, luteolin-7-O, luteolin-6-C-glucoside) had micellar destruction activity so that they could prevent cholesterol absorption in the gut. An *in vitro* study by Villalobos et al. (2021) showed that propionate was the predominant short-chain fatty acid (SCFA) produced fermentation from *C. citratus* total dietary fibre, and propionate inhibited HMGR activity *in vitro*.

C. citratus essential oil (Kumar et al., 2011), aerial hydroalcoholic extract (Betancourt et al., 2015), and leaves hydroalcoholic extract (Furtado et al., 2011) decreased serum triglycerides in the hyperlipidaemia model. *C. citratus* leaves aqueous extract (Adeneye and Agbaje, 2007) and total dietary fibre (Villalobos et al., 2021) decreased LDL and VLDL in normal and hyperlipidaemia models. *C. citratus* aerial hydroalcoholic extract (Betancourt et al. (2015), roots aqueous extract (Abbas et al., 2019), and powder (Abdelrahman and Omar, 2023) decreased LDL levels in the hyperlipidaemia model and whole plant water extract (Somparn et al., 2018) decreased LDL in normal rats.

Table 1. Studies on the effects of *Cymbopogon citratus* on obesity.

Author and year	Part used/ compound and dosage/ concentration	Research objectives	Study design (population, intervention, and comparison)	No. of subjects	Duration	Main outcomes/results
<i>In vivo</i>						
Adeneye and Agbaje (2007)	Leaf aqueous extract of <i>C. citratus</i> (daily oral dosing of 125-500mg/kg).	To investigate the hypoglycaemic and hypolipidemic effects of the single, daily oral dosing of 125–500 mg/kg of fresh leaf aqueous extract of <i>C. citratus</i> in normal, male Wistar rats.	Normal Wistar rats were divided into a control group given typical saline 10ml/kg/day and three treatment groups with 125, 250, and 500mg/kg/day leaf aqueous extract of <i>C. citratus</i> , respectively.	Four groups (n = 6 per group)	42 days	Leaf aqueous extract of <i>C. citratus</i> significantly induced weight loss in treated rats, lower fasting plasma glucose and lipid parameters (total cholesterol, LDL-c, and VLD-c) dose-dependently while raising the plasma HDL-c level (p<0.05) in the same dose-related mode but with no effect on plasma triglycerides level.
Agbafor and Akubugwo, (2007)	Leaves ethanol extract of <i>C. citratus</i> (100 and 200 mg/kg).	To investigate the hypocholesterolaemic effect of fresh leaves of <i>C. citratus</i> in albino rats.	Albino rats were divided into four groups. Two other groups were negative and positive control (high egg yolk diet). Two other groups were treated with a high egg yolk diet and 100 mg/kg or 200 mg/kg ethanol extract of <i>C. citratus</i> , respectively.	Four groups (n = 5 per group)	7 days	Leaves ethanol extract of <i>C. citratus</i> significantly lowered body weight and serum cholesterol in a dose-dependent manner compared with the untreated group. The serum cholesterol level in the animals given the higher dose (200 mg/kg) was almost at par with those of the animals that were never given the egg yolk diet (normal group).
Costa et al. (2011)	<i>C. citratus</i> essential oil (1, 10, or 100 mg/kg).	To investigate the toxicity and genotoxicity of this <i>C. citratus</i> essential oil in male Swiss mice.	Mice were randomly assigned to two control groups, saline- or Tween 80 0.01%-treated groups, or one of the three experimental groups receiving <i>C. citratus</i> essential oil (1, 10, or 100 mg/kg).	Five groups (n = 33)	21 days	No significant changes in gross pathology, body weight, absolute or relative organ weights, histology (brain, heart, kidneys, liver, lungs, stomach, spleen, and urinary bladder), urinalysis, or clinical biochemistry were observed in treated mice relative to the control groups. Blood cholesterol was reduced after essential oil treatment at the highest dose tested. During the 21-day acute toxicity treatment, a slight weight loss was observed among the mice treated with EO at 1 or 100 mg/kg, starting after 16 days of treatment.

Table 1. Studies on the effects of *Cymbopogon citratus* on obesity (continued...)

Author and year	Part used/ compound and dosage/ concentration	Research objectives	Study design (population, intervention, and comparison)	No. of subjects	Duration	Main outcomes/results
<i>In vivo</i>						
Furtado et al. (2011)	Leaves hydroalcoholic extract of <i>C. citratus</i> (0.5 g/kg and 1.0 g/kg).	To evaluate the effect of the hydroalcoholic extract of <i>C. citratus</i> in hyperlipidaemic rats.	Adult male Wistar rats were randomised and divided into five groups. Group I-IV were induced hyperlipidaemia with Triton WR 1339 (tyloxapol) at a dose of 0.3 g/kg and treated with saline, hydroalcoholic extract of <i>C. citratus</i> at 0.5 g/kg, 1.0 g/kg, and ciprofibrate, respectively. Group 5 (saline) received only the injection of 0.9% physiological NaCl solution.	Five groups (n = 6 per group)	24, 48, and 72 h	Hydroalcoholic extract of <i>C. citratus</i> at 0.5 g/kg and 1.0 g/kg reduced total cholesterol levels by 58% and 45% and triglycerides by 43% and 31%, respectively, and increased the HDL fraction by 38% and 45%, respectively, in hyperlipidaemic rats after 48 h of induction.
Kumar et al. (2011)	<i>C. citratus</i> oil (100 and 200 mg/kg, po.).	To evaluate the anti-hyperlipidaemic activity of <i>C. citratus</i> oil against dexamethasone-induced hyperlipidaemia in rats.	Adult male Wistar albino rats were divided into 5 groups. The first group of rats fed with a normal laboratory diet alone served as standard control. The second group of rats was administered with dexamethasone (10 mg/kg, sc.) for 8 consecutive days and served as pathogenic control. The third, fourth, and fifth groups of rats received dexamethasone (10 mg/kg, sc.) and simultaneously treated orally with 10 mg/kg atorvastatin, 100 mg/kg <i>C. citratus</i> oil and 200 mg/kg <i>C. citratus</i> oil, respectively, for 8 consecutive days.	Five groups (n = 6 per group)	8 days	<i>C. citratus</i> oil (100 and 200 mg/kg, po.) treatment has shown significant inhibition against dexamethasone hyperlipidaemia by maintaining the serum level of cholesterol, triglycerides, and atherogenic index near the normal levels.

Table 1. Studies on the effects of *Cymbopogon citratus* on obesity (continued...)

Author and year	Part used/ compound and dosage/ concentration	Research objectives	Study design (population, intervention, and comparison)	No. of subjects	Duration	Main outcomes/results
<i>In vivo</i>						
Modak and Mukhopadhaya (2011)	Citral (10, 15, and 20 mg/kg body weight).	To assess the effects of citral – an inhibitor of retinaldehyde dehydrogenase (the primary enzyme metabolising retinaldehyde), on body weight, glucose tolerance, fasting plasma glucose and insulin levels, metabolic rate, adipocyte size, and morphology in a diet-induced model of obesity.	In five groups of male Sprague–Dawley rats, 4 were maintained on an energy-intense, palatable, fat diet for– 42 days, while 1 was the control. After obesity had been induced, 3 groups were treated with daily doses of citral (10, 15, and 20 mg/kg body weight) for 28 days.	Five groups (n = 10 per group)	28 days	Citral-treated groups showed a dose-dependent reduction in body weight gain. They significantly had lower fasting glucose levels, improved glucose tolerance, higher metabolic rate (increased energy dissipation), and smaller adipocytes (reduced lipid accumulation) after citral administration.
Betancourt et al. (2015)	Hydroalcoholic extract of <i>C. citratus</i> aerial part (400 and 600 mg/kg).	To evaluate the lipid-lowering effect of <i>C. citratus</i> in a model of acute hyperlipidaemia induced by poloxamer 407, a non-ionic detergent.	Six experimental groups of C57BL/6J male mice were formed: Group I corresponded to the negative control, II to the control group of hyperlipidaemia, III and IV to control groups of simvastatin and nicotinic acid, as well as, groups V and VI corresponded to the evaluated doses of <i>C. citratus</i> extract.	Six groups (n = 8 per group)	24 and 48 h	<i>C. citratus</i> extract at the doses studied in the model of acute hyperlipidaemia presents hypolipidaemic activity. Cholesterol, TAG, and VLDL variables for groups V and VI showed significant differences to the control group of hyperlipidaemia (II) and behaved similarly to the control groups of simvastatin (III) and nicotinic acid (IV).
Dimgba et al. (2017)	Leaves aqueous extract of <i>C. citratus</i> (150, 300, and 600 mg/kg).	To evaluate the appetite suppressing potential of aqueous leaf extract of <i>C. citratus</i> in Wistar rats.	Twenty adults male Wistar rats were divided into four groups of five rats per group. Group I was the standard control and was only fed with normal rat feed and water. Groups II-IV were orally administered with 150, 300, and 600 mg/kg bw, respectively.	Four groups (n = 5 per group)	21 days	Aqueous extract of <i>Cymbopogon citratus</i> suppressed appetite, reducing animal weight. The quantity of food consumed by the control group significantly increased across treatment periods. However, the amount of food consumed by the treated group with <i>C. citratus</i> significantly decreased dose-dependent across treatment periods. The quantity of water consumed by the control group significantly increased across treatment periods, while a contrary observation was made on its treated counterpart. Evaluation of the weight of rats administered with varying doses of <i>C. citratus</i> indicated a significant reduction in body weight over treatment periods.

Table 1. Studies on the effects of *Cymbopogon citratus* on obesity (continued...)

Author and year	Part used/ compound and dosage/ concentration	Research objectives	Study design (population, intervention, and comparison)	No. of subjects	Duration	Main outcomes/results
<i>In vivo</i>						
Somporn et al. (2018)	Whole plant <i>C. citratus</i> water extract (250, 500, and 1000 mg/kg/day).	To investigate the effects of consuming <i>C. citratus</i> aqueous extract on rats' atherogenic index and antioxidant status.	Male Sprague-Dawley rats were divided into five groups of six rats each. The group I (control group) animals were orally administered vehicle solution (distilled water) for 30 days. The animals in groups II-IV were orally administered <i>C. citratus</i> water extract, which was dissolved in distilled water, at doses of 250, 500, and 1000 mg/kg/per day for 30 days. The animals in group V were orally administered simvastatin dissolved in distilled water at 10 mg/kg daily.	Five groups (n = 6 per group)	30 days	After treatment, the extract significantly decreased rats' total cholesterol, low-density lipoprotein, and atherogenic index. The expression of SREBP1c and HMGR genes and proteins was also significantly lowered in the treated groups.
Abbas et al. (2019)	Aqueous roots and flower extracts of <i>C. citratus</i> (500 mg/kg/day).	To investigate the antilipidemic effect of the aqueous extract <i>C. citratus</i> .	Five groups of albino mice (I: normal, II: hyperlipidaemic control, III: positive control with lovastatin, IV, IV, and V: hyperlipidaemic with roots and flower extract, respectively). An atherogenic diet induces the hyperlipidaemic model for 20 days or Triton for 48 hours.	Five groups (n = 6 per group)	14 days	Aqueous roots and flower extracts of <i>C. citratus</i> significantly decreased cholesterol and LDL levels, and increased HDL levels decreased compared to the cholesterol-induced group. Root extract had better anti-hypercholesterolemia activity.
Abdelrahman and Omar (2023)	<i>C. citratus</i> powder (7.5%).	To investigate the effect of <i>Cymbopogon citratus</i> and orlistat on hyperlipidaemia in rats fed on a high-fat diet.	Four groups of male albino rats of Sprague Dawley (I: negative control, II: high-fat diet group, III: high-fat diet +7.5% <i>C. citratus</i> powder, IV: high-fat diet + orlistat 60 mg/kg/body weight).	Four groups (n = 6 per group)	30 days	<i>C. citratus</i> powder 7.5% significantly decreased glucose levels, atherogenic index, body weight, total cholesterol, TG, LDL, ALT, AST, ALP, and liver weight, and increased HDL level compared with the high-fat diet group.

Table 1. Studies on the effects of *Cymbopogon citratus* on obesity (continued...)

Author and year	Part used/ compound and dosage/ concentration	Research objectives	Study design (population, intervention, and comparison)	No. of subjects	Duration	Main outcomes/results
<i>In vivo and in vitro</i>						
Villalobos et al. (2021)	Total dietary fibre (TDF) extracted from <i>C. citratus</i> (propionate) (400 mg/kg BW/day).	To analyse dietary fibre (DF) components of <i>C. citratus</i> , investigate the potential of the significant product from total dietary fibre fermentation to inhibit amylase and HMG-CoA reductase <i>in vitro</i> , critical enzymes of diabetes mellitus and hypercholesterolemia, respectively, and determine the serum glucose- and cholesterol-lowering potential of total dietary fibre in an animal model.	<i>C. citratus</i> dietary fiber components were analysed, TDF was fermented <i>in vitro</i> ; the primary fermentation product was isolated for enzyme inhibitory assays; and the postprandial blood glucose- and cholesterol-lowering potential of TDF was determined in Sprague-Dawley rats. Sprague-Dawley rats were modified to a high cholesterol, high sugar diet for two weeks, then were divided into three groups (total dietary fibre from <i>C. citratus</i> , acarbose + pravastatin as positive control, and saline as negative control) for two weeks while high cholesterol and sugar maintained.	Three groups (n = 5 per group)	Two weeks	TDF in <i>C. citratus</i> was 65.7 g/100g, and soluble DF was 2.8 g/100 g. A significant amount of propionate (10.9 mM/g TDF) was produced after TDF fermentation; propionate inhibited 20.4% amylase activity and 13.1% HMG-CoA reductase activity <i>in vitro</i> . In an animal model, total dietary fibre from <i>C. citratus</i> exhibited antihyperglycemic and cholesterol-lowering potential. Dietary fibre prevented the rise in fasting blood sugar levels, lowered the total cholesterol, and minimised the increase in LDL+VLDL levels.
<i>In vitro</i>						
Sri Devi and Ashokkumar (2018)	Citral (30, 40, and 50 μ M).	To investigate the inhibitory effect of citral against adipogenic genes in 3T3-L1 cells.	3T3-L1 preadipocytes were incubated with adipogenesis cocktail (DMEM with 3-isobutyl-1-methylxanthine, dexamethasone, and insulin) for 2 days and then replaced with DMEM containing insulin with or without citral (30, 40 and 50 μ M) for 8 days.	Four groups (differentiated control without citral and with citral 30, 40, 50 μ M).	8 days	Cells were treated with citral significantly attenuated intracellular triglyceride accumulation, suppressed the expression of PI3K/AKT, adipogenic specific transcription factors (PPAR γ , SREBP-1c, and FAS), and inflammatory biomarkers (TNF- α , IL-6, and MCP-1). The anti-obesity effects of citral decrease adipogenesis by modulating adipogenic transcriptional factors, PI3K/AKT signalling, and inflammatory signalling.

Table 1. Studies on the effects of *Cymbopogon citratus* on obesity (continued...)

Author and year	Part used/ compound and dosage/ concentration	Research objectives	Study design (population, intervention, and comparison)	No. of subjects	Duration	Main outcomes/results
<i>In vitro</i>						
Jo et al. (2019)	Ethanol extracts of <i>C. citratus</i> (50, 100, and 200 µg/mL).	To investigate the effect of ethanol extract of <i>C. citratus</i> on adipogenesis and its underlying mechanism in 3T3-L1 preadipocytes.	In the differentiation period, 3T3-L1 preadipocytes were treated with 50, 100, and 200 µg/mL of <i>C. citratus</i> ethanol extract.	Five groups (negative control, positive control, and treated group with 50, 100, and 200 µg/mL of <i>C. citratus</i> ethanol extract.	7 days	Ethanol extracts of <i>C. citratus</i> inhibit adipocyte differentiation in 3T3-L1 cells. Ethanol extracts of <i>C. citratus</i> effectively suppressed intercellular lipid accumulation at non-toxic concentrations. They were associated with the down-regulation of adipocyte-specific transcription factors, including C/EBPα and PPARγ, and increased phosphorylation of AMPKα. Ethanol extracts of <i>C. citratus</i> increased p21 expression, while the expression of CDK2, cyclin A, and cyclin B1 was reduced. Ethanol extracts of <i>C. citratus</i> seem to induce G0/G1 cell cycle arrest of 3T3-L1 cells. ERK and Akt signalling pathways were not involved in anti-adipogenesis by ethanol extracts of <i>C. citratus</i> .
Ngamdokmai et al. (2021)	<i>C. citratus</i> oil (12.5 and 25 µg/mL) and citral (50 and 100 µg/mL).	To investigate the activity of eight essential oils (including <i>C. citratus</i> oil) and two water extracts from the ingredients of the herbal compress together with nine monoterpenoid constituents (including citral) on the 3T3-L1 adipocytes for preventive and treatment effect.	To investigate the preventive effect, the samples were added to the media on days 3, 5, and 7 after the initiation of differentiation induction. To evaluate the treatment effect, the samples were incubated with the mature adipocyte on day 9 after the initiation, and their effects were measured on day 10.	<i>C. citratus</i> oil and nine other essential oil (ginger, black pepper, long pepper, turmeric, tea, cassumunar ginger, kaffir lime, coffee, and mixed oil) in 12.5-200 µg/mL compared to negative control, caffeine, and adrenaline as positive control. Citral and eight other monoterpenoid constituents (camphor, camphene, 3-carene, limonene, myrcene, alpha-pinene, beta-pinene and terpinene-4-ol) in 50 and 100 µg/mL compared to negative control, caffeine, and adrenaline as positive control.	Preventive effect: <i>C. citratus</i> oil and citral were added to media on days 3, 5, and 7 after the initiation differentiation induction of 3T3-L1. Treatment effect: <i>C. citratus</i> oil and citral were incubated with the mature adipocyte on day 9 after the initiation and their effects were measured on day 10.	<i>C. citratus</i> oil had preventive effects on adipogenesis in a dose-dependent manner. It demonstrated inhibition of lipid accumulations at a concentration of 12.5 µg/mL, which was 23 ± 6%, which was the lowest effective concentration of all samples tested. Citral significantly inhibited lipid accumulation compared to the control cells in preventive and treatment ways.

Table 1. Studies on the effects of *Cymbopogon citratus* on obesity (continued...)

Author and year	Part used/ compound and dosage/ concentration	Research objectives	Study design (population, intervention, and comparison)	No. of subjects	Duration	Main outcomes/results
<i>In vitro</i>						
Sprenger et al., (2022)	Citral (3,7-dimethyl-2,6-octadienal), citral dimethyl acetal (1,1-dimethoxy-3,7-dimethylocta-2,6-diene), and citral diethyl acetal (1,1-diethoxy-3,7-dimethylocta-2,6-diene) (1.25 x 10 ⁻³ %).	To investigate the effect of <i>C. citratus</i> essential oil major components citral in the modulation of adipogenesis and genetic expression in adipocytes.	Citral was added, achieving a final concentration of 1.25 x 10 ⁻³ % following the development of morphological characteristics of mature adipocytes (after 96 h differentiation induction).	Three groups: citral (3,7-dimethyl-2,6-octadienal), citral dimethyl acetal (1,1-dimethoxy-3,7-dimethylocta-2,6-diene), and citral diethyl acetal (1,1-diethoxy-3,7-dimethylocta-2,6-diene).	96 h	Citral significantly inhibited expression of sterol response binding protein 2 (SREBP2), cluster of differentiation 36 (CD36/FAT), fatty acid binding protein 4 (FABP4), and perilipin. These results indicate modulation of lipid accumulation through decreased lipid uptake, increased lipolysis, decreased differentiation, and downregulated lipid biosynthesis.
Da Ressurreição et al. (2022)	Aqueous extracts of <i>C. citratus</i> leaf (5-400 µg/mL). Phenolic fractions, flavonoids, and tannin fraction (0.001-200 µg/mL). Luteolin, luteolin-7-O-glucoside, and luteolin-6-C-glucoside (0.1-100 µg/mL).	To optimise an inexpensive colourimetric method to study <i>in vitro</i> , the micellar solubility of cholesterol was applied to plant extracts (<i>C. citratus</i> leaf extracts, phenolic fractions, and flavonoids were evaluated).	An assay was carried out on the effect of delipidified infusion, non-delipidified infusion, phenolic, flavonoid, tannin, luteolin, luteolin-7-O-glucoside, and luteolin-6-C-glucoside from <i>C. citratus</i> in various concentration on micellar solubility of cholesterol.	Delipidified and non-delipidified infusion of <i>C. citratus</i> : 5-400 µg/mL. Phenolic, flavonoid, and tannin fraction: 0.001-200 µg/mL. Luteolin, luteolin-7-O-glucoside, and luteolin-6-C-glucoside: 0.1-100 µg/mL.	-	<i>C. citratus</i> extracts and their polyphenols can prevent cholesterol absorption in the gut by micellar destruction and its contribution to cholesterol-lowering activity. For the fraction of flavonoids, the micellar destruction was 92.74% at 1 µg/mL, and for the tannin fraction, 99.45% at 25 µg/mL. Luteolin presented a percentage of micelle destruction of 94.83% in the concentration of 1 ng/mL, followed by luteolin-7-O-glucoside with 93.71% and luteolin-6-C-glucoside with 91.26% at the concentrations of 25 ng/mL and 50 ng/mL, respectively.

Table 1. Studies on the effects of *Cymbopogon citratus* on obesity (continued...)

Author and year	Part used/ compound and dosage/ concentration	Research objectives	Study design (population, intervention, and comparison)	No. of subjects	Duration	Main outcomes/results
In human						
Waheed et al. (2019)	<i>C. citratus</i> dried leaf powder (4, 8 and 12 g).	To assess and compare the prospect of ameliorative potential of sundried <i>C. citratus</i> leaf powder against lipid-lowering drugs (statins) in hyperlipidaemic non-smoker male patients and to execute its compositional analysis.	<i>C. citratus</i> powder was first subjected to proximate analysis. Then, nominated hyperlipidaemic, non-smoker males (age 25-50 years) were divided into four groups (G1, G2, G3, and G4), and each faction included 10 subjects. The first three sets were given deliberated amounts of <i>C. citratus</i> powder (4, 8, and 12 g, respectively) for 30 days. G4 set was prescribed the use of statins.	Four groups (n = 10 per group).	30 days	<i>C. citratus</i> attenuated the serum lipid parameters dose-dependently. The most desirable cholesterol reduction was witnessed in G2 and G3. Levels of TG diminished most significantly in G4 (statins). LDL reduction in both G2 and G3 were nearly the same.

Akt: protein kinase B; ALP: alkaline phosphatase; ALT: alanine transaminase; AMPK α : AMP-activated protein kinase alpha; AST: aspartate transaminase; C/EBP α : CCAAT/enhancer-binding protein α ; CD36: a cluster of differentiation 36; CDK2: Cyclin-dependent kinase 2; ERK: extracellular signal-regulated kinase; FABP4: fatty acid binding protein 4; FAS: fatty acid synthase; FAT: fatty acid translocase; HDL: high-density lipoprotein; HMGR: HMG-CoA reductase; IL-6: interleukin-6; LDL: low-density lipoprotein; MCP-1: monocyte chemoattractant protein-1; PI3K: phosphatidylinositol 3-kinase; PPAR γ : peroxisome proliferator-activated receptor γ ; SREBP1c: sterol regulatory element binding protein-1c; TAG= TG: triacylglycerols, triglycerides; TNF- α : tumour necrosis factor-alpha; VLDL: very low-density lipoproteins; ACC: acetyl-CoA carboxylase; LPL: lipoprotein lipase; CE: cholesterol ester; CETP: cholesteryl ester-transfer-protein; HL: hepatic lipase.

Table 2. Risk of bias assessment using the ADA quality criteria checklist for primary research.

Author and year	Relevance questions				Validity questions										Quality rating	
	1	2	3	4	1	2	3	4	5	6	7	8	9	10		
<i>In vivo</i>																
Adeneye and Agbaje (2007)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	+
Agbafor and Akubugwo (2007)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	+
Costa et al. (2011)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	+
Furtado et al. (2011)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	+
Kumar et al. (2011)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	+
Modak and Mukhopadhaya (2011)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	+
Betancourt et al. (2015)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	+
Dimgba et al. (2017)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	+
Sompam et al. (2018)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	+
Abbas et al. (2019)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	+
Abdelrahman and Omar (2023)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	+
<i>In vivo and in vitro</i>																
Villalobos et al. (2021)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	+
<i>In vitro</i>																
Sri Devi and Ashokkumar (2018)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	+
Jo et al. (2019)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	+
Ngamdokmai et al. (2021)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	+
Sprenger et al. (2021)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	+
Da Ressurreição et al. (2022)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	+
<i>In human</i>																
Waheed et al. (2019)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	+

Relevance questions

1. Would implementing the studied intervention, procedure or product (if found successful) improve outcomes for the patients/clients/target population group? (NA for some Epi studies)
2. Did the authors study an outcome (dependent variable) or topic the patients/clients/target population group would care about?
3. Is the focus of the intervention, procedure product (independent variable) or topic of study a common issue of concern to dietetics practice?
4. Is the intervention, procedure or product feasible for application in dietetic practice?

If the answers to the above relevant questions are "Yes," the report is eligible for designation with a plus (+) on the Evidence Quality Worksheet, depending on answers to the following validity questions.

Table 2. Risk of bias assessment using the ADA quality criteria checklist for primary research (continued...)

Validity questions	
1.	Was the <u>research question</u> clearly stated?
2.	Was the <u>selection</u> of study subjects/units free from bias?
3.	Were <u>study groups comparable</u> , or was an appropriate reference standard used?
4.	Did the study describe the methods for handling data losses from the original sample (e.g., withdrawals)?
5.	Was <u>blinding</u> used to prevent the introduction of bias?
6.	Was the intervention/treatment regimen/exposure factor, procedure, process or product of interest and any detailed comparison(s) described? Were <u>intervening factors</u> described?
7.	Were <u>outcomes, conditions</u> , or interest status clearly defined, and were the <u>measurements valid and reliable</u> ?
8.	Was the <u>statistical analysis</u> appropriate for the study design and type of outcome indicators?
9.	Do results with biases and limitations considered support conclusions?
10.	Is bias due to the study's <u>funding or sponsorship unlikely</u> ?
MINUS/NEGATIVE (-)	
If most (six or more) of the answers to the above validity questions are "No," the report should be designated with a minus (-) symbol on the Evidence Worksheet.	
NEUTRAL (∅)	
If the answers to validity criteria questions 2, 3, 6, and 7 are "Yes" but several other criteria indicate study weaknesses, the report should be designated with a neutral (∅) symbol on the Evidence Worksheet.	
PLUS/POSITIVE (+)	
If most (six or more) of the answers to the above validity questions are "Yes" (including criteria 2, 3, 6, 7), the report should be designated with a plus symbol (+) on the Evidence Worksheet.	
When a validity criteria question is NA	
Suppose any of the ten validity questions are NA. In that case, the report requires a majority of "Yes" answers (including 2, 3, 6, 7, as applicable) for a plus (+) or a majority of "No" answers for a minus (-) rating.	

A human study by Waheed et al. (2019) showed that *C. citratus* leaf powder decreased total cholesterol, triglycerides, and LDL in hyperlipidaemia subjects.

C. citratus leaves aqueous extract (Adeneye and Agbaje, 2007) increased HDL levels in normal rats. *C. citratus* leaves hydroalcoholic extract (Furtado et al., 2011), roots aqueous extract (Abbas et al., 2019), and powder (Abdelrahman and Omar, 2023) increased HDL in the hyperlipidaemia model. *C. citratus* essential oil (Kumar et al., 2011) and powder (Abdelrahman and Omar, 2023) decreased the atherogenic index in the hyperlipidaemia model. *C. citratus* whole plant water extract decreased atherogenic index in normal rats (Somparn et al., 2018)

Effect of Cymbopogon citratus on inhibiting adipogenesis, lipogenesis, and increasing lipolysis

In an *in vivo* study, whole plant water extract of *C. citratus* reduced the expression of SREBP-1c, which promotes lipogenesis in normal rats (Somparn et al., 2018). *In vitro* studies proved that citral (Sprenger et al., 2022; Sri Devi and Ashokkumar, 2018) and ethanol extract (Jo et al., 2019) from *C. citratus* inhibited adipogenesis in 3T3-L1 preadipocytes. Sri Devi and Ashokkumar (2018) study proved that 3T3-L1 preadipocytes treated with citral on differentiation process showed decreased expression of transcription factors and genes involved in adipogenesis, namely PPAR γ , SREBP-1c, and FAS. Citral also suppressed the expression of PI3K/AKT (a signalling pathway in-

volved in differentiation, inflammation, and proliferation) (Sri Devi and Ashokkumar, 2018).

The study of Jo et al. (2019) showed that ethanol extract of *C. citratus* reduced the expression of PPAR γ and C/EBP α . Ethanol extract of *C. citratus* also increased AMPK activity as an important regulator of cellular energy metabolism and regulated adipocyte differentiation. Sprenger et al. (2022) proved that citral and its isomers reduced adipocyte differentiation by decreasing FABP4 expression, decreased lipid uptake by decreasing SREBP-2 expression, decreased lipogenesis by decreasing peripilin expression, and increased lipolysis by decreasing CD36/FAT expression on 3T3-L1 preadipocytes.

Citral reduced lipid accumulation and adipocyte size in obesity model mice (Modak and Mukhopadhyaya, 2011). *C. citratus* essential oil (Ngamdokmai et al., 2021), citral (Ngamdokmai et al., 2021; Sri Devi and Ashokkumar, 2018), and ethanol extract (Jo et al., 2019) reduced lipid accumulation in 3T3-L1 adipocytes. Jo et al. (2019) also showed that *C. citratus* ethanol extract induced G0/G1 cell cycle arrest of 3T3-L1 cells by increasing zp21 and p21 expression and decreasing CDK2, cyclin A, and cyclin B1 expression.

Effect of Cymbopogon citratus on energy expenditure

Administration of citral to obese mice models increased the metabolic rate, suggesting more significant energy dissipation (Modak and Mukhopadhyaya, 2011).

Effect of Cymbopogon citratus on glucose level

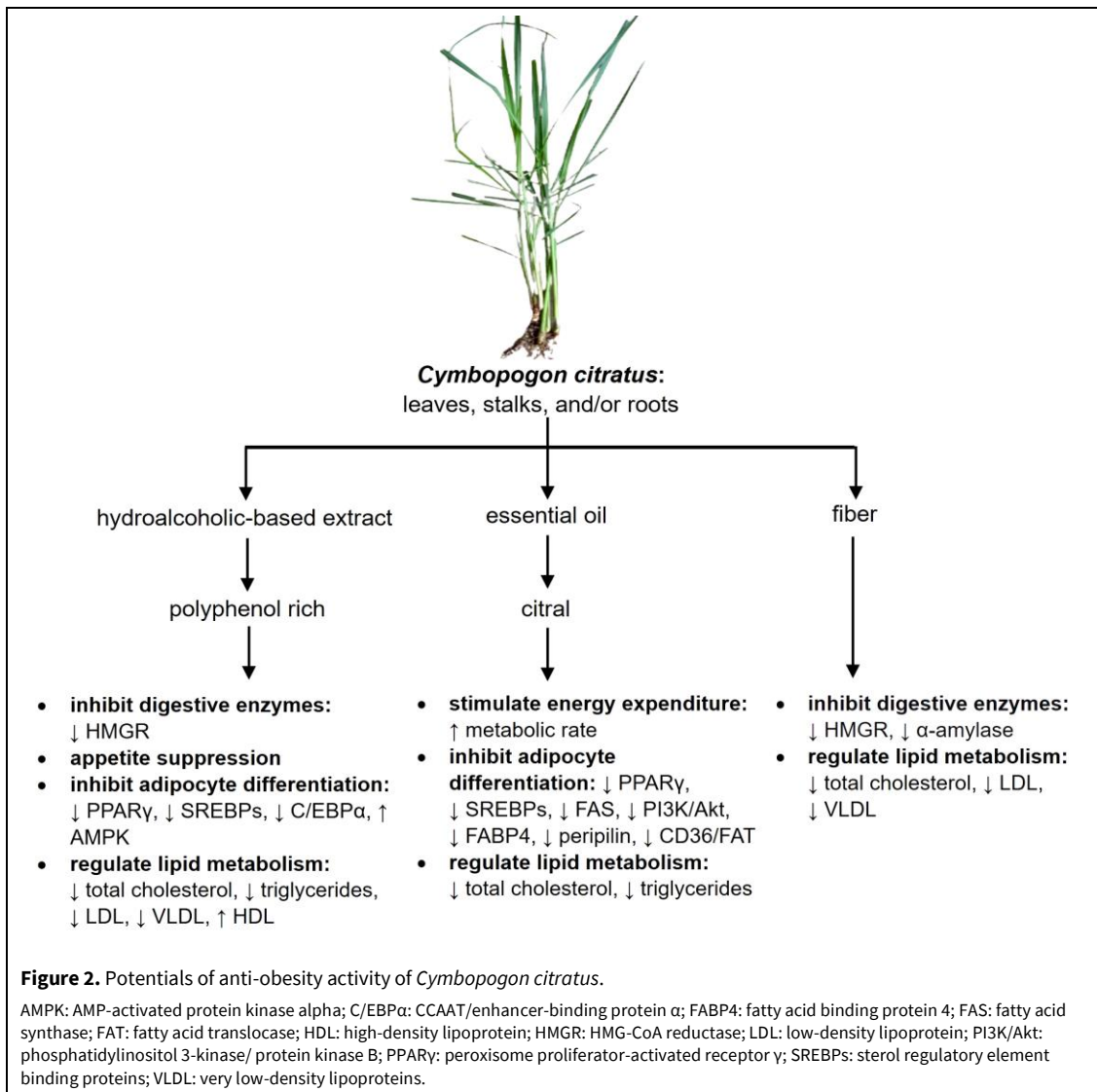
An *in vitro* study by Villalobos et al. (2021) showed that propionate from *C. citratus* total dietary fibre fermentation reduced α -amylase activity (an enzyme that causes the degradation of starch molecules to release glucose subunits). *C. citratus* leaves aqueous extract (Adeneye and Agbaje, 2007) and total dietary fibre (Villalobos et al., 2021) lowered fasting plasma glucose in normal rats and rats with high fat and glucose diets. Administration of citral to obese models reduced fasting plasma glucose and increased glucose tolerance (Modak and Mukhopadhyaya, 2011). *C. citratus* powder decreased glucose levels in rats with a high-fat diet (Abdelrahman and Omar, 2023).

DISCUSSION

This review showed that the potential of *C. citratus* as an anti-obesity agent could come from various parts of the plant (leaves, stalks, roots, or whole plant) and various preparations or extractions (aqueous extract, ethanol extract, powder, dietary fibre, or essential oil). This method, of course, affects the phytochemical content, which has anti-obesity effects. Sev-

eral studies have characterised the *C. citratus* preparations. Results of the characterisation of aqueous whole plant extract by Somparn et al. (2018) *C. citratus* water extract contains polyphenols, including gallic acid, isoquercetin, quercetin, rutin, catechin, and tannic acid. Rutin, isoquercetin, catechin, and quercetin are the flavonoids with the most content. Da Ressurreição et al. (2022) also showed that the phenolic compounds present in aqueous extracts of *C. citratus* leaves are phenolic acid (p-coumaric acid, caffeic and ferulic acid derivatives), flavonoids (flavone type, namely C- and O-glycosylated derivatives of luteolin), and tannins (mostly the condensed type, namely, type B procyanidins and derivatives of apigenin flavans and luteolin flavans). The results of phytochemical screening by Betancourt et al. (2015) from hydroalcoholic extract of *C. citratus* aerial parts also showed the presence of flavonoids, triterpenes, phenolics and tannins. Phytochemical analysis by Jo et al. (2019) showed the presence of the polyphenols caffeic acid and isoorientin in *C. citratus* ethanol extract. The essential oil from *C. citratus* leaves obtained through hydrodistillation extraction predominantly contains the monoterpenes citral (a mixture of geranial and neral stereoisomers), beta myrcene, and geraniol (Costa et al., 2011). Research by Villalobos et al. (2021) shows that propionate is the dominant SCFA content of total dietary fibre *C. citratus* fermentation products using fresh human faecal inoculum. Based on these, it can be concluded that the anti-obesity effect of *C. citratus* can come from its polyphenol, essential oil, or fibre content through the same or different mechanisms.

In general, different mechanisms of anti-obesity action are associated with inhibiting digestive enzymes, stimulating energy expenditure, suppressing appetite, inhibiting adipocyte differentiation, regulating lipid metabolism, and modulation of gut microbiota (Singh et al., 2020). Hydroalcoholic-based extract from *C. citratus* is rich in polyphenols, which have anti-obesity activity through inhibition of digestive enzymes (Somparn et al., 2018), appetite suppression (Dingba et al., 2017), modulation of lipid metabolism (Abbas et al., 2019; Adeneye and Agbaje, 2007; Agbafor and Akubugwo, 2007; Betancourt et al., 2015; Somparn et al., 2018), and adipogenesis inhibition (Somparn et al., 2018; Jo et al., 2019). *C. citratus* essential oil and citral as its major components have anti-obesity activity through stimulation of energy expenditure (Modak and Mukhopadhyaya, 2011), modulation of lipid metabolism (Costa et al., 2011; Kumar et al., 2011), and adipogenesis inhibition (Ngamdokmai et al., 2021; Sprenger et al., 2022; Sri Devi and Ashokkumar, 2018). Dietary fibre from *C. citratus* has anti-obesity activity by inhibiting digestive enzymes and modulation of lipid metabolism (Villalobos et al., 2021) (Fig. 2).



From inhibiting digestive enzymes, *C. citratus* whole plant water extract (Somparn et al., 2018) reduced the expression of HMGR (catalysator of endogenous cholesterol synthesis) in normal rats. *In vitro*, the study by Villalobos et al. (2021) showed propionate as the predominant SCFA-produced fermentation from *C. citratus* total dietary fibre inhibited HMGR and α -amylase (an enzyme that causes the degradation of starch molecules to release glucose subunits) activity *in vitro*. SCFA products from fermented *C. citratus* total dietary fibre can influence gut microbiota, contributing to anti-obesity. However, this review did not include and explore the article regarding the influence of *C. citratus* on the gut microbiota.

A study by Modak and Mukhopadhaya (2011) proved that citral administrated to obese mice increased the metabolic rate, suggesting more significant energy expenditure. This mode of action had not been explained. It opens up opportunities for future

research to examine the mechanism of citral in stimulating energy expenditure.

In the study by Dimgba et al. (2017), the aqueous leaf extract of *C. citratus* suppressed appetite in normal Wistar rats. The mechanism of appetite suppression by *C. citratus* had not been explained. Further research can be carried out regarding the effect of *C. citratus* water extract on neurological and hormonal processes that control appetite.

The fundamental cause of obesity is overconsumption of energy or lack of energy expenditure. Excessive food or energy intake causes adipose tissue expansion, including an increase in the number (adipogenesis/hyperplasia) and size (hypertrophy) of adipocytes. Thus, modulating the adipogenesis process is a potential therapeutic method to treat obesity (Sri Devi and Ashokkumar, 2018; Zhao et al., 2022). Adipogenesis is a complex multi-step process involving a cascade of transcription factors that regulate gene

expression, forming adipocytes. The transcription factors SREBP, C/EBP α , and PPAR γ are important determinants of adipocyte terminal differentiation by regulating the expression of genes involved in adipogenesis and lipogenesis, such as FABP4, acetyl-CoA carboxylase (ACC), and FAS (Ku et al., 2022; Sri Devi and Ashokkumar, 2018).

Lipid metabolism abnormalities are common in obesity. Lipid abnormalities in obesity include increased serum triglycerides, VLDL, LDL, and decreased HDL (Chan et al., 2016; Feingold, 2023; Klop et al., 2013). When lipid accumulation exceeds the storage capacity of adipocytes, it results in increased delivery of free acids to the liver. This process causes hepatic triglyceride accumulation and increases VLDL synthesis by the liver, which inhibits chylomicron lipolysis due to competition, especially for lipoprotein lipase (LPL) levels, with an increase in residual TG transported to the liver. Lipolysis is further impaired in obesity with reduced levels of LPL mRNA expression in adipose tissue and reduced LPL activity in skeletal muscle. Hypertriglyceridemia further induces an increased cholesterol ester (CE) and TG exchange between VLDL, HDL, and LDL by cholesteryl ester-transfer-protein (CETP). This condition then causes a decrease in HDL-C concentration and TG content in LDL. In addition, hepatic lipase (HL) removes TG and phospholipids from LDL for the final formation of small, dense LDL (Feingold, 2023; Klop et al., 2013).

Hypertrophic adipocytes release chemokines that induce macrophage recruitment from the bloodstream, increasing infiltration and inflammation with increased production of pro-inflammatory cytokines such as TNF- α and IL-6. This increase in residual triglycerides transported to the liver is achieved by increased FFA release and dysregulation of leptin, adiponectin, and resistin secretion. Adipokines derived from macrophages and adipose tissue act in a paracrine or autocrine, exacerbating adipose tissue inflammation. Altered adipokine secretion at the systemic level may decrease muscle and liver insulin sensitivity through increased ectopic lipid deposition and inflammation. This effect causes an increase in hepatic glucose production (via gluconeogenesis and glycogenolysis). In contrast, muscle metabolism is altered to a pattern of low glucose uptake and low FFA oxidation (with increased levels of the glycerol substrate for hepatic gluconeogenesis). This event causes an increase in plasma glucose and a subsequent increase in insulin resistance (Coelho et al., 2013; Rezaee and Dashty, 2013).

Administration of *C. citratus* dietary fibre (Villalobos et al., 2021), hydroalcoholic base extract (Adeneye and Agbaje, 2007), powder (Abdelrahman and

Omar, 2023), and citral (Modak and Mukhopadhaya, 2011) reduced plasma glucose levels *in vivo*. The administration of citral to 3T3-L1 preadipocytes reduces the inflammatory cytokines (Sri Devi and Ashokkumar, 2018). This result shows the potential of *C. citratus* in preventing the metabolic consequences of obesity.

As far as the author knows, research on *C. citratus* as an anti-obesity agent in humans is still limited. Further research, utilising a randomised controlled trial on humans, is needed to explore the potential of *C. citratus* in both *in vivo* and *in vitro* research. There is a need for further research regarding other mechanisms of *C. citratus* as an anti-obesity agent, namely its mechanism for increasing energy expenditure and suppressing appetite. This review also showed the potential for developing *C. citratus* as an anti-obesity functional food product, considering that all parts of the plant can provide therapeutic effects and, in general, the community uses only the stalks and roots of *C. citratus*. There is also a need to develop nutraceutical products from *C. citratus* based on its polyphenol, essential oil, and total dietary fibre content.

Strengths and limitation

This article is the first comprehensive systematic literature review on the anti-obesity activity of *C. citratus*, as the authors know. As far as the authors are concerned, they only found one study on the anti-obesity effects of *C. citratus* in humans. This review did not include articles regarding the effects of *C. citratus* on gut microbiota, which is one of the potential anti-obesity mechanisms. This review also did not include the effects of *C. citratus* on obesity, which are related to other metabolic syndromes or consequences of obesity, such as diabetes or cardiovascular disease.

CONCLUSION

The anti-obesity activity of *Cymbopogon citratus*, commonly known as lemongrass, could come from various parts of the plant (leaves, stalks, roots, or whole plant) and various preparations or extractions (aqueous or hydroalcoholic extract, powder, dietary fibre, or essential oil). Hydroalcoholic-based extract from *C. citratus* was rich in polyphenols, which had anti-obesity activity through inhibiting digestive enzymes, appetite suppression, modulation of lipid metabolism, and adipogenesis inhibition. *C. citratus* essential oil and citral as its primary component had anti-obesity activity through energy expenditure stimulation, lipid metabolism modulation, and adipogenesis inhibition. Dietary fibre from *C. citratus* had anti-obesity activity by inhibiting digestive enzymes and modulating lipid metabolism. However, further research is needed regarding the molecular mecha-

nisms of *C. citratus*'s influence in suppressing appetite and stimulating energy expenditure. Limited studies of the anti-obesity effects of *C. citratus* in humans encourage the need for proof in randomised controlled trials on humans. *C. citratus* has the potential to be developed as a functional food or nutraceutical product as an anti-obesity agent.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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AUTHOR CONTRIBUTION:

Contribution	Mashitah MW	Widodo N	Permatasari N	Rudijanto A
Concepts or ideas	x	x	x	x
Design	x	x	x	x
Definition of intellectual content	x	x	x	x
Literature search	x			x
Experimental studies	x			x
Data acquisition	x			x
Data analysis	x	x	x	x
Statistical analysis				
Manuscript preparation	x	x	x	x
Manuscript editing	x	x	x	x
Manuscript review	x	x	x	x

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