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Antiobesity Potential of Butterfly Pea Flower (*Clitoria Ternatea*): A Literature Review

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Abstract

Obesity is a health problem with an increasing prevalence every year in many countries including Indonesia. Obese patients are at risk for complications related to some non-communicable diseases. The difficulty of losing weight in obese patients is due to low awareness of a good lifestyle, appropriate dietary patterns, and discipline in taking drugs to prevent complications. However, the need for drug consumption takes a long time. The risk of side effects arising from long-term drug use needs to be considered. Using herbal plants as an additional dietary intervention could be a better choice. This review described the benefits of the butterfly pea (*Clitoria ternatea*) flower as antiobesity. This study is a literature review by searching preceding published articles in Pubmed, ScienceDirect, Cochrane, and Google Scholar journals. The keywords used are (*Clitoria ternatea*) OR (Bunga Telang) OR (Butterfly pea) AND (Obesity) OR (Antiobesity). Articles are limited by publication period from 2012 to 2022 and then selected based on the criteria. This literature review concluded that the administration of *Clitoria ternatea* extracts (CTE) can become an alternative antiobesity by inhibiting weight gain, increasing adipose lipolysis, and decreasing the expression of adipogenic and lipogenic proteins.

Keywords: antiobesity, bunga telang, butterfly pea flower

Review Article

INTRODUCTION

Obesity is a condition caused by excessive energy intake accompanied by increased free fatty acids in adipose tissue and a lack of physical activity as a form of energy expenditure (Sundaram et al., 2019) (Misra & Shrivastava, 2013). This condition was very worrying because obesity, especially central obesity, can lead to some chronic diseases. Obesity and overweight can affect health conditions due to excess accumulation of body fat. Obese patients with dyslipidemia showed elevation of TG and FFA levels. They increased plasma concentrations of apolipoprotein (apo) B. Impaired lipolysis of triglyceride-rich triglyceride lipoproteins can occur with decreased mRNA expression of lipoproteins in adipose tissue (Mehraban et al., 2021) In managing obesity and dyslipidemia, dietary recommendations play a crucial role in pharmacological interventions to prevent the side effects of chronic hypercholesterolemia (Sundaram et al., 2019; Misra & Shrivastava, 2013). Since 1975, the obesity rate has tripled. There are 39% of adults who are overweight and 13% have been diagnosed with obesity (Vaamonde & Álvarez-Món, 2020).

The burden of obesity is increasing in Indonesia. The prevalence of obesity from the Basic Health Survey (Riskesdas) (using a body mass index of 27 and over) among adults aged 18 years increased

from 10.5% in 2007 to 21.8% in 2018. The prevalence of obesity in adults in the territory of Indonesia, starting from the five highest are in Jakarta, Riau Islands, East Kalimantan, North Sulawesi, and West Papua. The increase in obesity rates over the past decade has been higher than overweight, which has increased from 8.% (2007) to 13.6 (2018). The Ministry of Health's Nutrition Status Monitoring (PSG) data shows a two-fold increase in the obesity rate in adults from 10.6% in 2016 to 25.8% in 2017 (Kemenkes RI, 2018; Ayuningtyas et al., 2022). The mortality rate for obesity is higher than in underweight patients in various countries (Vaamonde & Álvarez-Món, 2020). Obesity has been declared as a chronic disease with a high mortality rate and disability (Burki, 2021). However, obesity can be prevented through dietary modifications and physical activity. Various food and non-food ingredients were studied to find out their role in preventing obesity, such as butterfly peas (*Clitoria ternatea*) (WHO Regional Office for Europe, 2022).

Clitoria ternatea is a subgenus of Clitoria originating from the island of Ternate (Maluku Islands, Indonesia). This flower grows in South and East Africa, India, Madagascar, and other islands in the western Indian Ocean (Oguis et al., 2019). Butterfly pea flowers have been used traditionally for health as a supplement to improve cognitive function and as antipyretic, anti-inflammatory, anti-pain, and anti-diabetic. This flower has two colors, white and blue, but more research has been done on blue flowers. Butterfly pea flowers are known to contain many phenolic acids and other flavonoids (Hiromoto et al., 2013). Bioactive compounds, especially polyphenols, and flavonoids, are known to reduce inflammation and play an important role in preventing obesity (Ramírez-Moreno et al., 2022). The main color-producing substance in butterfly pea flowers is anthocyanin, a delphinidin derivative called termination. Ternatin is delphinidin 3-O-(6''-O-malonyl)-β-glucoside which has the structure of 3',5'-di-O-β-glucoside in ring B (Hiromoto et al., 2013). The application of anthocyanin in food products is limited because of its stability (Vidana Gamage et al., 2021). Cyclotide is the latest active compound found in butterfly pea flowers (Nguyen et al., 2016). Cyclotides are small circular peptides or mini proteins, consisting of 30 amino acids containing six conserved cysteine residues and three disulfide bonds which form the cyclic cystine knot (CCK) thereby making it more stable against acids, heat, and proteolytic degradation (Burman et al., 2015). The structure of proline as cis or trans determines the cyclotide subfamily, Mobius (Kalata B1) has a cis-proline, and Bracelet (cycloviolacin) structure O1) has a trans-proline structure. In addition, there are minor cyclotides, which inhibit trypsin (Andrew Gould, 2017). These compounds are known to have pharmacological effects such as antioxidant activity, antiglycation, antimicrobial, anti-platelet aggregation, anti-inflammatory, antipyretic, antihelmintic, antihyperglycemic, antihyperlipidemic, and antiobesity by attenuating adipogenesis (Chayaratanasin et al., 2019). Eliasen et al. inserted the melanocortin receptor-activation sequence into Kalata B1 to form a more stable melanocortin receptor agonist (Eliasen et al., 2012). Melanocortin-4 receptor (MC4R) is known to be an essential gene that causes obesity. Mutation in this gene cause a partial or complete loss of the ability of the MC4R to regulate dietary intake, homeostasis, and body weight (BW) (Marenne et al., 2020; Brouwers et al., 2021). The studies on *Clitoria ternatea* extract's effect in preventing obesity are still limited. However, several studies have been carried out both in vitro and in vivo methods. There are many useful ingredients in *Clitoria ternatea extracts* that can be used for antiobesity. We did not find literature in the form of a review regarding the benefits of pea flowers in obesity. Therefore, we would like to conduct a literature review to collect studies that have been conducted to improve insight into the potential of butterfly pea flowers in preventing obesity. So that this study can provide a reference for developing further studies on the benefits of butterfly pea flowers in overcoming obesity.

METHODS

The search method in this study is a scooping review. Article searches use a database of articles from PubMed, ScienceDirect, Cochrane, and Google Scholar. The search was limited to published literature with a range of 10 years from 2012 to 2022. The types of literature used were Indonesian and English literature related to the good of CTE in cases of obesity. The literature search strategy uses the

keywords (*Clitoria ternatea*) OR (Telang flower) OR (Butterfly pea) AND (Obesity) OR (Anti-obesity)). Based on the search results, four pieces of literature matched the topics to be discussed (Figure 1).

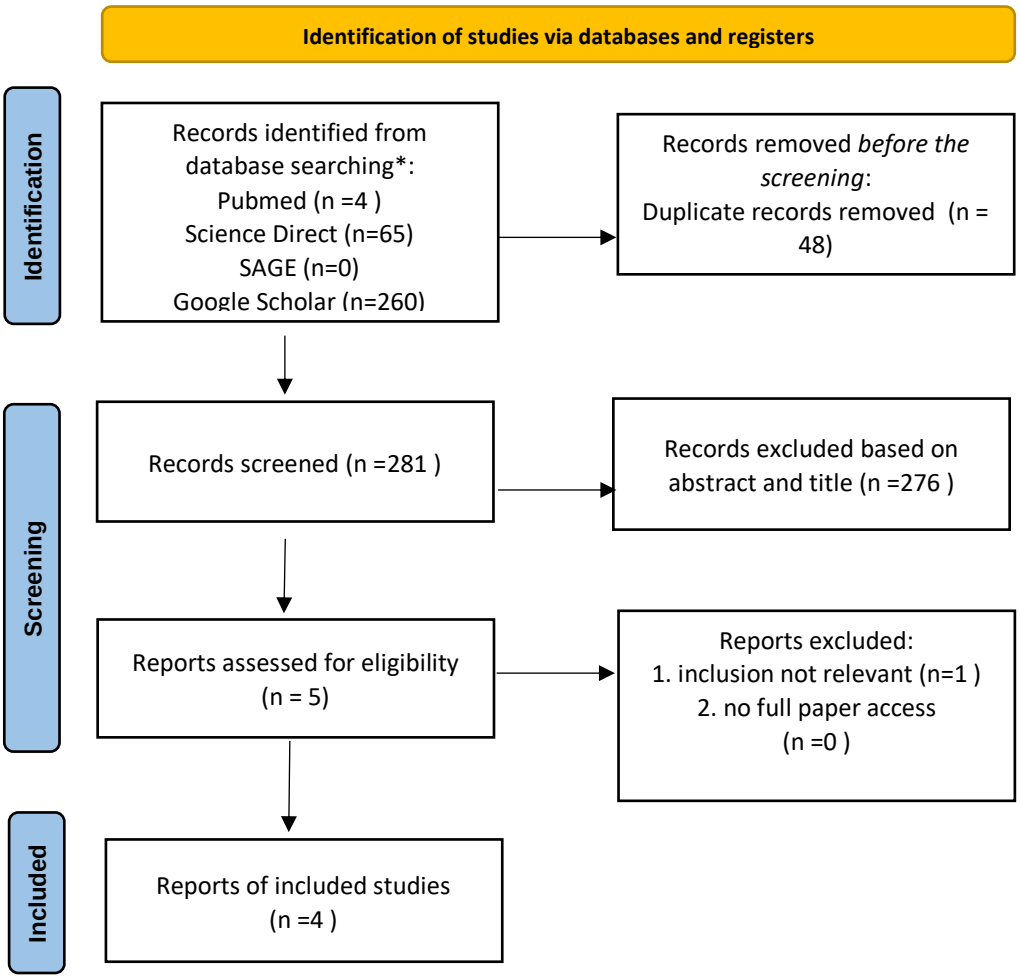

Figure 1. Literature searching strategy and identification via databases using keywords

RESULTS

In the search process, 329 articles were found, with 48 duplicate articles. The process continued with the selection of titles, relevant abstracts, appropriate inclusion and exclusion criteria, and articles with full text until four relevant articles were obtained (Figure 1). Based on advanced search and thorough selection to the relevant literature research purposes, there are 4 articles included selected reviews which are the results of in vivo and in vitro studies (Table 1).

Table 1. Summary of the *Clitoria ternatea* studies

No	References	Methods	General outcomes
1	Chayaratanasin et al, 2019	Invitro: preadiposit 3T3-L1 The phytochemical profile of CTE (Clitoria ternatea extracts) was analyzed by *liquid chromatography & tandem mass spectrometry* (LC-MS/MS)	1. Giving CTE 500-750 µg/mL significantly increased lipolysis of mature adipocytes 2. RT-PCR: Akt1 (T308) phosphorylation decreased significantly at a dose of 500 µg/mL; 750 µg/mL; 1000 µg/mL CTE

(*continue on next page*)

(continued)			b. ERK1/2 phosphorylation (T202/Y204) decreased significantly at a dose of 750 µg/mL; 1000 µg/mL CTE c. PPARγ & C/EBPα mRNA expression decreased significantly at doses of 500-1000 µg/mL CTE 4. Western blot: CTE (500-1000 µg/mL) a. The expression of an adipogenic protein, lipogenic PPARγ & C/EBPα decreased significantly
2	Thilavech et al, 2021	Clinical study (human) 1. 19-person early recruitment: 16 people (9 overweight dan 7 obese) finished the study 2. Three groups: 1. High fat meal + washout 1 week given 2g CTE+ High Fat meal + washout 1 week + 1gCTE+ HF meal 2. 1gCTE+ HF meal + washout 1 week + HF meal + washout 1 week + 2gCTE+ HF meal 2gCTE+ HF meal + washout 1 week + 1gCTE+ HF meal + washout 1 week + HF meal	1. Free fatty acids (FFA) decreased significantly at 360 min postprandial at 2g CTE 2. levels of antioxidants (FRAP & thiols) increased followed by a significant decrease in MDA at CTE 1g and 2g 5. Glutathione peroxidase (Gpx) activity increased significantly at 2g CTE, with decreased cytokine levels of IL-6 & TNFα and increased IL-1β
3	Wang et al, 2022	In vivo study. 40 C57BL/6J mice were fed a standard diet (SD) or a high-fat, high-fructose (HFFD) diet for 16 weeks, and the HFFD-fed animals were fed at doses of 0.25%, 0.5%, and 2% (w /w) of CTE in drinking water.	Administration of high doses of Aquadest + CTE (2%) significantly inhibited weight gain, and increased plasma adiponectin levels and FFA levels.
4	Permatasari et al, 2022	In vivo study: 40 Swiss albino male mice weighing 21.53 ± 1.92 g (3-5 weeks old). Probiotic drinks in the form of KBPF were given for six weeks. The treatment group was given KBPF with various doses of 65 mg/kg BW and 130 mg/kg BW,	In vivo studies: A dose of 130 mg/kg BW lowers the lipid profile; lowers oxidative stress levels, and increases levels of inflammatory markers (PGC-1α, TNFα, IL10).

DISCUSSION

The mechanism of adipogenesis inhibition is related to the reduction in the number and lipid content of adipocytes. Preadipocytes can proliferate to increase fat mass. The proliferation and differentiation of preadipocytes caused the number of adipocytes. The development of the herbal plant *Clitoria ternatea* provides safer additional opportunities for dietary intervention for patients with obesity. Many recent studies reported anti-obesity potential from leaf, root, and flower extracts from the *Clitoria ternatea*. The Polyphenols and flavonoid compounds in *Clitoria ternatea* extracts are powerful antioxidants and able to induce apoptosis in preadipocytes (Rayalam et al., 2008; T. Li et al., 2020). *Clitoria ternatea* extracts (CTE) affect 3T3-L1 preadipocytes. It inhibited the proliferation and cycle cell retardation. CTE at concentrations of 250, 500, and 750 µg/mL significantly delayed the cell cycle by increasing the cell distribution in G0/G1 phase and decreasing the G2/M phase. Furthermore, it

suppressed the phospho-Akt and phosphor-ERK1/2 signaling pathways and inhibited cell differentiation by decreasing PPARy and C/EBPy. Lipolytic activity in adipocytes was also increased induced by catecholamine. *Clitoria ternatea* extract attenuated adipogenesis by controlling cell cycle progression and decreased adipogenic gene expression (Chayaratanasin et al., 2019).

Permatasari et al. (2022) reported the *Clitoria ternatea* extracts effect (130 mg/kg BW) significantly relieved metabolic disorders caused by a high-fat diet. It also increased HDL levels and reduced LDL, TG, fasting blood glucose (FBG), and cholesterol levels. The addition of 65 and 130 mg/kg BW significantly decreased the activity of the lipase and amylase enzymes. Thilavech et al. (2021) demonstrated the role of CTE in postprandial glycemic and lipemic responses, antioxidant status, and pro-inflammatory markers in overnutrition men after consuming a high-fat meal. Administration of 2 g of CTE to obese patients has been shown to reduce serum triglycerides and postprandial serum free fatty acids 360 minutes post-eating HF food. It significantly improved plasma antioxidant status by gaining plasma FRAP and thiol levels. The plasma Gpx activity was significantly higher at 180 min after the HF meal with 2 g of CTE ingestion. This study supports that CTE can be used as an alternative natural agent to reduce postprandial lipemia and improve antioxidant status in overnutrition men after consuming HF foods (Thilavech et al., 2021). Very few studies, especially in humans, have looked at the role of CTE on adiponectin levels. Therefore, it needs future study explore how CTE can reduce adiponectin to support the development of CTE as an alternative therapy to support obesity.

Clitoria ternatea extracts might inhibit the progression of weight gain or the development of obesity. It is likely to occur because CTE can increase adiponectin levels, improve insulin resistance and lipid profiles (Wang et al., 2022). These results are similar to other studies, but Permatasari et al stated that there was no significant difference in body weight between the treatment and control groups. The amount of CTE given by Wang et al was not much different from Permatasari et al, which was at a dose of 2g CTE. However, Permatasari et al made observations for 6 weeks, shorter than Wang, who reached 16 weeks. Thilavech et al also administered a single dose of 2g CTE to humans which resulted in positive results for lipid profile and antioxidant levels. However, the effect of CTE on overnutrition respondents for a certain period cannot be observed, because Thilavech et al only observed the effects immediately after administration, only 60 – 360 minutes after administration. Improvements in blood glucose and lipid profiles after supplementation might play a role in inhibiting weight gain. Chayaratanasin et al found a decrease in triglycerides, an increase in mature adipocyte lipolysis, and a decrease in adipogenic protein expression with CTE administration. In vivo, Wang et al stated that CTE reduces hyperplasia and hypertrophy of abdominal fat tissue and accumulation of lipids in the liver.
Adiponectin levels were inversely related to body mass index (BMI) and fat mass. The CTE-improved energy balance by adiponectin is likely due to several mechanisms that align with the results of the four studies above. Clitoria Ternatea Extract reduces total cholesterol, LDL cholesterol (Wang et al., 2022), triglycerides (Thilavech et al., 2021), plasma glucose (Permatasari et al., 2022), and mature adipocyte lipolysis (Chayaratanasin et al., 2019). *Adiponectin* is a protein class hormone mainly produced by white adipose tissue (Rosa et al., 2021). Several studies state that adiponectin plays a role in energy homeostasis and lipid and carbohydrate metabolism (Halah et al., 2018)· Adiponectin increases the efficiency of energy use because it plays a role in increasing glucose tolerance & insulin sensitivity and reducing energetic expenditure (Cisternas et al., 2019). Wang et al (2022) conducted a study on obese rats. *C. ternatea* aqueous extract significantly inhibited high-fat diet-induced weight gain in rats. Supplementation of *Clitoria ternatea* improved high-fat-induced increases in plasma insulin, leptin, and HOMA-IR levels and significantly increased plasma adiponectin levels in rats. In addition, mice treated with CT showed a significant reduction in liver weight compared to mice fed a high-fat diet.

Insulin sensitivity rises because adiponectin reduces hepatic glucose production and improves hepatic insulin sensitivity (Bao et al., 2014). Adiponectin can gain the expression of gluconeogenesis enzymes, phosphoenol-carboxykinase, and glucose-6-phosphatase in the liver (Qin et al., 2022). Pancreatic beta cells treated with adiponectin showed improvement in insulin exocytosis and Pdx-1

and MafA gene expression, both co-activators of insulin gene transcription (Li et al., 2020). Adiponectin elevates glucose consumption by stimulating GLUT4 membrane translocation in muscle cells and adipocytes after AMPK phosphorylation (Wang et al., 2022). It is because the APPL1 protein activates the Rab5 protein. Rab5 is a GTPase enzyme involved in endosome biogenesis and a key in GLUT4 translocation from the endosome to the plasma membrane (Karvela et al., 2020). Adiponectin also inhibits the formation of glucose and glycogen. This is because it reduces the expression of the enzyme glucose-6-phosphatase and PEPCK, reducing glycogenolysis and gluconeogenesis in liver cells (Tang et al., 2022). Because of its role in AMPK activation, adiponectin also reduces glycogen production in muscle cells (Sung et al., 2022).

Increased adiponectin expression raised adipocyte differentiation, insulin sensitivity, and TG accumulation in adipocytes (Su et al., 2021). Visceral lipid deposits will be destroyed and stimulate the formation of new adipocytes in the subcutaneous tissue more sensitive to insulin (Yang et al., 2018). This situation is also related to increased FFA levels. Adiponectin stimulates the expression of fatty acid translocase enzyme, so it also increases the transport of fatty acids to muscle cells. Several enzymes involved in the β-oxidation process also increase in number and activity due to adiponectin, so fatty acid catabolism also increases (Ye et al., 2014). AMPK phosphorylation that occurs will inactivate ACC so that malonyl CoA production decreases and CPT-1 inhibition does not occur. CPT-1 is a transport protein that carries fatty acids to mitochondria, so it can be said that adiponectin increases fatty acid movements to mitochondria which β-oxidation enzymes will then degrade (Malandrino et al., 2015). Adiponectin elevates the expression of PPARγ so that it also influences the transcription of many genes involved in lipid catabolism (Zheng et al., 2014).

So from the previous studies, there are still opportunities to conduct further research on overnutrition animal models who are given 2g of CTE for 16 weeks or experimental people who experienced overnutrition receive 2g of CTE for 16 weeks. CTE as a support therapy for obesity must be accompanied by lifestyle changes. So further research that includes lifestyle changes in the form of improved intake and or increased physical activity is needed.

CONCLUSION

Based on the review of the literature studies conducted, it was concluded that the extract of the butterfly pea flower (*Clitoria ternatea*) has benefits in treating patients with obesity. In addition to losing weight, *Clitoria ternatea* also has a role in preventing obesity complications associated with dyslipidemia by improving HDL, LDL, total cholesterol, and amylase and lipase levels closer to normal.

CONFLICT OF INTEREST

All authors declare that there is no conflict of interest in this study

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REFERENCES

Adel, M. M. S., Tabatabaei-Malazy, O., Rahimi, R., Daniali, M., & Khashayar, P. (2021). Targeting dyslipidemia by herbal medicines: A systematic review of meta-analyses. *Journal of Ethnopharmacology*, 280. https://doi.org/https://doi.org/10.1016/j.jep.2021.114407

Andrew, G. J. A. C. (2017). Cyclotides: Overview and biotechnological applications Andrew. *Chembiochem*, *18*(14), 1350–1363. https://doi.org/10.1002/cbic.201700153.Cyclotides

Ayuningtyas, D., Kusuma, D., Amir, V., Tjandrarini, D. H., & Andarwati, P. (2022). Disparities in Obesity Rates among Adults: Analysis of 514 Districts in Indonesia. *Nutrients*, *14*(16), 1–18. https://doi.org/10.3390/nu14163332

Bao, Z., Yuan, X., Duan, S., & Dong, X. (2014). Clinical implication of changes in serum adiponectin in

patients with hepatogenic diabetes. *Scientific Reports*, 4, 10–12. https://doi.org/10.1038/srep05560

Brouwers, B., de Oliveira, E. M., Marti-Solano, M., Monteiro, F. B. F., Laurin, S. A……., & Mokrosiński, J. (2021). Human MC4R variants affect endocytosis, trafficking, and dimerization revealing multiple cellular mechanisms involved in weight regulation. *Cell Reports*, *34*(12). https://doi.org/10.1016/j.celrep.2021.108862

Burki, T. (2021). European Commission classifies obesity as a chronic disease. *The Lancet Diabetes and Endocrinology*, 9(7), 418. https://doi.org/10.1016/S2213-8587(21)00145-5

Burman, R., Yeshak, M. Y., Larsson, S., Craik, D. J., Rosengren, K. J., & Göransson, U. (2015). Distribution of circular proteins in plants: Large-scale mapping of cyclotides in the Violaceae. *Frontiers in Plant Science*, 6(October). https://doi.org/10.3389/fpls.2015.00855

Chayaratanasin, P., Caobi, A., Suparpprom, C., Saenset, S., Pasukamonset, P…… & Adisakwattana, S. (2019). Clitoria ternatea Flower Petal Extract Inhibits Adipogenesis and Lipid Accumulation in 3T3-L1. *Molecules*, 24(1894), 1–16.

Cisternas, P., Martinez, M., Ahima, R. S., William Wong, G., & Inestrosa, N. C. (2019). Modulation of Glucose Metabolism in Hippocampal Neurons by Adiponectin and Resistin. *Molecular Neurobiology*, 56(4), 3024–3037. https://doi.org/https://doi.org/10.1007/s12035-018-1271-x

Rosa, D. S. S. C., Liu, M., & Sweeney, G. (2021). Adiponectin synthesis, secretion, and extravasation from circulation to interstitial space. *Physiology*, 36(3), 134–149. https://doi.org/https://doi.org/10.1152/PHYSIOL.00031.2020

Eliasen, R., Daly, N. L., Wulff, B. S., Andresen, T. L., Conde-Frieboes, K. W., & Craik, D. J. (2012). Design, synthesis, structural, and functional characterization of novel melanocortin agonists based on the cyclotide kalata B1. *Journal of Biological Chemistry*, 287(48), 40493–40501. https://doi.org/10.1074/jbc.M112.395442

Halah, M. P., Marangon, P. B., Antunes-rodrigues, X. J., & Elias, X. L. L. K. (2018). *Neonatal nutritional programming impairs adiponectin effects on energy homeostasis in the adult life of male rats*. https://doi.org/10.1152/ajpendo.00358.2017

Hiromoto, T., Honjo, E., Tamada, T., Noda, N., Kazuma, K., Suzuki, M., & Kuroki, R. (2013). Crystal structure of UDP-glucose: anthocyanidin 3-O-glucosyltransferase from *Clitoria ternatea*. *Journal of Synchrotron Radiation*, 20(6), 894–898. https://doi.org/10.1107/S0909049513020712

Karvela, A., Kostopoulou, E., Rojas, G.A.P., Avgeri, A., Pappa, A., …..& Spiliotis, B. (2020). Adiponectin signaling and impaired GTPase Rab5 expression in adipocytes of adolescents with obesity. *Horm Res Paediatr*, 93, 287–296. https://doi.org/https://doi.org/10.1159/000510851

Kemenkes RI. (2018). Hasil Riset Kesehatan Dasar Tahun 2018. *Kementrian Kesehatan RI*, 53(9), 1689–1699.

Li, T., Zhang, L., Jin, C., Xiong, Y., Cheng, Y. Y., & Chen, K. (2020). Pomegranate flower extract bidirectionally regulates the proliferation, differentiation, and apoptosis of 3T3-L1 cells through the regulation of PPARγ expression mediated by the PI3K-AKT signaling pathway. *Biomedicine and Pharmacotherapy*, *131*(September), 110769. https://doi.org/10.1016/j.biopha.2020.110769

Li, X., Zhang, D., Vatner, D. F., Goedeke, L., Hirabara, S. M., & Zhang, Y. (2020). *Mechanisms by which adiponectin reverses high-fat diet-induced insulin resistance in mice*. *117*(51). https://doi.org/10.1073/pnas.1922169117

Malandrino, M. I., Fucho, R., Weber, M., Calderon-Dominguez, M., Mir, J. F., ……..& Herrero, L. (2015). Enhanced fatty acid oxidation in adipocytes and macrophages reduces lipid-induced triglyceride accumulation and inflammation. *American Journal of Physiology-Endocrinology and Metabolism*, *308*(9), E756–E769. https://doi.org/10.1152/ajpendo.00362.2014

Marenne, G., Hendricks, A. E., Perdikari, A., Bounds, R., Payne, F.,… & Barroso, I. (2020). Exome Sequencing Identifies Genes and Gene Sets Contributing to Severe Childhood Obesity, Linking PHIP Variants to Repressed POMC Transcription. *Cell Metabolism*, *31*(6), 1107-1119.e12. https://doi.org/10.1016/j.cmet.2020.05.007

Misra, A., & Shrivastava, U. (2013). Obesity and dyslipidemia in South Asians. *Nutrients*, *5*(7), 2708–2733. https://doi.org/10.3390/nu5072708

Nguyen, K. N. T., Nguyen, G. K. T., Nguyen, P. Q. T., Ang, K. H., Dedon, P. C., & Tam, J. P. (2016). Immunostimulating and Gram-negative-specific antibacterial cyclotides from the butterfly pea (Clitoria ternatea). *FEBS Journal*, *283*(11), 2067–2090. https://doi.org/10.1111/febs.13720

Oguis, G. K., Gilding, E. K., Jackson, M. A., & Craik, D. J. (2019). Butterfly pea (Clitoria ternatea), is a cyclotide-bearing plant with applications in agriculture and medicine. *Frontiers in Plant Science*, *10*(May), 1–23. https://doi.org/10.3389/fpls.2019.00645

Permatasari, H. K., Nurkolis, F., Gunawan, W., Ben, Yusuf, V. M., ……. & Tsopmo, A. (2022). Modulation of gut microbiota and markers of metabolic syndrome in mice on cholesterol and fat-enriched diet by butterfly pea flower kombucha. *Current Research in Food Science*, *5*(August), 1251–1265. https://doi.org/10.1016/j.crfs.2022.08.005

Qin, C., Zhao, W., Yan, X., Yang, G., Yang, L., ……& Nie, G. (2022). Effects of Adiponectin on Glucose Metabolism in the Hepatopancreas of Grass Carp (Ctenopharyngodon idella). *Aquaculture Nutrition*, *2022*, 1–14. https://doi.org/10.1155/2022/5699931

Ramírez-Moreno, E., Arias-Rico, J., Jiménez-Sánchez, R. C., Estrada-Luna, D., Jiménez-Osorio, A. S., …… & Sandoval-Gallegos, E. M. (2022). Role of Bioactive Compounds in Obesity: Metabolic Mechanism Focused on Inflammation. *Foods*, *11*(9), 1–23. https://doi.org/10.3390/foods11091232

Rayalam, S., Della-Fera, M. A., & Baile, C. A. (2008). Phytochemicals and regulation of the adipocyte life cycle. *Journal of Nutritional Biochemistry*, *19*(11), 717–726. https://doi.org/10.1016/j.jnutbio.2007.12.007

Su, S. C., Chiang, C. F., Hsieh, C. H., Lu, G. H., Liu, J. S., …… & Lee, C. H. (2021). Growth arrest-specific 6 modulates adiponectin expression and insulin resistance in adipose tissue. *Journal of Diabetes Investigation*, *12*(4), 485–492. https://doi.org/10.1111/jdi.13412

Sundaram, S., Palaniappan, B., Nepal, N., Chaffins, S., Sundaram, U., & Arthur, S. (2019). Mechanism of dyslipidemia in obesity—unique regulation of ileal villus cell brush border membrane sodium–bile acid cotransport. *Cells*, *8*(10). https://doi.org/10.3390/cells8101197

Sung, H. K., Mitchell, P. L., Gross, S., Marette, A., & Sweeney, G. (2022). ALY688 elicits adiponectin-mimetic signaling and improves insulin action in skeletal muscle cells. *American Journal of Physiology - Cell Physiology*, *322*(2), C151–C163. https://doi.org/10.1152/ajpcell.00603.2020

Tang, Y., Wang, Y., Chen, C., Chan, C., Tsai, F., & Chen, S. (2022). *Genetic and Functional Effects of Adiponectin in Type 2 Diabetes Mellitus Development*.

Thilavech, T., Adisakwattana, S., Channuwong, P., Radarit, K., Jantarapat, K., Ngewlai, K., Sonprasan, N., & Chusak, C. (2021). Clitoria ternatea flower extract attenuates postprandial lipemia and increases plasma antioxidant status responses to a high-fat meal challenge in overweight and obese participants. *Biology*, *10*(10). https://doi.org/10.3390/biology10100975

Vaamonde, J. G., & Álvarez-Món, M. A. (2020). Obesity and overweight. *Medicine (Spain)*, *13*(14), 767–776. https://doi.org/10.1016/j.med.2020.07.010

Vidana Gamage, G. C., Lim, Y. Y., & Choo, W. S. (2021). Anthocyanins From Clitoria ternatea Flower: Biosynthesis, Extraction, Stability, Antioxidant Activity, and Applications. *Frontiers in Plant Science*, *12*(December), 1–17. https://doi.org/10.3389/fpls.2021.792303

Wang, Y., Liu, T., Xie, Y., Li, N., Liu, Y., ….. & Granato, D. (2022). Clitoria ternatea blue petal extract protects against obesity, oxidative stress, and inflammation induced by a high-fat, high-fructose diet in C57BL/6 mice. *Food Research International*, *162*(September). https://doi.org/10.1016/j.foodres.2022.112008

WHO Regional Office for Europe. (2022). *WHO European Regional Obesity Report 2022*.

Yang, W., Yang, C., Luo, J., Wei, Y., Wang, W., & Zhong, Y. (2018). Adiponectin promotes preadipocyte differentiation via the PPARγ pathway. *Molecular Medicine Reports*, *17*(1), 428–435.

https://doi.org/10.3892/mmr.2017.7881

Ye, R., Holland, W. L., Gordillo, R., Wang, M., Wang, Q. A., ….. & Scherer, P. E. (2014). Adiponectin is essential for lipid homeostasis and survival under insulin deficiency and promotes β-cell regeneration. *ELife*, *3*, 1–21. https://doi.org/10.7554/eLife.03851

Zheng, F., Zhang, S., Lu, W., Wu, F., Yin, X., ….. & Li, H. (2014). Regulation of insulin resistance and adiponectin signaling in adipose tissue by liver X receptor activation highlights a cross-talk with PPARγ. *PLoS ONE*, *9*(6), 1–11. https://doi.org/10.1371/journal.pone.0101269