Review

Anti-obesity effects of medicinal plants from Asian countries and related molecular mechanisms: a review

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Medicinal plants have been used as an alternative medicine for obesity prevention, and Asian countries, which are major habitats of various medicinal plant species, have traditionally used these medicines for centuries. Obesity is a global health problem caused by excessive fat accumulation linked to abnormal lipid metabolism, such as adipogenesis, lipogenesis, and lipolysis. Accordingly, the effects of medicinal plants on obesity-related mechanisms and biomarkers have been evaluated in various experimental studies. For example, adipogenesis and lipogenesis are regulated by several transcription factors, such as peroxisome proliferator-activated receptor gamma, CCAAT/enhancer binding protein alpha, and fatty acid synthase. Moreover, activation of the adenosine monophosphate-activated protein kinase pathway is accompanied by promotion of lipolysis. However, few reports have consolidated studies of the effects of various Asian medicinal plants on obesity and related mechanisms. Therefore, in this review, we examined the associations of medicinal plants originating from Asian countries with obesity and discussed the related mechanisms and biomarkers from *in vitro* and *in vivo* studies.

Keywords

Medicinal plants; Asia; Obesity; Adipogenesis; Biomarker; Review

1. Introduction

Obesity is a global health problem that is expected to continuously increase in incidence in upcoming years [1]. According to the World Health Organization (WHO), in 2016, more than 650 million adults (approximately 13% of the population) worldwide were considered obese [2]. Because obesity causes various health complications, including insulin resistance, hepatic steatosis, and dyslipidemia [3–5], obesity is considered a major risk factor for chronic diseases, such as type 2 diabetes, cardiovascular diseases, and cancer [6, 7]. Thus, obesity prevention and management are essential for individual health and the national healthcare system.

To prevent obesity, it is generally recommended to reduce energy intake and improve lifestyle. When obesity becomes severe, anti-obesity drugs have been used as a mechanism to promote metabolism and suppress appetite; however, the use of these drugs is often limited owing to various side effects, such as neuropathy and cardiovascular disease [8]. For example, the appetite suppressant sibutramine was widely used after approval, but was then withdrawn from the market in 2010 due to the risk of cardiovascular disease [8]. Obesity is currently treated with long-term use of anti-obesity drugs that target various mechanisms of action, including gastric/pancreatic lipases, neurotransmitters, glucagon-like peptide-1 (GLP-1) analogs, and catecholamine release [9]. However, these drugs have been reported to exhibit various side effects, including insomnia, vomiting, hyperpyrexia, and constipation [9].

Accordingly, medicinal plants have emerged as alternative preventive agents because of their weak side effects, ease of availability, low cost, and richness in bioactive compounds [10]. A recent meta-analysis of clinical trials demonstrated that intake of green tea, *Phaseolus vulgaris*, and *Nigella sativa* improved obesity-related parameters, such as weight, body mass index, waist circumference, and lipid levels [11]. In addition, several plants, including garcinia and Yerba mate, have been developed as dietary supplements for weight management [12–14], and weight loss products in the form of pills have widely used for obesity management [15, 16].

Medicinal plants are currently used worldwide; in particular, Asian countries, including China, Japan, Thailand, Indonesia, and Himalayan countries, have traditionally used medicinal plants for more than two centuries [17–20]. Asian medicinal plants also account for 45% of global profits in trades of medicinal plants, and approximately 39,000 species of medicinal plants are found naturally in Asian countries [21, 22]. However, an overview of the effects of various Asian medicinal plants on obesity and related mechanisms has rarely been reported.

Therefore, in this study, we study aimed to examine the association of medicinal plants originating from Asian countries with obesity and related mechanisms and biomarkers *in vitro* and *in vivo*.

2. Obesity related mechanisms and biomarkers

The development of obesity can be influenced by various factors, such as diet, physical activity, environment and genetic susceptibilities [23]. In general, however, obesity is

simply defined as status of abnormal fat accumulation in adipose tissue, and caused by excessive fat accumulation resulting from an imbalance between high energy intake and low energy expenditure at the cellular level [23]. Adipose tissue consists of white adipose tissue and brown adipocytes. White adipose tissue stores energy in the form of lipids or breaks down stored lipids to use them when energy is needed, whereas brown adipocytes use them to generate heat and contain large numbers of mitochondria [24]. In particular, adipose tissue generates heat and consumes energy through regulation of various proteins, such as uncoupling protein 1 (UCP1) [25]. Fat accumulation includes adipogenesis, which involves accumulation of lipids in the form of triglycerides (TGs) in adipocytes and increased size of adipocytes [26, 27]. Lipolysis, which is the alteration of stored TG to free fatty acids and glycerol, is also a process of abnormal lipid metabolism [28]. In addition, obesity is followed by dyslipidemia, which is characterized by high TG levels and low high-density lipoprotein cholesterol or high low-density lipoprotein cholesterol (LDL-C) levels [29].

Various adipogenic markers are also involved in the development of obesity. Expression of CCAAT/enhancer binding protein (C/EBP) β and C/EBPδ during adipogenesis induces the expression of C/EBPα and peroxisome proliferator-activated receptor gamma (PPARγ), resulting in the expression of fatty acid synthase (FAS) and fatty acid binding protein 4 (FABP4) [24, 30]. Fatty acids act as ligands of PPARγ, and adipocyte protein 2 (aP2) affects the transport and metabolism of intracellular fatty acids into cells [24, 30]. In addition, the expression of sterol regulatory element binding protein-1c (SREBP1c) cooperates with C/EBPα and PPARγ to increase the expression of aP2 and FAS [24, 30]. The expression of SREBP1c is also related to the expression of acetyl-CoA carboxylase (ACC) [31]. ACC, a controller of malonyl-CoA, allosterically inhibits the expression of carnitine palmitoyl transferase-1 (CPT-1), thereby inhibiting β-oxidation [32]. During adipose tissue development, the expression of adipokines, which are secreted by adipose tissue, is regulated by several transcription factors, including PPARγ and C/EBPα [33, 34]. Therefore, inhibition of various adipogenic markers is widely used to develop effective drugs or natural agents for obesity.

3. General characteristics of Asian medicinal plants

We searched articles from PubMed and Google Scholar using the keywords "plant", "obesity", "anti-obesity", "fat", "lipid", "cell", and "mice" from April 2019 to October 2020. We considered only *in vitro* and *in vivo* studies using medicinal plants that generally originated from Asian countries in the article and mainly targeted adipogenesis, lipid or fat accumulation, and obesity. Articles written in languages other than English were excluded. As a result, fourteen medicinal plants from 12 articles were reviewed. We extracted the following information from the articles: general characteristics of medicinal plants, including order, family, genus, scientific name, major habitat, extraction method, plant part, and major components; *in vitro* or *in vivo* models used in the article; administration and dose; anti-obesity activities, such as anti-adipogenesis; and related biomarkers. The characteristics of medicinal plants were based on information in the original article; however, several parameters, including order, family, and genus, which were not specified in the original article, were based on the information of the National Institute of Biological Resources of the Ministry of Environment in Korea (URL: https://species.nibr.go.kr/).

The general characteristics of the Asian medicinal plants are described in Table 1 (Ref. [35–46]). The major habitat countries are North East Asia, including Korea, China, and Japan, as well as India, Malaysia, and Russia. In total, 11 orders, 12 families, and 14 genera were identified. The orders and families of medicinal plants were Apiales-Araliaceae, Asterales-Asteraceae, Capparales-Brassicaceae, Moringaceae, Cornales-Cornaceae, Dipsacales-Valerianaceae, Myrtales-Melastomataceae, Nymphaeales-Nelumbonaceae, Rosales-Saxifragaceae, Sapindales-Aceraceae, Urticales-Moraceae, and Violales-Violaceae. The types of plant extraction were generally water and ethanol, although petroleum ether and methanol were also used. The major compounds in medicinal plants were flavonoids, such as quercetin, as well as catechin, rutin, and phenolic acids. The effects of medicinal plants were demonstrated using *in vitro* models in nine studies and *in vivo* models in eight studies (Table 1).

4. Anti-obesity effects of Asian medicinal plants and their underlying mechanisms *in vitro*

All *in vitro* studies selected in this study used 3T3-L1 cells to examine the effects of Asian medicinal plants on adipogenesis, lipogenesis, lipolysis, and other obesity-related activities (Table 2, Ref. [35, 36, 38–41, 44]). Adipogenesis, also called adipocyte differentiation, is a process through which preadipocytes develop into mature adipocytes [47]. Adipocytes are major components of white adipose tissue that mediate physiological and pathological processes, such as appetite, immunological and inflammatory responses, glucose metabolism, and blood pressure regulation [47, 48]. 3T3-L1 cells are pre-adipocytes that originate from mouse embryonic fibroblasts and have been commonly used to evaluate anti-obesity effects [49]. Notably, many medicinal plants, including *Acer okamotoanum* Nakai and *Astilbe chinensis* Franch. et Savat., *Cirsium setidens* Naki, *Cornus kousa*, *Dendropanax morbifera*, *Moringa oleifera*, and a mixture of *Nelumbo nucifera* L., *Morus alba* L., and *Raphanus sativus*, attenuate pre-adipocyte differentiation by suppressing lipid accumulation and reducing the size and number of lipid droplets in adipocytes. In particular, studies of *Astilbe chinensis* Franch. et Savat., *Dendropanax morbifera*, and *Moringa oleifera* showed that these plants decrease TG accumulation in adipocytes. In

Table 1. General characteristics of Asian medicinal plants with anti-obesity effects described in this study.

Order/Family/Genus	Plant name/Scientific name	Major habitat	Reference
Apiales			
Araliaceae	Dendropanax morbifera	Korea (Jeju Island)	Song *et al.* [35]
Dendropanax			
Asterales			
Asteraceae	Cirsium setidens Naki	Korea (Gangwon province)	Cho *et al.* [36]
Cirsium			
Cosmos	Cosmos caudatus Kunth	Malaysia	Rahman *et al.* [37]
Solidago	Solidago virgaurea var. gigantea	North East Asia	Wang *et al.* [38]
Capparales			
Brassicaceae	Raphanus Sativus	China, Mostly Asia	Sim *et al.* [39]
Raphanus			
Moringaceae	Moringa oleifera Lam.	India, Africa	Xie *et al.* [40]
Moringa			
Cornales			
Cornaceae	Cornus kousa	China, Japan, Korea	Khan *et al.* [41]
Cornus			
Dipsacales			
Valerianaceae	Valeriana dageletiana Nakai ex F. Maek.	Korea (Ulung Island)	Wang *et al.* [42]
Valeriana			
Myrtales			
Melastomataceae	Melastoma malabathricum var Alba Linn	Malaysia	Karupiah *et al.* [43]
Melastoma			
Nymphaeales			
Nelumbonaceae	Nelumbo Nucifera L.	China (Mostly Asia)	Sim *et al.* [39]
Nelumbo			
Rosales			
Saxifragaceae	Astilbe chinensis Franch. et Savat.	Russia, China, Japan, Korea	Zhang *et al.* [44]
Astilbe			
Sapindales			
Aceraceae	Acer okamotoanum Nakai	Korea (Ulung Island)	Kim *et al.* [45]
Acer			
Urticales			
Moraceae	Morus Alba L.	China, Mostly Asia	Sim *et al.* [39]
Morus			
Violales			
Violaceae	Viola mandshurica W. Becker	China, Japan, Korea	Sung *et al.* [46]
Viola			

addition, extracts of *Acer okamotoanum* Nakai, *Cirsium setidens* Naki, *Cornus kousa*, *Dendropanax morbifera*, and *Moringa oleifera* inhibit lipogenesis or stimulate lipolysis. Extracts of *Cirsium setidens* Naki increase glycerol release from mature adipocytes and stimulate triglycerol lipolysis. In particular, effect of glycerol release of extracts of *Cirsium setidens* Naki was stronger than the effect of *Garcinia cambogia*, a well-known plant for anti-adipogenic and anti-lipogenesis activities [50, 51]. Extracts of *Dendropanax morbifera* inhibit lipid accumulation by reducing glucose uptake, but do not significantly decrease lipolysis.

As shown in Table 3 (Ref. [36, 40, 41, 44, 45]), the expression of adipogenesis- and lipogenesis-related biomarkers is downregulated by treatment with *Acer okamotoanum* Nakai, *Astilbe chinensis* Franch. et Savat., *Cirsium setidens* Naki, *Cornus kousa*, *Dendropanax morbifera*, and *Moringa oleifera* in differentiated adipocytes. Additionally, treatment with *Cirsium setidens* Naki extract reduces the expression of PPARγ, C/EBPα, C/EBPβ, and C/EBPδ. Moreover, the protein expression of PPARγ, C/EBPα, C/EBPβ, SREBP1, and FAS is inhibited by *Dendropanax morbifera* and *Moringa oleifera* extracts, whereas treatment with *Acer okamotoanum* Nakai, *Astilbe chinensis* Franch. et Savat., and *Cornus kousa* extracts decreases the protein expression of PPARγ, C/EBPα, SREBP1, and FAS. The gene expression of transcription factors, including PPARγ, C/EBPα, C/EBPβ, C/EBPδ, and SREBP1, has been reported to regulate adipogenesis and lipogenesis [47, 52]. Furthermore, FAS is a well-known enzyme related to fatty acid synthesis [53] and may inhibit fat synthesis in adipocytes following treatment with medicinal

Table 2. Anti-obesity activities of Asian medicinal plants as demonstrated using *in vitro* models.

Activities	Plants	Plant part	Extraction	Major components	Objects	Dose	References
Reduced intercellular lipid accumulation and lipid droplet sizes and numbers during adipogenesis	*Acer okamotoanum* Nakai	Leaf	Methanol extraction	-	3T3-L1 cells	P, A + None, A + 50 μg/mL, A + 100 μg/mL	Kim *et al.* [45]
	Astilbe chinensis Franch. et Savat.	Whole plant	Ethanol extraction	Astilbic acid (Triterpenoids)	3T3-L1 cells	P, A + None, A + 20 μg/mL, A + 40 μg/mL	Zhang *et al.* [44]
	Cirsium setidens Naki	Leaf	Ethanol extraction	Pectolinarin	3T3-L1 cells	P, A + PC (*Garcinia cambogia* extract) 100 μg/mL, A + 100 μg/mL, A + 200 μg/mL	Cho *et al.* [36]
	Cornus kousa	Leaf	Ethanol extraction	Anthocyanins	3T3-L1 cells	A + None, A + 5 μg/mL, A + 30 μg/mL, A + 60 μg/mL, A + 100 μg/mL	Khan *et al.* [41]
	Dendropanax morbifera	Leaf	Water extraction	Vitamin C Tannic acid	3T3-L1 cells	P, A + None, A + 50 μg/mL, A + 100 μg/mL, A + 300 μg/mL, A + 500 μg/mL	Song *et al.* [35]
	Moringa oleifera	Leaf	Petroleum ether extract	Isoquercitrin, Chrysin-7-glucoside, Quercitrin	3T3-L1 cells	A + None, A + 25 μg/mL, A + 50 μg/mL, A + 100 μg/mL, A + 200 μg/mL, A + 400 μg/mL	Xie *et al.* [40]
	Nelumbo Nucifera L., *Morus Alba* L., *Raphanus Sativus*	Leaf, leaf, root	Ethanol extraction	Quercetin-3-O-glucuronide	3T3-L1 cells	P, A + PC (*Garcinia cambogia*) 100 μg/mL, A + EM11[a] 100 μg/mL, A + EM12[b] 100 μg/mL, A + EM01[c] 100 μg/mL, A + Q3OG[d] 7.8 μM	Sim *et al.* [39]
	Solidago virgaurea var. *gigantea*	Whole plant	Ethanol extraction	Protocatechuic acid, Chlorogenic acid, Rutin	3T3-L1 cells	P, A + None, A + water extract 10 μg/mL, A + 10% ethanol extract 10 μg/mL, A + 30% ethanol extract 10 μg/mL, A + 50% ethanol extract 10 μg/mL, A + 70% ethanol extract 10 μg/mL, A + 100% ethanol extract 10 μg/mL	Wang *et al.* [38]
Decreased TG accumulation in adipocytes	*Astilbe chinensis* Franch. et Savat.	Whole plant	Ethanol extraction	Astilbic acid (Triterpenoids)	3T3-L1 cells	P, A + None, A + 20 μg/mL, A + 40 μg/mL	Zhang *et al.* [44]
	Dendropanax morbifera	Leaf	Water extraction	Vitamin C Tannic acid	3T3-L1 cells	P, A + None, A + 50 μg/mL, A + 100 μg/mL, A + 300 μg/mL, A + 500 μg/mL	Song *et al.* [35]
	Moringa oleifera	Leaf	Petroleum ether extract	Isoquercitrin, Chrysin-7-glucoside, Quercitrin	3T3-L1 cells	A + None, A + 25 μg/mL, A + 50 μg/mL, A + 100 μg/mL, A + 200 μg/mL, A + 400 μg/mL	Xie *et al.* [40]
Inhibited lipogenesis or promoted lipolysis	*Acer okamotoanum* Nakai	Leaf	Methanol extraction	-	3T3-L1 cells	P, A + None, A + 50 μg/mL, A + 100 μg/mL	Kim *et al.* [45]
	Cirsium setidens Naki	Leaf	Ethanol extraction	Pectolinarin	3T3-L1 cells	C, A + PC (*Garcinia cambogia* extract) 100 μg/mL, A + 100 μg/mL, A + 200 μg/mL	Cho *et al.* [36]
	Cornus kousa	Leaf	Ethanol extraction	Anthocyanins	3T3-L1 cells	A + None, A + 5 μg/mL, A + 30 μg/mL, A + 60 μg/mL, A + 100 μg/mL	Khan *et al.* [41]
	Dendropanax morbifera	Leaf	Water extraction	Vitamin C Tannic acid	3T3-L1 cells	P, A + None, A + 50 μg/mL, A + 100 μg/mL, A + 300 μg/mL, A + 500 μg/mL	Song *et al.* [35]
	Moringa oleifera	Leaf	Petroleum ether extract	Isoquercitrin, Chrysin-7-glucoside, Quercitrin	3T3-L1 cells	A + None, A + 25 μg/mL, A + 50 μg/mL, A + 100 μg/mL, A + 200 μg/mL, A + 400 μg/mL	Xie *et al.* [40]

P, preadipocyte; A, adipocyte (differentiated cell); PC, positive control.

[a,b,c] The ethanol extract mixture ratios of *Nelumbo Nucifera*, L. *Morus Alba* L., *Raphanus Sativus* — EM11 (100:0:0), EM12 (0:100:0), EM01 (80:20:0), respectively. [d] quercetin-3-O-glucuronide.

Table 3. TAnti-obesity mechanisms and biomarkers of Asian medicinal plants as demonstrated using *in vitro* models.

Mechanisms	Plants	Related biomarkers	References
Adipogenesis, lipogenesis, and lipolysis	*Acer okamotoanum* Nakai	PPARγ ↓, C/EBPα ↓, SREBP1 ↓, FAS ↓	Kim *et al.* [45]
	Astilbe chinensis Franch. et Savat.	PPARγ ↓, C/EBPα ↓, SREBP1 ↓, FAS ↓, SCD-1 ↓	Zhang *et al.* [44]
	Cirsium setidens Naki	PPARγ ↓, C/EBPα ↓, C/EBPβ ↓, C/EBPδ ↓ phospho-HSL ↑	Cho *et al.* [36]
	Cornus kousa	PPARγ ↓, C/EBPα ↓, SREBP1 ↓, FAS ↓, aP2 ↓, LPL ↓	Khan *et al.* [41]
	Dendropanax morbifera	PPARγ ↓, C/EBPα ↓, C/EBPβ ↓, SREBP1 ↓	Song *et al.* [35]
	Moringa oleifera	PPARγ ↓, C/EBPα ↓, C/EBPβ ↓, FAS ↓ HSL ↑	Xie *et al.* [40]
Activation of the AMPK pathway	*Astilbe chinensis* Franch. et Savat.	Phospho-AMPKα ↑, phospho-ACC ↑, PGC-1α ↑, PPARα ↑, ATGL ↑, HSL ↑	Zhang *et al.* [44]
	Cirsium setidens Naki	Phospho-AMPK ↑, phospho-ACC ↑, CPT-1 ↑	Cho *et al.* [36]
	Cornus kousa	Phospho-AMPK ↑	Khan *et al.* [41]
	Moringa oleifera	Phospho-AMPKα (Thr172) ↑, phospho-ACC (Ser79) ↑	Xie *et al.* [40]
Inactivation of PI3K/AKT signaling	*Acer okamotoanum* Nakai	PI3K 110α ↓, PI3K 110β ↓, PI3K 110δ ↓ phospho-AKT (Ser 473) ↓ phospho-mTOR (Ser 2481) ↓ phospho-p70S6K (Ser371) ↓	Kim *et al.* [45]
Activation of β-catenin signaling	*Acer okamotoanum* Nakai	β-Catenin ↑ phospho-β-catenin (Ser 552) ↑ phospho-β-catenin (Ser 33, 37/Thr 41) ↓ phospho-GSK3β ↑	Kim *et al.* [45]

plants. In addition, extracts of *Astilbe chinensis* Franch. et Savat. reduce the expression of stearoyl-CoA desaturase (SCD)-1, and extracts of *Cornus kousa* reduce the expression of aP2 and lipoprotein lipase (LPL) in 3T3-L1 differentiated adipocytes. Adipocyte-specific gene promoters, such as SCD-1, aP2, and LPL, are also well-known transcription factors that regulate adipogenesis and lipogenesis, as has been confirmed in several studies [54–56].

By contrast, promotion of lipolysis is also related to inhibition of lipid accumulation, and lipolysis-related biomarkers have been evaluated in adipocyte cell model studies. In this review, we found that treatment with *Moringa oleifera* and *Cirsium setidens* Naki upregulated hormone-sensitive lipase (HSL) protein levels and phosphorylation, respectively. HSL is a key regulator of TAG lipolysis [57].

The effects of *Astilbe chinensis* Franch. et Savat. and *Cornus kousa* on adipogenesis inhibition or lipolysis stimulation are mediated by activation of the adenosine monophosphate (AMP)-activated protein kinase (AMPK) pathway. Extracts of *Astilbe chinensis* Franch. et Savat. upregulate phospho-AMPKα and phospho-ACC as well as the mRNA levels of PPARγ coactivator (PGC-1α), PPARα, adipose TG lipase (ATGL), and HSL in 3T3-L1 cells. This indicated that the extract of *Astilbe chinensis* Franch. et Savat. attenuates adipogenesis and promotes lipolysis via the AMPK pathway. Extracts of *Cornus kousa* also activate the phosphorylation of AMPK, whereas extracts of *Moringa oleifera* activate the phosphorylation of both AMPKα and ACC. Treatment with *Cirsium setidens* Naki extract promotes the metabolism of lipid synthesis to fatty acid oxidation through activation of the AMPK pathway, enhancing the phosphorylation of AMPK and ACC, the expression of CPT I, and the production of ATP.

Leaf extracts of *Acer okamotoanum* Nakai show anti-adipogenic activity by regulating phosphatidylinositol-3 kinase (PI3K)/AKT and β-catenin signaling. Treatment with *Acer okamotoanum* Nakai decreases the protein levels of PI3K 110α, PI3K 110β, PI3K 110δ, and phospho-AKT (Ser 473). The PI3K/AKT signaling pathway is involved in stimulation of glucose uptake and adipocyte differentiation, and activation of PI3K and phosphorylation of AKT facilitates PPARγ expression at the beginning of adipocyte differentiation. Thus, decreased levels of PI3K and phospho-Akt by *Acer okamotoanum* Nakai are linked to the suppression of insulin metabolism and lipid synthesis. Moreover, activation of the PI3K/AKT signaling pathway is associated with glucose uptake and 3T3-L1 adipogenesis in a chlorophyll pigment-derived branched-chain fatty alcohol, phytol [58]. In addition, in a study of *Acer okamotoanum* Nakai, mammalian target of rapamycin (mTOR) was found to be related to AKT downstream metabolism, whereas phosphorylation of ribosomal protein S6 kinase (p70S6K) was found to be related to the downstream metabolism of mTOR. Both factors, i.e., mTOR and p70S6K, are also involved in adipogenesis, and inhibition of mTOR and p70S6K phosphorylation resulting from attenuation of the PI3K/AKT signaling pathway decreases adipocyte differentiation after treatment with *Acer okamotoanum* Nakai. Furthermore, inhibition of AKT and mTOR signaling pathways induces adipogenesis and lipogenesis, as demonstrated in a previous study of oligonol, an oligomerized polyphenol [59].

Treatment with *Acer okamotoanum* Nakai extract stimulates β-catenin signaling by inhibiting PPARγ expression and preventing adipogenesis. The increased phosphorylation of glycogen synthase kinase 3β, a key factor of β-catenin signaling, induces cytoplasmic β-catenin levels, and β-catenin is associated with inhibition of adipogenesis through down-regulation of PPARγ activity.

5. Anti-obesity effects of Asian medicinal plants and their underlying mechanisms *in vivo*

As described in Table 4 (Ref. [36–40, 42–44, 46]), major anti-obesity activities *in vivo*, such as reduced body weight, adipose tissue weight (e.g., epididymal or retroperitoneal fat), and adipocyte size, have been demonstrated by all Asian medicinal plants discussed in this review. A high-fat diet (HFD) supplemented with extracts of *Astilbe chinensis* Franch. et Savat., *Cirsium setidens* Naki, *Cosmos caudatus* Kunth, *Melastoma malabathricum* var Alba Linn, *Moringa oleifera*, a mixture of *Nelumbo nucifera* L., *Morus alba* L., and *Raphanus sativus*, *Solidago virgaurea* var. *gigantea*, *Valeriana dageletiana* Nakai ex F. Maek., and *Viola mandshurica* W. Becker was provided to C57BL/6 or Sprague-Dawley rats for 7 to 14 weeks. The findings showed that supplementation with the extracts of most plants resulted in a decrease in serum lipid levels. Extracts of *Astilbe chinensis* Franch. et Savat., *Cosmos caudatus* Kunth, *Melastoma malabathricum* var Alba Linn, and *Viola mandshurica* W. Becker reduce serum TG, total cholesterol (TC), and LDL-C levels. *Moringa oleifera* extracts decrease TC and LDL-C levels, and a mixture of *Nelumbo nucifera* L., *Morus alba* L., and *Raphanus sativus* extracts decreases TC levels. Extracts of *Solidago virgaurea* var. *gigantea* and *Valeriana dageletiana* Nakai ex F. Maek. decrease TG and TC levels, whereas extracts of *Astilbe chinensis* Franch. et Savat., *Cosmos caudatus* Kunth, and *Viola mandshurica* W. Becker also show potential for controlling diabetes-related parameters by regulating glucose or insulin plasma levels. Additionally, extracts of *Nelumbo nucifera* L., *Morus alba* L., and *Raphanus sativus* improve glucose levels in HFD-fed mice, as demonstrated in a glucose tolerance test. The effects of extracts of *Cirsium setidens* Naki, *Moringa oleifera,* a mixture *of Nelumbo Nucifera* L., *Morus Alba* L., and *Raphanus Sativus, Solidago virgaurea* var. *gigantea, Valeriana dageletiana* Nakai ex F. Maek, and *Viola mandshurica* W. Becker were also similar when compared to positive controls, *Garcinia cambogia*, Lovastatin, or Orlistat.

Anti-adipogenic effects on the liver have also been observed in medicinal plants. For example, extracts of *Cosmos caudatus* Kunth, *Melastoma malabathricum* var Alba Linn, *Moringa oleifera*, and a mixture of *Nelumbo nucifera* L., *Morus alba* L., and *Raphanus sativus*, *Solidago virgaurea* var. *gigantea*,

Table 4. Anti-obesity activities of Asian medicinal plants as demonstrated using *in vivo* models.

Activities	Plants	Plant part	Extraction	Major components	Animal model	Administration/Dose	Period	References
Reduced body weight, adipose tissue weight, and adipocyte size	*Astilbe chinensis* Franch. et Savat.	Whole plant	Ethanol extraction	Astilbic acid (Triterpenoids)	C57BL/6N	Supplementation with HFD ND, HFD, HFD + 100 mg/kg, HFD + 200 mg/kg	8 weeks	Zhang *et al.* [44]
	Cirsium setidens Naki	Leaf	Ethanol extraction	Pectolinarin	C57BL/6J	Oral administration with HFD ND, HFD, HFD + 25 mg/kg/day, HFD + 50 mg/kg/day, HFD + 100 mg/kg/day, HFD + 200 mg/kg/day, HFD + PC (*Garcinia cambogia* extract) 100 mg/kg/day	14 weeks	Cho *et al.* [36]
	Cosmos caudatus Kunth	Leaf	Ethanol extraction	Quercetin, Catechin, Rutin, Chlorogenic acid	C57BL/6N	Supplementation with HFD ND, ND + 175 mg/kgBW, ND + 350 mg/kgBW, HFD, HFD + 175 mg/kgBW, HFD + 350 mg/kgBW	10 weeks	Rahman *et al.* [37]
	Melastoma malabathricum var Alba Linn	Whole plant	Methanol extraction	Epicatechin, Flavonoids	Sprague-Dawley rats	Supplementation with HFD ND, HFD, HFD + 5%	8 weeks	Karupiah *et al.* [43]
	Moringa oleifera	Leaf	Petroleum ether extract	Isoquercitrin, Chrysin-7-glucoside, Quercitrin	C57BL/6N	Supplementation with HFD ND, HFD + PC (Lovastatin) 10 mg/kg, HFD + 0.125 g/kg, HFD + 0.25 g/kg, HFD + 0.5 g/kg	10 weeks	Xie *et al.* [40]
	Nelumbo Nucifera L., *Morus Alba* L., *Raphanus Sativus*	Leaf, leaf, root	Ethanol extraction	Quercetin-3-O-glucuronide	C57BL/6J	Oral administration with HFD ND, HFD, HFD + PC (*Garcinia cambogia*) 245 mg/kg, HFD + EM11[a] 100 mg/kg, HFD + EM12[b] 100 mg/kg, HFD + EM01[c] 50 mg/kg, HFD + EM01[c] 100 mg/kg, HFD + Q3OG[d] 10 mg/kg	8 weeks	Sim *et al.* [39]
	Solidago virgaurea var. *gigantea*	Whole plant	Ethanol extraction	Protocatechuic acid, Chlorogenic acid, Rutin	C57BL/6J	Oral administration with HFD ND, HFD, HFD + 1% PC (*Garcinia cambogia* extract), HFD + 0.5% of 10% ethanol extract, HFD + 2% of 10% ethanol extract	7 weeks	Wang *et al.* [38]
	Valeriana dageletiana Nakai ex F. Maek	Stem and leaf	Ethanol extraction	Camphene, α-therpineol, Azulene, Geraniol	Sprague-Dawley rats	Supplementation with HFD ND, HFD, HFD + 1% PC (*Garcinia combogia* extract), HFD + 1%	8 weeks	Wang *et al.* [42]
	Viola mandshurica W. Becker	Whole plant	Ethanol and water extraction	Esculetin, Schaftoside	Sprague-Dawley rats	Oral administration with HFD ND, HFD, HFD + 200 mg/kg of ethanol extract, HFD + 100 mg/kg of ethanol extract, HFD + 50 mg/kg of ethanol extract, HFD + 200 mg/kg of water extract, HFD + 100 mg/kg of water extract, HFD + 50 mg/kg of water extract, HFD + PC1 (Orlistat) 50 mg/kg, HFD + PC2 (*Garcinia combogia* extract) 100 mg/kg	11 weeks	Sung *et al.* [46]

Table 4. Continued.

Activities	Plants	Plant part	Extraction	Major Components	Animal model	Administration/Dose	Period	References
	Astilbe chinensis Franch. et Savat.	Whole plant	Ethanol extraction	Astilbic acid (Triterpenoids)	C57BL/6N	Supplementation with HFD ND, HFD, HFD+100 mg/kg, HFD+200 mg/kg	8 weeks	Zhang *et al.* [44]
	Cosmos caudatus Kunth	Leaf	Ethanol extraction	Quercetin, Catechin, Rutin, Chlorogenic acid	C57BL/6N	Supplementation with HFD ND, ND + 175 mg/kgBW, ND + 350 mg/kgBW, HFD, HFD + 175 mg/kgBW, HFD + 350 mg/kgBW	10 weeks	Rahman *et al.* [37]
Decreased lipid levels of serum	*Melastoma malaba-thricum* var Alba Linn	Whole plant	Methanol extraction	Epicatechin, Flavonoids	Sprague-Dawley rats	Supplementation with HFD ND, HFD, HFD + 5%	8 weeks	Karupiah *et al.* [43]
	Moringa oleifera	Leaf	Petroleum ether extract	Isoquercitrin, Chrysin-7-glucoside, Quercitrin	C57BL/6N	Supplementation with HFD ND, HFD + PC (Lovastatin) 10 mg/kg, HFD + 0.125 g/kg, HFD + 0.25 g/kg, HFD + 0.5 g/kg	10 weeks	Xie *et al.* [40]
	Nelumbo Nucifera L., *Morus Alba* L., *Raphanus Sativus*	Leaf, Leaf, Root	Ethanol extraction	Quercetin-3-O-glucuronide	C57BL/6J	Oral administration with HFD ND, HFD, HFD + PC (*Garcinia cambogia*) 245 mg/kg, HFD + EM11 100 mg/kg, HFD + EM12 100 mg/kg, HFD + EM01 50 mg/kg, HFD + EM01 100 mg/kg, HFD + Q3OG 10 mg/kg	8 weeks	Sim *et al.* [39]
	Solidago virgaurea var. *gigantea*	Whole plant	Ethanol extraction	Protocatechuic acid, Chlorogenic acid, Rutin	C57BL/6J	Oral administration with HFD ND, HFD, HFD + 1% PC (*Garcinia cambogia* extract), HFD + 0.5% of 10% ethanol extract, HFD + 2% of 10% ethanol extract	7 weeks	Wang *et al.* [38]
	Valeriana dageletiana Nakai ex F. Maek.	Stem and leaf	Ethanol extraction	Camphene, α-therpineol, Azulene, Geraniol	Sprague-Dawley rats	Supplementation with HFD ND, HFD, HFD + 1% PC (*Garcinia combogia* extract), HFD + 1%	8 weeks	Wang *et al.* [42]
	Viola mandshurica W. Becker	Whole plant	Ethanol and water extraction	Esculetin, Schaftoside	Sprague-Dawley rats	Oral administration with HFD ND, HFD, HFD + 200 mg/kg of ethanol extract, HFD + 100 mg/kg of ethanol extract, HFD + 50 mg/kg of ethanol extract, HFD + 200 mg/kg of water extract, HFD + 100 mg/kg of water extract, HFD + 50 mg/kg of water extract, HFD + PC1 (Orlistat) 50 mg/kg, HFD + PC2 (*Garcinia combogia* extract) 100 mg/kg	11 weeks	Sung *et al.* [46]

Table 4. Continued.

Activities	Plants	Plant part	Extraction	Major Components	Animal model	Administration/Dose	Period	References
Regulated plasma glucose and insulin levels	*Astilbe chinensis* Franch. et Savat.	Whole plant	Ethanol extraction	Astilbic acid (Triterpenoids)	C57BL/6N	Supplementation with HFD ND, HFD, HFD + 100 mg/kg, HFD + 200 mg/kg	8 weeks	Zhang *et al.* [44]
	Cosmos caudatus Kunth	Leaf	Ethanol extraction	Quercetin, Catechin, Rutin, Chlorogenic acid	C57BL/6N	Supplementation with HFD ND, ND + 175 mg/kgBW, ND + 350 mg/kgBW, HFD, HFD + 175 mg/kgBW, HFD + 350 mg/kgBW	10 weeks	Rahman *et al.* [37]
	Nelumbo Nucifera L., *Morus Alba* L., *Raphanus Sativus*	Leaf, Leaf, Root	Ethanol extraction	Quercetin-3-O-glucuronide	C57BL/6J	Oral administration with HFD ND, HFD, HFD + PC (*Garcinia cambogia*) 245 mg/kg, HFD + EM11 100 mg/kg, HFD + EM12 100 mg/kg, HFD + EM01 50 mg/kg, HFD + EM01 100 mg/kg, HFD + Q3OG 10 mg/kg	8 weeks	Sim *et al.* [39]
	Viola mandshurica W. Becker	Whole plant	Ethanol and water extraction	Esculetin, Schaftoside	Sprague-Dawley rats	Oral administration with HFD ND, HFD, HFD + 200 mg/kg of ethanol extract, HFD + 100 mg/kg of ethanol extract, HFD + 50 mg/kg of ethanol extract, HFD + 200 mg/kg of water extract, HFD + 100 mg/kg of water extract, HFD + 50 mg/kg of water extract, HFD + PC1 (Orlistat) 50 mg/kg, HFD + PC2 (*Garcinia combogia* extract) 100 mg/kg	11 weeks	Sung *et al.* [46]
	Cosmos caudatus Kunth	Leaf	Ethanol extraction	Quercetin, Catechin, Rutin, Chlorogenic acid	C57BL/6N	Supplementation with HFD ND, ND + 175 mg/kgBW, ND + 350 mg/kgBW, HFD, HFD + 175 mg/kgBW, HFD + 350 mg/kgBW	10 weeks	Rahman *et al.* [37]
Decreased liver weight and lipid accumulation in the liver	*Melastoma malabathricum* var Alba Linn	Whole plant	Methanol extraction	Epicatechin, Flavonoids	Sprague-Dawley rat	Supplementation with HFD ND, HFD, HFD + 5%	8 weeks	Karupiah *et al.* [43]
	Moringa oleifera	Leaf	Petroleum ether extract	Isoquercitrin, Chrysin-7-glucoside, Quercitrin	C57BL/6N	Supplementation with HFD ND, HFD + PC (Lovastatin) 10 mg/kg, HFD + 0.125 g/kg, HFD + 0.25 g/kg, HFD + 0.5 g/kg	10 weeks	Xie *et al.* [40]

Table 4. Continued.

Activities	Plants	Plant part	Extraction	Major Components	Animal model	Administration/Dose	Period	References
	Nelumbo Nucifera L., *Morus Alba* L., *Raphanus Sativus*	Leaf, leaf, root	Ethanol extraction	Quercetin-3-O-glucuronide	C57BL/6J	Oral administration with HFD ND, HFD, HFD + PC (*Garcinia cambogia*) 245 mg/kg, HFD + EM11 100 mg/kg, HFD + EM12 100 mg/kg, HFD + EM01 50 mg/kg, HFD + EM01 100 mg/kg, HFD + Q3OG 10 mg/kg	8 weeks	Sim *et al.* [39]
	Solidago virgaurea var. *gigantea*	Whole plant	Ethanol extraction	Protocatechuic acid, Chlorogenic acid, Rutin	C57BL/6J	Oral administration with HFD ND, HFD, HFD + 1% PC (*Garcinia cambogia* extract), HFD + 0.5% of 10% ethanol extract, HFD + 2% of 10% ethanol extract	7 weeks	Wang *et al.* [38]
	Valeriana dageletiana Nakai ex F. Maek	Stem and leaf	Ethanol extraction	Camphene, α-therpineol, Azulene, Geraniol	Sprague-Dawley rats	Supplementation with HFD ND, HFD, HFD + 1% PC (*Garcinia combogia* extract), HFD + 1%	8 weeks	Wang *et al.* [42]
	Viola mandshurica W. Becker	Whole plant	Ethanol and water extraction	Esculetin, Schaftoside	Sprague-Dawley rats	Oral administration with HFD ND, HFD, HFD + 200 mg/kg of ethanol extract, HFD + 100 mg/kg of ethanol extract, HFD + 50 mg/kg of ethanol extract, HFD + 200 mg/kg of water extract, HFD + 100 mg/kg of water extract, HFD + 50 mg/kg of water extract, HFD + PC1 (Orlistat) 50 mg/kg, HFD + PC2 (*Garcinia combogia* extract) 100 mg/kg	11 weeks	Sung *et al.* [46]
Reduced hepatic lipid metabolites	*Solidago virgaurea* var. *gigantea*	Whole plant	Ethanol extraction	Protocatechuic acid, Chlorogenic acid, Rutin	C57BL/6J	Oral administration with HFD ND, HFD, HFD + 1% PC (*Garcinia cambogia* extract), HFD + 0.5% of 10% ethanol extract, HFD + 2% of 10% ethanol extract	7 weeks	Wang *et al.* [38]
	Valeriana dageletiana Nakai ex F. Maek.	Stem and leaf	Ethanol extraction	Camphene, α-therpineol, Azulene, Geraniol	Sprague-Dawley rats	Supplementation with HFD ND, HFD, HFD + 1% PC (*Garcinia combogia* extract), HFD + 1%	8 weeks	Wang *et al.* [42]

ND, normal diet; HFD, high-fat diet; PC, positive control.

[a,b,c] The ethanol extract mixture ratios of *Nelumbo Nucifera* L., *Morus Alba* L., *Raphanus Sativus* — EM11 (100:0:0), EM12 (0:100:0), EM01 (80:20:0), respectively.

[d] quercetin-3-O-glucuronide.

Valeriana dageletiana Nakai ex F. Maek., and *Viola mandshurica* W. Becker decrease liver weight and lipid accumulation in the liver. In particular, *Moringa oleifera* reduces hepatic TG levels. Furthermore, several medicinal plants, including *Solidago virgaurea* var. *gigantea* and *Valeriana dageletiana* Nakai ex F. Maek, lower hepatic lipid metabolite levels, as measured using nuclear magnetic resonance. Both plants reduce the levels of fatty acids, cholesterol, phospholipids, and lipid moieties, which are induced by consumption of an HFD. Extracts of *Cosmos caudatus* Kunth or a mixture of *Nelumbo nucifera* L., *Morus alba* L., and *Raphanus sativus*, *Solidago virgaurea* var. *gigantea*, *Viola mandshurica* W. Becker, and *Valeriana dageletiana* Nakai ex F. Maek. were also used for evaluation of liver function and toxicity by analyzing aspartate transaminase, alanine transferase, and gamma-glutamyl transferase levels.

Similar to the results of *in vitro* studies, obesity-related mechanisms and biomarkers have also been identified from *in vivo* studies (Table 5, Ref. [38–40, 42, 44, 46]). Supplementation with extracts of *Astilbe chinensis* Franch. et Savat. downregulates PPARγ, C/EBPα, SERBP1, FAS, and SCD-1, and extracts of *Viola mandshurica* W. Becker downregulates C/EBPα, C/EBPβ, and SREBP1c in epididymal adipose tissue, whereas extracts of *Nelumbo nucifera* L., *Morus alba* L., and *Raphanus sativus* decrease the expression of PPARγ, SERBP1c, FAS, SCD-1, and DGAT1 in liver and epididymal adipose tissues. Specifically, extracts of a mixture of *Nelumbo nucifera* L., *Morus alba* L., and *Raphanus sativus*, and *Viola mandshurica* W. Becker increase the gene expression of PPARα, uncoupling protein (UPC)-1, and UPC-2 in adipose tissue and abdominal subcutaneous fat. Moreover, extracts of *Moringa oleifera* decreases the expression of PPARγ and FAS and increase the expression of ATGL by controlling lipolysis in epididymal adipose tissue and the liver. Furthermore, extracts *of Solidago virgaurea* var. *gigantea* reduce the expression of PPARγ, C/EBPα, aP2, FAS, and SCD-1 by inhibiting adipogenesis in epididymal tissue and suppress the expression SREBP1c, FAS, SCD-1, and CD36 by inhibiting lipogenesis in the liver. Hence, the expression of adipogenesis- and lipogenesis-related genes, including PPARγ, C/EBPα, aP2, FAS, and SCD-1, is downregulated in epididymal white adipose tissue, whereas the expression of lipogenesis-related genes, including SERBP1c, FAS, SCD-1, and CD36, is downregulated in liver by treatment with extracts of *Valeriana dageletiana* Nakai ex F. Maek.

The AMPK pathway is a well-known mechanism that regulates lipid metabolism. Several medicinal plants have been evaluated to determine their ability to regulate lipolysis through the activation of AMPK signaling in the adipose tissue and liver of HFD-induced obese mice. Extracts of *Astilbe chinensis* Franch. et Savat. promote AMPK pathways by increasing the protein levels of phospho-AMPK, phospho-ACC, and PGC-1α and the levels of lipolysis-related targets, such as ATGL and phospho-HSL, in epididymal adipose tissue. In addition, extracts of *Moringa oleifera* stimulate the phosphorylation of AMPKα (Thr172) and ACC (Ser79) in epididymal adipose tissue and the liver by inhibiting adipogenesis. Moreover, the mRNA expression of AMPKα1 and AMPKα2 is upregulated in both epididymal adipose tissue and the liver, and the levels of phospho-AMPK and ACC are upregulated in the liver after supplementation with *Viola mandshurica* W. Becker extract.

6. Conclusions

Various species of medicinal plants originate from Asian countries, including Korea, China, Japan, India, and Malaysia. Plants are generally extracted with ethanol, and flavonoids, such as quercetin, as well as catechin, anthocyanins, and other phenolic acids are the major components of these plants. The effects of Asian medicinal plants on obesity have been examined through many *in vitro* and *in vivo* studies. In this study, we found that eight types of Asian medicinal plants, including *Acer okamotoanum* Nakai, *Astilbe chinensis* Franch. et Savat., *Cirsium setidens* Naki, *Cornus kousa*, *Dendropanax morbifera*, *Moringa oleifera*, a mixture of *Nelumbo nucifera* L., *Morus alba* L., and *Raphanus sativus*, and *Solidago virgaurea* var. *gigantea*, reduce intercellular lipid accumulation and decrease the sizes and numbers of lipid droplets during adipogenesis. These plants also inhibit lipogenesis or promote lipolysis in 3T3-L1 cells. The major transcription factors related to adipogenesis and lipogenesis are PPARγ, C/EBPα, C/EBPβ, SREBP1, and FAS. In particular, upregulation of lipolysis via the AMPK pathway has been observed in several medicinal plants. Additionally, we evaluated the effects of nine types of Asian medicinal plants, including *Astilbe chinensis* Franch. et Savat., *Cirsium setidens* Naki, *Cosmos caudatus* Kunth, *Melastoma malabathricum* var Alba Linn, *Moringa oleifera*, *Solidago virgaurea* var. *gigantea*, *Valeriana dageletiana* Nakai ex F. Maek, *Viola mandshurica* W. Becker, and a mixture of *Nelumbo nucifera* L., *Morus alba* L., and *Raphanus sativus* on obesity in HFD-induced obesity mouse models. The results showed that supplementation with these medicinal plants reduces body weight, adipose tissue weight, and adipocyte size; decreases serum lipid levels; regulates glucose and insulin levels; and improves lipid accumulation in the liver. Similar to *in vitro* studies, these *in vivo* reports showed that the expression levels of PPARγ, C/EBPα, C/EBPβ, SREBP1, FAS, SCD-1, CD36, UCP-1, UCP-2, and ATGL are related to adipogenesis, lipogenesis, and lipolysis in the adipose tissue and liver. The possible anti-obesity mechanisms and related biomarkers of Asian medicinal plants from this study is illustrated in Fig. 1. Although many studies have reported the anti-obesity effects of Asian plants, most results have been reported from *in vitro* or *in vivo* studies, and there is a lack of clear evidence demonstrating these effects, as well as the safety of the medicines, in the human body. Furthermore, the mechanisms of absorption and metabolism, as well as the effects of the medicinal plants on various tissues and organs, as related to their anti-obesity effects, have still not been elucidated. Studies on the signaling

Table 5. Anti-obesity mechanisms and biomarkers of Asian medicinal plants as demonstrated using *in vivo* models.

Mechanisms	Plants	Related organs	Related biomarkers	References
Adipogenesis and lipogenesis in adipose tissue and the liver	*Astilbe chinensis* Franch. et Savat.	Epididymal adipose tissue	PPARγ ↓, C/EBPα ↓, SERBP1 ↓, FAS ↓, SCD-1 ↓	Zhang *et al.* [44]
	Moringa oleifera	Epididymal adipose tissue, liver	PPARγ ↓, FAS ↓	Xie *et al.* [40]
	Nelumbo Nucifera L., *Morus Alba* L., *Raphanus Sativus*	Liver, epididymal adipose tissue Adipose tissue, abdominal subcutaneous fat tissue	PPARγ ↓, SREBP1c ↓, FAS ↓, SCD-1 ↓, DGAT1 ↓ PPARα ↑, UCP-1 ↑, UCP-2 ↑,	Sim *et al.* [39]
	Solidago virgaurea var. *gigantea*	Epididymal adipose tissue Liver	PPARγ ↓, C/EBPα ↓, aP2 ↓, FAS ↓, SCD-1 ↓ SREBP1c ↓, FAS ↓, SCD-1 ↓, CD36 ↓	Wang *et al.* [38]
	Valeriana dageletiana Nakai ex F. Maek.	Epididymal white adipose tissue Liver	PPARγ ↓, C/EBPα ↓, aP2 ↓, FAS ↓, SCD-1 ↓ SREBP1c ↓, FAS ↓, SCD-1 ↓, CD36↓	Wang *et al.* [42]
	Viola mandshurica W. Becker	Epididymal adipose tissue Adipose tissue, abdominal subcutaneous fat tissue	C/EBPα ↓, C/EBPβ ↓, SREBP1c ↓ UCP-2 ↑	Sung *et al.* [46]
Lipolysis in adipose tissue and the liver	*Astilbe chinensis* Franch. et Savat.	Epididymal adipose tissue	ATGL ↑, phospho-HSL ↑	Zhang *et al.* [44]
	Moringa oleifera	Epididymal adipose tissue, liver	ATGL ↑	Xie *et al.* [40]
Inhibitory effects of lipid accumulation by AMPK activation in adipose tissue and the liver	*Astilbe chinensis* Franch. et Savat.	Epididymal adipose tissue	Phospho-AMPK ↑, phospho-ACC ↑, PGC-1α ↑	Zhang *et al.* [44]
	Moringa oleifera	Epididymal adipose tissue, liver	Phospho-AMPKα (Thr172) ↑, Phospho-ACC (Ser79) ↑	Xie *et al.* [40]
	Viola mandshurica W. Becker	Epididymal adipose tissue Liver	AMPKα1↑, AMPKα2 ↑ Phospho-AMPK ↑, ACC ↑	Sung *et al.* [46]

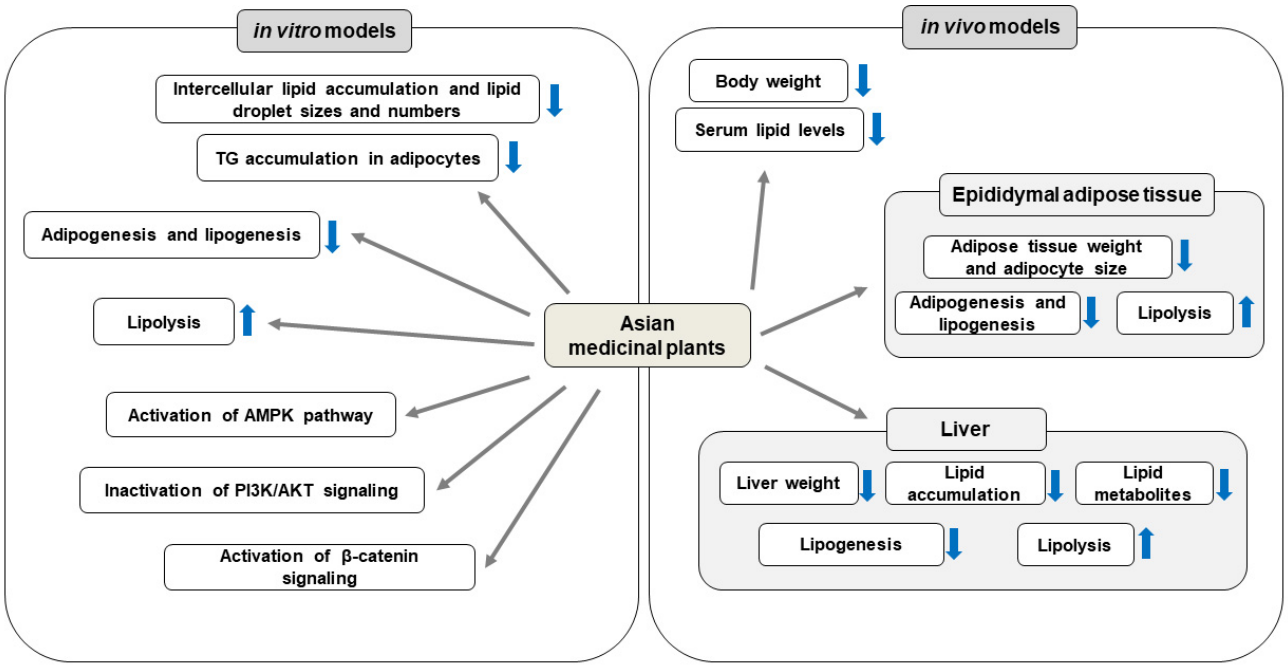

Fig. 1. Anti-obesity effects of Asian medicinal plants and their underlying mechanisms *in vitro* and *in vivo* models. Asian medicinal plants inhibit fat accumulation and promote lipolysis by AMPK activation, PI3K/AKT signaling inactivation, and activation of β-catenin signaling pathway.

pathways and biomarkers of anti-obesity have also been insufficient. Therefore, further studies are needed to improve our knowledge of these aspects in the future. Nevertheless, the findings from this review highlight the anti-obesity effects of Asian medicinal plants and support the use of these plants as alternative medicines for obesity prevention.

Abbreviations

UCP1, uncoupling protein 1; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol; C/EBP, CCAAT/enhancer binding protein; PPAR, peroxisome proliferator-activated receptor; FAS, fatty acid synthase; FABP4, fatty acid binding protein 4; aP2, adipocyte protein 2; SREBP, sterol regulatory element binding protein; ACC, acetyl-CoA carboxylase; CPT-1, carnitine palmitoyl transferase-1; LPL, lipoprotein lipase; SCD, stearoyl-CoA desaturase; HSL, hormone-sensitive lipase; AMP, adenosine monophosphate; AMPK, AMP-activated protein kinase; PGC, peroxisome proliferator-activated receptor gamma coactivator; ATGL, adipose triglyceride lipase; PI3K, phosphatidylinositol-3 kinase; mTOR, mammalian target of rapamycin; p70S6K, phosphorylation of ribosomal protein S6 kinase; HFD, high-fat diet; TC, total cholesterol; UPC, uncoupling protein.

Author contributions

JTH received a review invitation; SC and JTH developed the research question, and SC and SHP collected and screened the relevant articles; JHP and JTH selected the final articles and extracted the data from the articles; SC wrote the manuscript; All authors critically reviewed the manuscript and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

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Conflict of interest

The authors declare no conflict of interest.

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