CHAPTER

18

Botanicals as Medicinal Food and Their Effects against Obesity

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OUTLINE

18.1 INTRODUCTION

An excess deposition of body fat in adipose tissue may result in overweight and/or obesity and the proportionate increase in risks caused with increasing-degrees of obesity. According to World Health Organization (WHO) the definition of obesity is established on the body mass index (BMI), which is computed as weight in kilograms divided by height in meters squared (kg/m^2). Obesity is defined as a BMI greater than 30 kg/m^2, and overweight is determined as a BMI from 25 to 30 kg/m^2. The metabolic syndrome

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is a collective term that refers to obesity-associated metabolic abnormalities/risk factors [1]. There are several health risks associated with obesity and according to WHO can be categorized into three groups: diseases that are greatly increased due to obesity (type 2 diabetes, gall bladder diseases, dyslipidemia); those which are moderately increased (coronary heart disease, hypertension, osteoarthritis); and finally diseases that are mildly increased (cancer especially breast cancer in postmenopausal women, endometrial and colon cancer, reproductive hormone abnormalities, polycystic ovary syndrome). On June 2013, the American Medical Association officially recognized obesity as a disease [2].

Utilization of plant components and its derived products has a prospective future for controlling the prevalence of metabolic syndrome. Several evidences are exploring to support the use of herbs as an alternative way of obesity control and weight management [3]. The pathogenesis of obesity is very complex and requires different intervention strategies to undertake this problem. Despite going for lifestyle modification or pharmacotherapy in terms of weight loss, there has always been disappointing results which indicated the need of other treatment modalities to produce better and long-lasting results. Diet-based therapies and herbal supplements are among the most common complementary and alternative medicine modalities for weight loss. The great ratio of the population depends on traditional practitioners and their prescription of medicinal plants in society to assemble health care needs [4]. Hence, it is really obvious that plants may offer an efficient option for the treatment of obesity.

18.2 PATHOGENESIS OF OBESITY AND MANAGEMENT STRATEGIES

18.2.1 Etiology

A hypothesis suggests that obesity is linked to genetic predisposition and environmental factors which leads to the accumulation of excess adipose tissue. Usually, both the environmental factors and genetic factor(s) should be present for the occurrence of obesity. This hypothesis is indubitably true for majority of obese people worldwide. There are two parts to the obesity equation:

(1) An excessive intake of food items with increased amounts of fat, salt, and sugars, but lesser amounts of minerals, vitamins, and other nutrients; and (2) decrease in physical activity because of sedentary lifestyles, comfortable modes of transportation, lack of maintenance of daily routines, and increasing urbanization. Thus, the energy discrepancy between calorie intake and those expended is the fundamental cause of obesity and overweight [5].

18.2.2 Pathophysiology

Although multiple candidate genes contribute to the pathogenesis of obesity, these findings are not consistent. The genes include the chromosome 10p, melanocortin-4 receptor gene, β_3-adrenergic receptor gene, peroxisome proliferators activated receptor gamma two gene, and other genetic polymorphisms. Hormones such as adipokines, gut-related hormones, and many others are involved in the regulation and pathophysiology of obesity. One of them is ghrelin, which is a circulating peptide hormone derived from the stomach. It is the only known peripherally acting orexigenic hormone that is responsible for stimulating appetite. But the gut-derived hormones act as anorectic agents that attenuate food intake to attain optimal digestion and absorption rather avoiding the cost of overconsumption, such as insulin resistance and hyperinsulinemia [6].

Peptide YY (PYY) is present in the intestine at increasingly higher levels, having maximum levels in colon and rectum. It is mainly secreted by the L cells of the distal small bowel and colon. PYY reduces gastric secretion by modulating signals to the hypothalamus, ensuing in delayed gastric emptying. Food consumption is decreased if PYY is administered before meal [7]. Cholecystokinin (CCK) is produced in the pancreas, stomach, and gallbladder. Dietary fat is responsible for the release of CCK and accumulated in the small intestine. The major functions of CCK involve pancreatic exocrine secretion, gastric emptying, gallbladder contraction, and gut motility. CCK increases satiety and simultaneously decreases appetite by acting centrally via subtype CCK-A receptors on the afferent brain vagal fibers, causing inhibition of appetite. Oxyntomodulin is released postprandially resulting in the limitation of food intake. Secretion of this peptide occurs from the intestinal cells that also are responsible for the secretion of PYY. Oxyntomodulin suppresses appetite and reduces food intake for a long period that is also associated with a decline in fasting ghrelin levels. Intravenous administration of glucagon-like peptide-1 in humans enhances satiety and also reduces food intake [6].

Adipokines are a group of hormones produced by the adipocytes. Adipokines secretion is regulated by tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), leptin, and adiponectin. The role of TNF-α in obesity has been associated with insulin resistance via the liberation of free fatty acids, decreased production of adiponectin, and modulate insulin signaling. Inflammatory mediators are recruited in vascular tissue through the activation of nuclear factor-kappa B(NF-κB) by TNF-α. Immune, endothelial, fibroblasts, and adipocytes cells are secreting one of the pleiotropic circulating cytokine, intreleukin-6 (IL-6) which causes

inflammation, impairment of host defenses, and tissue injury. It acts by inhibiting insulin receptor signal transduction in hepatocytes, increasing circulating free fatty acids from adipose tissue, and reducing adiponectin secretion [6]. Leptin is one type of adipokine that plays a key role in regulating energy intake and expenditure, including appetite and hunger, metabolism, and behavior. Leptin can cross the blood–brain barrier by binding to specific receptors in the hypothalamus resulting in the suppression of appetite. True leptin deficiency in humans is rare; however, obese humans are, in part, leptin-resistant [8]. Adiponectin is a 244 amino acid long polypeptide derived from plasma protein. The role of adiponectin is glucose regulation and fatty acid oxidation [6].

The level of inflammatory mediators such as IL-6, TNF-α, and CCK are increased by increasing the visceral fat, as a result proinflammatory mediators like adiponectin and interleukin-10 levels are decreased that leads to increases in the chances of metabolic dysfunction which is one of the prime causes of obesity. Neuroendocrine diseases are secondary causes of obesity.

18.2.3 Obesity Pharmacotherapy by Phytocostituents

A huge number of plants, phytochemicals, and plant derivatives possess antiobesity activity by their unique mode of action. Broadly, phytocostituents generally act through modulating physiological functions that may restore balance between energy intake and expenditure. Phytoconstituents encompass antiobesity activity and their mechanism of action is discussed. Schematic representation of major targets for antiobesity phytoconstituents is seen in Figure 18.1.

18.2.3.1 Pancreatic Lipase

A diet containing fat is neither digested nor absorbed in the intestine until it has been possessed by the action of pancreatic lipase enzyme. Hence, one of the most promising strategies to inhibit fat absorption from intestine can achieve by blocking the action of pancreatic lipase through phytochemicals. Phytochemicals covalently bond to the active serine site on pancreatic lipases enzyme in the gut lumen. By forming the covalent bond,

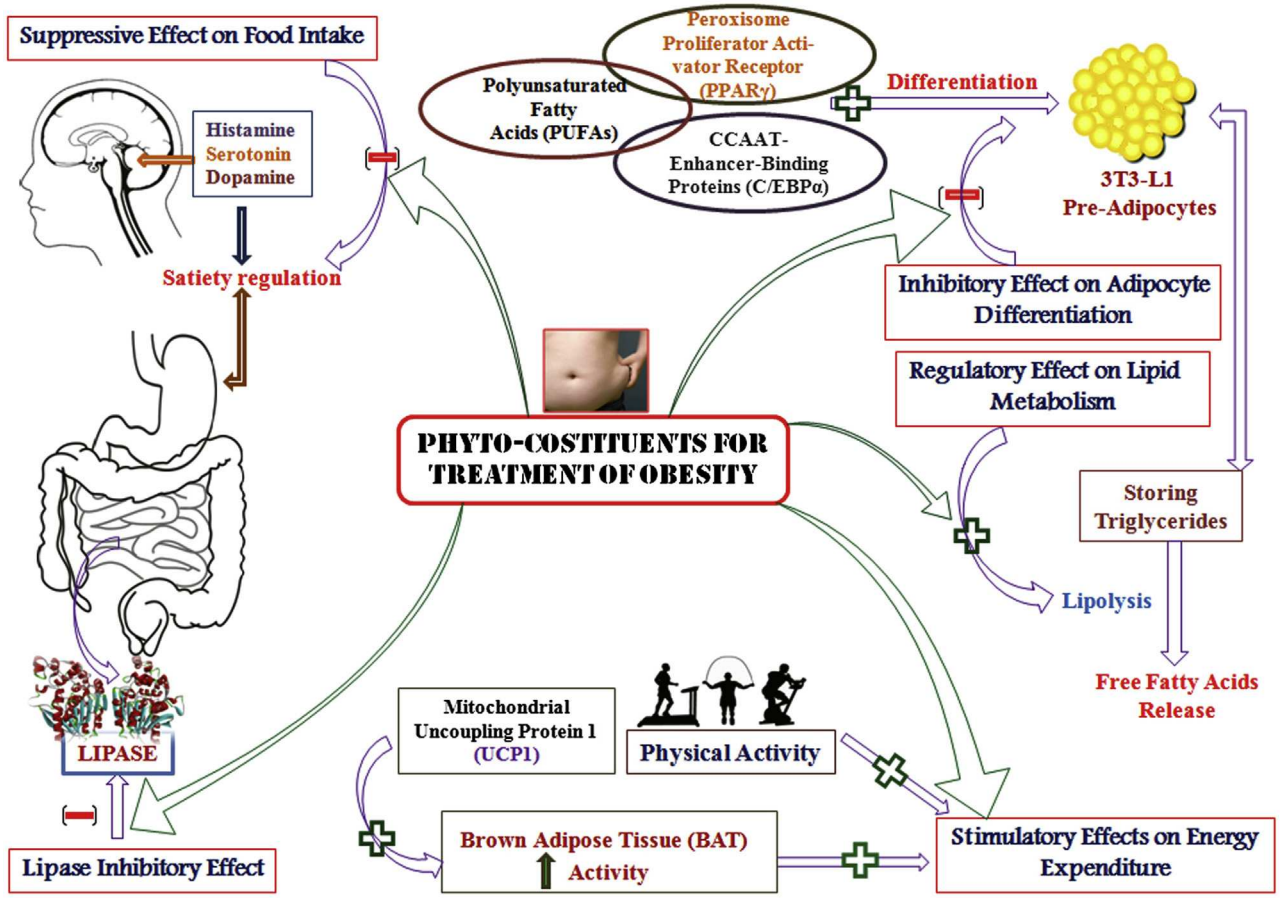


FIGURE 18.1 Major targets for anti-obesity phyto-constituents. (Five major target for anti-obesity activity possess phyto-constituents: satiety regulation; lipase inhibitory effect; stimulatory effect on energy expenditure; regulatory effect on lipid metabolism; inhibitory effect on adipocyte differentiation).

it inhibits lipases activity to hydrolysis of dietary fats into absorbable monoglycerides and fatty acids. Therefore, fats then tend to be excreted in feces rather than being absorbed to be used as a source of energy, in turn leading to weight loss in individuals [9].

18.2.3.2 *Adipocyte Differentiation and Proliferation*

Adipocytes, also known as lipocytes and fat cells, are the cells that primarily compose of adipose tissue, play a central role in the maintenance of lipid homeostasis and energy balance by storing triglycerides and releasing free fatty acids in response to changing energy demands. There are two types of adipose tissue, white adipose tissue and brown adipose tissue (BAT). Growth of the adipose tissue depends on hyperplasia and hypertrophy of adipocytes. Therefore, several studies are performed to focus on the processes of adipocyte proliferation and differentiation. In research, uses of 3T3-L1 preadipocyte cells are advantageous in vitro model for the study of obesity, due to its triglycerides accumulation ability during differentiation in cell culture [10]. This process is accomplished by expression of adipocyte specific genes, such as peroxisome proliferator-activated receptors-γ (PPARγ) and CCAAT/enhancer-binding protein-α (C/EBPα). Research is done to find the potential natural product which shows a promising inhibitory activity on adipogenesis, with regard to the potential treatment of obesity. However, current studies in this area suggest that inhibiting adipogenesis is unhealthy, leading to type 2 diabetes and other metabolic diseases, such as atherosclerosis [11]. Polyunsaturated fatty acids (PUFAs) are integral molecules of phospholipids of cell membrane and act as a signal transducer in adipocyte differentiation via regulating adipocyte-specific gene expression. Moreover, PUFA can withstand to the formation of triglycerides then other saturated and monounsaturated fatty acid. Therefore, PUFA plays an essential role in limiting fatty acid synthesis and regulating adipocyte differentiation through the suppression of late-phase adipocyte differentiation [9].

18.2.3.3 *Lipid Metabolism*

The lipolysis of fats can be achieved in two different ways. The first approach is stimulating triglyceride hydrolysis in order to diminish fat stores and another option is augmented fatty acid oxidation which is released from triglyceride store, thereby combating obesity. β_3-Adrenergic agonists played a pivotal role in this regard. However, excessive lipolysis causes high circulating fatty acid levels in the blood stream leading to dyslipidemia; a blockade of such a fatty acid release may be of therapeutic interest [9].

18.2.3.4 *Energy Intake and Energy Expenditure*

Appetite control can suppress body weight gain through a cascade of multifactorial events, which is typically interrelated with neurological and hormonal function of the body. Histamine, dopamine, and their closely associated receptor activities are responsible for satiety regulation. Appetite suppression can be achieved by modifying various hypothalamic neuropeptides' levels and/or via decrease in the function of monoamine neurotransmitters in the central nervous system (CNS). It may be suitable targets for appetite suppressant drug development [12]. Serotonin is a monoaminergic neurotransmitter of sensory and motor neurons that may modulate behavioral processes by acting through 5-hydroxy tryptamine (5-HT) receptor subtypes. These receptors played a crucial role in the energy intake reduction and may be useful for antiobesity drug development from natural product [13]. A potential appetite suppressant should be considered in terms of: (1) the psychological experience and behavioral expression of appetite, (2) metabolism and peripheral physiology, and (3) the CNS neural pathways' functioning [12].

Hunger is a sensation experienced when one feels the physiological need to eat food. In contrast, satiety is the absence of hunger. It is the sensation of feeling full. However, ghrelin secretion from stomach may increase the desire of food intake in animals and humans. Thus, ghrelin antagonism may decrease or blunt the desire for food; consequently decreased feeding, may be a possible adjunctive treatment for obesity [14]. Melanin-concentrating hormone receptor antagonism may also prove an important target for obesity treatment through appetite regulation. Increased adipose tissue concentration causes excessive food intake as a result of insufficient energy expenditure. To regulate body weight and energy expenditure, mammalian BAT plays an imperative role in energy homeostasis, BAT dissipates energy in the form of heat, a process called nonshivering thermogenesis. UCP-1 (mitochondrial uncoupling protein-1) is a key player in this process, which discharges the proton gradient generated in oxidative phosphorylation and thereby dissipating energy as heat. Thus, phytoconstituents work on the upregulation of UCP-1 gene expression may be considered as prospective agents for obesity control through increasing energy expenditure. UCP-3 is an analog of UCP-1; UCP-3 is also regulating thermogenesis by the thyroid hormone, β_3-adrenergic agonists and leptin in some organs may be recognized as a potent target for antiobesity drug development in future [9].

18.2.4 Antiobesity Drugs

The currently available antiobesity drugs can be divided into two classes: central acting and peripheral

acting. Orlistat is the sole representative of the group of peripheral-acting drugs. Drugs that act on the CNS (modulating monoamine levels in the synaptic cleft) do so by means of three mechanisms, namely catecholaminergic (noradrenaline and dopamine), serotoninergic (5-hydroxytriptamine), or both [15].

Orlistat is a Food and Drug Administration (FDA)-approved weight-loss drug that is available without a prescription. Orlistat inhibits gastrointestinal lipases, reducing fat absorption. Its most common side effect is steatorrhea [16]. Some cases of severe liver injury have been reported. It is advisable to stop the drug immediately if there are any symptoms of liver problems which may include dark urine, itching, light-colored stools, loss of appetite, and sometimes yellow coloration of eyes and skin [15]. Lorcaserin is another FDA-approved antiobesity drug, for long-term use. Lorcaserin is a selective agonist of 5-HT2C receptors (subtype of 5-HT receptor). A rare but serious side effect of this drug is serotonin syndrome (high fever, muscle rigidity, and confusion), which most commonly occurs if the drug is taken along with antidepressant drugs like selective serotonin reuptake inhibitors or monoamino oxidase inhibitors. Other serious side effects are psychiatric disorders with cognitive impairment, bradycardia, hematological changes, and prolactin elevation [16].

Numerous complex etiologies are involved in obesity in human. So, monotherapy will not be sufficient to reverse the disease condition. Therefore, combination therapies have been evaluated clinically and it shows promising results in the management of obesity. One such combination therapy that has recently been approved in the United States is phentermine/topiramate extended-release formulation for the treatment of obesity [17]. The role of phentermine is the downregulation of catecholamines concentration in the satiety centers of the hypothalamus; as a result appetite is suppressed. Topiramate exerts its effects through partial antagonism of α-amino-3-hydroxy-5-methyl-4-isoxazole propionate/kainite receptors, although induction of γ-aminobutyric acid receptor-mediated inhibitory currents and modification of voltage-gated calcium and sodium channels may also play a role [16]. It must not be used during pregnancy because it may cause harm to the baby. Rare side effects associated with topiramate include kidney stones and acute glaucoma.

18.3 PHYTOCHEMICALS USEFUL AGAINST METABOLIC DISORDER

Phytochemicals derived from vegetables, fruits, herbs, and spices have beneficial health effects such as antiobesity, lipid-lowering, and/or antidiabetic properties [18]. Considering the above-mentioned facts, several phytochemicals possessing antiobesity activity have been summarized in Table 18.1.

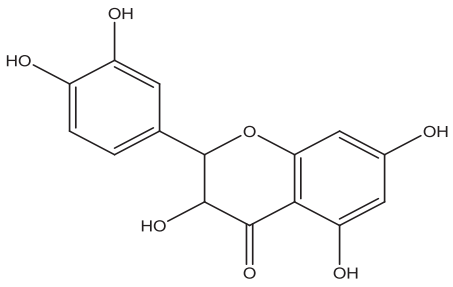
18.3.1 Phenolic Acids

Phenolic acids are composed of a basic phenol moiety with one carboxylic acid group. Chlorogenic and coumaric acids caused significant inhibition of cell growth as well as enhancing apoptosis on mouse preadipocytes. Gallic acid was not affecting the adipocyte cell cycle, but increased the number of apoptotic cells. A recent study explored that ferulic acid can suppress the high fat diet (HFD) induced weight gain by inhibiting fatty acid biosynthesis on lipid metabolism of mice [24].

18.3.2 Flavonoids

The most common expression of phenolic compounds is flavonoids abundantly present in plants, fruits, seeds, and vegetables. Flavonoids have the basic chemical structure of diphenylpropanes ($C_6{-}C_3{-}C_6$), and most often aglycones e.g., quercetin (**3**) or kaempferol (**4**), moieties are found attached to sugars (glycosides).

Quercetin [3]



Kaempferol [4]

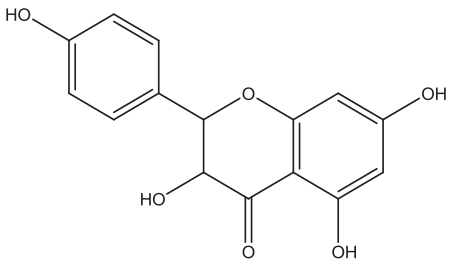
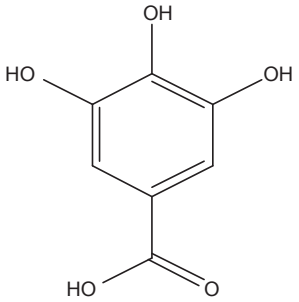
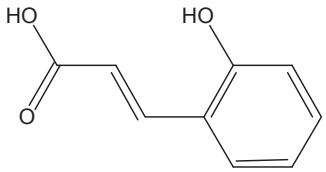
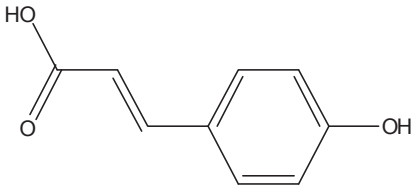
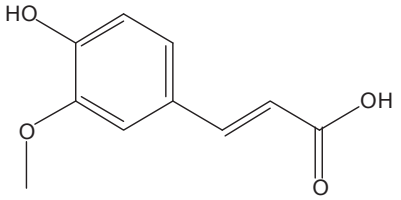
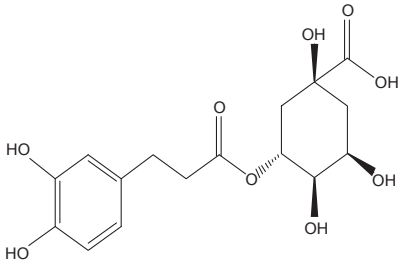


TABLE 18.1 Several Phytochemicals Possessing Antiobesity Potential

Name	Structure	Mode of action	Role in antiobesity	References
PHENOLIC ACID				
Gallic acid		↓ Triglyceride (TG), phospholipid, total cholesterol, low density lipoprotein-cholesterol (LDL-C), insulin and leptin levels	↓ Dyslipidemia, hepatosteatosis, and oxidative stress	[19]
		Inhibiting pancreatic lipase activity, ↓ TG	↓ Weight gain	[20]
		Upregulation of Peroxisome proliferator-activated receptors-γ (PPARγ) expression and Akt activation	Improves glucose tolerance and lipid metabolism	
Coumaric acid	O-Cumaric acid 	↓ Serum lipid profiles, insulin, and leptin ↓ TG and cholesterol levels ↓ Oxidative stress and glutathione disulfide(GSSG) content ↑ Glutathione (GSH), GSH peroxidase (GPx), GSH reductase (GRd), and GSH S-transferase (GST)	↓ Dyslipidemia, hepatosteatosis, and oxidative stress	[21]
	P-Cumaric acid 	↓ Expression of CCAAT/enhancer-binding protein α (C/EBPα), PPARγ, sterol regulatory element-binding protein-1c (SREBP-1c), and aP2 ↓ Fatty acid synthase and adiponectin mRNAs ↑ adenosine monophosphate-activated protein kinase (AMPK) and acetyl-CoA carboxylase (ACC) phosphorylation	Inhibited adipogenesis	[22]
Ferulic acid		Improved the hepatic steatosis	↓ Body weight gain ↓ Hyperglycemia ↓ Hypercholesterolemia	[23]
		↑ Fecal lipid excretion and antioxidant ↑ Lipogenic enzymes activities	Hypolipidemic	[24]
Chlorogenic acid		Inhibit fatty acid synthase, 3-hydroxy-3-methylglutaryl CoA reductase and acyl-CoA:cholesterol acyltransferase activities ↑ Fatty acid beta-oxidation activity and PPARα expression ↓ TG, leptin, and insulin ↑ Absorption and utilization of glucose	↓ Body weight gain improve lipid metabolism ↓ Body mass and body fat	[25]

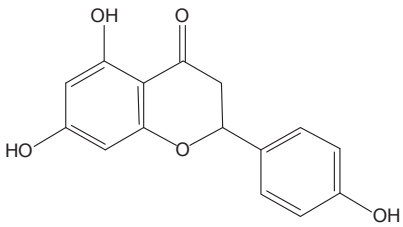
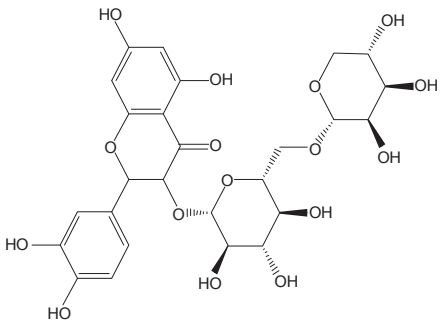
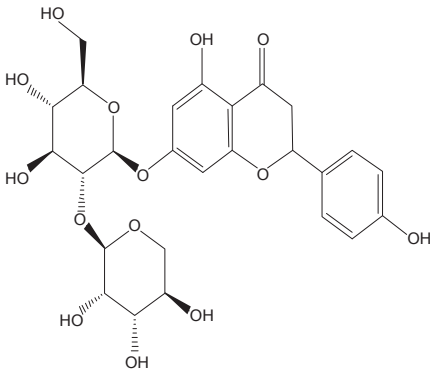
FLAVONOIDS				
Naringenin		↑ Fatty acid oxidation ↓ Very-low-density lipoprotein (VLDL) overproduction ↓ Hepatic cholesterol and cholesterol ester synthesis Improved overall insulin sensitivity and glucose tolerance	↓ Hepatic steatosis ↓ Dyslipidemia	[26]
		Inhibits toll-like receptors expression during adipocyte differentiation ↓ Tumor necrosis factor-alpha (TNF-α) and monocyte chemotactic protein-1	Antihyperglycemia Anti-inflammatory	
		Inhibits adipogenesis and impairs mature fat cell function ↓ Insulin receptor substrate 1 tyrosine phosphorylation Inhibited adiponectin protein expression	Antihyperlipidemic	[27]
Rutin		In vivo ↓ body weight gain ↓ PPARγ and C/EBPα	Suppressing adipocyte differentiation	[21]
		↓ Serum lipid profiles, insulin, and leptin ↓ TG and cholesterol levels ↓ Oxidative stress and GSSG content ↑ GSH, GPx, GRd, and GST	↓ Dyslipidemia, hepatosteatosis and oxidative stress	
		↓ Endoplasmic reticulum (ER) stress and production of reactive oxygen species Protect fatty liver and insulin resistance ↑ Energy expenditure	Blocking macrophage mediated inflammation and inflammation induced obesity	[28]
Naringin		↓ Cholesterol and TG concentrations ↓ 3-Hydroxy-3-methylglutaryl-coenzyme A reductase activity ↓ Cholesterol acyltransferase activity	Hypolipidemic ↓ Hepatic cholesterol biosynthesis	[29]
		↓ Inflammatory cell infiltration, oxidative stress, plasma lipid concentrations ↑ Liver mitochondrial function	Cardioprotective	
		↓ Plasma acute-phase protein and haptoglobin concentrations—naringin (0.1%)	Improve the obesity-related inflammatory state	[30]

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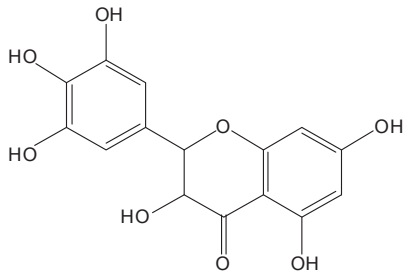
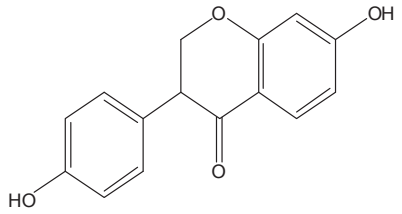
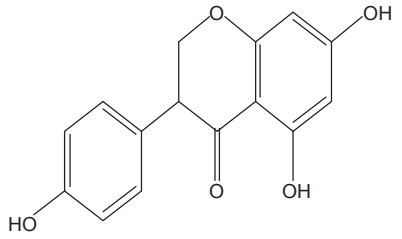
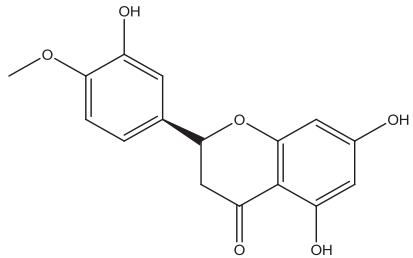
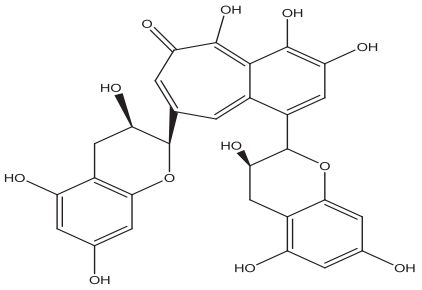
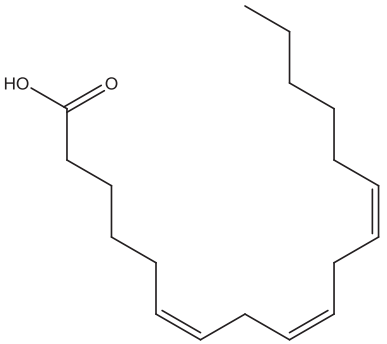
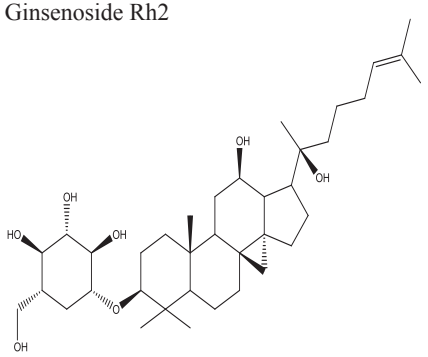
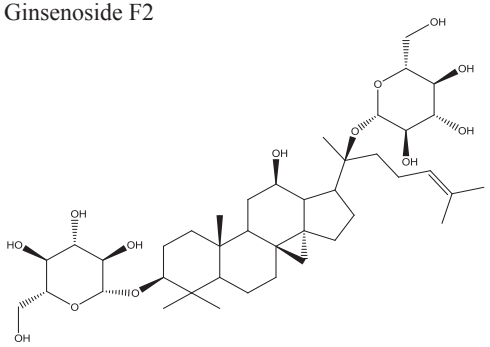
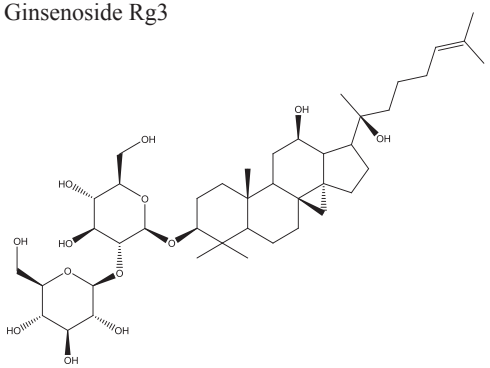
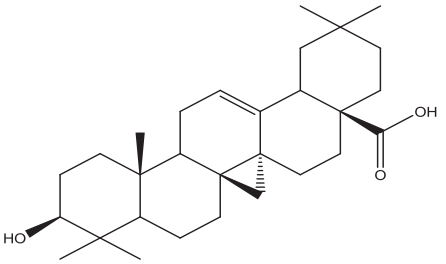
TABLE 18.1 Several Phytochemicals Possessing Antiobesity Potential—cont'd

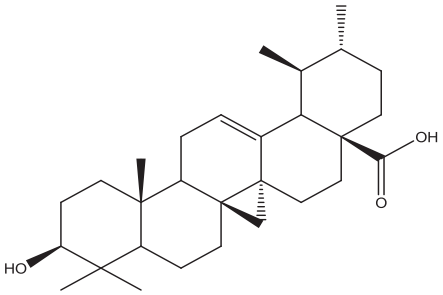
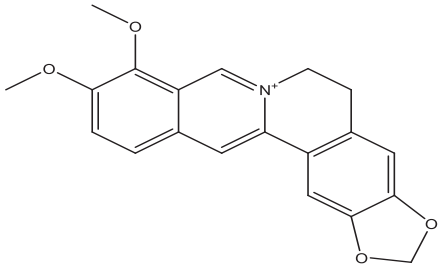
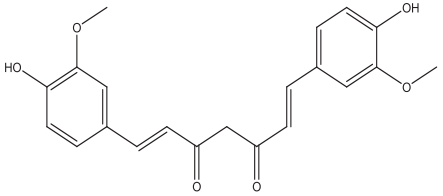
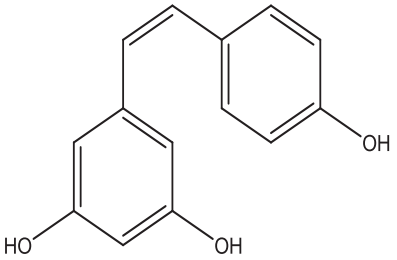
Name	Structure	Mode of action	Role in antiobesity	References
Myricetin		↓ PPARα ↓ Acyl-CoA oxidase and cytochrome P450 isoform 4A1 ↑ Expressions of hepatic SREBPs	↓ Body weight gain and body fat accumulation	[31]
Daidzein		↓ Glucose-6-phosphatase and phosphoenolpyruvate carboxykinase activities ↓ Fatty acid beta-oxidation and carnitine palmitoyltransferase ↑ Malic enzyme and glucose-6-phosphate dehydrogenase	Insulin-dependent diabetes mellitus	[32]
		↑ Leptin ↓ Adiponectin ↑ Uncoupling protein 1 ↓ Expression of stearoyl coenzyme A desaturase	Hepatic steatosis ↓ Weight gain and fat content	
Genistein		↑ Methylation of six cytosine–guanine sites in a retrotransposon upstream of the transcription start site of the agouti gene Permanently altering the epigenome	Alters susceptibility to obesity in adulthood	[33]
		↓ PPARγ and C/EBPα ↓ Glycerol-3-phosphate dehydrogenase ↓ Adipocyte fatty acid binding protein, fatty acid synthase, ↓ SREBP-1, leptin, lipoprotein lipase	Inhibited adipogenic differentiation	[34]
Hesperetin		↓ PPARγ2 ↓ TG and cholesterol levels ↓ Body weight	Inhibited the adipocyte differentiation	[35]
		↑ Release of cholecystokinin ↑ Intracellular Ca(2+) concentrations ([Ca(2+)]i)	Suppression of appetite	[36]

Theaflavin		Theaflavin digallate as potential plasminogen activator inhibitor type one inhibitor	↓ Body weight	[37]
		↓ Lipid accumulation, fatty acid synthesis Inhibited ACC activities	Prevention of fatty liver and obesity	[38]
		↓ Total Cholesterol (TC), TG, and LDL-C ↓ Atherogenic index, ↑ Insulin sensitive index Inhibited the hepatic lipase activity ↓ Leptin ↓ Serum alanine transaminase activity ↑ Serum superoxide dismutase activity	Reduce the risk of type 2 diabetes and cardiovascular disease in obesity	[39]
TERPINOIDS				
Gamma linolenic acid		↓ Body weight ↓ Adipose fatty acids	Weight loss in humans	[40]
		↑ Insulin-mediated glucose transport activity Reductions in the glucose-insulin index	Insulin-resistant obesity	
		Poly(ethylene glycol) + 1 conjugated linoleic acid ↓ PPARγ ↓ C/EBPα ↓ aP2	Antiadipogenic	[41]
Ginsenosides (Rh2, F2 and Rh3)	Ginsenoside Rh2 	↓ PPARγ activity ↑ AMPK signaling pathway	Antiadipogenesis	[42]
		Glucocorticoid receptor through ↑ Adipogenesis	↑ Lipogenesis in adipose tissue	

Continued

TABLE 18.1 Several Phytochemicals Possessing Antiobesity Potential—cont'd

Name	Structure	Mode of action	Role in antiobesity	References
	Ginsenoside F2 	PPARγ and perilipin gene expression	Antiadipogenesis	[43]
	Ginsenoside Rg3 	↓ Blood glucose ↑ Insulin secretion ↑ Fatty acid oxidation	Hyperglycemia	[44]
		↓ Fat accumulation ↓ PPARγ AMPK inhibition	Antiadipogenesis	[45]
Oleanolic acid		↓ PPARγ ↓ C/EBPα Visfatin (a proinflammatory and visceral fat-specific adipokine expressed in adipocytes) inhibition	Suppress obesity-associated inflammation	[46]
		↓ Body weights, visceral adiposity, plasma lipids ↑ Leptin ↓ Ghrelin	↑ Glucose tolerance ↑ Carbohydrate and fat metabolism	[47]

Ursolic acid		Translocating hormone-sensitive lipase ↓ Perilipin A expression by the protein kinase A pathway ↑ Adipose triglyceride lipase	↑ Lipolysis	[48]
		Ursolic acid stearoyl glucoside by ↓ Lipid parameters, TG ↓ Body weight, parametrial adipose tissue weight	Inhibiting pancreatic lipase activity	[49]
		↑ AMPK ↑ Liver kinase B1	Inhibit preadipocyte differentiation and adipogenesis	
OTHER GROUP OF PHYTO-CHEMICAL				
Berberine		↑ AMPK − in peripheral tissues ↓ Level of malonyl-CoA and stimulated the expression of fatty acid oxidation genes, centrally	Improve fatty liver	[50]
		↓ Weight gain and food intake ↓ Serum glucose, TG, and total cholesterol levels ↓ PPARγ expression ↑ GATA-binding protein 3 expression	Inhibited adipogenesis	[51]
		Modulation of the gut microbiota ↑ Levels of serum lipopolysaccharide-binding protein, monocyte chemoattractant protein-1 (MCP1), and leptin ↓ Level of adiponectin	Obesity-mediated insulin resistance	
Curcumin		Curcumin from *Curcuma longa* extract (0.09%) ↓ α1-acid glycoprotein	Improve the obesity-related inflammatory state	[30]
Resveratrol		↓ Body weight gain ↓ Levels of TG, free fatty acid, total cholesterol, glucose ↓ TNF-α and monocyte chemoattractant protein-1 ↓ Galanin-mediated adipogenesis signaling cascade	Antiadipogenic, anti-inflammatory	[52]
		Resveratrol-enriched rice DJ-526 rice ↓ Body weights and abdominal fat ↓ Lipid and glucose levels	Antiobesity	

↑ Increase the effect, ↓ decrease the effect.

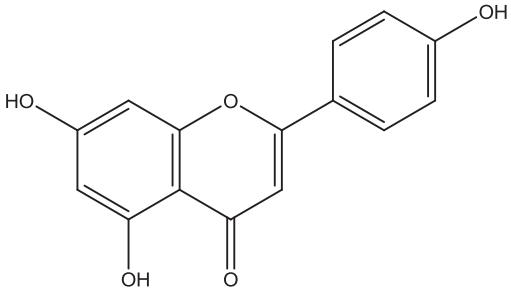
18.3.2.1 Flavonols

Quercetin and kaempferol are a common dietary flavonol found in plants and they have potential antiobesity effects. Quercetin has been shown to inhibit adipogenesis and induce apoptosis in mouse preadipocytes [19]. In a recent study, quercetin was seen to amplify the adenosine monophosphate-activated protein kinase (AMPK) signal pathway in 3T3-L1 preadipocytes cells that may be responsible for antiadipogenesis activity of the compound, while the quercetin-induced apoptosis of mature adipocytes was mediated by modulation of the extracellular signal-regulated kinases and c-Jun N-terminal kinase pathways, which play a key role during apoptosis [53]. Effect of quercetin with a combination of genistein and resveratrol was observed in human adipocytes (HAs). The combined treatments caused an enhanced inhibition of lipid accumulation in maturing HAs that was greater than the responses to individual compounds. Kaempferol has also possessed antiobesity effect to a lesser extent [54].

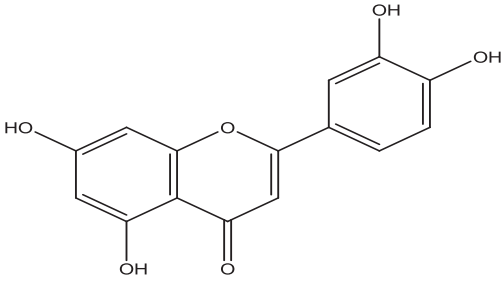
18.3.2.2 Flavones

Natural flavones are mainly apigenin (**5**), luteolin (**6**), chrysin (**7**), baicalein (**8**), scutellarein (**9**), wogonin (**10**), and their glycosides. Luteolin inhibited intracellular triglyceride (TG) accumulation of murine 3T3-L1 preadipocytes in a dose-dependent manner without producing cytotoxicity. Its antiadipogenic effects were exerted through suppressing adipogenic transcription factors and by inhibiting the *trans*-activation of PPARγ. An earlier study on apigenin suggests that it induced lipolysis in rat adipocytes [53].

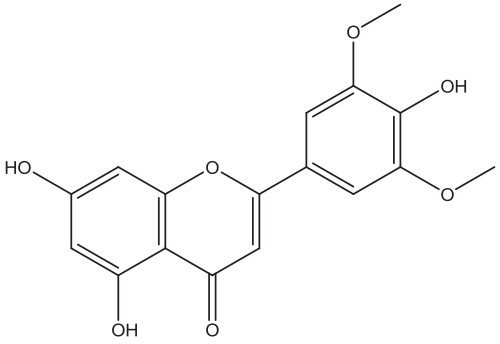
Apigenin [5]



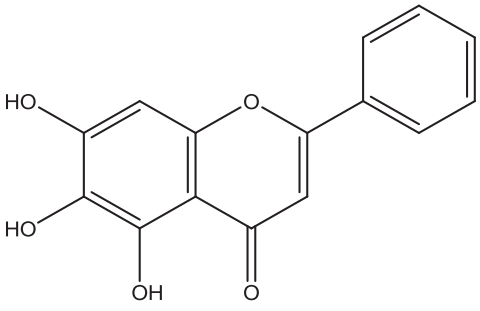
Luteolin [6]



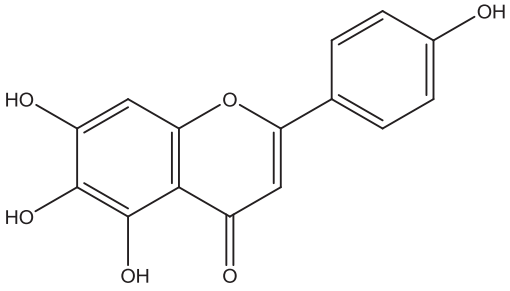
Crysin [7]



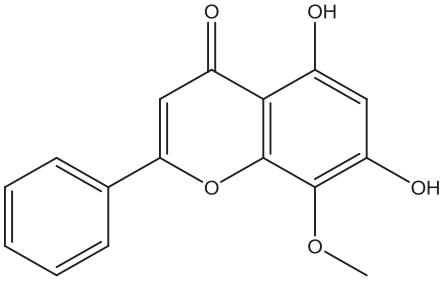
Baicalein [8]



Scutellarein [9]



Wogonin [10]



18.3.2.3 Anthocyanins

Anthocyanins are another class of flavonoids mostly water-soluble pigments that may appear red, purple, or blue depending on the pH and biosynthesized via the phenylpropanoid pathway. It has conquered the HFD-induced obesity in mice significantly. Cyanidins (**11**) are considered as the most widely spread anthocyanin in the plant kingdom. Cyanidin can reduce blood glucose levels as well as downregulating inflammatory protein cytokines such as monocyte chemoattractant protein-1 (MCP-1) in the adipose tissue of mice [53]. A study was revealed that cyanidin 3-glucoside stimulated in vitro insulin secretion from rodent pancreatic beta-cells. Among cyaniding glycosides, cyanidin 3-rutinoside and cyanidin 3-galactoside have been proposed as new noncompetitive α-glucosidase inhibitors [55]. These recent studies suggest that cyanidins have a unique therapeutic advantage and important implications in the prevention of obesity and diabetes.

18.3.3 Terpenoids

The terpenoids, sometimes called isoprenoids, were derived from five-carbon isoprene units (CH_2=$C(CH_3)$−CH=CH_2) assembled and modified in different ways. The daily eating of plant-derived terpenoids might be useful for the management for obesity and obesity associated syndrome, such as type 2 diabetes, hyperlipidemia, insulin resistance, cardiovascular disorder (CVD), and a lower prevalence of metabolic syndrome. Astaxanthin (**12**) belongs to the xanthophyll class of carotenoids was reduced the hepatic accumulation of TG and hyperlipidemia in HFD-induced mice [18]. Six closely related bicyclic diterpene was isolated from *Commiphora mukul* Gum possess lipid peroxidation and COX enzyme inhibitory activities. PPARs are dietary lipid sensors that control energy homeostasis. Researchers have observed abiotic acid, geranylgeraniol, bixin, geraniol, farnesol, phytol and auraptene are potential terpinoids activate PPARs significantly [56].

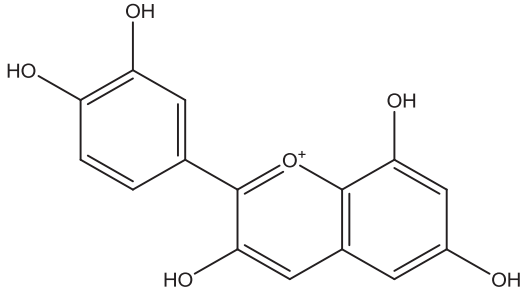
18.3.4 Carotenoids

Carotenoids belong to the category of tetraterpenoids (i.e., they contain 40 carbon atoms, being built from four terpene units each containing 10 carbon atoms). Hydrocarbons (carotenes) and their oxygenated derivatives (xanthophylls) are two main categories of carotenoids. β-carotene inhibits inflammatory gene expression in lipopolysaccharide-stimulated macrophages and has been suggested that its antioxidant activity contributes to beneficial effect on obesity and CVD. Possible pharmacological actions of α- and β-carotene have been postulated based on the finding lower level of plasma carotenoids among overweight and obese children compared to healthy weight children [53]. A similar result was also found when investigated the relationship between abdominal adiposity and serum levels of carotenoids in a healthy Japanese population [57].

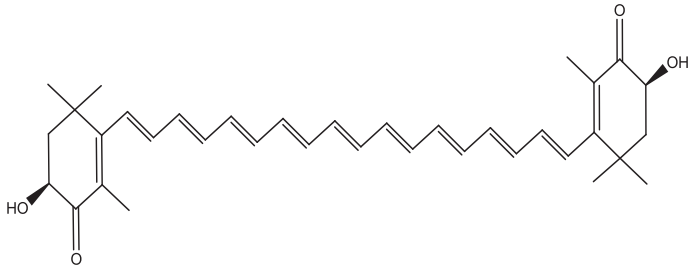
18.3.5 Organosulphurs

Organosulfur are sulfur containing organic compounds. Vegetables like garlic, onion, scallion, chive, shallot, and leek are the major source of bioactive organosulfur compounds such as allicin (**13**), allixin (**14**), and allyl sulfides. Allicin is the principal constituent of allium vegetables, which has induced apoptosis of human tumor cells [53]. Elkayam and coauthors [58] observed that pure allicin can lower blood pressure, insulin, and triglycerides levels in fructose-fed rats. In the same experiment, the control group was treated with fructose enriched diet that's shown continued to weight gain, whereas the groups fed allicin did not. Thus, allicin could be established as a useful therapeutic agent to combat obesity. In another study, antiobesity potential of ajoene was evaluated in 3T3-L1 adipocytes. The ajoene induced apoptosis in 3T3-L1 adipocytes was occurred mainly due to regulating fat cell numbers via generation of hydrogen peroxide, which leads to activation of mitogen-activated protein kinases, degradation

Cyanidins [11]



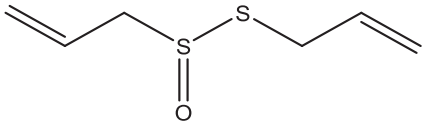
Astaxanthin [12]



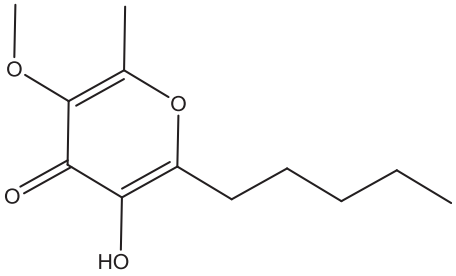
of PARP-1, translocation of apoptosis-inducing factor, and fragmentation of DNA [59].

The glucosinolates (**15**) are sulfur containing natural occurring organosulfurs of many pungent plants such as mustard, cabbage and horseradish. Breakdown products of glucosinolate are biologically active most notably the isothiocyanates and indoles, this byproduct has received much attention for its apparent anticarcinogenic activity and possible antiobesity effects. Sulforaphane (SFN), a member of the aliphatic isothiocyanate family, is a biologically active compound extracted from cruciferous vegetables such as broccoli, cauliflower, radishes and cabbage [53]. In a recent study, Choi and coworkers investigated the effect of sulforaphane on HFD induced obesity in C57BL/6N mice. Experimental results suggest that the role of antiadipogenesis activity of SFN possibly through downregulation of PPARγ and CCAAT/enhancer-binding protein α (C/EBPα) and by suppressing lipogenesis through activation of the AMPK pathway. Perhaps clinical trials are required to confirm the antiobesity effects of these phytochemicals [60].

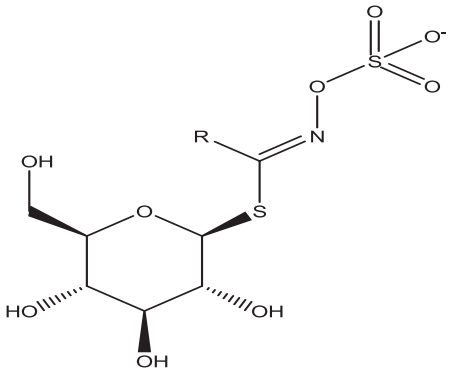
Allicin [13]



Allixin [14]



Glucosinolates [15]



18.3.6 Phytosterol

Phytosterols are natural compounds structurally similar to mammalian cell-derived cholesterol. The main sources of phytosterols are vegetable oils, nuts, grains, and grain derived products. The sterols are abundant in nature, they exist in both esterified and free alcohol forms. Phytosterols with potential effects of obesity are diosgenin (**16**), campesterol, brassicasterol, β- and γ-sitosterol (**19, 20**), stigmasterol, and guggulsterone E (**22**). High intakes of these compounds can also protect against atherosclerosis and decrease serum low density lipoprotein-cholesterol (LDL-C) levels [61]. Dietary plant sterols are reducing intestinal cholesterol absorption by increase fecal excretion of cholesterol as well as via regulating the expression of cholesterol homeostasis genes in the liver [62]. In another study explored that phytosterols can inhibit cholesterol absorption by competitive solubilization of mixed micelle formation of cholesterol in the intestinal lumen [63].

A bioactive phytochemical, protodioscin, isolated from the rhizomes of *Dioscorea nipponica*, was identified for its antihyperlipidemic effect. In hyperlipidemic rats, the administration of protodioscin significantly reduced the blood levels of TG, cholesterol, LDL and high-density lipoproteins (HDL) [64]. Dioscin and diosgenin the active components of *D. nipponica* are a potent porcine pancreatic lipase inhibitor. Diosgenin (5 and 10 μmol/L) inhibited the accumulation of TG and the expression of lipogenic genes in HepG2 cells. It is also ameliorates

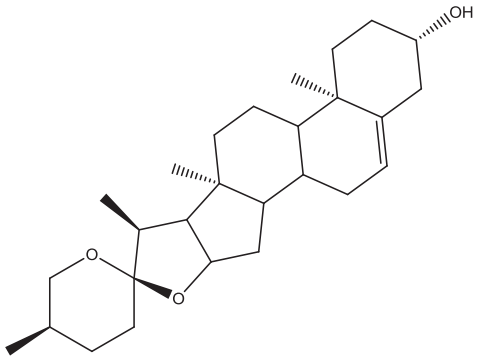
dyslipidemia by decreasing the hepatic lipid content in diabetic mice [65]. Furthermore, diosgenin is improving the lipid profile of rats feed with a high-cholesterol diet supplemented. Diosgenin showed significant therapeutic and preventive effect on hypercholesterolemia in mice. The serum total cholesterol level was decreased when rats were pretreated with diosgenin [66].

Guggulsterone (GS) is an active agent of the guggul plant (*Commiphora mukul*) which is used for treatment of obesity, arthritis, cancer, and CVD. GS and its isomers exert antiobesity effects by inhibiting differentiation of preadipocytes, and by inducing apoptosis and promoting lipolysis of mature adipocytes [67]. It is also potentiates antiadipogenic and proapoptotic effects in maturing 3T3-L1 preadipocytes considered as a potential antiobesity agent [68]. Researchers have discovered that GS can selectively decrease the expression of bile acid genes by act as an antagonist for farnesoid X receptor. It is hypoglycemic and hypolipidemic activity was tested on HFD induced rat [69]. Finally, studies indicate that GS can significantly lower lipid, cholesterol and TG and help in rising HDL in serum.

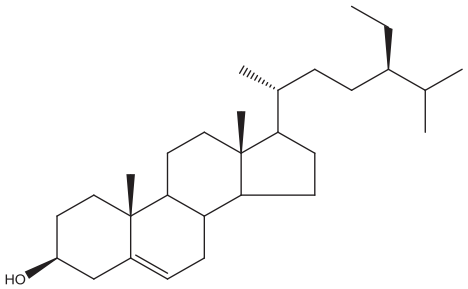
18.4 HERB AS FOOD USEFUL IN OBESITY MANAGEMENT

The best and most useful option for overweight and obese individual is calorie restriction and exercise. Obesity prevention through diets may be accomplished by bioactive constituents of herbal food supplements that could modulate molecular pathways and gene/protein expressions of the obese individual along with diet control and physical activity. Most recent researches on food were shown its ability to modulate some specific physiological functions in the organism through food intake [70]. Body weight control by food supplements requires knowledge of the process by which body gaining weight. Serrano and Sánchez-González [71] reported the main strategies for body weight control by the functional food ingredients: inhibition of food intake (by inhibiting orexigenic signals or enhancing anorexigenic signals), limiting the bioavailability of nutrients (by suppressing the digestive enzymes and/or interacting with them to physically prevent their absorption), stimulation of energy expenditure (thermogenesis), and

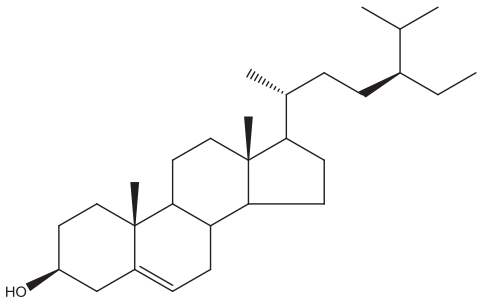
Diosgenin [16]



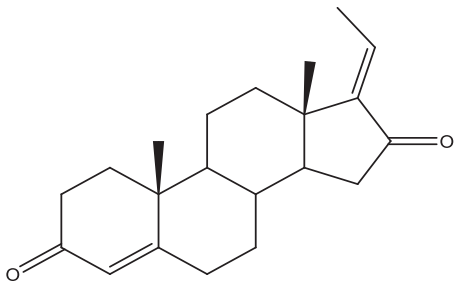
β-Sitosterol [19]



γ-sitosterol [20]



Guggulsterones E [22]



modifying the composition of the gut microbiota. The specific roles of gut microbiota are modulating metabolic energy storage by increase the capacity to harvest energy from the diet and modulate plasma lipopolysaccharides levels, which activate the inflammatory tone and the onset of obesity and type 2 diabetes [72]. This section is discussed the role of herbal food as medicine in alleviating obesity and associated complications. Table 18.2 summarized some important antiobesity activity possesses food plants.

18.4.1 Berries

The word berry is used for many dissimilar kinds of small fruits that bear many seeds and can be used as food. Some examples are raspberry, blueberry and lingonberry. In that respect are different species of berries which contains different types of ingredients most frequently polyphenols. Acai berries (*Euterpe oleracea* Mart.) are known as "superfood" with antiaging and weight loss properties. This fruit is small and reddish purple in color. This fruit pulp is rich in antioxidant component. It reduces fasting glucose, insulin levels, total cholesterol and LDL-cholesterol, in healthy overweight adults [112].

Blackberry is an edible fruit produced by many species in the *Rubus* genus in the Rosaceae family. It contains 87% cyanidin-3-O-β-d-glucoside (C_3G). C_3G is an anthocyanin compound which is having powerful antioxidative and anti-inflammatory activity. It has been sorted from the literature review that consumption of C_3G-rich blackberries are effective in prevention of

TABLE 18.2 Food Plants Possessing Antiobesity Potential

Plants	Parts used	Active principle	Mechanism of action	References
Aegle marmelos Correa. (Rutaceae)	Leaves	Coumarines, umbelliferone, and esculetin	↑ Lipolysis	[73]
Allium cepa L.(Amaryllidaceae)	Peels	Quercentin	Suppression of preadipocyte differentiation and inhibition of adipogenesis.	[74]
	Bulb	Cycloalliin, S-methyl-L-cysteine, S-propyl-L-cysteine sulfoxide and dimethyl trisulfide	↓ Serum TG and free fatty acid (FFA) levels on diabetes rats Inhibit formation of oil drop in the cells-suppressing obesity	
Brassica juncea L. Czern (Brassicaceae)	Oil	Crude extract	Regulate body weight gain, adipose tissue mass, lipid, and glucose metabolism	[75]
Brassica oleracea L. (Brassicaceae)	Sprouts	Crude extract	Cholesterol-lowering effect and potentially reduce lipid storage	[76]
Carica papaya L. (Caricaceae)	Fruit	Crude extract	↓ Triglyceride (TG), Total cholesterol (TC), low density level (LDL), and Very-low-density lipoprotein (VLDL) while high density lipoprotein -cholesterol (HDL-C) elevated	[77]
Cinnamomum zeylenicum Nees (Lauraceae)	Fruit	Crude extract	↓ TG, TC, and LDL-cholesterol	[78]
Citrus sinensis L. Osbeck (Rutaceae)	Peels	Pectin, synephrine	Pectin reduce blood cholesterol levels by decreasing its reabsorption in the colon and synephrine, reduces the production of cholesterol in the liver	[79]
Coffea canephora robusta (Rubiaceae)	Seeds and leaves	Caffeine, chlorogenic acid, Neochlorogenic acid, Feruloyquinic acids	Decrease the body weight Gain, ↓ hepatic TG level, and inhibit the fact accumulation in liver	[80]
Coriandrum sativum L. (Apiaceae)	Seed	Crude extract	↑ Hepatic bile acid synthesis and the degradation of cholesterol to fecal bile acids and neutral sterols	[81]

TABLE 18.2 Food Plants Possessing Antiobesity Potential—cont'd

Plants	Parts used	Active principle	Mechanism of action	References
Crocus sativus L. (Iridaceae)	Stigma	Crocin	Inhibit the absorption of dietary fat and cholesterol by hydrolysis of fat, pancreatic lipase inhibitor	[82]
Cuminum cyminum L. (Apiaceae)	Fruits	Crude extract	Reduction of macro vesicular steatosis in hepatic tissues and a significantly decreased number of lipid droplets and size of adipocytes	[83]
Curcuma longa L (Zingiberaceae)	Rhizome	Curcumin	Fatty acid oxidation, adipocyte apoptosis, AMPK activation, decrease expression of Peroxisome proliferator-activated receptors-γ (PPARγ) and CCAAT/enhancer-binding protein α (C/EBPα)	[84]
			Inhibited pancreatic lipase activity	
			Anti-inflammatory and improved metabolic conditions in obesity and improves glycemic control of type 2 diabetes in mouse models	
Emblica officinalis Gaertn. (Phyllanthaceae)	Fruit	Crude extract	Normalize adipose mRNA expression of nuclear transcription factor, peroxisome and inhibit lipid accumulation in mouse adipocytes	[85]
Ferula asafetida L. (Umbelliferae)	Oleo gum resin	Rhizome and root	↓ Body weights, abdominal fat, and size of epididymal adipocyte, serum leptin	[86]
Foeniculum vulgare Mill. (Apiaceae)	Fruit	Phenolics and flavonoids	Restricts the increase in body weight, fat pad weights, and disturbance of Total cholesterol (TC), HDL, LDL, and TGs	[87]
Garcinia cambogia Desr. (Guttiferae)	Fruit	Hydroxyl citric acid	Lipogenesis inhibition, lower body weight and reduce fat mass in humans	[9]
Glycine max (L.) Merr (Fabaceae)	Seeds	Protein	Pancreatic lipase inhibitor	[88]
Gymnema sylvestre R. Br (Asclepiadaceae)	Leaves	Gymnemic acids	↑ Fecal cholesterol and cholic acid-derived bile acid excretion	[89]
			↓ Serum leptin, insulin, LDH, LDL-C, total cholesterol, TG, and apolipoprotein-B levels	
Lagenaria siceraria (Molina) Standl (Cucurbitaceae)	Fruit	Crude extract	Fat amassment, ↓ TG and TC	[90]
Litchi chinensis Sonn. (Sapindaceae)	Litchi water extract	Crude extract	↓ TG and FFA	[91]
Malus domestica Borkh. (Rosaceae)	Fruit	Polyphenols	↓ Plasma and LDL cholesterol and triglyceride accumulation in heart and liver	[92]
Mangifera indica L. (Anacardiaceae)	Seed kernel	Crude extract	↓ The activity of glycerol 2-phosphate dehydrogenase in 3T3-	[93]

Continued

TABLE 18.2 Food Plants Possessing Antiobesity Potential—cont'd

Plants	Parts used	Active principle	Mechanism of action	References
			L1 adipocytes, and inhibit cellular lipid accumulation through downregulation of transcription factors such as PPARγ and C/EBPα	
Momordica charantia L. (Cucurbitaceae)	Fruit juice	Crude extract	Reduced adiposity mass with increased in lipid oxidative enzyme activities and uncoupling of protein expression	[94]
			Anti-inflammation and reduced oxidative stress, modulates mitochondrial activity, suppresses apoptosis activation, and inhibits lipid accumulation in liver	
			Reduce insulin resistance antidiabetic Downregulation of expressions of lipogenic genes inhibit visceral fat accumulation and adipocyte hypertrophy	[95]
			Reduced adipose tissue inflammation in diet-induced obese mice. ↓ Mast cell recruitment and proinflammatory cytokine monocyte chemotactic protein-1 (MCP-1) expression recruitments in epididymal adipose tissues (EAT), ↓ interleukin-6 (IL-6) and TNF-α expression in EAT	
Moringa oleifera Lam (Moringaceae)	Leaves	Polyphenolic, flavonoids	↓ TG, LDL, Very-low-density lipoprotein (VLDL), Total cholesterol (TC)	[96]
Murraya koenigii L. Spreng (Rutaceae)	Leaves	Carbazole alkaloids, mahanimbine	Pancreatic lipase inhibitor	[97]
Myristica fragrans Houtt. (Myristicaceae)		2,5-Bis-aryl-3, 4-dimethyltetrahydrofuran lignans, tetrahydrofuroguaiacin B, saucernetindio, verrucosin, nectandrin B, nectandrin A and galbacin	Activators of AMP-activated protein kinase	[98]
Phaleous vulgaris L. (Fabaceae)	Whole	α-amylase inhibitor, starch blocker	α-Amylase inhibitor	[99]
Psidium guajava L. (Myrtaceae)	Fruit peel	Crude extract	↓ TG, LDL, Very-low-density lipoprotein (VLDL), Total cholesterol (TC)	[100]
Spinacia oleracea (Amaranthaceae)	Leaves	Crude form	Improve abnormal postprandial hyperglycemic or hyperlipidemic responses	[101]
Solanum tuberosum L. (Solanaceae)	Tubers	Crude extract	Inhibition of lipid metabolism	[102]
Syzygium aromaticum L. Merr. et Perry. (Myrtaceae)	Dried flower buds	Crude extract	Regulation of genes related to lipid metabolism in the liver and white adipose tissue, ↓ lipid accumulation	[103]
Tamarindus indica L. (Fabaceae)	Pulp	Crude extract	Significant reduction in adipose tissue weights, as well as lowers the degree of hepatic steatosis	[104]

TABLE 18.2 Food Plants Possessing Antiobesity Potential—cont'd

Plants	Parts used	Active principle	Mechanism of action	References
Terminalia chebula Retz (Combretaceae)	Fruit, leaves	Myrobalan	Prevent cholesterol absorption, cholesterol excretion, enhanced lecithin: Cholesterol acyl transferase activity, lowers TG and TC	[105]
Trichosanthes dioica Roxb. (Cucurbitaceae)	Fruit	Flavonoids, alkaloids, glycosides, terpenes, sterols, lectins	↓ TG, LDL and Very-low-density lipoprotein (VLDL)	[106]
Trigonella foenum-graecum L., (Fabaceae)	Seed	Crude extract	↓ Very-low-density lipoprotein (VLDL), TGs, lactate dehydrogenase, and ↑ serum HDL-C ↓ Body weight gain	[107]
Vitis vinifera L. (Vitaceae)	Seeds	Cyanidol chloride (7%), Monomer (30%)	↓ Weight gain ↓ Blood lipid concentration ↑ Serum HDL-C concentration ↑ mRNA levels of lipolytic genes ↓ mRNA levels of lipogenic genes	[108]
	Grape skin	Resveratrol	↓ Adipogenic transcription factors (PPAR, C/EBPα, and their target genes (fatty acid synthase, aP2, SCD-1, and lipoprotein lipase)	[109]
	Seeds	Phenolic content	Inhibited lipid accumulation of C3H10T1/2 and 3T3-L1 adipose cells ↓ Expression of PPARγ	
Zingiber officinale Roscoe. (Zingiberaceae)	Rhizome	Crude extract, Gingerols and shogaol	Inhibition of dietary fat absorption ↓ Body weight, glucose, insulin, and lipid levels Inhibition of carbohydrate metabolism enzymes, ↑ insulin release ↓ Lipid content	[110]
Ziziphus jujuba Mill. (Rhamnaceae)	Fruit	Crude extract	Suppression of lipid accumulation and glycerol-3-phosphate dehydrogenase	[111]

↑ Increase the effect, ↓ decrease the effect.

weight gain and inflammation associated with ovariectomy-induced menopause in a rat model. The study was modeled for 100 days and after 100 days treatment revealed that a diet containing 10% blackberry (w/w) decreased hepatic NF-κB, and cyclooxygenase-2 expression levels in female Sprague—Dawley rats [113].

Blackcurrant (*Ribes nigrum*) berries are a woody shrub rich source of anthocyanin content. The concentration of anthocyanin in this type of berries are fourfold greater than those of other common fruits. 80% of the total anthocyanin content contains four major anthocyanins such as cyanidin-3-glucoside, cyanidin-3-rutinoside, delphinidin-3-glucoside and delphinidin-3-rutinoside. Maximum anthocyanins are found in fully ripe stage. In vitro or in vivo evidence suggested that anthocyanins are effective as natural antioxidants, anticarcinogenic, anti-inflammatory, vasoprotective, and antiobese agent [114]. Blueberries (vaccinium) are the perennial flowering plants with indigo-colored berries containing several bioactive compounds like anthocyanins (anthocyanidins, or phenolic aglycone conjugated with sugar), chlorogenic acid, flavonoids, α-linolenic acid, pterostilbene, resveratrol, and vitamins. The mechanism behind its obesity management involves the suppression of adipocyte differentiation, adipogenesis, and cell proliferation [115].

Bilberry is low-growing shrubs of the Ericaceae family. The obesity management potential of bilberries has been studied by Lehtonen, in 2011. It was found that bilberries decrease weight, waist limits, vascular cell adhesion molecule and intercellular adhesion molecule of obese women [116]. The extract of bilberry is enriched

with anthocyanidins which inhibited adipocyte differentiation by affecting the genes expressions of the insulin pathway; decreased PPAR, sterol regulatory element-binding protein 1c and tyrosine residues of insulin receptor substrate 1 phosphorylation [117]. Black chokeberry (*Aronia melanocarpa*) is native to eastern North America belonging to the family of Rosaceae found to contain high concentrations of anthocyanins and procyanidins. Chokeberry reduces weight gain and modulates insulin, adipogenic and inflammatory signaling pathways in epididymal adipose tissue of rats on a fructose-rich diet [118].

Indian gooseberry (amla) has been traditionally used in Ayurvedic herbal preparation or rejuvenating medicine. In an HFD induced mice model it significantly inhibited body weight gain as well as adipose tissue weight. Amla normalized adipose mRNA expression of nuclear transcription factor, PPARγ. Its aqueous extract was more effective in inhibiting lipid accumulation in 3T3-L1 mouse adipocytes treated during differentiation [85]. Mulberry is a long multiple fruit of Moraceae family. Peng and coauthors have investigated the potential of mulberry in obesity management. Mulberry water extracts (MWE) contain polyphenolic components like gallic acid, chlorogenic acid, rutin, and anthocyanins may responsible for hypolipidemic action by reducing serum triacylglycerol, cholesterol, free fatty acid, LDL/HDL ratio in 6-week-old male hamsters. MWE protects livers from impairment by decreasing hepatic lipids through regulating lipogenesis and lipolysis [119].

Rubus idaeus is a type of berries known to be effective in obesity management. The major aromatic component responsible for the obesity management is raspberry ketone (RK), 4-(4-hydroxyphenyl) butan-2-one; which is the main compound of red raspberry. It has structural similarity with capsaicin and synephrine. RK decreases the hepatic triacylglycerol content in HFD-induced mice. It translocate hormone sensitive lipase from the cytosol to lipid droplets in rat epididymal fat cells, thereby significantly increases norepinephrine-induced lipolysis. Specifically RK alters the lipid metabolism and increases norepinephrine-induced lipolysis in white adipocytes. In these ways RK prevented elevations in HFD-induced body weight and the weights of the liver and visceral adipose tissues [120].

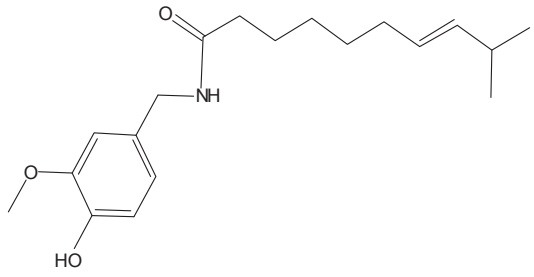
The *Solanum lycopersicum* is the edible red fruit/berry. It is commonly known as a tomato plant. In a recent investigation the effect of red and green tomato extract on has been studied in high-fat-diet-induced C57BL/6 mice. The investigation indicated that the green tomato extract attenuates obesity, which may be associated with activation of the AMPK pathway [60]. In another investigation into the effect of tomato vinegar (TV) containing phytochemicals has been evaluated in vitro and in vivo. In HFD-induced rats TV inhibited adipocyte differentiation of 3T3-L1 preadipocyte and lipid accumulation during differentiation. TV supplementation markedly decreased visceral fat weights, hepatic TG and cholesterol level without changing the food and calorie intakes. Furthermore, plasma LDL-cholesterol and antherogenic index has been lowered. It also elevates HDL-cholesterol to total cholesterol ratio. Thereby this study suggested that TV can be used as an antiobesity therapeutic agent [121].

18.4.2 Capsicum

Capsicum is the fruit of different species of capsicum plants. Capsicum is also known as red pepper or chili pepper or bell pepper, variety of names depending on place and type. Capsaicin (8-methyl-N-vanillyl-6-nonenamide) (**23**) is the most common naturally occurring capsaicinoids which is present all varieties of Capsicum plants. Other capsaicinoids are capsaicin, dihydrocapsaicin, nordihydrocapsaicin, homocapsaicin and homodihydrocapsaicin. Antiobesity effects of water extracts of *Capsicum annuum* L. were examined through the evaluation of lipoprotein lipase (LPL) mRNA expression level in mouse preadipocytes. In another study of antiadipogenic effect of *C. annuum* L. seeds in 3T3-L1 adipocytes cells were examined [122]. From the experimental outcome, it has observed significant decrease in the expression of LPL mRNA level, adipogenic transcription factors C/EBPβ, C/EBPα, and PPARγ, may possible mechanism of antiobesity activity of capsicum. Red chili pepper consumption can be augmented satiety and reduced energy and fat intake, the stronger reduction with oral exposure suggests a sensory effect of capsaicin [123]. In another possible mechanism of antiobesity effects of capsaicin may be thermogenesis caused by primary sensory neurons of the "pain" pathway to stimulate the transient receptor potential vanilloid receptor 1 [124]. Capsaicin can also increase catecholamine (epinephrine, norepinephrine (NE) and dopamine) secretion from sympathetic nervous system and as a result, increases blood pressure. The explored evidence may be another postulate of thermogenesis [125]. Furthermore, prospective antiobesity effects of capsicum were examined in diet-induced obese rats. The result suggests that capsaicin may diminish body weight and fat accumulation in obese rats significantly. These effects may be arbitrated by the up regulation of uncoupling protein 2 (UCP2) gene expressions and its ability to inhibit glycerol-3-phosphate dehydrogenase activity [126]. Clinical studies have shown that diet-induced thermogenesis has amplified by capsaicin. The most recent study reveals capsaicin to the diet has been shown to increase energy expenditure by negative energy balance and promotes fat oxidation [127]. In

addition, nanoemulsion oleoresin capsicum was explored as a potential antiobesity agent in HFD induced rats. Very few studies have been executed to measure safety issues of capsinoids. One of the study indicate 6 mg/day capsinoids consumption is safe which will improve the obesity condition by decrease body weight (abdominal fat loss) and changes in metabolism specially increase oxidation of fat [128]. Several studies indicate Capsicum fruit may consider as a potential antiobesity food.

Capsaicin [23]



18.4.3 Citrus

Citrus is one of the most popular food stuff in the world and is a rich source of nutrients and bioactive compounds. Citrus fruits contain vitamins, minerals, dietary fibers, and pectins along with abundant of bioactive compounds, including coumarins, flavonoids, carotenoids, and limonoids. Antiobesity and cardiovascular toxic effects of *Citrus aurantium* extracts in the rat were observed by Calapai et al. [129]. In this study citrus fruit extract was standardized by synephrine. Repeat dose administration had shown significantly reduced the food intake and body weight gain in rats. The immature peel extract of *Citrus sunki* Hort. was tested on HFD induced obese C57BL/6 mice and mature 3T3-L1 adipocytes. In vitro results suggest that *C. sunki* extract (CSE) had an antiobesity effect via elevated β-oxidation and lipolysis in adipose tissue. *In vivo* study of animal was explored *Citrus* peel extract causes decrease body weight gain, adipose tissue weight, reduce serum total cholesterol, and TG in the CSE-administered group significantly compared to the HFD group [130]. In another study, nomilin from citrus fruit and seeds causes lower body weight, serum glucose, serum insulin, and enhanced glucose tolerance in male HFD-induced C57BL/6J mice [131]. Limonin (Lim) is a white crystalline substance, usually found in orange and lemon seeds. Halder et al. [35] report the antiobesity effects of cyclodextrin (CD)-treated Lim along with naringenin (Ng) and hesperetin (Hes). The results were indicated that Lim, Ng, and Hes decreased cell viability in 3T3-L1 preadipocyte cells. Lim, Ng, and Hes inhibited the adipocyte differentiation in response to adipogenic inducers. The evidence for this inhibition included fewer Oil Red O positive droplets and a decreased expression of the adipocyte-specific gene PPARγ2. In animal studies, Lim-, Hes-, and combination-treated mice gained less body weight than control mice without treatment. The plasma TG and cholesterol levels were significantly reduced by Lim and the other substances. Furthermore, Lim increased the mRNA expression on lipid metabolism-related genes, including Acox1, UCP2. and carnitine palmitoyltransferase1 in the liver. In another experiment on Lim and its glycoside isolated from *Citrus reticulate*, was shown induction of mitochondria mediated intrinsic apoptosis in colon adenocarcinoma (SW480) cells [132]. In conclusion, we found that citrus fruits can prevent the development of obesity induced by an HF diet and lowers hyperlipidemia.

18.4.4 Garlic

Allium sativum (garlic) is a well known food plant gaining popularity as hyperlipidemic as well as a hypoglycemic agent. It is the member of Liliacae family got attractiveness both as food and medicine for many years. It is reported to contain a variety of effective compounds such as sulfur containing compounds, trace minerals etc. [133]. The sulfur compounds found in garlic cloves are mainly two types present in equal amount S-alkylcysteine sulfoxides and the γ-glutamyl-S-alkylcysteines. The most abundant sulfur compound is allicin (detail in Section 18.3.5). A thorough literature study has revealed that it lowers cholesterol level and decrease lipid peroxidation. In an in vitro experimental evidence showing garlic components suppress LDL oxidation and short-term supplementation of garlic in human has exhibited inhibition of LDL oxidation [134]. Three hundred and sixty days randomized, single-blind, placebo controlled study of garlic supplementation was conducted on Type 2 diabetic patients. The results of the garlic treated group significantly decrease total cholesterol, LDL-C and increase HDL cholesterol compared to placebo treated group. This study suggests garlic possess cardioprotective activity [135]. In addition, garlic can prevent the aortic plaque formation on cholesterol-fed rabbits. Moreover, vascular calcification is inhibited in human patients with high blood cholesterol by supplementation with garlic extract [136]. Garlic is also used for its hypoglycemic activity. The probable mechanism of garlic's hypoglycemic effects is increased insulin oozing and sensitivity. Evidence suggests that garlic possess antioxidative, anti-inflammatory, and antiglycative properties [137]. Garlic supplementation has been shown to boost testosterone levels and decrease plasma

corticosterone, hormones associated with protein anabolism, in rats fed a high protein diet [138]. Thus, garlic may emerge as an effective medicine for diabetic obese patient.

18.4.5 Grains

Whole grain contains a number of bioactive constituents' e.g., dietary fiber, polyphenolic compounds, carotenoids, tocotrienols, tocopherols, phytoestrogens, and vitamins. Its consumption was declining body mass index in school children, even after taking high calorie diet [139]. It also possesses protective action against stroke and metabolic syndrome. Due to poor digestibility rice protein reduced mammals' body weight and lipid level by increasing lipolysis and decreasing lipogenesis [140]. Barley Flakes: of all the grains, ceryain forms of barley have among the lowest glycemic indexes. Pearled barley (glycemic index (GI) = 36) and cracked barley (GI = 72) have lower GI than sweet corn (GI = 78), rolled barley (GI = 94), and instant white rice (GI = 128). Barley is a low glycemic source of carbohydrates and a great source of fiber (1.5%), both of which are advantageous in maintaining good glucose levels and weight control [141]. Nuts (tree nuts and peanuts) are rich sources of nutrient such as minerals, protein, unsaturated fats, fiber, phytosterols, phenolics, and other bioactive compounds and they do not contribute to weight gain rather its consumption showed reduced coronary heart disease and gallstones incidences in both genders and diabetes in women [142]. Early life soya intake produces higher leptin and MCP-1 levels, which contribute to the prevention of obesity. The polyphenol-rich black soybean seed coat extract containing cyanidin 3-glucoside, catechins, and procyanidins, suppresses abdominal fat accumulation, plasma glucose level and enhances insulin sensitivity, UCP-1 and UCP-2 expression in HFD mice, to deter obesity and diabetes by enhancing energy expenditure and suppressing inflammation [143].

18.4.6 Punica

Punica granatum L. (pomegranate) is a fruit bearing plant is probably originated in Iran and now cultivated throughout India. Till date several researches have been performed for investigating of its antitumor, antibacterial, astringent, antidiarrheal, and antiobesity activities. The presence of a wide range of bioactive components in leaf, flower, seed, and juice of pomegranate may attribute to its antiobesity effects [144].

The fruit of *P. granatum* could be considered as a functional food because it has contained a number of bioactive compounds that display functional and medicinal effects. Gallic acid, ursolic acid, and oleanolic acid are the major metabolites found in pomegranate fruit extract (PFE) posses' antihyperlipidemic properties. Along with the secondary metabolites the peels are also a rich in complex polysaccharides, and minerals, including potassium, nitrogen, calcium, magnesium, phosphorus, and sodium [144]. The antihyperlipidemic potential of PFE has been investigated by many researchers and it has been observed that PFE consumption decrease hepatic triacylglycerol and fatty droplets content without altering total cholesterol and it lowers serum lipids and glucose levels by 18−25% [145]. In another study, endothelial NO synthase expression by pomegranate juice (PJ) and seed oil was studied in obese Zucker rats, a model of metabolic syndrome. Results indicated that PJ significantly decreased the expression of vascular inflammation markers, thrombospondin (TSP), and cytokine TGFβ1, whereas prominent downregulation of TSP-1 expression occurred by seed oil. Plasma nitrate and nitrite (NO (x)) levels were significantly increased by PJ [146]. These data emphasize promising clinical applications of PJ in metabolic disorder. The pomegranate seeds represent about 3% of the fruit weight. The oil constitutes 12−20% of the total seed weight contains a high concentration of fatty acids such as linoleic acid and linolenic acid, as well as other lipids, including punicic, oleic, other than lipids, decent amounts of proteins, fibers, vitamins and minerals, polyphenols, and isoflavones are present. Investigation on seed hypolipidemic profile Vroegrijk and coworker speculated that the administration of 1 g seed oil had decreased body weight and fat mass in male C57Bl/J6 mice for 12 weeks [147]. Vroegrijk et al. also reported that supplementation with pomegranate seed oil improved insulin sensitivity in HFD-fed mice. Hontecillas, studied the effect of catalpic acid in C57Bl/67 obese mice and observed the reduction in the white adipose tissue accumulation, triacylglycerol content as well as augmented HDL in plasma [148]. Numerous in vitro, animal, and human experiments have demonstrated the enormous potential benefits of pomegranate. Therefore, it is necessary to establish the therapeutic profile of all the constituents in the diet and commercialized forms to understand about the potential benefits of the pomegranate for the prevention of obesity and related disorders.

18.4.7 Tea

Tea is the most widely consumed aromatic beverage in worldwide. The variety of chemical compounds within this plant plays an important role in management of human health. The three categories of teas are black, green, and oolong-tea. Among these three types, black tea is mostly consumed. The antiobesity potential of black tea (*Camellia sinensis*) is due to the presence of

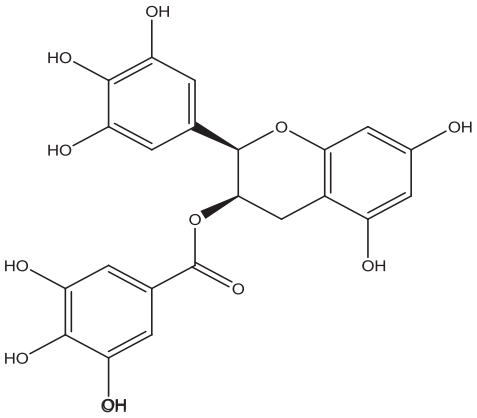
variety of polyphenolic compounds such as theaflavins, theaflavin 3-O-gallate, theaflavin 30-O-gallate, theaflavin 3, 30-O-gallate, epigallocatechin gallate (**24**), epicatechin gallate, catechins (**25**), quercetin glycosides, quinic acid, gallic acid and caffeine (**26**). These polyphenols inhibits pancreatic lipase thereby produces the antiobesity effect [149].

Green tea is another category of tea produced by the unfermented dried leaves of *C. sinensis*. Diverse mechanisms are involved behind the antiobesity effect of this tea. The main constituents of the green tea are the polyphenols like flavonols, flavones and flavon-3-ols, out of which flavan-3-ols also known as the catechins are the most widely found accounting to 60–80% of the polyphenols. This catechin helps in reducing metabolic syndrome and decrease the body weight of overweight/obese men, without affecting blood pressure or metabolic function biomarkers [150]. Catechin gallate is the strongest inhibitor of fatty acid synthase found in green tea. Green tea helps in increasing the energy utilization by increasing the potency of NE which is responsible for increasing energy utilization and fat oxidation. It also increases the lipolytic pathway, reduces adipose tissue and low-grade inflammation in HFD animal model. The other health beneficial role of green tea may be partly because of the caffeine present in it which increases energy utilization [151].

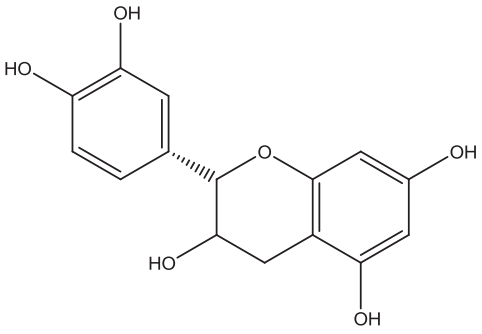
White tea is the category of tea produced from the unfermented young shoots of *C. sinensis*. The catechins level in this plant is more than green tea. It reduces blood triacylglycerols by increasing fecal lipids and reduces oxidative stress in the liver and adipose tissue without reducing food intake, body weight, visceral adiposity, and cholesterol lipoprotein profile [152].

Oolong tea is partially fermented tea. It may have some impact on increasing energy expenditure due to its catechin content. It also treats obesity, diabetes, atherosclerosis, high cholesterol, and skin allergies such as eczema; and boosts the immune system which is due to the presence of caffeine. Literature survey has revealed that three days of oolong tea consumption at five cups per day increases the resting metabolic rate 3–4%. This attributed to the increased fat oxidation, thereby decreasing the body fat stores [141].

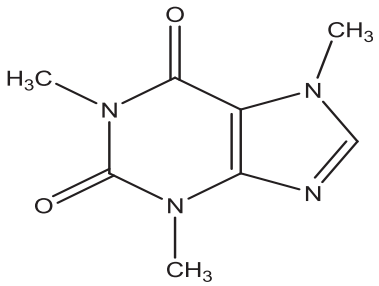
Epigallocatechin Gallate [24]



Catechin [25]



Caffeine [26]



18.5 MEDICINAL PLANT FOR TREATMENT OF OBESITY

Miscellaneous plant products such as plant protein, dietary fiber, prebiotic having the highest diversity in their properties which can reduce body weight and prevent diet-induced obesity. Therefore, in this section, we are discussing about antiobesity activity possesses plants and plant-derived products.

18.5.1 Plant Extract and Herbal Supplement

Several evidences suggested that not only isolated compounds from the plant, but crude plant extracts also possess desired therapeutic effects. Occasionally synergistic interaction of a plant's different groups of chemicals may improve the therapeutic activity in testing animals and also in humans. In Unani and Ayurvedic system of medicine, *Nigella sativa* (NS) seed extracts are used in the treatment of metabolic disorders, including dyslipidemia and obesity. The antiobesity activity of NS was clinically studied, which showed that the activity of different treatment group was not statistically significant but produced better activity than the control group. Results suggested that larger dose and longer duration of NS consumption will give better results [153]. In another clinical study, antihypertensive and hypolipidemic activity of *Hibiscus sabdariffa* extract was explored [154]. Furthermore, an acute and chronic effect of *Opuntia ficus-indica* extract was investigated on obese prediabetic patients. The result shows acute blood glucose lowering effects among the treatment group [155]. *Carum carvi* L. (caraway), an effective medicinal plant, is conventionally recommended for treating obesity. A randomized, triple-blind, placebo-controlled clinical trial on obese women suggests that caraway can successfully be used for obesity control in women without having any side effects [156]. Snacking is an uncontrolled eating habit, resulting in weight gain and obesity. Satiereal (Inoreal Ltd, Plerin, France) is an oral dietary supplement containing *Crocus sativus* L. (saffron) extract that may reduce snacking and enhance satiety through its suggested mood-improving effect. In addition, researchers are postulating that antioxidant rich compounds of saffron, e.g., crocins, picrocrocins, and safranal, may exert potential antiobesity activity but sufficient research has not yet been done [82].

Herbal supplements are nonfood substances intended to supplement the diet, contain one or more dietary ingredients (including vitamins, minerals, herbs, or other botanicals, amino acids, and certain other substances) or their constituents, and are generally available in forms such as tablet, capsule, powder, softgel, gelcap, or liquid. Herbal supplements and diet-based therapies for weight loss are among the most common in complementary and alternative medicine modalities. Additionally, traditional system of medicine used polyherbal preparation (combination of two or more plants) for the purpose of enhancement of effects. In this context, researchers have been examining the synergistic interaction of therapeutically active plant extracts in combinations; positive results are obtained which shows combination can increase or decrease the individual therapeutic activity or toxicity. While the exact mechanism of action of a combination of herbal preparation is not yet explored, a number of published data indicate that the herbal extract in combination being more efficacious than a single dose of one of its components alone. A combination of *Citrus pinnatifida* fruit and *Citrus unshiu* peel extracts shows superior antiobesity effects of HFD-induced obese rats [157]. A randomized, double blind, placebo-controlled clinical trial of herbal supplement (combination of *Asparagus officinalis* (*C. sinensis*), black tea, *Guarana Paullinia* cupana (guarana), *Phaseolus vulgaris* (kidney bean), *Garcinia cambogia* and chromium yeast) shows significant changes of the Body Composition Improvement Index and decrease in body fat in herbal supplement subjects compared to placebo [158]. In a recent study, Chinese herbal supplement (RCM-104) was examined for the management of simple obesity. A double-blind, randomized, placebo-controlled trial result studied RCM-104 and it was seen to be well tolerated and beneficial in reducing body weight and BMI in obese subjects [159].

18.5.2 Plant-derived Proteins

Some plants are good sources of protein, e.g., whole grains, soy, legumes, nuts, fruits, and seeds. We can get sufficient essential amino acids by eating a variety of plant proteins. Dietary proteins are considered to increase thermogenesis and satiety that may help in the prevention of obesity. Stem bromelain is a proteolytic enzyme obtained from *Ananas comosus* (pineapple) and this showed inhibitory effects on 3T3-L1 adipocyte differentiation. It may be attributed to antiobesity activity by suppressing the PPARγ-regulated adipogenesis pathway and by augmenting TNF-α-induced lipolysis and apoptosis in mature 3T3-L1 adipocytes [70]. Soy protein (SP) is an important component of soybeans and provides an abundant source of dietary protein. The antiobesity activity of dietary SP has been investigated in Wistar fatty rats. Results suggested that SP efficiently reduced the body weight of fatty rats by suppressing the lipogenic enzyme gene. In addition, this effect of SP has been examined on genetically modified obese rodents by Aoyama and coauthors [160]. Experimental results indicate that SP significantly

decreased body weight and plasma glucose level. Consequent research on SP recognized that it is a suitable protein source in energy-restricted diets for the treatment of obesity. Sixty days randomized single-blind study compared the effects of soy protein and pork-meat protein and carbohydrate diet on 24-h energy expenditure. The 24-h energy expenditure was higher with the pork followed by soy and then carbohydrate diet. The result suggests that soy has a greater thermogenic effect, than a carbohydrate diet which may be relevant for the prevention and treatment of obesity. Allison and coworkers [161] performed a 12-week randomized controlled trial of a low calorie soy-based meal replacement program in 100 obese subjects. Soy-based dietary formula was effective in lowering body weight, fat mass, and decreasing LDL cholesterol level in serum. However, long-term effects of dietary soy protein on obesity have not yet revealed. Further research is required to identify bioactive protein from plant sources that may play an important role against metabolic disorders.

18.5.3 Dietary Fiber and Prebiotics

Regulation of energy intake can be controlled by increased intake of dietary fiber (DF). DFs are nondigestible and nonstarch polysaccharides derived from plants. An increased intake of DF is useful in the management of obesity and diabetes. The obesity management potential is related to its unique physical and chemical properties, which aid in the early signals of satiation and/or prolonged signals of satiety. Sufficient amount of fiber in diet controls satiety via diverse mechanisms which includes cut-off in excessive food intake and deposits of fat accumulation, lowering the energy density of the diet, increasing sensory exposure time to a food in the oral cavity, slowing down gastric emptying, modifying the postprandial glucose response, promoting intestinal satiety, and changing neural and humoral signals in the gut [162]. Pectin, β-glucan, xylan, arabinoxylan, insulin, resistant starch, and guar gum are some of the examples of DFs which are beneficial in obesity. Guar gum slows down the gastric emptying and highly viscous fibers like oat reduce fasting glucose levels and elevated LDL-cholesterol level without changing the HDL fraction [163]. Whole-grain cereals significantly lower the risk of obesity, diabetes, coronary heart disease, stroke, hypertension, gastrointestinal diseases, and boosts the immune system and stimulates the growth of beneficial microbes in the colon. High amylose maize resistant starch (RS) is effective in treating obesity. RS supplementation (15–30 g/day) improved insulin sensitivity in overweight and obese subjects, thereby helping in the alleviation of complications associated with insulin resistance. Wheat arabinoxylan supplementation decreased adiposity, body weight gain, serum, and hepatic cholesterol and insulin resistance to HFD-induced obese mice [70].

Prebiotics are nondigestible oligosaccharides that pass undigested through the upper gastrointestinal tract and stimulate the growth and/or activity of advantageous bacteria. They are produced by enzymatic hydrolysis of polysaccharides or by transglycosylations. Gut microbiota (namely prebiotics) plays a nutritional role in the management of obesity by inducing a host response, controlling the gut's barrier, and endocrine functions [164]. Prebiotics like fructooligosaccharides, galactooligosaccharides, and lactulose have already been approved by the European Union. The effectiveness of some prebiotics is yet to be established. Supplementation of inulin (a type of fructans found in onion, banana, chicory, and artichokes) in the diet reduces liver and abdominal fat weight, enhances satiety, decreases energy intake, and regulates body weight in human and animal studies [70]. Therefore, proper and careful dietary manipulations can help in the prevention or management of obesity and other degenerative disorders.

18.6 PROSPECT OF PHYTOCHEMICALS, FOODS AND BOTANICALS IN OBESITY MANAGEMENT

Published data indicate that phytochemicals play a promising role for the treatment of obesity and its associated metabolic diseases. Several in vivo studies have repeatedly indicated that the intake of some phytochemicals could inhibit HFD-induced obesity in mice, hamsters, rats, or even humans [53]. The adipose tissue mass can be scaled down by inhibiting adipogenesis and/or inducing apoptosis in adipocytes. The pathway is important for the investigation of mode of action that natural products exert on antiobesity activity as well as for defining the strategies for future investigation.

Ghrelin is the only known circulating orexigenic hormone. Its effect on obesity is associated with increased appetite and food intake while reducing energy expenditure. Blocking ghrelin's action via a decrease in ghrelin secretion in the stomach may provide a promising target for antiobesity drug development programs [16]. A randomized, double-blind, placebo-controlled clinical trial on obese women was done and it was found that green tea extract significantly reduced the obesity-related hormone peptides such as adiponectin and ghrelin [165].

An effective weight-management product should provide improvements in blood pressure, lipids, glycemia, or other beneficial outcomes that are commensurate with the degree of weight loss [166]. Body fat

homeostasis typically balances body's energy regulation. Thus, drugs which are acting on either energy intake or expenditure fail to make the desired outcome after long-term treatment because compensatory mechanism balances the body weight. In the time to come, it is possible that plant derivatives, herbal supplement, and phytochemicals, combat the problem by their multiple mechanisms and emerge as effective antiobesity drugs.

18.7 CONCLUSION

Herbal food and plant-derived phytoconstituents along with regular exercise may provide efficient control over weight gain. However, there remains a heavy heap of research and understanding about the herb–drug interaction, pharmacokinetic measures, toxicological limitation, and beneficial effect of combination therapy. Progressive research on the recognition of new phytochemicals, functional food, or botanicals could be relevant for future advanced therapies and preventive steps to develop safe and effective therapeutics for obesity.

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LIST OF ABBREVIATIONS

5-HT Hydroxy tryptamine
AIF Translocation of apoptosis-inducing factor
AMPK Adenosine monophosphate-activated protein kinase
BAT Brown adipose tissue
BCI Body composition improvement
BMI Body mass index
C/EBPα CCAAT/enhancer-binding protein-α
CAM Complementary and alternative medicine
CAPs Capsaicins
CCK Cholecystokinin
CDSCO Central Drug Standard Control Organization
COX-2 Cyclooxygenase-2
CVD Cardio vascular disorder
EBPα Enhancer-binding protein α
EMA European Medicines Agency
eNOS Endothelial NO synthase
ERK Extracellular signal-regulated kinases
FDA Food and Drug Administration
FXR Farnesoid X receptor
GABA-γ Aminobutyric acid
GI Glycemic index
GPDH Glycerol-3-phosphate dehydrogenase
HAs Human adipocytes
HDL High density lipoprotein
IL-6 Interleukin-6
JNK- c Jun N-terminal kinase-c
LDL Low density lipoprotein
LPL Lipoprotein lipase
MAOi Monoamino oxidase inhibitors
MAPK Mitogen-activated protein kinase
MCH Melanin-concentrating hormone
MCP-1 Monocyte chemoattractant protein-1
NE Norepinephrine

NF-κB Nuclear factor-kappa B
NO Nitric oxide
PGE2 Prostaglandin E2
PPARγ Peroxisome proliferator-activated receptors-γ
PUFAs Polyunsaturated fatty acids
PYY Peptide YY
mRNA Messenger RNA
SNS Sympathetic nervous system
SSRIs Selective serotonin reuptake inhibitors
TG Triglyceride
TNF-α Tumor necrosis factor-alpha
TRPV1 Transient receptor potential vanilloid receptor-1
TV Tomato vinegar
UCP-1 Uncoupling protein 1
UCP-2 Uncoupling protein 2
WAT White adipose tissue
WHO World Health Organization