Pharmacogn. Res., 2025; 17(2):358-369.
https://www.phcogres.com

Review Article

Exploring the Therapeutic Potential of Natural Products in Obesity Treatment: Molecular Mechanisms and Isolation Techniques

Sandhya Jaiswal[1,*], Aaditee Sharma[1], Anjoo Kamboj[2], Jaspreet Kaur[3], Parminder Nain[4]

[1]Department of Pharmaceutics, Chandigarh College of Pharmacy, Landran, Mohali, Punjab, INDIA.
[2]Department of Pharmaceutical Chemistry, Chandigarh College of Pharmacy, Landran, Mohali, Punjab, INDIA.
[3]Department of Pharmacognosy, School of Pharmaceutical Sciences, RIMT University, Mandi-Gobindgarh, Punjab, INDIA.
[4]Department of Pharmacy Practice, School of Pharmaceutical Sciences, RIMT University, Mandi-Gobindgarh, Punjab, INDIA.

ABSTRACT

The present review focuses on the investigation of natural chemical constituents that contribute to anti-obesity activity, along with their mechanisms of action and potential therapeutic applications. Extensive literature searches from reputed and indexed journal data sets were performed. Review highlights bioactive compounds derived from various plants and natural sources that show promising anti-obesity properties. Resolving the complexity of mechanisms by which these bioactive components function provides a valuable insight for the development of innovative interventions in obesity management, ultimately promoting complete wellness. This review emphasizes the significance of understanding and utilizing the potential of naturally occurring substances to fight against obesity and to find a way for novel therapeutic strategies. The identification of head compounds and their anti-obesity properties not only broadens the understanding of physiological processes but also offers a structure for the advancement of targeted and effective interventions. This comprehensive analysis contributes to the ongoing discussion on anti-obesity approaches, emphasizing the role of natural compounds as potential agents for improving obesity-related challenges. This review will serve as a platform for researchers and health practitioners in the further search of developing evidence-based strategies for obesity management, aligning with the pattern shift towards integrative and nature-inspired healthcare solutions.

Keywords: Anti-obesity activity, Bioactive components, Innovative interventions, Natural Chemical Constituents, Novel therapeutic strategies, Obesity management, Therapeutic indications.

Correspondence:
Dr. Sandhya Jaiswal
Department of Pharmaceutics,
Chandigarh College of Pharmacy,
Landran, Mohali-140307, Punjab, INDIA.
Email: sandhya@cgc.edu.in

Received: 24-09-2024;
Revised: 15-11-2024;
Accepted: 09-01-2025.

INTRODUCTION

Globally, the prevalence of obesity is on the rise. Chronic diseases often contribute to obesity and overweight conditions, with a Body Mass Index (BMI) of 25 to 30 indicates 'overweight' and a BMI exceeding 30 signifies 'obese.[1] These results from an imbalance between excessive caloric intake and inadequate energy expenditure, leading to chronic inflammation and altered cytokine levels in the bloodstream. Obesity treatments primarily focus on weight reduction and associated comorbidities through pharmacological or non-pharmacological approaches.[2] Current pharmaceutical intervention to reduce obesity includes Bupropion-naltrexone, Liraglutide, Orlistat, Phentermine-topiramate, Semaglutide and Setmelanotide, but may cause side effects.[3] Ethnobotanical and ethnopharmaceutical research highlights the potential of medicinal plants, such as *Achillea millefolium, Bellis perennis* (L.) *Camellia sinensis* (L.) and *Fumaria officinalis* (L.), with antioxidant properties in treating obesity and their associated complications.[4] As obesity level remains high worldwide, therefore developing effective and safe approaches of body weight control is important, emphasizing the significance of herbal medicines in this context.[5] In our study, we extensively searched publications using PubMed, Scopus, Web of science from 2022 to 1997 utilizing keywords natural anti-obesity agents, pharmacological treatment, obesity management, Indian herbal drugs, ethnopharmacological plants, etc. To minimize the duplicity, bibliographic references were also searched. All authors independently searched publications to decrease the probability of bias.

DOI: 10.5530/pres.20252016

Pathogenesis

Pathogenesis of obesity may be caused by overstimulation of the appetite leading to energy imbalance or reduced utilization of calories via various cell mechanisms including exercise this leads to the generation of more adipocytes that increase cytokines which develop vascular complication.[6] These results into hyperlipidemia, a defect of the cardiovascular system as well as atherosclerosis which results into serious pathologies viz. colon cancer, gallstones, liver disease, stomach pathologies, etc.[7] So, it is necessary to take actions against obesity. Reducing appetite to increase calorie expenditure are common ways to control obesity. Hormones and receptors that control appetite expression can be adjusted to control hunger.[8] These results in an increase in physical activity to avoid the buildup of white adipose tissue, leading to prevention as well as its complications of obesity. Excessive fatty acid and triglycerol levels in the blood cause adipocyte buildup in the body, especially in the development of atherosclerosis thus resulting into hypertriglyceridemia, oxidative stress, lipotoxicity and other metabolic disorders like diabetes and various metabolic syndromes.[9] Furthermore, leads to the diminishing of circulated fatty acids. Therefore, a decrease in oxidative stress have been helpful in controlling many pathologies related to obesity.[10] Additionally, they release lectin, adiponectin and visfatin, which come together to form an adipocytokine complex. These may initiate cytotoxic autophagy in the carcinogenesis of the breast, colon, prostate and gynecologic tissues.[11] Consequently, adiponectin suppression may aid in lowering the risk of obesity-related carcinogenesis. The release of insulin, which helps to control body fat and blood glucose levels, is triggered by these three hormones. Therefore, any dysregulation in physiological model causes imbalance, which in turn leads to obesity.[12] Figure 1 apart from representing the pathogenesis of obesity, illustrates the role of insulin in the management of obesity and the connection between diabetes and obesity. Adipose tissue, the pancreas and the gastrointestinal system are all regulated by dopamine to release their corresponding hormones. These hormones keep hunger in check.

Phytochemical Constituents Responsible for Anti-Obesity Activity

Individuals' genetic makeup, nutritional habits, lifestyle and environmental factors interact to create obesity, a lifestyle disorder. These factors cause an excessive build-up of body fat.[13] Natural compounds alter body's regulating system by preventing or obstructing the work of α- amylase that further breaks down starch into individual sugars, α-glucosidases and other lipases of the gastrointestinal tract. Amylases and glucosidases are glucose transporters, an enzyme that release glucose into the bloodstream after breaking down carbohydrates.[14] When blood glucose levels rise above normal, pancreatic cells release insulin and start processes that lower blood glucose levels: glycogenesis, de novo lipogenesis and glycolysis.[15] Obesity results from the metabolism of glucose to produce lipids and fatty acids, which are then esterified to form triglycerides and stored in adipose tissue combine to form monoglycerides. Triglycerides, phospholipids and fatty acids are hydrolyzed by lipases to produce monoglycerides. The monoglycerides form the micellar structure and chylomicrons when they combine with sugars, lysophosphatidic acid and bile salts that structure enters in enterocytes, causing triglycerides to be synthesized and stored in adipose tissue.[16] After being treated with plant products, these enzymes are inhibited, which ultimately leads to a decrease in obesity. Now a day, holistic

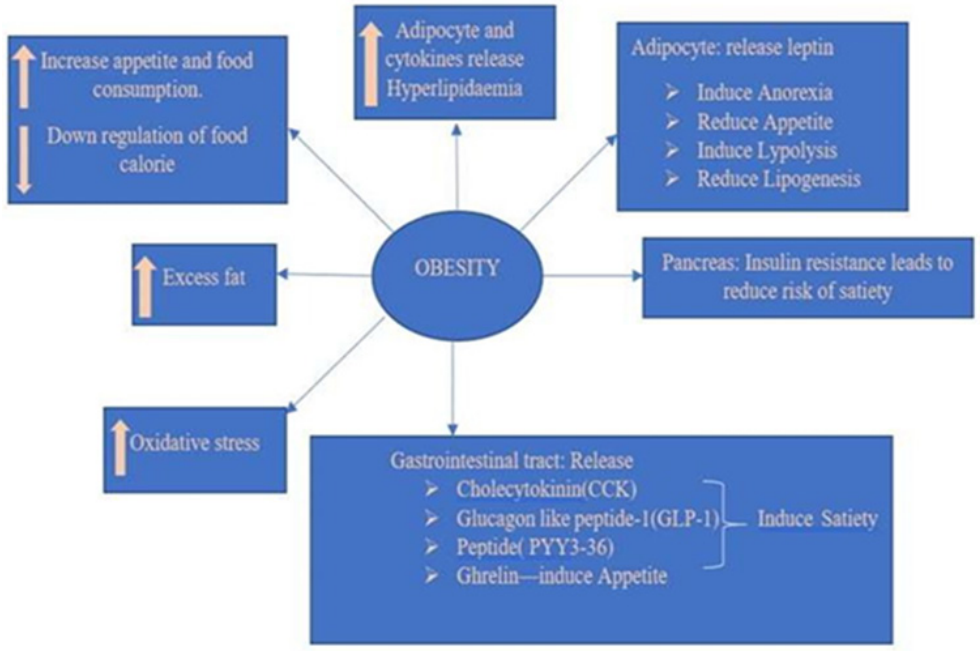


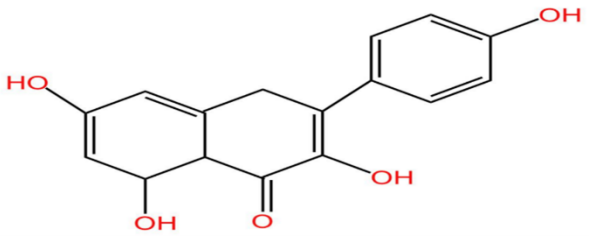
Figure 1: Pathogenesis of obesity.

wellness model based on Ayurveda principles and practices have changed the whole paradigm of our health system. Post covid there has been a sudden surge in demand for the Phyto pharma medicines. Studies have also indicated that majority of bioactive compounds derived from indigenous plants can reduce the disease burden and out of pocket expenditure for the treatment of lifestyle diseases like hypertension, diabetes, obesity etc. Table 1 represents some of the plants with their phytoconstituent's responsible for antiobesity activity like Diospyros kaki, Nelumbo nucifera, Lonicera caerulea etc. these contains flavonoids as their primary active ingredients and whose basic moiety Hydroxyl group (-OH) reported in literature is responsible for its pharmacological activity has changed the pathology of disease without any side effects. Similarly, plants like Capsicum annuum, *Araucaria angustifolia* contain Phenolic compounds as their key constituent responsible for its pharmacological activity. In phenolic compounds the presence of monohydoxyl group and polyhydroxyl group are reported in studies which is responsible for the anti-obesity activity. These hydroxyl groups contribute to phenolic compound's ability to neutralize free radicals and act as a potent antioxidant. Terpenoids are also reported to show anti-obesity activity. The basic moiety responsible for the antioxidant activity is the presence of conjugated double bonds in their structure. This characteristic allows terpenoids to act as free radical scavengers, neutralizing reactive oxygen species and providing antioxidant benefits. The presence of hydroxyl groups in some terpenoids was also reported to contribute to its antioxidant activities. Basic moiety present in these bioactive constituents have encouraged scientist to synthesize new phytochemical drugs for the treatment of diseases. Commercial Herbal Medicines available in the market for weight management are given in Table 2.

Polyphenol

Polyphenols are natural occurring substances mostly found in fruits, vegetables and cereals.[39] Dysfunction in individuals' energy metabolism leads to obesity. Figure 2 represents the systematic depiction of their role in weight management. The Adenosine 5′- Monophosphate (AMP)-Activated Protein Kinase (AMPK) signaling pathway is crucial for energy metabolism, diabetes and other disorders. AMPK can be activated by a variety of bodily stimuli, such as cell pressure, exercise, hormones and chemicals that alter cell metabolism. It is expressed in several organs linked to metabolism. Its activation helps in reduction in the type II diabetes-related metabolic imbalance. The energy-sensing domains of AMPK regulate phosphorylation, which in turn controls AMPK activity. Different metabolic conditions cause changes in the AMP, ATP ratio and alterations brought on by glycogen. Polyphenolic compounds contain one or more aromatic ring, present with mono hydroxyl and poly hydroxyl groups.[40] On the basis of number of aromatic rings, polyphenols can be categorized into tannins, stilbenes, phenolic acid, flavonoids, lignans, lignin's and coumarins.[41,42] These compounds have health benefits when consumed through fruits, vegetables and herbs, because of their antioxidant and anti-inflammatory activity.[43] Polyphenols mechanisms for preventing obesity is via lowering of food consumption and ultimately reducing obesity through polyphenols intake reduce lipogenesis and fat storage and increase lipolysis and fat mobilization.[44] Fatty acid beta oxidation and suppression of adipocyte differentiation in acids diminish inflammation enhancing both development and growth attenuating inflammatory responses and suppressing oxidative stress.

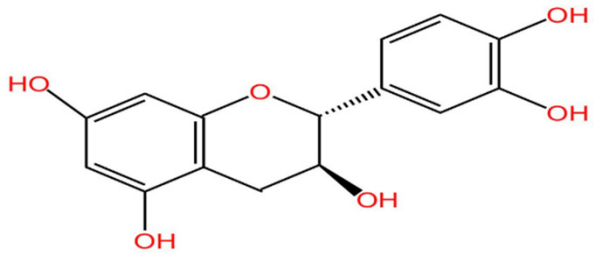
Basic structure of Polyphenols



Some of the Polyphenols present in Plants

Kaempferol

Free radicals can be neutralized by kaempferol within the body. Free radicals are extremely reactive chemicals that can lead to oxidative stress, harming cells and playing a role in aging and chronic illnesses. As an antioxidant, kaempferol contributes to the stabilization of these free radicals by releasing electrons, thus stopping their harmful effects. It has been reported that kaempferol increases the activity of several antioxidant enzymes in cells. These enzymes, which include catalase and superoxide dismutase, are essential for the body's defense against oxidative stress.[45]



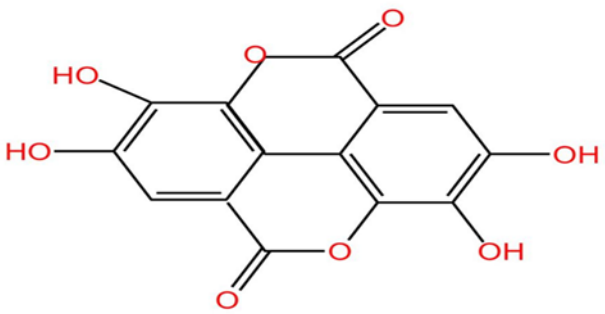
Catechin

All diastereoisomers of catechin share the same chemical structure, which consists of phenolic hydroxyl groups with the ability to stabilize free radicals.[46] This characteristic allows catechins to function as free radical scavengers, which is what gives them their direct antioxidant activity.

Table 1: List of plants with their phytochemicals responsible for Anti-obesity Activity.

Sl. No.	Plant	Plant part used	Chemical Constituents	Research findings	References
1.	*Camellia sinensis*	Leaves	Catechins	Inhibition of Pancreatic lipase Elevate the concentrations of ghrelin in plasma.Inhibitor of pancreatic lipase; Lower levels of plasma TAG and postprandial lipaemia.Trigger the release of serotonin, which decreases appetite Increase energy usageAlters the gut microbiota's makeup to promote satiety.	M. Nakai *et al.* [2005].[17]
2.	*Gymenma sylvestre*	Leaves	Gymnemic acids	Regulates obesity brought on by diabetes.	P. Kanetkar *et al.* [2007].[18]
3.	*Ginkgo biloba*	Leaves	Terpene tri lactone, including ginkgolides and bilobalide	Lowering blood cholesterol levels by blocking pancreatic lipase.	Y. Bustanji *et al.* [2011].[19]
4.	*Garcinia cambogia* or Garcinia gummi-gutta	Berries	Hydroxy citric acid	Regulating lipid biosynthesis.	F. Márquez *et al.* [2012].[20]
5.	Black soyabean	Seeds	Polyphenolic pigment	Affects lipolysis, differentiation and growth of 3T3-L1 cells Prevent the division of pre-confluent pre-adipocytes and the maturation of post confluent adipocytes.	H.-K. Kim *et al.* [2012].[21]
6.	*Morus austrails* poir (mulberry)	Leaves	Fructan	Regulation of appetite by modifying hormones like GLP-1 and leptin 7.	H. Lim *et al.* [2013].[22]
7.	*Nelumbo nucifera*	Leaves	Flavonoids and phenolic compounds	Stop the pancreatic lipase. α-amylase Block LDL, triglycerides, total cholesterol and malondialdehyde are among the lipid components whose levels are decreased by blocking α-glucosidase.	S. Liu *et al.* [2013].[23]
8.	*Araucaria angustifolia*	Seed coat	Polyphenols and tannins.	It inhibits pancreatic lipase and decreases plasma triglyceride levels by blocking absorption.Cease α-amylase.	R.F. Oliveira *et al.* [2015].[24]
9.	*Calotropis procera* Aiton	Roots	Bis (2-methyl propyl) ester, 1,2-benzedenedicarboxylic acid and 2,4 bis (1, 1-dimethyl ethyl) ester.	Pancreatic lipase inhibition.	S.G. Patil *et al.* [2015].[25]
10.	*Dioscorea oppositifolia*	Rhizomes	3,5-dimethoxy-2,7-phenanthrene diol and (3R,5R) phenanthrene diol-3.5% dihydroxy-1.7% bis(4-hydroxyphenyl)-3,5-hexanediol	Inhibition of pancreatic lipase.The anti-adipogenic effect. Reduce body weight as well as adipose tissue weight. Reduces the levels of triglycerides, total cholesterol and LDL.	E.J. Jeong *et al.* [2016].[26]
11.	*Diospyros kaki*	Unripe fruit	Flavonoids and phenolic compounds	Significant reduction of visceral fat, total cholesterol and serum triacylglycerol by inhibition of pancreatic lipase.	G.-N. Kim *et al.* [2016].[27]

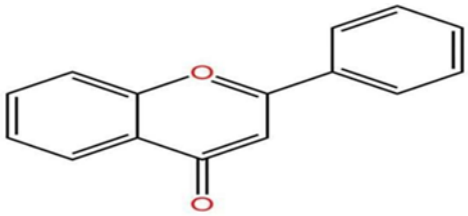
12.	*Betula platyphylla*	Bark	Platyphylloside, diarylheptanoid	Adipocyte-specific gene promoters such as aP2, FAS, SCD-1, LPL, Adiponectin, perilipin and HSL, as well as PPARζ, C/EBPα and SREBP1-induced adipogenesis, can be blocked to prevent 3T3-L1 from differentiating into adipocytes. Excessive TNFα synthesis.	M. Lee *et al.* [2016].[28]
13.	*Curcuma longa*	Tubers	Curcumin	Control of inflammatory responses and obesity brought on by oxidative stress.	A. Jarzab *et al.* [2016].[29]
14.	*Lonicera caerulea*	whole plant	Phenolic compounds and flavonoids.	Regulates the lipid profile in serum.	D.H. Suh *et al.* [2016].[30]
15.	*Morus alba*	Root bark	Carnosol, carnosic acid, flavonoids, xanthines, purine alkaloids and polyphenols.	Decrease in body weight gain.	M. Yimam *et al.* [2016].[31]
16.	*Capsicum annuum*	Flowers	Flavonoids and phenolic compounds.	Inhibition of antioxidants and pancreatic lipase.	M. Marrelli *et al.* [2016].[32]
17.	*Peucedanum japonicum* Thunb	Leaves	Hellactone cis-3',4'-diisovaleryl (cDIVK).	Increased glucose absorption; decreased adipocyte differentiation and fat deposition Increased activation of AMPK α-glucosidase activity inhibition and decreased protein and mRNA expression of key adipogenic transcriptional factors in 3T3-L1 cells, such as C/EBPα, PPARγ and SREBP-1c.	R.-Y. Choi *et al.* [2016].[33]
18.	*Eclipta alba*	whole plant	Luteolin, Apigenin	It has anti-dyslipidemia and lipolytic properties. In 3T3-L1 pre-adipocytes, it inhibits adipocyte differentiation and has anti-adipogenic properties.Prevents the growth of mitotic clones and brought about cell cycle arrest in the G1 and S phases.	A. Gupta *et al.* [2017].[34]
19.	*Eugenia caryophyllus*	Flower bud	Fatty acid synthase, eugenol, acetyl eugenol, caryophyllene and humulene.	Halt OP9 cell adipocyte differentiation and HepG2 cell S-phase DNA replication. A decrease in total body weight, the weight of abdominal adipose tissue and lipid buildup in the liver and epididymal adipose tissue.Controls the levels of low-density Lipoprotein Cholesterol (LDL-C) and total Triglycerides (TG).	Y. Ding *et al.* [2017].[35]
20.	*Euphorbia supina*	whole plant	Quercetin, gallic acid, scopoletin, etc.,	Serum leptin levels were considerably lowered by ESEE.Elevated levels of adiponectin.Notable decreases in Proliferator-Activated Receptor γ (PPARγ) and CCAAT/Enhancer Binding Protein alpha (C/EPBα) mRNA and protein levels in WAT and liver tissues.	S. Nepali *et al.* [2018].[36]
21.	*Carissa carandas*	Bark	Oroxylin A, chrysin and baicalein are flavonoids.	Effects against adipogenesis and inhibition of pancreatic lipase.	P. Mangal *et al.* [2018].[37]
22.	*Malus hupehensis*	Fruit	Hyperoside, kaempferol, quercetin, naringenin, myricetin and ursolic acid.	Reduces the level of serum lipids.	C. Wen *et al.* [2018].[38]



Flavonoids

Numerous plants contain flavonoids. Flavonoids' basic structure consists of a 15-C phenylpropanoid core, two linked aromatic rings and a six membered heterocyclic. The characteristics of the second bond inside the heterocyclic ring and its oxidation state divide flavonoids into six groups.[47] Luteolin and apigenin are among other flavones which contain flavanols or catechins, cyanin pigment and flavanones like narigenin and herpertin. Additionally, isoflavones like genistein and flavin, as well as chalcones (butein, xanthoangelol). Flavonoids inhibit weight gain lowering calorie consumption while increasing the feeling of fullness.[48] Figure 3 provides an illustration of flavonoids role in weight management. Their impact on overweight people by reducing hunger and increasing feeling of being satisfied after a meal. White adipose tissue first is specialized for storing the extra energy in the form of triglycerides, while the second is referred to as Brown adipose tissue, which is predominantly specially designed for high metabolism and intense energy utilization.[49] Adipocyte UCP-1 protein expression both regulates thermogenesis and acts as an engine that uses up energy. Thermogenesis' various methods make the activity of the sympathetic nervous system even stronger. This causes the release of norepinephrine by the nervous system. PGC1-α proteins play a major role in thermogenesis, particularly through transcription. AMPK and SIRT1 are the key determinants that have flavonoids as their main contributor, which is the most active component in the process. PGC1α. Normally, browning of fat cells is caused by the process, which is mediated by thermogenesis and AMPK/PGC1α signaling.[50] Different bacterial populations can be found in the gastrointestinal tract, including Actinobacteria, Firmicutes, Proteobacteria, Bacteroides and others.[51] About one percent (1.9%) of total floral composition is determined by the genetic process while more than twenty percent (20%) of its species depends on the mechanism it is mainly involved in issues such as consumption patterns. There is also a diversity in the intestinal microbiome that can lead to an imbalance of microbial presence could lead to endotoxin accumulation with possible damaging effects on the circulatory system causing chronic inflammation and being associated with obesity.[52] After the fermentation of bacteria some indigestible metabolites such as polyphenols, a product known as the Short-Chain Fatty Acids (SCFAs) is synthesized primarily by polysaccharides and proteins mostly energy. The body produces sympathetic factors and enters gluconeogenesis. Bile Acid derived from liver cholesterol might be processed using intestinal bacterium.[53] The structure of microbial composition is influenced by bile acid which permits orderly growth.

Basic structure of flavonoids



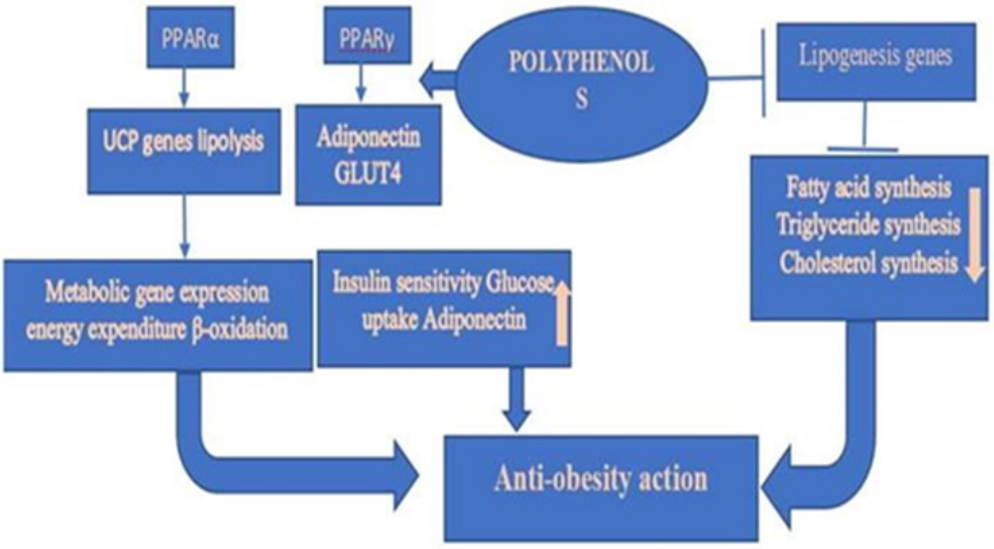


Figure 2: Role of polyphenols in weight management.

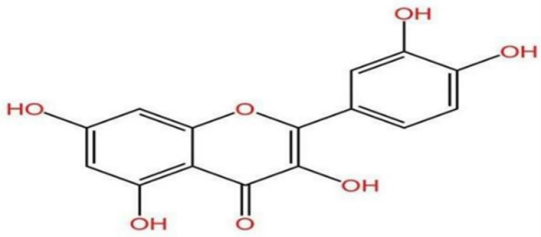
Table 2: Commercial Herbal Medicines available in the market for Weight Management.

Sl. No.	Plant	Marketed name	Formulation	Manufacturing unit
1.	Vrikshamla (*Garcinia cambogia*)	Vrikshamla weight wellness	Tablets	Himalaya
2.	Green coffee, *Garcinia cambogia*, Green tea *Caralluma* extract	Fat burner	Tablets	Dr. Morepen
3.	Caffeine, *Coffee arabica, Piper nigrum*, L-Carnitine, *Garcinia cambogia, Choline bitartrate* and *Carathmus tinctorius* L. Seed oil	HK Vitals	Tablets	Healthkart
4.	*Terminal abele, Terminalia chebula, Picrorhiza kurroa, Embelia, Embelia ribes, Commiphoramuku, Asphallum*	Divya Medohar Vati	Tablets	Divya pharmacy Patanjali.
5.	Guduchi	Obesidat	Tablets	Guduchi the Ayurvedism.
6.	Gugglu, Triphala, Trikatu, Haritaki, Bibhitaki, Amla, Ginger, Pipalli, Chitrak, Maricha, Vidang, Mustak	Medohar gugglu	Tablets	Gynoveda
7.	*Terminalia chebula, Crotalaria juncea, Ricinus communis, Berberis aristata, Stevia rebaudiana, Terminalia bellirica, Phyllanthus emblica*	Fat reducer	Juice	Krishna's Herbal and Ayurveda.
8.	*Curcuma longa, Piper nigrum*	Nutriburst turmeric ultra-Gummies	Gummies	Nutriburst
9.	Vrikshamla, Medohar Guggul, Meshashringi, Methi	Herbolism	Tablets	Dr. Vaidya's
10.	*Garcinia cambogia, Terminalia chebula, Coffee arabica, Camellia sensis, Cinnamonum zeylanicum, Commiphora mukul, Gymnea sylvestre*	Weight loss support	Tablets	Satvam

Some of the flavonoids present in plant

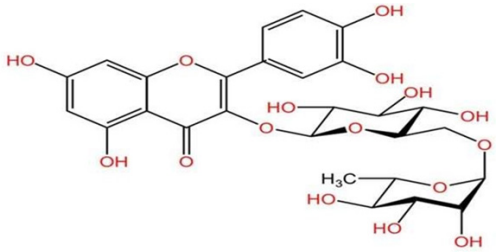
Quercetin

According to the studies, quercetin inhibits the adipogenesis and apoptosis by decreasing the activity of adipogenesis-related enzymes; however, MAPK and its substrate Acetyl-CoA Carboxylase (ACC) were upregulated.[54] Apoptosis was induced simultaneously and ERK and JNK phosphorylation levels decreased. The implication is that quercetin inhibits adipogenesis by stimulating the MAPK signaling pathway. At the same time, quercetin induced apoptosis in mature adipocytes by controlling the critical ERK and JNK pathways.[55]



Rutin

Rutin is a low molecular weight polyphenolic molecule that belongs to the class of citrus flavonoids. Rutin and similar flavonoids have a variety of physiological roles in the body of humans and other organisms, including plants. As an antioxidant, it aids in the body's defense against free radicals. This antioxidant action may shield cells from harm and promote general health, which may have an impact on variables associated to weight.[56]



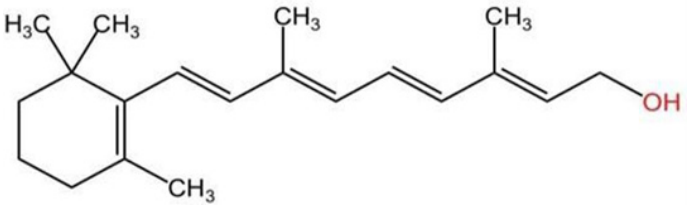
Diterpenoids

Diterpenoids are secondary metabolite groups made up of two terpene units with four isoprene units each and the molecular formula $C_{30}H_{32}$.[57] There are numerous beneficial effects of diterpenoids, like anti- obesity effect derived from *Taxus taxanes*[58] and carnosic acid, as well as steviol and its derivatives.[59,60] Secondly, inhibition of protein tyrosine phospendense 1b exerts a negative effect on leptin transduction and insulin.[61] Diterpenoids prevents the differentiation of adipocytes, which had an anti-obesity effect. The compounds carnosic acid.[62,63] and 14-deoxy-11,12-dihydro andrographolide, which was isolated

from Andrographis paniculata,[64] have shown to alter the ratio of various C/EBP-β proteins, inhibit the expression of C/EBPα and PPAR-α, decrease lipoprotein mRNA expression through Tumor Necrosis Factor (TNF-α) and interleukin-6 and activate the TOR pathways.[65,66] Studies suggested that geranylgeraniol (alcoholic derivatives of diterpenoids), which are primarily present in certain fruits and herbs, activates the human PPARα and PPARγ in CV1 cells and controls the expression of these receptors responsible for lipid metabolism in 3T3-L1 cells and Hep G2.[67,68]

Retinol diterpenoid

It is a known fact that retinol alters the activity of several antioxidant enzymes in cells. These enzymes i.e., catalase and superoxide dismutase, are essential for the body's defense against oxidative stress. By controlling their activity, retinal strengthens the antioxidant defense systems within cells. Retinol helps in neutralizing the free radicals which further stabilize and lessens their ability to damage cells and tissues.



Commonly used Techniques for The Isolation of Natural Chemical Compounds

Scientists analyze solvents like methanol, hexane and ethyl alcohol for antioxidant extraction from plant parts like leaves and seeds. Used to extract the highly potent antioxidant from the plants.[69] Anokwuru *et al.*, discovered that acetone and DMF are effective for extracting antioxidants, whereas Koffi *et al.*, discovered that methanol is more effective solvents for extracting phenolic content from walnut fruits.[70-72]

Microwave-Assisted Extraction (MAE)

MAE is a green technology that reduces the use of organic solvents. There are solvent-free and solvent-based extraction techniques.[73] Microwaves interact with polar compounds in the plant matrix, resulting in the generation of heat and mass in MAE. This synergistic effect speeds up extraction, increases yield and decreases thermal degradation. MAE has piqued the interest of researchers as a technique for extracting bioactive compounds from a wide range of plants and natural residues.[74] Microwaves emit electromagnetic radiation at frequencies ranging from 300 MHz to 300 GHz and wavelengths ranging from 1 cm to 1 m. These electromagnetic waves have both an electrical and a magnetic field. These are two perpendicular fields. The first application of microwaves was to heat up objects that can absorb a portion of electromagnetic energy and convert it to heat.[75] Commercial microwave instruments commonly use the frequency 2450 MHz, which corresponds to an energy output of 600-700 Watts.[76] Advanced techniques have recently become available to reduce bioactive compound loss without increasing extraction time. As a result, microwave-assisted extraction has been shown to be a good technique in a variety of fields, particularly in the medicinal plant field. Furthermore, this technique reduced the biochemical compound extraction losses.[77] Microwave-Assisted Extraction (MAE) has been shown to be more effective than conventional methods in increasing antioxidant activity and phenolic content. The efficiency of microwave extraction can be affected by factors such as extraction temperature, solvent composition and extraction time. The best temperature for extracting phenolic compounds from Chinese tea is 170°C. MAE has advantages such as lower solvent consumption, shorter extraction times and higher sensitivity to target molecules.[78-80]

Ultrasound Assisted Extraction (UAE)

Ultrasonic-Assisted Extraction (UAE), also known as ultrasonic extraction. Sonication employs ultrasonic wave energy in the extraction process. Ultrasound in the solvent causes' cavitation, which accelerates solute dissolution and diffusion as well as heat transfer, increasing extraction efficiency.[81] Another advantage of UAE is the reduced extraction temperature and time. UAE is suitable for the extraction of thermolabile and unstable compounds. UAE is commonly used in the extraction of a wide range of natural products.[82,83] A higher yield of polyphenols from *Thymus serpyllum* L. by UAE at an optimized condition (50% ethanol as solvent; 1:30 solid- to-solvent ratio; 0.3 mm particle size; and 15 min time) than maceration and heat-assisted extraction methods.[84] There was no statistically significant difference in extracting ginsenosides, including ginsenosides Rg1 and Rb1, chikusetsusaponins V, IV and IV a and pseudo ginsenoside RT1 from the TCM Panacis Japonici Rhizoma between UAE and reflux using 70% aqueous methanol to extract for 30 min.[85,86] Both the reflux method and UAE had the advantages of time-saving, convenient operation and high extract yield and that UAE is relatively better than reflux methods for TCM Dichroae Radix using the extract yield and content of febrifugine as the criteria.[87]

Pulsed Electric Field (PEF) extraction

By increasing mass transfer and reducing thermolabile compound degradation, pulsed electric field extraction improves extraction yield and reduces time. Its effectiveness is dependent on field strength, energy input, pulse number and treatment temperature. By using PEF extraction to achieve the highest ginsenoside yield (12.69 mg/g), outperforming MAE, heat reflux extraction, UAE and PLE methods.[88] When compared to untreated samples, PEF treatment increased phenolic content and antioxidant activity in Norway spruce bark.[89,90]

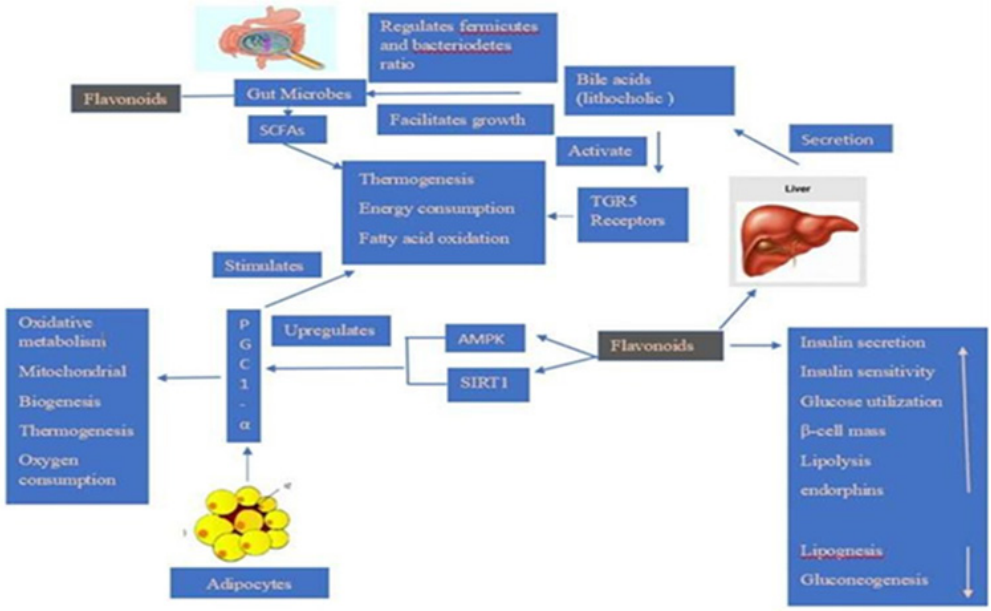


Figure 3: Role of flavonoids in weight management.

DISCUSSION

The present review highlights the plants responsible for anti-obesity action with their bioactive compounds and their potential role in combating obesity is being explored in current research. Several aspects were being explored; future developments include deep understanding about mechanisms as it may provide deeper insight into the molecular mechanisms underlying the anti-obesity effects of natural compounds. Understanding these compounds interacts with metabolic pathways and adipose tissue. Further synergistic effects of combining different natural compounds or integrating them with conventional weight management strategies might be explored. This could lead to more effective and comprehensive obesity treatment options. Research focuses on personalized approaches, considering individual variations in genetics, microbiome composition and lifestyle factors helps to enhance the efficacy of natural compounds in obesity management. So, it is concluded that combining the benefits of traditional natural compounds with lifestyle modifications, could be a realistic approach towards obesity management.

CONCLUSION

In conclusion the diverse array of natural chemical constituents highlighted in this study demonstrates their potential as effective agents for combating obesity. The multifaceted mechanism of action ranging from metabolic modulation to appetite regulation, underscores the richness of nature's resources in addressing this global health challenge. More research and clinical trials are needed to validate these findings and translate them into practical applications for the development of safe and effective anti-obesity interventions based on natural compounds. Using the power of these constituents to promote sustainable and holistic approaches to obesity management is a promising avenue.

ACKNOWLEDGEMENT

Authors would like to acknowledge Head of Department, Chandigarh college of Pharmacy for their kind support in accomplishing review cum research work.

CONFLICT OF INTEREST

The authors report no conflict of interest including financial and non-financial. The authors alone are responsible for the content and writing of this article.

AUTHORS CONTRIBUTIONS

The author's contribution to the paper as follows: study conception and design: Sandhya Jaiswal; data collection: Aaditee Sharma; analysis and interpretation of results: Sandhya Jaiswal, Anjoo Kamboj; draft manuscript: Sandhya Jaiswal, Aaditee Sharma, Jaspreet Kaur, Parminder Nain. All authors reviewed the results and approved the final version of the manuscript.

CONSENT FOR PUBLICATION

Authors give their consent to publish the article in your esteemed journal.

ABBREVIATIONS

BMI: Body Mass Index; **CCK:** Cholecystokinin; **GCP:** Glucagon like Peptide; **AMP:** Adenosine 5'-Monophosphate; **AMPK:** Activated Protein Kinase; **SCFA:** Short Chain Fatty Acid; **ACC:** Acetyl- CoA Carboxylase; **MAPK:** Mitogen Activated Protein Kinase; **JNK:** Jun N-Terminal Kinase; **DMF:** Dimethyl

Formamide; **MAF:** Microwave Assisted Extraction; **UAE:** Ultrasound Assisted Extraction; **PEF:** Pulsed Electric Field; **BAT:** Brown Adipose Tissue.

SUMMARY

Obesity arises from an imbalance between excessive calorie intake and low energy expenditure, leading to metabolic disorders like diabetes, atherosclerosis and oxidative stress. Pharmaceutical treatments exist but often cause side effects, highlighting the potential of herbal remedies as safer alternatives. Herbal medicines show promise for safe and effective weight control. Polyphenols, naturally occurring compounds in fruits, vegetables and cereals, play a significant role in managing obesity and metabolic disorders. They exert their effects by activating the AMP-Activated Protein Kinase (AMPK) pathway, crucial for regulating energy metabolism and reducing metabolic imbalances, including those associated with type II diabetes. AMPK activation, triggered by stimuli like exercise and hormonal changes, improves energy sensing and balances phosphorylation activity. Their anti-obesity mechanisms include reducing food intake, suppressing lipogenesis and fat storage, enhancing lipolysis and fat mobilization, promoting fatty acid beta-oxidation and inhibiting adipocyte differentiation. Kaempferol is a potent antioxidant that neutralizes free radicals in the body, preventing oxidative stress and its associated damage to cells, which contributes to aging and chronic diseases. Flavonoids, found in many plants, have a core structure composed of aromatic rings and a heterocyclic ring. Flavonoids help manage weight by reducing calorie intake and promoting satiety. They influence adipose tissue, enhancing the function of Brown Adipose Tissue (BAT), which increases metabolism and energy expenditure through thermogenesis. Additionally, flavonoids can impact the gut microbiome, which plays a role in obesity. An imbalance in gut bacteria can lead to chronic inflammation, while bacterial fermentation of polyphenols produces Short-Chain Fatty Acids (SCFAs), aiding energy production and influencing metabolic processes. The composition of bile acids, affected by gut bacteria, also contributes to metabolic regulation. Different solvents, including methanol, acetone and hexane, are used to extract antioxidants from plant parts. Studies show that methanol is particularly effective for extracting phenolic compounds, while acetone and DMF are also efficient.

REFERENCES

1. Boutari C, Mantzoros CS. A 2022 update on the epidemiology of obesity and a call to action: as its twin COVID-19 pandemic appears to be receding, the obesity and dysmetabolism pandemic continues to rage on. Metabolism. 2022;133:155217. doi: 10.1016/j.metabol.2022.155217, PMID 35584732.
2. Ruban A, Stoenchev K, Ashrafian H, Teare J. Current treatments for obesity. Clin Med (Lond). 2019;19(3):205-12. doi: 10.7861/clinmedicine.19-3-205, PMID 31092512.
3. Tchang BG, Aras M, Kumar RB, Aronne LJ. Pharmacologic treatment of overweight and obesity in adults.2021; 2021.
4. Chaachouay N, Benkhnigue O, Fadli M, El Ibaoui H, Zidane L. Ethnobotanical and ethnopharmacological studies of medicinal and aromatic plants used in the treatment of metabolic diseases in the Moroccan Rif. Heliyon. 2019;5(10):e02191. doi: 10.1016/j.heliyon.2019.e02191, PMID 31720440.
5. Wilborn C, Beckham J, Campbell B, Harvey T, Galbreath M, La Bounty P, *et al.* Obesity: prevalence, theories, medical consequences, management and research directions. J Int Soc Sports Nutr. 2005;2(2):4-31. doi: 10.1186/1550-2783-2-2-4, PMID 18500955.
6. Karri S, Sharma S, Hatware K, Patil K. Natural anti-obesity agents and their therapeutic role in management of obesity: A future trend perspective. Biomed Pharmacother. 2019;110:224-38. doi: 10.1016/j.biopha.2018.11.076, PMID 30481727.
7. Redinger RN. The pathophysiology of obesity and its clinical manifestations. Gastroenterol Hepatol (N Y). 2007;3(11):856-63. PMID 21960798.
8. Yeung AY, Tadi P. Physiology, obesity neurohormonal appetite and satiety control. 2023; 2023.
9. Manna P, Jain SK. Obesity, oxidative stress, adipose tissue dysfunction and the associated health risks: causes and therapeutic strategies. Metab Syndr Relat Disord. 2015;13(10):423-44. doi: 10.1089/met.2015.0095, PMID 26569333.
10. Obesity: causes, consequences, treatments and challenges. J Mol Cell Biol. 2021;13(7):463-5. doi: 10.1093/jmcb/mjab056, PMID 34673982.
11. Muppala S, Konduru SK, Merchant N, Ramsoondar J, Rampersad CK, Rajitha B, *et al.* Adiponectin: its role in obesity-associated colon and prostate cancers. Crit Rev Oncol Hematol. 2017;116:125-33. doi: 10.1016/j.critrevonc.2017.06.003, PMID 28693794.
12. Ahmed B, Sultana R, Greene MW. Adipose tissue and insulin resistance in obese. Biomed Pharmacother. 2021;137:111315. doi: 10.1016/j.biopha.2021.111315, PMID 33561645.
13. Khanna D, Welch BS, Rehman A. Pathophysiology of obesity.2022; 2022.
14. Kojta I, Chacińska M, Błachnio-Zabielska A. Obesity, bioactive lipids and adipose tissue inflammation in insulin resistance. Nutrients. 2020;12(5):1305. doi: 10.3390/nu12051305, PMID 32375231.
15. Bhuyan DJ, Basu A. Phenolic compounds: potential health benefits and toxicity. In: Vuong QV, editor. Utilisation of bioactive compounds from agricultural and food production waste. Boca Raton, FL: CRC Press, Taylor & Francis Group; 2017. p. 27-59.
16. Naczk M, Shahidi F. Phenolics in cereals, fruits and vegetables: occurrence, extraction and analysis. J Pharm Biomed Anal. 2006;41(5):1523-42. doi: 10.1016/j.jpba.2006.04.002, PMID 16753277.
17. Nakai M, Fukui Y, Asami S, Toyoda-Ono Y, Iwashita T, Shibata H, *et al.* Inhibitory effects of oolong tea polyphenols on pancreatic lipase *in vitro*. J Agric Food Chem. 2005;53(11):4593-8. doi: 10.1021/jf047814+, PMID 15913331.
18. Kanetkar P, Singhal R, Kamat M. Gymnema sylvestre: a memoir. J Clin Biochem Nutr. 2007;41(2):77-81. doi: 10.3164/jcbn.2007010, PMID 18193099.
19. Bustanji Y, Al-Masri IM, Mohammad M, Hudaib M, Tawaha K, Tarazi H, *et al.* Pancreatic lipase inhibition activity of trilactone terpenes of *Ginkgo biloba*. J Enzyme Inhib Med Chem. 2011;26(4):453-9. doi: 10.3109/14756366.2010.525509, PMID 21028941.
20. Márquez F, Babio N, Bulló M, Salas-Salvadó J. Evaluation of the safety and efficacy of hydroxycitric acid or *Garcinia cambogia* extracts in humans. Crit Rev Food Sci Nutr. 2012;52(7):585-94. doi: 10.1080/10408398.2010.500551, PMID 22530711.
21. Kim HK, Kim JN, Han SN, Nam JH, Na HN, Ha TJ. Black soybean anthocyanins inhibit adipocyte differentiation in 33-L1 cells. Nutr Res. 2012;32(10):770-7. doi: 10.1016/j.nutres.2012.06.008, PMID 23146774.
22. Lim HH, Lee SO, Kim SY, Yang SJ, Lim Y. Anti-inflammatory and antiobesity effects of mulberry leaf and fruit extract on high fat diet-induced obesity. Exp Biol Med (Maywood). 2013;238(10):1160-9. doi: 10.1177/1535370213498982, PMID 24000381.
23. Liu S, Li D, Huang B, Chen Y, Lu X, Wang Y. Inhibition of pancreatic lipase, α-glucosidase, a-amylase and hypolipidemic effects of the total flavonoids from *Nelumbo nucifera* leaves. J Ethnopharmacol. 2013;149(1):263-9. doi: 10.1016/j.jep.2013.06.034, PMID 23811214.
24. Oliveira RF, Gonçalves GA, Inácio FD, Koehnlein EA, De Souza CG, Bracht A, *et al.* Inhibition of pancreatic lipase and triacylglycerol intestinal absorption by a pinhão coat (*Araucaria angustifolia*) extract rich in condensed tannin. Nutrients. 2015;7(7):5601-14. doi: 10.3390/nu7075242, PMID 26184295.
25. Patil SG, Patil MP, Maheshwari VL, Patil RH. *In vitro* lipase inhibitory effect and kinetic properties of di- terpenoid fraction from *Calotropis procera* (Aiton). Biocatal Agric Biotechnol. 2015;4(4):579-85. doi: 10.1016/j.bcab.2015.08.014.
26. Jeong EJ, Jegal J, Ahn J, Kim J, Yang MH. Anti-obesity effect of *Dioscorea oppositifolia* extract in high-fat diet-induced obese mice and its chemical characterization. Biol Pharm Bull. 2016;39(3):409-14. doi: 10.1248/bpb.b15-00849, PMID 26700066.
27. Kim GN, Shin MR, Shin SH, Lee AR, Lee JY, Kim MY, *et al.* Study of antiobesity effect through inhibition of pancreatic lipase activity of *Diospyros kaki* fruit and *Citrus unshiu* peel. BioMed Res Int. 2016;32:770-7.
28. Lee M, Sung SH. Platyphylloside isolated from Betula platyphylla inhibit adipocyte differentiation and induce lipolysis via regulating adipokines including PPARγ in 3T3-1 Cells. Pharmacogn Mag. 2016;12(48):276-81. doi: 10.4103/0973-1296.192208, PMID 27867269.
29. Jarząb A, Kukula-Koch W. Recent advances in obesity: the role of turmeric tuber and its metabolites in the prophylaxis and therapeutical strategies. Curr Med Chem. 2018;25(37):4837-53. doi: 10.2174/0929867324666161118095443, PMID 27855627.
30. Suh DH, Jung ES, Park HM, Kim SH, Lee S, Jo YH, *et al.* Comparison of metabolites variation and antiobesity effects of fermented versus nonfermented mixtures of *Cudrania tricuspidata, Lonicera caerulea* and soybean according to fermentation *in vitro* and *in vivo*. PLOS One. 2016;11(2): e0149022: e0149022. doi: 10.1371/journal.pone.0149022, PMID 26848749.

31. Yimam M, Jiao P, Hong M, Brownell L, Lee YC, Hyun EJ, *et al.* Appetite suppression and antiobesity effect of a botanical composition composed of *Morus alba*, yerba mate and *Magnolia officinalis*. J Obes. 2016; 2016:4670818. doi: 10.1155/2016/4670818, PMID 27699065.
32. Marrelli M, Menichini F, Conforti F. Hypolipidemic and antioxidant properties of hot pepper flower (*Capsicum annuum* L.). Plant Foods Hum Nutr. 2016;71(3):301-6. doi: 10.1007/s11130-016-0560-7, PMID 27372805.
33. Choi RY, Nam SJ, Ham JR, Lee HI, Yee ST, Kang KY, *et al.* Anti-adipogenic and antidiabetic effects of cis- 3′,4′-diiso-valerylkhellactone isolated from *Peucedanum japonicum* Thunb. leaves *in vitro*. Bioorg Med Chem Lett. 2016;26(19):4655-60. doi: 10.1016/j.bmcl.2016.08.056, PMID 27575482.
34. Gupta A, Kumar A, Kumar D, Nandan S, Shankar K, Varshney S, *et al.* Ethyl acetate fraction of *Eclipta alba*: a potential phytopharmaceutical targeting adipocyte differentiation. Biomed Pharmacother. 2017;96:572-83. doi: 10.1016/j.biopha.2017.10.002, PMID 29032341.
35. Ding Y, Gu Z, Wang Y, Wang S, Chen H, Zhang H, *et al.* Clove extract functions as a natural fatty acid synthesis inhibitor and prevents obesity in a mouse model. Food Funct. 2017;8(8):2847-56. doi: 10.1039/c7fo00096k, PMID 28726934.
36. Nepali S, Kim DK, Lee HY, Ki HH, Kim BR, Hwang SW, et al. *Euphorbia supina* extract results in inhibition of high-fat- diet-induced obesity in mice. Int J Mol Med. 2018;41(5):2952-60. doi: 10.3892/ijmm.2018.3495, PMID 29484428.
37. Mangal P, Khare P, Jagtap S, Bishnoi M, Kondepudi KK, Bhutani KK. Screening of six Ayurvedic medicinal plants for anti-obesity potential: an investigation on bioactive constituents from *Oroxylum indicum* (L.) Kurz bark. J Ethnopharmacol. 2017;197:138-46. doi: 10.1016/j.jep.2016.07.070, PMID 27469197.
38. Wen C, Wang D, Li X, Huang T, Huang C, Hu K. Targeted isolation and identification of bioactive compounds lowering cholesterol in the crude extracts of crab apples using UPLC-DAD-MS-SPE/NMR based on pharmacology-guided PLSDA. J Pharm Biomed Anal. 2018;150:144-51. doi: 10.1016/j.jpba.2017.11.061, PMID 29232626.
39. Pandey KB, Rizvi SI. Plant polyphenols as dietary antioxidants in human health and disease. Oxid Med Cell Longev. 2009;2(5):270-8. doi: 10.4161/oxim.2.5.9498, PMID 20716914.
40. Aloo SO, Ofosu FK, Kim NH, Kilonzi SM, Oh DH. Insights on dietary polyphenols as agents against metabolic disorders: obesity as a target disease. Antioxidants (Basel). 2023;12(2):416. doi: 10.3390/antiox12020416, PMID 36829976.
41. Bešlo D, Golubić N, Rastija V, Agić D, Karnaš M, Šubarić D, *et al.* Antioxidant activity, metabolism and bioavailability of polyphenols in the diet of animals. Antioxidants (Basel). 2023;12(6):1141. doi: 10.3390/antiox12061141, PMID 37371871.
42. Karioti A, Carta F, Supuran CT. Phenols and polyphenols as Carbonic Anhydrase Inhibitors. Molecules. 2016;21(12):1649. doi: 10.3390/molecules21121649, PMID 27918439.
43. Galleano M, Verstraeten SV, Oteiza PI, Fraga CG. Antioxidant actions of flavonoids: thermodynamic and kinetic analysis. Arch Biochem Biophys. 2010;501(1):23-30. doi: 10.1016/j.abb.2010.04.005, PMID 20388486.
44. Nieuwenhuizen AG, Laere KM, Raggers RJ. Combination of flavonoids and procyanidin for the reduction of the mammalian appetite. U.S.; 2006. p. 258.
45. Wang J, Fang X, Ge L, Cao F, Zhao L, Wang Z, *et al.* Antitumor, antioxidant and anti-inflammatory activities of kaempferol and its corresponding glycosides and the enzymatic preparation of kaempferol. PLOS One. 2018;13(5):e0197563. doi: 10.1371/journal.pone.0197563, PMID 29771951.
46. Virtanen KA, Lidell ME, Orava J, Heglind M, Westergren R, Niemi T, *et al.*, Functional brown adipose tissue in healthy adults. Functional brown adipose tissue in healthy adults. N Engl J Med. 2009;360(15):1518-25. doi: 10.1056/NEJMoa0808949, PMID 19357407. N. Engl. J. Med. Overseas Ed. 2009;360:1518-1525.
47. Bernatoniene J, Kopustinskiene DM. The role of catechins in cellular responses to oxidative stress. Molecules. 2018;23(4):965. doi: 10.3390/molecules23040965, PMID 29677167.
48. Zhang X, Zhang QX, Wang X, Zhang L, Qu W, Bao B, *et al.* Dietary luteolin activates browning and thermogenesis in mice through an AMPK/PGC1α pathway-mediated mechanism. Int J Obes (Lond). 2016;40(12):1841-9. doi: 10.1038/ijo.2016.108, PMID 27377953.
49. Musso G, Gambino R, Cassader M. Interactions between gut microbiota and host metabolism predisposing to obesity and diabetes. Annu Rev Med. 2011;62:361-80. doi: 10.1146/annurev-med-012510-175505, PMID 21226616.
50. Chourpiliadis C, Mohiuddin SS. Biochemistry, gluconeogenesis.2023; 2023.
51. Quispe M, Herrera-Bravo C, Rahaman J, Hossain MM, Sarkar R, *et al.*, Activities and Molecular Mechanisms of Diterpenes, Diterpenoids and Their Derivatives in Rheumatoid Arthritis. Is Iam T. Evid Based Complement Alternat Med. 2022;2022.
52. Rowinsky EK, Eric K. The development and clinical utility of the taxane class of antimicrotubule chemotherapy agents. Annu Rev Med. 1997;48:353-74. doi: 10.1146/annurev.med.48.1.353, PMID 9046968.
53. Lipina C, Hundal HS. Carnosic acid stimulates glucose uptake in skeletal muscle cells via a PME- 1/PP2A/PKB signaling axis. Cell Signal. 2014;26(11):2343-9. doi: 10.1016/j.cellsig.2014.07.022, PMID 25038454.
54. Ahn J, Lee H, Kim S, Park J, Ha T. The anti-obesity effect of quercetin is mediated by the AMPK and MAPK signaling pathways. Biochem Biophys Res Commun. 2008;373(4):545-9. doi: 10.1016/j.bbrc.2008.06.077, PMID 18586010.
55. Jung CH, Cho I, Ahn J, Jeon TI, Ha TY. Quercetin reduces high-fat diet- induced fat accumulation in the liver by regulating lipid metabolism genes. Phytother Res. 2013;27(1):139-43. doi: 10.1002/ptr.4687, PMID 22447684.
56. Patel K, Patel D, Chapter 26. The beneficial role of Rutin, A naturally occurring flavonoid in Health Promotion and disease prevention: A systematic review and update, bioactive food as dietary interventions for arthritis and related inflammatory diseases. Academic Press; 2019. p. 457-79.
57. De Vincenzi M, Maialetti F, Silano M. Constituents of aromatic plants: teucrin A. Fitoterapia. 2003;74(7-8):746-9. doi: 10.1016/s0367-326x(03)00145-x, PMID 14630189.
58. Johnson RK. Dietary intake-how do we measure what people are really eating? Obes Res. 2002;10 Suppl 1: 63S-8S. doi: 10.1038/oby.2002.192, PMID 12446861.
59. Na M, Oh WK, Kim YH, Cai XF, Kim S, Kim BY, *et al.* Inhibition of protein tyrosine phosphatase 1B by diterpenoids isolated from Acanthopanax koreanum. Bioorg Med Chem Lett. 2006;16(11):3061-4. doi: 10.1016/j.bmcl.2006.02.053, PMID 16545563.
60. Romo Vaquero M, García Villalba R, Larrosa M, Yáñez-Gascón MJ, Fromentin E, Flanagan J, *et al.* Bioavailability of the major bioactive diterpenoids in a rosemary extract: metabolic profile in the intestine, liver, plasma and brain of Zucker rats. Mol Nutr Food Res. 2013;57(10):1834-46. doi: 10.1002/mnfr.201300052, PMID 23625681.
61. Lee EJ, Hwang JS, Kang ES, Lee SB, Hur J, Lee WJ, *et al.* Nanoemulsions improve the efficacy of turmeric in palmitate- and high fat diet-induced cellular and animal models. Biomed Pharmacother. 2019;110:181-9. doi: 10.1016/j.biopha.2018.11.006, PMID 30469082.
62. Takahashi Y, Kushiro M, Shinohara K, Ide T. Dietary conjugated linoleic acid reduces body fat mass and affects gene expression of proteins regulating energy metabolism in mice. Comp Biochem Physiol B Biochem Mol Biol. 2002;133(3):395-404. doi: 10.1016/s1096-4959(02)00164-1, PMID 12431407.
63. Seo DB, Jeong HW, Kim YJ, Kim S, Kim J, Lee JH, *et al.* Fermented green tea extract exhibits hypolipidaemic effects through the inhibition of pancreatic lipase and promotion of energy expenditure. Br J Nutr. 2017;117(2):177-86. doi: 10.1017/S0007114516004621, PMID 28132656.
64. Rahman HA, Sahib NG, Saari N, Abas F, Ismail A, Mumtaz MW, *et al.* Antiobesity effect of ethanolic extract from *Cosmos caudatus* Kunth leaf in lean rats fed a high fat diet. BMC Complement Altern Med. 2017;17:1.
65. Wong PY, Kitts DD. Studies on the dual antioxidant and antibacterial properties of parsley (*Petroselinum crispum*) and cilantro (*Coriandrum sativum*) extracts. Food Chem. 2006;97(3):505-15. doi: 10.1016/j.foodchem.2005.05.031.
66. Ruan ZP, Zhang LL, Lin YM. Evaluation of the antioxidant activity of *Syzygium cumini* leaves. Molecules. 2008;13(10):2545-56. doi: 10.3390/molecules13102545, PMID 18927517.
67. Koffi E, Sea T, Dodehe Y, Soro S. Effect of solvent type on extraction of polyphenols from twenty-three Ivorian plants. J Anim Plant Sci. 2010;5:550-8.
68. Anokwuru CP, Anyasor GN, Ajibaye O, Fakoya O, Okebugwu P. Effect of extraction solvents on phenolic, flavonoid and antioxidant activities of three Nigerian medicinal plants. Nat Sci. 2011;9:53-61.
69. Chemat F, Cravotto G. Microwave-assisted extraction for bioactive compounds. Boston: Springer; 2013. p. 2013.
70. Ballard TS, Mallikarjunan P, Zhou K, O'Keefe S. Microwave-assisted extraction of phenolic antioxidant compounds from peanut skins. Food Chem. 2010;120(4):1185-92. doi: 10.1016/j.foodchem.2009.11.063.
71. Kingston HM, Jessie LB. Introduction to microwave sample preparation. Washington, DC: American Chemical Society; 1998. p. 1998.
72. Li H, Deng Z, Wu T, Liu R, Loewen S, Tsao R. Microwave-assisted extraction of phenolics with maximal antioxidant activities in tomatoes. Food Chem. 2012;130(4):928-36. doi: 10.1016/j.foodchem.2011.08.019.
73. Tsubaki S, Sakamoto M, Azuma J. Microwave-assisted extraction of phenolic compounds from tea residues under autohydrolytic conditions. Food Chem. 2010;123(4):1255-8. doi: 10.1016/j.foodchem.2010.05.088.
74. Christophoridou S, Dais P, Tseng LH, Spraul M. Separation and identification of phenolic compounds in olive oil by coupling high-performance liquid chromatography with post column solid-phase extraction to nuclear magnetic resonance spectroscopy (lcspenmr). J Agric Food Chem. 2005;53(12):4667-79. doi: 10.1021/jf040466r, PMID 15941298.
75. Andrews SS. Electromagnetic waves. In: Light and waves. Cham: Springer; 2023.
76. Barba FJ, Zhu Z, Koubaa M, Sant'Ana AS, Orlien V. Green alternative methods for the extraction of antioxidant bioactive compounds from winery wastes and by-products: a review. Trends Food Sci Technol. 2016;49:96-109. doi: 10.1016/j.tifs.2016.01.006.
77. Chemat F, Rombaut N, Sicaire AG, Meullemiestre A, Fabiano-Tixier AS, Abert-Vian M. Ultrasound assisted extraction of food and natural products. Mechanisms, techniques, combinations, protocols and applications. A review. Ultrason Sonochem. 2017;34:540-60. doi: 10.1016/j.ultsonch.2016.06.035, PMID 27773280.
78. Jovanović AA, Đorđević VB, Zdunić GM, Pljevljakušić DS, Šavikin KP, Gođevac DM, *et al.* Optimization of the extraction process of polyphenols from *Thymus serpyllum* L. herb using maceration, heat- and ultrasound-assisted techniques. Sep Purif Technol. 2017;179:369-80. doi: 10.1016/j.seppur.2017.01.055.
79. Wu QS, Wang CM, Lu JJ, Lin LG, Chen P, Zhang QW. Simultaneous determination of six saponins in Panacis Japonici rhizoma using quantitative analysis of multi-components with single-marker method. Curr Pharm Anal. 2017;13(3):289-95. doi: 10.2174/1573412912666160526165500.

80. Liang J, Yang Z, Ai X. Comparative study on extraction of febrifugine from traditional Chinese medicine *Dichroa febrifuga* by reflux method and ultrasonic method. Shizhen Guoyi Guoyao.2015. Zt Guo, Xq Luo. 1532-1533;26.
81. Lipeng S, Pang S, Zhong M, Sun Y, Qayum A, Liu Y, *et al.* A comprehensive review of ultrasonic assisted extraction (UAE) for bioactive components: principles, advantages, equipment and combined technologies, Ultrasonics Sonochemistry. 2023; 101. Vol. 4177; 1350.
82. Hou J, He S, Ling M, Li W, Dong R, Pan Y, *et al.* A method of extracting ginsenosides from *panax ginseng* by pulsed electric field. J Sep Sci. 2010;33(17-18):2707-13. doi: 10.1002/jssc.201000033, PMID 20715136.
83. Bouras M, Grimi N, Bals O, Vorobiev E. Impact of pulsed electric fields on polyphenols extraction from Norway spruce bark. Ind Crops Prod. 2016;80:50-8. doi: 10.1016/j.indcrop.2015.10.051.
84. Zhang QW, Lin LG, Ye WC. Techniques for extraction and isolation of natural products: a comprehensive review. Chin Med. 2018;13:20. doi: 10.1186/s13020-018-0177-x, PMID 29692864.
85. Wu QS, Wang CM, Lu JJ, Lin LG, Chen P, Zhang QW. Simultaneous determination of six saponins in panacis japonici rhizoma using quantitative analysis of multi-components with single-marker method. Curr Pharm Anal. 2017;13(3):289-95. doi: 10.2174/1573412912666160526165500.
86. Tu Y, Li L, Fan W, Liu L, Wang Z, Yang L. Development of Green and Efficient Extraction of Bioactive ginsenosides from *panax ginseng* with Deep Eutectic Solvents. Molecules. 2022;27(14):4339. doi: 10.3390/molecules27144339, PMID 35889211.
87. Ma Y, Meng A, Liu P, Chen Y, Yuan A, Dai Y, *et al.* Reflux extraction optimization and antioxidant activity of phenolic compounds from *Pleioblastus amarus* (Keng) Shell. Molecules. 2022;27(2):362. doi: 10.3390/molecules27020362, PMID 35056677.
88. Bocker R, Silva EK. Pulsed electric field assisted extraction of natural food pigments and colorings from plant matrices. Food Chem X. 2022;15:100398. doi: 10.1016/j.fochx.2022.100398, PMID 36211728.
89. Athanasiadis V, Chatzimitakos T, Kotsou K, Kalompatsios D, Bozinou E, Lalas SI. Polyphenol Extraction from Food (by) Products by Pulsed Electric Field: a review. Int J Mol Sci. 2023;24(21):15914. doi: 10.3390/ijms242115914, PMID 37958898.
90. Bouras M, Grimi N, Bals O, Vorobiev E. Impact of pulsed electric fields on polyphenols extraction from Norway spruce bark. Ind Crops Prod. 2016;80:50-8. doi: 10.1016/j.indcrop.2015.10.051.

Cite this article: Jaiswal S, Sharma A, Kamboj A, Kaur J, Nain P. Exploring the Therapeutic Potential of Natural Products in Obesity Treatment: Molecular Mechanisms and Isolation Techniques. Pharmacog Res. 2025;17(2):358-69.