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## Obesity and its Treatment with Natural Product

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#### **Abstract**

A condition known as obesity is defined by an abnormal buildup of body fat. It occurs as a result of an imbalance between calories burned and calories ingested. Long-term disregard for this illness could result in serious complications such as fatty liver, cardiac problems, stroke, diabetes, and arthritis. Obesity's rising prevalence causes more deaths globally. Controlling the complications has indeed been accomplished by treatment. This review will concentrate on using natural cures to manage obesity.

Keywords: Obesity, Abnormal buildup of body fat, Rising prevalence, Treatment, Natural cures

#### Introduction

Obesity is a complex disorder involving an excessive accumulation of body fat. It is usually caused by the consumption of more calories than the body can use. Simply, it may be defined as a state of imbalance between calorie intake and calorie expenditure, leading to abnormal fat accumulation. Obesity is not just a cosmetic concern. It is also a medical problem. It is not a single disorder but a heterogeneous group of conditions with multiple causes which is expressed as an obese phenotype. It is not the same as being overweight. Being overweight may be due to extra muscle, bone, or water, as well as too much fat. [1]

Obesity is a metabolic syndrome. World Health Organization [WHO] considers a "NEW WORLD SYNDROME" due to a lack of physical activity. Being overweight and obese are increasing problems that lead to significant health and social difficulties for people. It is commonly determined by measuring BMI [Body Mass Index]. [2]

#### Types of obesity

According to some studies, obesity is of 6 types. They are:

- Nervous obesity: In this type, obesity was caused by anxiety, stress, and depression.
- Genetic obesity: It is genetically transferred obesity. In this type, obese people have a swollen stomach like a balloon, and fat accumulated in the middle parts of the body.
- **Dietary obesity:** It is caused by leading a sedentary lifestyle and eating more calories than burned.
- Obesity due to poor regulation: This type of obesity is due to continuously feeling unsatisfied eating.

- Endocrine obesity: In this type, obesity was caused by an imbalance of thyroid hormones.
- Thermogenic Obesity: In this type, the body does not reach the temperature required for burning calories.

## **Etiology**

The following causes are responsible for getting obesity.

- Obesogenic environmental factor (sedentary lifestyle). [3][4][5][6]
- Medications (anti-seizures, antidepressants, anti-psychotics, steroids, and beta-blockers).
- Psychological factors.
- Hormones (leptin, insulin, sex hormones, growth hormones, thyroid hormones). [7][8][9]
- Bacteria (Gut microbiome, Bacteroidetes, Firmicutes).[10][11]
- Genetics (body weight, body fat, and other obesity-related traits are linked to 15 chromosomal loci that lead to Prader-Willi Syndrome and Cushing Syndrome. [12]

## **Epidermilogy**

- ➤ Obesity is defined as an increasing body mass index greater than 30 or 30.<sup>[13]</sup>
- ➤ Obesity prevalence can increase the day by day in developing countries.
- ➤ In the 1970s obesity is a rare condition but in nowadays obesity is a common disease.
- ➤ In the 21<sup>st</sup> century; obesity or overweight is an endemic condition.
- ➤ Overweight or obesity in children and adolescents is 95% of a specified population. [14]

- ➤ Worldwide obesity has nearly tripled since 1975.
- ➤ In 1975, 20.2% of individuals were obese or overweight.
- ➤ In the 1980s, 4.8% of men and 7.9% of women increase their obesity yearly.
- According to the United States, obesity increased by 12% in 1990.
- ➤ In 1997, the World Health Organization formally recognized obesity as a global epidemic condition.
- ➤ In 2003-2004, 32.9% of adults 20-75 years old were obese and more than 17% of teenagers are noted as obese patients.<sup>[15]</sup>
- ➤ In 2016, more than 1.9 billion adults 18 years older were overweight or obese.
- ➤ 39 billion children under 5 years were overweight in 2020.
- ➤ The overall worldwide prevalence of obesity nearly tripled between 1975 and 2016.
- ➤ The prevalence of obesity doubled between 1980 and 2014.
- ➤ As of 2008, WHO estimates that at least 500 million adults are obese with higher rates among women than men.<sup>[16]</sup>
- ➤ In 2014, more than 600 million adults were obese.
- ➤ In 2013 has estimated 2.1 billion adults were overweight as compared with 857 million in 1980.<sup>[17]</sup>
- ➤ Obesity has reached epidemic proportions in India in the 21<sup>st</sup> century. [18]
- ➤ In India, the obesity rate is increased in urban areas than in rural areas. [19]
- Obesity rates have increased in all ages and both sexes irrespective of geographical locality, ethnicity, or socioeconomic status, although the

- prevalence of obesity is generally greater in older persons and women.<sup>[19]</sup>
- ➤ In the United States, obesity among adults and overweight among children and adolescents has increased markedly since 1980. [20]
- ➤ A complex, multifactorial disease, with genetic, behavioral, socioeconomic, and environmental origins, obesity raises the risk of debilitating morbidity and mortality. [21][22]

#### Risk factor

- Hereditary (inheritance of eating habits)
- Unhealthy diet (junk food)
- Sedentary lifestyle <sup>[23][24][25]</sup>
- Sudden stoppage of smoking<sup>[26]</sup>
- Drugs used in pregnancy and insomnia condition<sup>[27]</sup>
- Arthritis<sup>[28][29]</sup>
- Gender (more women are obese than men in developing countries & more men are obese than in developed countries). [30]

#### **Factor affecting obesity**

- ✓ **Genetic factors:** Obesity tends to continue in families not only through sharing of genes, but family members also share eating habits and activities.
- ✓ Energy imbalance: An imbalance between the consumption of high calories daily without the expenditure of that calories.
- ✓ **Sedentary lifestyle:** It is known that around 31% of people over 15 years lead a sedentary lifestyle. [31]

## **Complications**

Obesity can cause severe complications to the body. [32]

- Diabetes Mellitus. Hypertension, Dyslipidemia, Heart disease, Coronary artery disease, Heart failure, Atrial fibrillation, Cerebrovascular disease. Obstructive sleep asthma, apnoea, Gastroesophageal reflux, Hepatobiliary disease, Fatty liver, Osteoarthritis, certain types of cancers, Psychosocial problems, Gynecological and obstetric complications, chronic kidney disease. [33]
- Inflammation, Gut microbiome, stroke, neurological disease, dysregulated immune system, Infertility, and Musculoskeletal problems. [34]

## **Pathogenesis**

The generation of adipose tissue, known as adipogenesis, is the primary source of obesity. Adipose tissue is one of the most sophisticated organs in the human body. Preadipocytes undergo a process of cell differentiation to become adipocytes. Several transcription factors control the differentiation of adipocytes. It consists of the melanocortin-4 receptor gene, the beta-3-adrenergic receptor gene, the peroxisome-proliferatoractivated receptor gamma chromosome 10p, and additional genetic polymorphisms. Peroxisome proliferatoractivated receptor (PPAR)-mediated activation of adipocyte-specific genes and CCAAT/enhancer binding protein (C/EBP-1) is demonstrated. [35][36]

They have a significant role in the growth arrest necessary for adipocyte differentiation. Triglyceride molecules are digested by lipoprotein lipase (LPL). In adipose tissue, it

is plentiful. Since LPL mRNA production is frequently seen as an early indicator of adipocyte development, it is essential for regulating lipid synthesis. Blood glucose levels are regulated, and fatty acid oxidation is promoted by a protein hormone called adiponectin, which is produced by adipose tissue. The etiology of obesity necessitates the resetting of body weight and a persistent positive energy balance (energy intake) energy expenditure). [37]

These days consumption of calories will is higher than what the body needs. The calories that are not used by the body are stored as fat. This causes fat cells to grow, which in turn causes an increase in the number of fat cells. Even if a person regulated their food intake after their number of fat cells increased, the size of their adipose cells may have decreased, but their total number of fat cells did not change. Lack of self-control or lack of willpower may be the cause of eating a high-calorie diet or eating a lot of food. One can simply get rid of this illness by making small modifications to their lifestyle. [38]

The basic issue with obesity is eating habits, which have significantly changed in recent decades. Examples include irregular mealtime, bad timing, wrong proportions between different product groups, or excessive consumption of certain items, particularly fats and monosaccharides. In 1961, the average person consumed 2,300 calories per day. It climbed to 2,800 in 1998 and surpassed 3,000 in 2015. Additionally, because food is so inexpensive, there is a greater overall supply of it. Consumption of fruits and vegetables is also down in the same period. Only 30% of boys and 37% of girls (aged 13 to 15)

consume fruit every day, according to the WHO European Office.

#### **Treatment**

To reduce obesity, one should cut back on calories and adopt healthy eating practices (Eat less, Work more). Exercise may result in lipolysis, which releases free fatty acids from triglycerides stored in fat for later usage by muscle as an energy source. [39]

A moderate and steady weight loss over time is seen to be the safest approach to losing weight and the greatest way to keep it off permanently, even though may initially drop weight quickly. The subjects who had engaged in the daily exercise had successfully lost weight over the long term, as seen in multiple research projects. [40][41]

# Natural products for the treatment of obesity

To solve this issue, numerous anti-obesity drugs have been tried. The depressing history of anti-obesity drugs points to their unreliability and the necessity for other methods. Currently offered anti-obesity drugs are pharmacological therapies that can lower or manage weight by changing appetite, metabolism, or calorie intake. They are not only challenging to create, but they also have negative side effects.

Furthermore, restricting the intake of sugar and fatty foods and increasing physical exercise are the cornerstones of treatment interventions for the condition of obesity. However, due to their bioactive components, plant-based meals have garnered significant attention in recent years as a unique preventative and potential therapeutic

approach for the treatment of numerous disorders, particularly obesity. Along with calorie restriction and exercise, management through meals can be accomplished by discovering active ingredients that could modify molecular pathways and gene/protein expressions in a good way.

Various crops include active or functional components that may have anti-obesity benefits and lower the chance of becoming obese. In order to reduce the oxidative inflammatory condition linked to weight gain to be utilized for the treatment of numerous ailments brought on by obesity, antioxidants such as polyphenols, flavonoids, and quercetin are believed to work as a protective-agents. This paper's objective is to investigate new research on plant-derived active ingredients and how it affects the control of obesity. [42][43]

#### **Flavonoids**

The most abundant phenolic substances found in plants, fruits, seeds, and vegetables are flavonoids, which are also known polyphenols. Flavonoids are the most coupled frequently found to sugars (glycosides) or aglycones and have the same fundamental structure as Di phenylpropanes (C6-C3-C6). Flavonoids are divided into 13 categories that include more than 5,000 different chemicals. Flavones, flavanols, and their glycosides are the most prevalent flavonoids. The anti-obesity benefits of flavonoids such as rutin, quercetin, kaempferol, myricetin, hesperidin, naringenin, naringin, green tea catechins (catechin, epigallocatechin gallate, and epicatechin gallate), theaflavins, cyanidins, isoflavones have been the subject of several

research (genistein, daidzein, and glycitien). [44][45]

#### Quercetin

The most frequent flavonoid, quercetin, serves as the building block for numerous other flavonoids, including rutin (glycosylated hesperidin, quercetin), and naringenin. Numerous foods consumed by people contain quercetin, including red onions, grapes, apples, berries, cherries, broccoli, citrus fruits, and tea (Camellia Sinensis), with capers and lovage having the highest quantities (180 mg per 100g). Depending on dietary patterns, the typical daily intake of quercetin for human's ranges from 10 to 100 mg. [46] demonstrated in animal models and, to some extent, in people, quercetin has a wide range of biological actions, including lowering blood pressure [47][48], reducing body weight [47], and ameliorating disorders connected to hyperglycemia [49][50]. By lowering the potential of the mitochondrial membrane, inhibiting peroxisome proliferator-activated receptors (PPARs) and Bcl-2, and activating caspase 3, Bax, and Bak, quercetin causes preadipocytes to undergo apoptosis. [51]

# Active components for plant sources with anti-obesity activity

#### Mulberry leaf

The scientific names of red mulberry and white mulberry are *Morus rubra* and *Morus Alba* respectively. This belongs to the Moraceae family. These are grown in Asian nations. Numerous phytochemical components, including flavonoids and polyphenolic chemicals, are present in these leaves. HPLC is used to extract Mulberry Leaf Extract (MLE) and Mulberry Leaf Poly

Extract (MLPE). The mulberry-water extract has demonstrated some biological effects, antiobesity, antidiabetic, such inflammatory, and antioxidant properties. In comparison to other solvents, ethanol works best to extract the phenolic component from mulberry leaves. Mulberry leaves contain polyphenol, quercetin, caffeic acid, hydroxy Flavin, and hesperidin, which are all active substances. These substances work by inhibiting the expression of the target genes adipocyte-specific fatty acid binding protein and fatty acid synthase, as well as PPAR proteins and sterol regulatory element binding proteins-1c.[52][42]

## **Pepper**

The scientific name of pepper is *Capsicum* annuum *L*. The main agricultural by-product and waste product created during the manufacturing of pepper paste or powder is pepper seeds. Due to its possible antioxidant, antifungal, and antiadipogenic properties, pepper seed has attracted a lot of attention as a useful resource. Additionally, pepper seeds include beneficial bioactive substances such as tocopherols, sterols, triterpenes, and organic acids. Pepper's active ingredient is Capsicoside G, a furostanol saponin. Adenosine monophosphate-activated protein is activated in order to decrease adipogenesis. [53][42]

#### Cocoa

The scientific name of cocoa is *Theobroma cacao*. Polyphenols from cocoa have been shown to be effective in preventing visceral fat accumulation. Additionally, flavonols, the primary class of polyphenols, have been proposed to have anti-obesity properties. By utilizing column chromatography, high-

performance liquid chromatography, and 80% ethanol, the polyphenolic components in the cocoa powder were extracted. Cocoa polyphenols are the cocoa bean's active ingredient (CPs). The device is to control obesity-induced steatosis indicators, genes in lipid catabolism, particularly in fatty acid oxidation, were up-regulated, whereas genes in lipid synthesis pathways were downregulated. [54][42]

#### **Barley**

The scientific name of barley is *Hordeum vulgare L*. Hull less barley is also known as naked barley, is separated from the husk, and hulled barley, also known as covered barley. Ferulic acid, along with coumaric acid are the active ingredients in barley. The mechanism is dysregulated lipid profiles, inhibited adipocyte development, and prevention of body weight increase. [55][42]

#### Citrus lemon

The scientific name of lemon is Citrus limon L. It belongs to the Rutaceae family. It has been reported that dietary lemon polyphenols extracted from the lemon peel (0.5% w/w) on high-fat diet-induced obesity in C57BL/6j mice for 12 weeks suppressed body weight gain (44%) and body fat accumulation (36%). Citrus Limon contains many important phytochemicals, including phenolic (primary compounds flavonoids). Upregulation of acyl-CoA oxidase mRNA levels in the liver and white adipose tissues, which was likely mediated by up-regulation of the mRNA levels of peroxisome proliferatoractivated receptor (PPAR), is one anti-obesity mechanism identified for lemon. [42]

#### **Black soyabeans**

The scientific name of black soyabean is Glycine max L. These are only a dark-colored kind of sovabean that contains several phytochemicals. These black soyabean compounds may be beneficial to human health. Black soyabeans- decrease hunger, heighten feelings of fullness, and result in fewer calories consumed overall. Black soyabean seed coat extract, a dietary item rich in polyphenols, contains 39.8% procyanidins, and 9.2% 6.2% catechins, cyanidin-3glycoside. The anti-obesity benefits of black soyabean seed coating can counteract the negative effects of a high-fat diet on body weight, adipose tissue weight, and serum lipid content. These include phytochemicals such as isoflavones, saponins, and anthocyanins. It has been widely employed in oriental medicine for centuries. One of the most common natural plant pigments, anthocyanins come in a wide spectrum of hues, from orange and red to purple and blue shades. [56][42]

## Red chili pepper

The scientific name of red chili is Capsicum annuum. The hot ingredient in red chili peppers known as capsaicin has been shown to enhance energy expenditure in part via activating the sympathetic nerve-adrenergic receptors in humans. Chronic use of capsaicin has been shown to prevent diet-induced obesity, and it has been hypothesized that UCP1(uncoupling protein 1) plays a role in this action. Capsaicin can treat human obesity, however, it is challenging to utilize because of its extreme pungency. Capsinoids, which are less potent counterparts of capsaicin derived from CH-19 sweet peppers, include dihydrocapsiate, capsiate, and

nordihydrocapsiate. The mechanism is suppressing diet-induced obesity through an uncoupling protein 1-dependent mechanism. [57][42]

#### Garlic

The scientific name of garlic is Allium sativum L. According to studies, dried garlic's main constituents are fructose-containing carbohydrates, followed by sulfur-containing compounds, protein, fiber, and free amino acids. Garlic is a species of the onion genus and has been used as both a flavoring agent complementary medicine. organosulfur chemicals oversee both garlic's favorable health effects and distinctive odor. The active ingredient in garlic is S-ally-1cysteine sulphoxide and S-allyl-cysteine. In high fat diet, decreased relative masses of liver and fat tissues, serum triacyl glyceride levels, hepatic oxidative stress, and increased fecal lipid contents were associated with upregulation of Sirtuin 1. adenosine monophosphate-activated protein kinase, adipose triacyl glyceride lipase, hormonesensitive lipase, Acyl-CoA oxidase, palmitoyl transferase 1 were down regulated. [58][42]

#### **Saffron**

The active ingredient is Crocin. It can able to reduce the plasma levels of triacylglycerol and total cholesterol. [59][42]

#### Oiltea Camellia

The active ingredient of camellia ispolyphenols. The metabolic effects appear to be partially mediated by inhibiting fatty acid synthase activity and suppressing adipogenesis in adipocytes. These effects include suppressed increases in body weight

and fat storage, decreased serum levels of total cholesterol and triacylglycerols, and activity of fatty acid synthase in the animal liver was significantly lower in the inhibited adipogenesis. [60][42]

## **Strawberry and Raspberry**

The active ingredient is salidroside. It inhibits inflammation and triglyceride accumulation brought on by obesity in the liver and the muscles while promoting adiponectin signaling, fatty acid oxidation in the liver and skeletal muscle, and liver PPARs.<sup>[61][42]</sup>

#### Coffee

The active ingredients in polyphenols. It acts by down regulating sterol regulatory element binding protein, acetyl-CoA carboxylase-1 and -2, stearoyl-CoA desaturase-1, and pyruvate dehydrogenase kinase-4 in the liver, suppressed postprandial hyperglycemia and hyperlipidemia prevented lipogenesis. [62][42]

#### References

- 1. Kopelman PG. Obesity as a Medical Problem. Nature 2000 April, 404 (6778), 635–643.
- 2. Poston II, W. S.; Foreyt, J. P. Obesity Is an Environmental Issue. Atherosclerosis 1999 October 1, 146 (2), 201–209.
- 3. Wright, S. M.; Aronne, L. J. Causes of Obesity. Abdom. Rad. 2012 October, 37 (5), 730–732.
- 4. Martinez JA. Body-Weight Regulation: Causes of Obesity. Proc. Nutr. Soc. 2000 August, 59 (3), 337–345.
- Rosin O. The Economic Causes of Obesity: A Survey. J. Econ. Surv. 2008 September, 22 (4), 617–647.
- 6. P.H. Wilding, J. Causes of Obesity. Pract. Diabetes Int. 2001 October, 18 (8), 288–292.
- 7. Leeners, B.; Geary, N.; Tobler, P. N.; Asarian, L. Ovarian Hormones and Obesity. Hum. Reprod. Update 2017 May 1, 23 (3), 300–321.

## **Bilberry**

The active ingredient in bilberry is anthocyanidins. It acts by lowering PPARs, sterol regulatory element-binding protein-1c, and tyrosine residues of insulin receptor substrate-1- phosphorylation, which all served to inhibit adipocyte development. [63][42]

#### Conclusion

Obesity is a condition that is rapidly becoming more prevalent in the modern world, and it causes numerous health complications and death in some instances, though usage of medications will cure the conditions to an extent, the side effects that arise from these are not be overlooked so, utilizing natural products will be giving us a chance to avoid the forthcoming adverse effects that occur due to this disease and sometimes they may also show greater action when compared to the allopathic drugs.

- 8. Reinehr, T.; Andler, W. Thyroid Hormones before and After Weight Loss in Obesity. Arch. Dis. Child. 2002 October 1, 87 (4), 320–323.
- 9. Mayes, J. S.; Watson, G. H. Direct Effects of Sex Steroid Hormones on Adipose Tissues and Obesity. Obes. Rev. 2004 November, 5 (4), 197– 216.
- 10. Chen, X.; Devaraj, S. Gut Microbiome in Obesity, Metabolic Syndrome, and Diabetes. Curr. Diabetes Rep. 2018 December, 18 (12), 129.
- Hullar, M. A.; Lampe, J. W. The Gut Microbiome and Obesity. In Inobesity Treatment and Prevention; Vol. 73; New Directions; Karger Publishers, 2012.
- 12. Vitale, S. A. Parent Recommendations for Family Functioning with Prader-Willi Syndrome: A Rare Genetic Cause of Childhood Obesity. J. Pediatr. Nurs. 2016 January 1, 31 (1), 47–54.

- 13. Ogden, C. L.; Carroll, M. D.; Flegal, K. M. Epidemiologic Trends in Overweight and Obesity. Endocrinol. Metab. Clin. North Am. 2003 December 1, 32 (4), 741–760.
- 14. Dietz, W. H. Health Consequences of Obesity in Youth: Childhood Predictors of Adult Disease. Pediatrics 1998 March 1, 101 (3 Pt 2) (Supplement\_2), 518–525.
- 15. Phinney, S. D. Exercise During and After Very-Low-Calorie Dieting. Am. J. Clin. Nutr. 1992 July 1, 56 (1) (Suppl.), 190S–194S.
- Pasco, J. A.; Nicholson, G. C.; Brennan, S. L.; Kotowicz, M. A. Prevalence of Obesity and the Relationship between the Body Mass Index and Body Fat: Cross-Sectional, Population-Based Data. PLOS ONE 2012 January 13, 7 (1), e29580.
- 17. Ng, M.; Fleming, T.; Robinson, M.; Thomson, B.; Graetz, N.; Margono, C.; Mullany, E. C.; Biryukov, S.; Abbafati, C.; Abera, S. F.; Abraham, J. P.; Abu-Rmeileh, N. M.; Achoki, AlBuhairan, F. S.; Alemu, Z. A.; Alfonso, R.; Ali, M. K.; Ali, R.; Guzman, N. A.; Ammar, W.; Anwari, P.; Banerjee, A.; Barquera, S.; Basu, S.; Bennett, D. A.; Bhutta, Z.; Blore, J.; Cabral, N.; Nonato, I. C.; Chang, J. C.; Chowdhury, R.; Courville, K. J.; Criqui, M. H.; Cundiff, D. K.; Dabhadkar, K. C.; Dandona, L.; Davis, A.; Dayama, A.; Dharmaratne, S. D.; Ding, E. L.; Durrani, A. M.; Esteghamati, A.; Farzadfar, F.; Fay, D. F.; Feigin, V. L.; Flaxman, A.; Forouzanfar, M. H.; Goto, A.; Green, M. A.; Gupta, R.; Hafezi-Nejad, N.; Hankey, G. J.; Harewood, H. C.; Havmoeller, R.; Hay, S.; Hernandez, L.; Husseini, A.; Idrisov, B. T.; Ikeda, N.; Islami, F.; Jahangir, E.; Jassal, S. K.; Jee, S. H.; Jeffreys, M.; Jonas, J. B.; Kabagambe, E. K.; Khalifa, S. E.; Kengne, A. P.; Khader, Y. S.; Khang, Y. H.; Kim, D.; Kimokoti, R. W.; Kinge, J. M.; Kokubo, Y.; Kosen, S.; Kwan, G.; Lai, T.; Leinsalu, M.; Li, Y.; Liang, X.; Liu, S.; Logroscino, G.; Lotufo, P. A.; Lu, Y.; Ma, J.; Mainoo, N. K.; Mensah, G. A.; Merriman, T. R.; Mokdad, A. H.; Moschandreas, J.; Naghavi, M.; Naheed, A.; Nand, D.; Narayan, K. M.; Nelson, E. L.; Neuhouser, M. L.; Nisar, M. I.; Ohkubo, T.; Oti, S. O.; Pedroza, A.; Prabhakaran, D.; Roy, N.; Sampson, U.; Seo, H.; Sepanlou, S. G.; Shibuya, K.; Shiri, R.; Shiue, I.; Singh, G. M.; Singh, J. A.; Skirbekk, V.; Stapelberg, N. J.; Sturua, L.; Sykes,
- B. L.; Tobias, M.; Tran, B. X.; Trasande, L.; Toyoshima, H.; van de Vijver, S.; Vasankari, T. J.; Veerman, J. L.; Velasquez-Melendez, G.; Vlassov, V. V.; Vollset, S. E.; Vos, T.; Wang, C.; Wang, X.; Weiderpass, E.; Werdecker, A.; Wright, J. L.; Yang, Y. C.; Yatsuya, H.; Yoon, J.; Yoon, S. J.; Zhao, Y.; Zhou, M.; Zhu, S.; Lopez, A. D.; Murray, C. J.; Gakidou, E. Global, Regional, and National Prevalence of Overweight and Obesity in Children and Adults During 1980–2013: A Systematic Analysis for the Global Burden of Disease Study 2013. Lancet 2014 August 30, 384 (9945), 766–781.
- 18. Caballero, B. The Global Epidemic of Obesity: An Overview. Epidemiol. Rev. 2007 January 1, 29 (1), 1–5.
- 19. Chooi, Y. C.; Ding, C.; Magkos, F. The Epidemiology of Obesity. Metabolism 2019 March 1, 92, 6–10.
- 20. Ogden, C. L.; Yanovski, S. Z.; Carroll, M. D.; Flegal, K. M. The Epidemiology of Obesity. Gastroenterology 2007 May 1, 132 (6), 2087–2102.
- 21. Nguyen, D. M.; El-Serag, H. B. The Epidemiology of Obesity. Gastroenterol. Clin. North Am. 2010 March 1, 39 (1), 1–7.
- 22. Hruby, A.; Hu, F. B. The Epidemiology of Obesity: A Big Picture. Pharmacoeconomics 2015 July, 33 (7), 673–689.
- Tudor-Locke, C.; Craig, C. L.; Thyfault, J. P.; Spence, J. C. A Step-Defined Sedentary Lifestyle Index: < 5000 Steps/Day. Appl. Physiol. Nutr. Metab. 2013, 38 (2), 100–114.
- Tremblay, M. S.; Colley, R. C.; Saunders, T. J.; Healy, G. N.; Owen, N. Physiological and Health Implications of a Sedentary Lifestyle. Appl. Physiol. Nutr. Metab. 2010 December, 35 (6), 725–740.
- Manson, J. E.; Skerrett, P. J.; Greenland, P.; VanItallie, T. B. The Escalating Pandemics of Obesity and Sedentary Lifestyle: A Call to Action for Clinicians. Arch. Intern. Med. 2004 February 9, 164 (3), 249–258.
- Bush, T.; Lovejoy, J. C.; Deprey, M.; Carpenter, K. M. The Effect of Tobacco Cessation on Weight Gain, Obesity, and Diabetes Risk. Obesity (Silver Spring) 2016 September, 24 (9), 1834–1841.

- 27. Henriksen, T. The Macrosomic Fetus: A Challenge in Current Obstetrics. Acta Obstet. Gynecol. Scand. 2008 January 1, 87 (2), 134–145.
- 28. Stavropoulos-Kalinoglou, A.; Metsios, G. S.; Panoulas, V. F.; Douglas, K. M.; Nevill, A. M.; Jamurtas, A. Z.; Kita, M.; Koutedakis, Y.; Kitas, G. D. Associations of Obesity with Modifiable Risk Factors for the Development of Cardiovascular Disease in Patients with Rheumatoid Arthritis. Ann. Rheum. Dis. 2009 February 1, 68 (2), 242–245.
- 29. Leveille, S. G.; Wee, C. C.; Iezzoni, L. I. Trends in Obesity and Arthritis among Baby Boomers and Their Predecessors, 1971–2002. Am. J. Public Health 2005 September, 95 (9), 1607–1613.
- 30. Kanter, R.; Caballero, B. Global Gender Disparities in Obesity: A Review. Adv. Nutr. 2012 July, 3 (4), 491–498.
- 31. Martin-Biggers, J.; Spaccarotella, K.; Berhaupt-Glickstein, A.; Hongu, N.; Worobey, J.; Byrd-Bredbenner, C. Come and Get It! A Discussion of Family Mealtime Literature and Factors Affecting Obesity Risk. Adv. Nutr. 2014 May, 5 (3), 235–247.
- 32. Daniels, S. R. Complications of Obesity in Children and Adolescents. Int. J. Obes. (Lond) 2009 April, 33 (1) (Suppl. 1), S60–S65.
- 33. Malnick, S. D.; Knobler, H. The Medical Complications of Obesity. J. Assoc. Phys. 2006 September 1, 99 (9), 565–579.
- Kinlen, D.; Cody, D.; O'Shea, D. Complications of Obesity. Q.J.M. An Int. J. Med. 2018 July 1, 111 (7), 437–443.
- 35. Harsha, KS, Kamireddy S, Obilineni I, Prasana, KL, Manasa GA, Indrani B, Vyshnavi PA. Review on Global Health Complication Obesity and Its Treatment with Natural Products. J. Cardiovasc. Dis. Res. 2021, 12 (5), 1687–1693.
- 36. Kaila, B.; Raman, M. Obesity: A Review of Pathogenesis and Management Strategies. Can. J. Gastroenterol. 2008 January 1, 22 (1), 61–68.
- 37. Mejia de Grubb, M. C.; Levine, R. S.; Zoorob, R. J. Diet and Obesity Issues in the Underserved. Phys. Assist. Clin. 2019 January 1, 4 (1), 155–169.
- 38. Oussaada, S. M.; van Galen, K. A.; Cooiman, M. I.; Kleinendorst, L.; Hazebroek, E. J.; van Haelst, M. M.; Ter Horst, K. W.; Serlie, M. J. The Pathogenesis of Obesity. Metabolism 2019 March 1, 92, 26–36.

- 39. Fujioka, K.; Seaton, T. B.; Rowe, E.; Jelinek, C. A.; Raskin, P.; Lebovitz, H. E.; Weinstein, S. P.; Sibutramine/Diabetes Clinical Study Group. Weight Loss with Sibutramine *Improves* Glycaemic Control and Other Metabolic Parameters in Obese Patients with Type 2 Diabetes Mellitus. Diabetes Obes. Metab. 2000 May, 2 (3), 175–187.
- Klem, M. L.; Wing, R. R.; McGuire, M. T.; Seagle, H. M.; Hill, J. O. A Descriptive Study of Individuals Successful at Long-Term Maintenance of Substantial Weight Loss. Am. J. Clin. Nutr. 1997 August 1, 66 (2), 239–246.
- 41. Nordmann, A. J.; Nordmann, A.; Briel, M.; Keller, U.; Yancy, W. S.; Brehm, B. J.; Bucher, H. C. Effects of Low-Carbohydrate vs Low-Fat Diets on Weight Loss and Cardiovascular Risk Factors: A Meta-analysis of Randomized Controlled Trials. Arch. Intern. Med. 2006 February 13, 166 (3), 285–293.
- 42. Mir, S. A.; Shah, M. A.; Ganai, S. A.; Ahmad, T.; Gani, M. Understanding the Role of Active Components from Plant Sources in Obesity Management. J. Saudi Soc. Agric. Sci. 2019 April 1, 18 (2), 168–176.
- 43. Park, T.; Kim, Y. Phytochemicals as Potential Agents for Prevention and Treatment of Obesity and Metabolic Diseases. Anti-Obes. Drug Discov. Dev. Bentham, Dubai 2011 July 7, 1, 150–185.
- 44. Havsteen, B. H. The Biochemistry and Medical Significance of the Flavonoids. Pharmacol. Ther. 2002 November 1, 96 (2–3), 67–202.
- 45. Bravo, L. Polyphenols: Chemistry, Dietary Sources, Metabolism, and Nutritional Significance. Nutr. Rev. 1998 November 1, 56 (11), 317–333.
- 46. Bischoff, S. C. Quercetin: Potentials in the Prevention and Therapy of Disease. Curr. Opin. Clin. Nutr. Metab. Care 2008 November 1, 11 (6), 733–740.
- 47. Yamamoto, Y.; Oue, E. Antihypertensive Effect of Quercetin in Rats Fed with a High-Fat High-Sucrose Diet. Biosci. Biotechnol. Biochem. 2006, 70 (4), 933–939.
- 48. Edwards, R. L.; Lyon, T.; Litwin, S. E.; Rabovsky, A.; Symons, J. D.; Jalili, T. Quercetin Reduces Blood Pressure in Hypertensive Subjects. J. Nutr. 2007 November 1, 137 (11), 2405–2411.

- 49. Fang, X. K.; Gao, J.; Zhu, D. N. Kaempferol and Quercetin Isolated from Euonymus Alatus Improve Glucose Uptake of 3T3-L1 Cells Without Adipogenesis Activity. Life Sci. 2008 March 12, 82 (11–12), 615–622.
- Rivera, L.; Morón, R.; Sánchez, M.; Zarzuelo, A.; Galisteo, M. Quercetin Ameliorates Metabolic Syndrome and Improves the Inflammatory Status in Obese Zucker Rats. Obesity (Silver Spring) 2008 September, 16 (9), 2081–2087.
- Hsu, C. L.; Yen, G. C. Induction of Cell Apoptosis in 3T3-L1 Pre adipocytes by Flavonoids Is Associated with Their Antioxidant Activity. Mol. Nutr. Food Res. 2006 November, 50 (11), 1072– 1079.
- 52. Chang, Y. C.; Yang, M. Y.; Chen, S. C.; Wang, C. J. Mulberry Leaf Polyphenol Extract Improves Obesity by Inducing Adipocyte Apoptosis and Inhibiting Preadipocyte Differentiation and Hepatic Lipogenesis. J. Funct. Foods 2016 March 1, 21, 249–262.
- 53. Sung, J.; Lee, J. Capsicoside G, a Furostanol Saponin from Pepper (Capsicum annuum L.) Seeds, Suppresses Adipogenesis Through Activation of AMP-Activated Protein Kinase in 3T3-L1 Cells. J. Funct. Foods 2016 January 1, 20, 148–158.
- 54. Ali, F.; Ismail, A.; Esa, N. M.; Pei, C. P.; Kersten, S. Hepatic Genome-Wide Expression of Lipid Metabolism in Diet-Induced Obesity Rats Treated with Cocoa Polyphenols. J. Funct. Foods 2015 August 1, 17, 969–978.
- 55. Seo, C. R.; Yi, B.; Oh, S.; Kwon, S. M.; Kim, S.; Song, N. J.; Cho, J. Y.; Park, K. M.; Ahn, J. Y.; Hong, J. W.; Kim, M. J.; Lee, J.; Park, K. W. Aqueous Extracts of Hulled Barley Containing Coumaric Acid and Ferulic Acid Inhibit Adipogenesis In Vitro and Obesity In Vivo. J. Funct. Foods 2015 January 1, 12, 208–218.
- 56. Kim, S. Y.; Wi, H. R.; Choi, S.; Ha, T. J.; Lee, B. W.; Lee, M. Inhibitory Effect of Anthocyanin-Rich Black Soybean testa (Glycine max (L.) Merr.) On the Inflammation-Induced Adipogenesis in a DIO Mouse Model. J. Funct. Foods 2015 April 1, 14, 623–633.

- Okamatsu-Ogura, Y.; Tsubota, A.; Ohyama, K.; Nogusa, Y.; Saito, M.; Kimura, K. Capsinoids Suppress Diet-Induced Obesity Through Uncoupling Protein 1-Dependent Mechanism in Mice. J. Funct. Foods 2015 December 1, 19, 1–9.
- 58. Chen, Y. C.; Kao, T. H.; Tseng, C. Y.; Chang, W. T.; Hsu, C. L. Methanolic Extract of Black Garlic Ameliorates Diet-Induced Obesity via Regulating Adipogenesis, Adipokine Biosynthesis, and Lipolysis. J. Funct. Foods 2014 July 1, 9, 98–108.
- 59. Mashmoul, M.; Azlan, A.; Yusof, B. N. M.; Khaza'ai, H.; Mohtarrudin, N.; Boroushaki, M. T. Effects of Saffron Extract and Crocin on Anthropometrical, Nutritional and Lipid Profile Parameters of Rats Fed a High Fat Diet. J. Funct. Foods 2014 May 1, 8, 180–187.
- 60. Chen, Q.; Wu, X.; Liu, L.; Shen, J. Polyphenol-Rich Extracts from Oiltea Camellia Prevent Weight Gain in Obese Mice Fed a High-Fat Diet and Slowed the Accumulation of Triacylglycerols in 3T3-L1 Adipocytes. J. Funct. Foods 2014 July 1, 9, 148–155.
- 61. Goto, T.; Teraminami, A.; Lee, J. Y.; Ohyama, K.; Funakoshi, K.; Kim, Y. I.; Hirai, S.; Uemura, T.; Yu, R.; Takahashi, N.; Kawada, T. Tiliroside, a Glycosidic Flavonoid, Ameliorates Obesity-Induced Metabolic Disorders via Activation of Adiponectin Signaling Followed by Enhancement of Fatty Acid Oxidation in Liver and Skeletal Muscle in Obese–Diabetic Mice. J. Nutr. Biochem. 2012 July 1, 23 (7), 768–776.
- 62. Murase, T.; Yokoi, Y.; Misawa, K.; Ominami, H.; Suzuki, Y.; Shibuya, Y.; Hase, T. Coffee Polyphenols Modulate Whole-Body Substrate Oxidation and Suppress Postprandial Hyperglycaemia, Hyperinsulinaemia and Hyperlipidaemia. Br. J. Nutr. 2012 June, 107 (12), 1757–1765.
- 63. Suzuki, R.; Tanaka, M.; Takanashi, M.; Hussain, A.; Yuan, B.; Toyoda, H.; Kuroda, M. Anthocyanidins-Enriched Bilberry Extracts Inhibit 3T3-L1 Adipocyte Differentiation via the Insulin Pathway. Nutr. Metab. (Lond) 2011 December, 8 (1), 14.