

# Atiology, prevention and management of obesity: a nutritional approach

## Abstract

Obesity is a chronic, multifactorial condition with complex metabolic and behavioral causes and consequences. Epidemiological studies have shown that obesity contributes to the increase in mortality from cancers of the colon, breast (in postmenopausal women), endometrium, kidney (renal cell), esophagus (adenocarcinoma), gastric cardia, pancreas, gallbladder and liver and possibly other types while some experimental investigations have revealed that obesity is a major risk factor for type 2 diabetes, atherosclerosis, cancer and other chronic diseases. Factors such as high caloric intake, genetic factors and psychological factors can lead to obesity. Furthermore, pharmaceuticals, sleep duration, environmental temperature and endocrine disruptors have been established to also be a causative factor of obesity. The therapeutic approach for the treatment of obesity involves different mechanisms and strategies. Plant-based diets are increasingly being recognized for their health benefits in weight management, satiety effects and glycemic control. Therefore, dietary agents that have a potential to decrease body fat or improve hyperglycemia may be used as therapeutic agents for the treatment and/or management of obesity. This review therefore focus on the role of functional foods and nutraceuticals in the treatment and/or management of obesity

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## Introduction

Obesity is a chronic, multifactorial condition with complex psychological, environmental (social and cultural), genetic, physiologic, metabolic and behavioral causes and consequences. There are indications that prevalence of overweight and obese people is increasing worldwide in many developing and developed countries. Environmental and behavioral changes brought about by economic development, modernization and urbanization have been linked to the rise in global obesity. Rising rates of obesity have been linked to food supply trends and to the increase in the consumption of energy-dense foods.<sup>1-3</sup> An increased consumption of snacks,<sup>4</sup> caloric beverages<sup>5,6</sup> and fast foods<sup>7</sup> by children and young adults has been shown repeatedly to be associated with obesity and excess weight gain. Studies have examined the contribution to the obesity epidemic of dietary sugars and fats,<sup>8</sup> larger portion sizes<sup>9</sup> and the lower nutrient density of foods eaten away from home.<sup>10</sup>

Epidemiological studies have shown that obesity contributes to the increase in mortality from cancers of the colon, breast (in postmenopausal women), endometrium, kidney (renal cell), esophagus (adenocarcinoma), gastric cardia, pancreas, gallbladder and liver and possibly other types<sup>11</sup> while some experimental investigations have revealed that obesity is a major risk factor for type 2 diabetes, atherosclerosis, cancer and other chronic diseases.<sup>12</sup>

The common approach to the measurement and identification of overweight and obesity is the use of body mass index (BMI). Although some reports have supported the use of BMI, it is not a perfect measurement. BMI is not a direct measure of adiposity and as a consequence it can overestimate or underestimate adiposity. BMI is a derived value that correlates well with total body fat and markers of secondary complications, e.g., hypertension and dyslipidemia. An abnormally high body mass index does not address the distribution of body fat. BMI is solely dependent on height and weight and does not consider other factors such as a person's physical activity level, sex or

age. Obesity is a risk factor for metabolic syndromes and therapeutic approach for the treatment of obesity involves different mechanisms and strategies

## Factors that induce overweight and obesity

### High caloric intake

Food intake can be affected by many factors such as portion size, taste, variety and accessibility of foods. A high fat diet enriched with saturated fatty acids is the common diet in many developed countries while vegetarian diet is common to developing countries.<sup>13</sup> Liu et al.,<sup>14</sup> reported that diet may affect body weight by controlling satiety and metabolic efficiency, or by modulating insulin secretion and action. Thus, the calorie dense diet common in the western world may induce obesity via increase in postprandial insulin levels resulting from the high carbohydrate intake which leads to increased triglyceride storage in the adipose tissue depots.<sup>15</sup> High insulin levels may also provoke a vicious metabolic cycle. Insulin induces hunger by depleting the glucose levels of the blood and this promotes further food intake which leads to greater insulin secretion. This metabolic cycle will lead to overweight and chronic hyperinsulinaemia.<sup>16,17</sup> Moreover, some researchers have reported that obese subjects have a high preference for fatty foods<sup>13</sup> which will heighten the release of insulin and storage of triglyceride.

Furthermore, previous studies have shown that there is a positive correlation between high fat diet and obesity.<sup>18,19</sup> This also agrees with the report of<sup>20</sup> and Piers et al.,<sup>21</sup> which revealed that food containing saturated fat causes weight gain compared to food containing unsaturated fatty acids. This is because Fatty acids activate peroxisome proliferator-activated receptors delta and gamma (PPAR  $\delta$ , PPAR  $\gamma$ ), which promote adipogenesis and expansion of adipose tissue depots.<sup>22</sup> The common diet in many developed and developing countries contains more fat and considerably less fibre than the recommended levels which leads to the prevalence of obesity.

## Genetic factors

The genes may act as determinant factor of BMI by modulating energy balance. More than 300 genes, markers and chromosomes have been discovered to be linked with physical characteristics related with human obesity<sup>23</sup> and it has been estimated that 30–70% of the variance in BMI in humans can be explained by genetic factors.<sup>24</sup> Some reports have linked the leptin gene with the role adipose tissues play in the regulation of energy balance and appetite.<sup>25</sup> Leptin play a major role by reducing food take via its action within the arcuate nucleus of the hypothalamus which decreases the expression of orexigenic signals and increase the levels of anorexigenic signals.<sup>26</sup> There are many other genes which are expressed in the hypothalamus that controls appetite. However the mutation of these genes contributes to low cases of human obesity which makes it difficult to understand the pathologic process of this condition. Nevertheless, recent experimental investigations involving gene screening techniques have revealed that some genes may induce the deposition of adipose tissues. Many of these genes have been found to be present in the central nervous system and are responsible for the regulation of food intake.<sup>27</sup>

## Psychological factors

The psyche of humans can influence eating habits, due to the fact that many people eat in response to negative emotions. Also stress for example, not only increases consumption of food but also shifts consumption toward high caloric foods that are normally avoided.<sup>28</sup> An experimental investigation using rodent models reported by Dallman et al.,<sup>29</sup> revealed that high levels of adrenal glucocorticoid (GC) which are released due to stress can induce increase in food intake which in turn causes abdominal obesity. Furthermore some neurological disorders can induce high intake of food which contributes to the accumulation fat.<sup>30</sup> A study carried out by Johanssen et al.,<sup>31</sup> and Blisset et al.,<sup>32</sup> revealed that families of patients with morbid obesity have proposed that abnormal or irrational eating habits of families, parental conflicts and parents' psychopathology may influence weight gain in children.

## Other factors

Other factors that may contribute to the pathogenesis of obesity include

**Pharmaceuticals:** Some synthetic drugs such as antidepressants (e.g. serotonin re-uptake inhibitors), contraceptives, corticosteroids, antidiabetic agents (e.g. insulin, sulphonylureas and thiazolidinediones) and some antihypertensive agents (e.g. beta adrenergic receptor antagonists) may lead to increase in weight gain.<sup>33</sup>

**Sleep duration:** It has been shown in human studies that longer sleep duration is associated with high BMI.<sup>34</sup>

**Endocrine disruptors:** The by-products of industrial processes can leak into the environment and hence into the food chain. These molecules are able to elicit endocrine responses and include agents that have oestrogen-like effects (e.g. vinclozolin and bisphenol A) and also substances that are able to activate adipogenesis via interaction with transcription factors.<sup>34</sup>

**Environmental temperature:** The advent of air conditioners has meant that humans spend less time in temperatures outside the thermoneutral zone (TNZ). The TNZ is the range of temperatures over which changes in metabolic rate are not required to maintain normal body temperature. Once a person leaves the TNZ, energy expenditure will increase in an attempt to maintain body temperature

at the required level. Thus, in humans who are constantly within the TNZ, energy expenditure is reduced and this predisposes to weight gain at lower levels of energy intake when compared to subjects who do not spend large periods of time within the TNZ.<sup>34</sup>

## Role of functional foods and nutraceuticals in the treatment and/or management of obesity

Given the worldwide increase in obesity and its health consequences, efficient strategies for its prevention and treatment are important. Since obesity arises from an energy imbalance whereby energy intake exceeds energy expenditure, prevention and treatment of obesity requires some changes in one or both components of energy balance. Strategies to weight management targets multiple aspects of the energy balance systems: dietary energy intake, physical energy expenditure, energy storage and lifestyle changes via the use of natural and synthetic compounds. However, the use of functional foods designed for weight management may be a more attractive approach than the use of synthetic drugs due to their side effects.<sup>35</sup>

Plant-based diets are increasingly being recognized for their health benefits in weight management, satiety effects and glycemic control. Therefore, dietary agents that have a potential to decrease body fat or improve hyperglycemia may be used as therapeutic agents for the treatment and/or management of obesity. Several functional food ingredients are known to post absorptively influence substrate utilization or thermogenesis. Characteristics and supporting data on conjugated linoleic acid, diglycerides, medium-chain triglycerides, green tea, ephedrine, caffeine, capsaicin and calcium, are examples of compounds that alter energy expenditure or appetite control.

## Dietary interventions

**Reduction of energy intake:** Functional foods are foods that are capable of demonstrating physiological effects and can reduce the risk of chronic diseases beyond their basic nutritional functions. Functional foods have the potential to reduce energy intake by inducing satiety. These foods can increase the sense of fullness and discourage overeating thereby reducing energy intake. There are three strategies that can be used to increase satiety. These include;

- Modification of the energy density of the diet;
- Modification of the macronutrient composition of the diet; and
- Modification of the glycemic index of the diet. Satiety is physiologically associated with the total volume of food consumed.

Therefore, modification of the energy density could contribute to the reduction of total energy intake and therefore reduce obesity and overweight.<sup>36</sup> One physiological signal for satiety may relate to the total weight or volume of food ingested. This suggests that modifying the energy density of the diet could be a way to reduce total energy intake and therefore reduce obesity. The main determinant of energy density is the non-caloric content of the food, primarily the water content. Foods with high water content have a lower energy density.<sup>37,38</sup>

Research has shown that fiber also reduces energy density since it contributes substantially more to food weight than to caloric content. Dietary fiber intake seems to affect total energy intake. Increase in fiber diets have been linked to lower food intake. This is due to the fact that fiber diets may trigger maximal sensory stimulation in the mouth due to the increased need for chewing, reduce gastric emptying

and a slow rate of nutrient absorption and reduce the energy density of the overall diet. Moreover, scientific investigations have shown that increase in dietary fiber is generally thought to aid in weight management.<sup>39</sup>

Further, macronutrient composition of a diet can affect its energy density. Some reports have revealed that fat has a higher energy-density than either protein or carbohydrate. Therefore reducing the proportion of fat in the diet can have a major impact on reducing the energy density of the diet. Previous reports show that reducing energy density reduces energy intake (at least in the short term), functional foods aimed at modifying energy density may be useful in managing obesity.<sup>36</sup>

The glycemic index of a food is determined by the level of postprandial glucose that occurs after eating that food in relation to the rise in glucose seen after eating a standardized food such as white bread. High glucose levels following eating would stimulate insulin secretion which may consequently increase appetite and facilitate other disease processes linked to insulin action. Whether or not the glycemic index of the diet affects energy intake and obesity remains controversial. There is no convincing evidence that food intake is directly related to glycemic index, although there is some evidence that high glycemic diets are linked to weight gain. The glycemic index of the total diet could be modified by eating foods with a low glycemic index. If the glycemic index were shown to affect food intake, a good target would be to develop more good-tasting, low-glycemic foods.<sup>40</sup>

### Functional foods to increase energy expenditure

Increase in the total energy expenditure without increasing energy intake is another approach for the management and/or prevention of obesity. Some bioactive compounds mostly known as nutraceuticals which are present in functional foods are capable of enhancing energy expenditure.

**Caffeine and ephedrine:** A combination of caffeine and ephedrine has shown to be effective in long-term weight management, likely due to different mechanisms that may operate synergistically, e.g., respectively inhibiting the phosphodiesterase-induced degradation of cAMP and enhancing the sympathetic release of catecholamines. There has, however, been recent concern about the longterm safety of ephedrine.<sup>41</sup>

**Tea:** Green tea, by containing both tea catechins and caffeine, may act through the inhibition of catechol O-methyl-transferase and the inhibition of phosphodiesterase. Here, the mechanisms may also operate synergistically. In addition, tea catechins have antiangiogenic properties that may prevent the development of obesity. Furthermore green, black and oolong teas may cause decreased energy intake from the gastrointestinal tract due to their interactions with pancreatic lipase. Previous reports have shown that bioactive components present in some teas (catechin and epigallocatechin-3-gallate) are capable of enhancing weight loss.<sup>42,43</sup> Furthermore polyphenols such as L-epicatechin, epicatechin-3-gallate, epigallocatechin, epigallocatechin-3-gallate which were isolated from tea extracts are potent inhibitors of pancreatic lipase which contributes to weight loss.<sup>44,45</sup>

Oolong tea also contribute to increasing energy expenditure, perhaps through its catechin content. Resting metabolic rate was increased by 3–4% during three days of oolong tea consumption at five cups per day. Interestingly, most of the rise in metabolic rate was from increased fat oxidation, which would have the greatest impact upon decreasing body fat stores.<sup>46</sup> The mechanism for increasing

energy expenditure by green tea has been postulated to be its flavonoid content and even more specifically its polyphenolic content. One class of these compounds, the catechins, has been shown to inhibit catechol O-methyltransferase (COMT), an enzyme that degrades norepinephrine.<sup>47</sup> Although there are numerous catechins in green tea, probably the most influential is epigallocatechin gallate (EGCG). This cannot be obtained in appreciable amounts from any other food source. The inhibition of COMT by catechins allows norepinephrine to exert a prolonged influence on thermogenesis and fat metabolism. Both of these metabolic processes are controlled by the sympathetic nervous system via norepinephrine. The delay in degrading norepinephrine allows it to remain in the sympathetic synaptic cleft longer and there for exert its effect. Caffeine also has an effect on norepinephrine by inhibiting phosphodiesterases and prolonging the life of cAMP in the cell. These actions coupled with the sustained effect of norepinephrine caused by EGCG greatly affect thermogenesis.<sup>48</sup>

**Capsaicin:** Capsaicin the main bioactive compound in pepper fruits has been shown to be effective in the management of obesity but when it is used clinically it requires a strong compliance to a certain dosage. This dosage has not been shown to be feasible yet. Scientists are reporting new evidence that capsaicin may cause weight loss and fight fat buildup by triggering certain beneficial protein changes in the body.<sup>49</sup>

**Calcium:** Recent reports have revealed that diets rich in calcium may contribute to weight loss and that part of the mechanism may be an increase in energy expenditure.<sup>50</sup> In some previous studies, high Ca intake was associated with a lower BMI, but there has yet been no clear demonstration that this is a causal relationship.<sup>51</sup>

### Other compounds helpful in weight reduction

**Brain serotonin:** An experimental investigation conducted by Bell & Goodrick<sup>47</sup> revealed that brain serotonin can reduce overeating. This work suggests a role for amino acids in regulating food intake. The brain neurotransmitter serotonin is produced via the conversion of tryptophan to 5-HTP. Serotonin enhances energy balance and induces the circadian patterns of eating (i.e., three times a day) by activating the neurons responsible for satiety in the medial hypothalamus. Serotonin also decreases rate of appetite and carbohydrate intake by interacting with norepinephrine antagonistically.

**Dietary chromium:** Dietary chromium is an essential trace element that is capable of enhancing insulin action. Chromium deficiency can lead to impaired glucose metabolism, insulin resistance and hyperglycemia. Supplementation can reduce the severity of these symptoms. Adequate insulin utilization can lead to decrease in body fat. In addition, correcting insulin resistance may have a positive effect on muscle mass by slowing its catabolism.<sup>52</sup>

### Naturally occurring bioactive compounds

Some bioactive compounds such as phenolic compounds, lipoic acid and n-3 LC-PUFA have been discovered to have antiobesity activity.

**Phenolic compounds:** Some in vivo and in vitro experiments have shown the anti-obesity activity of some flavonoids and phenolic acid. Mahat et al.,<sup>53</sup> reported that flavonoids such as kaempferol, apigenin and luteolin have the ability to block molecular mechanisms involved in triggering the inflammatory response, especially the signaling pathway of the transcription factor NF- $\kappa$ B, which increases the expression of genes that encode proteins involved in obesity-related inflammation

Apigenin is capable of reducing food intake by inducing gene expression of anorexigenic neuropeptides.<sup>54</sup> The potential of kaempferol to increase energy expenditure Kaempferol may cause increase in skeletal myocyte oxygen consumption and high energy expenditure da Silva et al.<sup>55</sup> Furthermore, the anti-inflammatory, anti-oxidant and proapoptotic effects of quercetin have been linked to its antiobesity activity. An animal experiment conducted by Stewart et al.,<sup>56</sup> using mice fed with high fat diet revealed that there was increase in energy expenditure due to the supplementation of the rat feed with quercetin. The anti obesity activity of reveratrol has been linked with its ability to decrease lipid synthesis in adipocytes by PPAR- $\gamma$  suppression, increase lipolysis and reduce lipid accumulation in maturing preadipocytes,<sup>57,58</sup> through the inhibition of lipogenesis and differentiation of 3T3-L1 adipocytes *via* activation of AMPK in a dose-dependent manner<sup>59</sup> and inhibition of adipogenesis by means of GSH up-regulation.<sup>60</sup>

Curcumin is the most important polyphenolic compound in turmeric (*Curcuma Longa L.*) which is a rhizome ginger (*Zingiber officinale*). Ejaz et al.,<sup>61</sup> reported that curcumin can reduce body weight gain and adiposity, decrease serum cholesterol, suppress angiogenesis in adipose tissue, inhibits adipocyte differentiation<sup>62,63</sup> and decrease lipid accumulation by reducing the expression of fatty acid synthase (FAS).

Some reports have revealed the potentials of catechins (the most abundant phenolic compound present in tea and beverages) in the management of obesity. Wang et al.,<sup>64</sup> and Basu et al.,<sup>65</sup> reported that catechins are capable of improving body composition and lower and reduce oxidative. In an experiment involving diabetic patients, it was reported that catechin rich beverages reduced body weight, increased adiponectin secretion and recovered insulin secretory ability and abdominal adiposity in moderately overweight subjects. In diabetic subjects, catechin-rich beverages have also contributed to reducing body weight, increasing adiponectin secretion and recovering insulin-secretory ability.<sup>66</sup> Other researchers have also linked the anti-obesity activity of catechins to their ability to reduce adipocyte differentiation, proliferation, lipogenesis,<sup>59,67,68</sup> fat mass, body weight, oxidised LDL-c and blood pressure and can improve glycemic control.<sup>69–72</sup> Furthermore phenolic acids have been reported to inhibit adipocyte proliferation and enzymes involved in carbohydrate metabolism and lipid pathways and improve adipocyte metabolism.<sup>73–76</sup> Son et al.,<sup>77</sup> also reported the antiobesity activity of ferulic acid and its derivative, gamma-oryzanol which was associated with regulation of insulin secretion and hepatic glucose-regulating enzyme activities which reduces the risk of hyperglycemia induced by high fat

**n-3 Long-chain polyunsaturated fatty acids:** Some experimental investigations have revealed that some polyunsaturated fatty acids such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) show some physiological effects in the adipose tissue. In-vitro studies reported by 89-92 revealed the EPA and DHA has the capacity to inhibit adipocyte differentiation, increase cell apoptosis and up-regulate the expression of PPAR- $\gamma$ , proteins that enhance glucose uptake and improve insulin resistance. Furthermore, results from in vivo experiment conducted by Flachs et al.,<sup>78</sup> and Perez-Matute et al.,<sup>79</sup> revealed that EPA improved insulin resistance and hypolipidemia in animals fed with a high-fat diet, reduces adipose tissue inflammation and visceral adiposity, increases adipocyte apoptosis and serum adiponectin and up-regulates mitochondrial biogenesis, which may induce  $\beta$ -oxidation in white fat.

**Lipoic acid:** Lipoic acid is an organo-sulfur compound derived from caprylic acid that acts as a co-factor of mitochondrial enzymes. It is synthesised in the human body, but is also present in foods and has

gain much interest due to its therapeutic potential.<sup>80</sup> Lipoic acid has been considered to be effective in the management of obesity due to its ability to modulate adipogenesis<sup>81</sup> and induce the release of adipokines, such as leptin, adiponectin and apelin. The anti-obesity mechanisms of lipoic acid improve mitochondrial function via the stimulation of organelle biogenesis and consistent activation of Beta oxidation metabolic pathway.<sup>82,83</sup> Prieto-Hontoria et al.,<sup>84</sup> and Salinthonne et al.,<sup>85</sup> associated the antiobesity activity of lipoic acid to reduction of inflammation *via* cAMP, prevention of high-fat diet induced weight gain, slight increase in apelin expression and decrease in intestinal sugar uptake and insulin resistance.

## Medicinal plants

Herbal supplements are common therapies for weight loss and are used as complementary and alternative therapeutic approach for the treatment and/or management of obesity.<sup>86</sup> Many natural bioactive compounds and medicinal plants, including crude extracts and isolated compounds from plants can be used to induce weight loss and prevent diet-induced obesity. Many researchers have reported the use of herbal supplements in the management of obesity due to containing a large variety of several components with different anti-obesity and anti-oxidant effects on body metabolism and fat oxidation.

Anti-obesity activity of some medicinal plants have been linked to the reduction in lipid absorption, reduced energy intake, increased energy expenditure, decreased pre-adipocyte differentiation and proliferation, or decreased lipogenesis and increased lipolysis.

Moreover, chitosan, levan, mate tea, oolong tea, jasmine tea and green tea have been reported to inhibit pancreatic lipase.<sup>87–92</sup> Further medicinal plants such as turmeric, capsicum, palm oil, banana leaf, brown algae, flaxseed, garlic and soybean are capable of preventing adipocyte differentiation.<sup>93–96</sup> Okuda et al.,<sup>90</sup> and Smyth & Heron<sup>97</sup> reported that herb teas and cinnamon enhances lipid metabolism while pine nut, pomegranate leaf and ginseng helps to decrease appetite.<sup>98–100</sup> Yun<sup>101</sup> reported that *Nigella Sativa* showed was able to enhance weight loss and re-duce waist circumference with a mild reduction in fasting blood sugar, triglycerides and low-density lipoprotein levels.<sup>102</sup> Pistachio,<sup>103</sup> Psyllium Fibre,<sup>104</sup> black Chinese Tea,<sup>43</sup> *Camellia Sinensis*,<sup>105</sup> Yacon Syrup,<sup>106</sup> Oolong Tea,<sup>107</sup> Xantigen<sup>108</sup> and olive oil<sup>109</sup> also show similar antiobesity activity with *Nigella sativa*. Furthermore, previous reports on the anti-obesity effects of whole grain, pistachio, virgin olive oil and nuts revealed that these herbal plants were capable of reducing obesity.<sup>110,111</sup>

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## Conflict of interest

The author declares no conflict of interest.

## References

- Putnam J, Allshouse J, Kantor LS. U. S. per capita food supply trends: more calories, refined carbohydrates, and fats. *Food Review*. 2002;25(3):2–15.
- Nielsen SJ, Siega-Riz AM, Popkin BM. Trends in energy intake in US. between 1977 and 1996; similar shifts seen across age groups. *Obes Res*. 2002;10(5):370–378.
- Kant AK. Consumption of energy-dense, nutrient-poor foods by adult Americans: nutritional and health implications. The Third National Health and Nutrition Examination Survey, 1988–1994. *Am J Clin Nutr*. 2000;72(4):929–936.

4. Zizza C, Siega-Riz AM, Popkin BM. Significant increase in young adults' snacking between 1977–1978 and 1994–1996 represents a cause for concern! *Prev Med.* 2001;32(4):303–310.
5. Harnack L, Stang J, Story M. Soft drink consumption among U. S. children and adolescents: nutritional consequences. *J Am Diet Assoc.* 1999;99(4):436–441.
6. Ludwig DS, Peterson KE, Gortmaker SL. Relation between consumption of sugar-sweetened drinks and childhood obesity: a prospective, observational analysis. *Lancet.* 2001;357(9255):505–508.
7. French SA, Story M, Jeffery RW. Environmental influences on eating and physical activity. *Annu Rev Public Health.* 2001;22:309–335.
8. Bray GA, Popkin BM. Dietary fat intake does affect obesity! *Am J Clin Nutr.* 1998;68(6):1157–1173.
9. Young LR, Nestle M. The contribution of expanding portion sizes to the obesity epidemic. *Am J Public Health.* 2002;92(2):246–249.
10. McCrory MA, Fuss PJ, Hays NP, et al. Overeating in America: association between restaurant food consumption and body fatness in healthy adult men and women ages 19–80. *Obes Res.* 1999;7(6):564–71.
11. Yi Zhang, Ju Liu, Jianliang Yao, et al. Obesity: Pathophysiology and Intervention. *Nutrients.* 2014;6(11):5153–5183.
12. Wilhelmsen L, Rosengren A, Eriksson H, et al. Heart failure in the general population of mendmorbidty, risk factors and prognosis. *J Intern Med.* 2001;249(3):253–261.
13. Willett WC. Dietary fat plays a major role in obesity. *Obes Rev.* 2002;3(2):59–68.
14. Cordain L, Eaton SB, Sebastian A, et al. Origins and evolution of the western diet: Health implications for the 21<sup>st</sup> century. *Am J Clin Nutr.* 2005;81(2):341–354.
15. Liu S, Willett WC, Manson JE, et al. Relation between changes in intakes of dietary fiber and grain products and changes in weight and development of obesity among middle aged women. *Am J Clin Nutr.* 2003;78(5):920–927.
16. Ludwig DS. Dietaryglycemicindex and obesity. *J Nutr.* 2000;130(2):280S–283S.
17. Cosford R. Insulin resistance, obesity and diabetes: the connection. *J Aus Coll Nutr Environ Med.* 1999;18(1):3–10.
18. polonski K, Given B, Van Cauter E. Twenty-four hour profiles and pulsatile patterns of insulin secretion in normal and obese subjects. *J Clin Invest.* 1988;81(2):442–448.
19. Bes-Rastrollo M, van Dam RM, Martinez-Gonzalez MA, et al. Prospective study of dietary energy density and weight gain in women. *Am J Clin Nutr.* 2008;88(3):769–777.
20. Savage JS, Marini M, Birch LL. Dietary energy density predicts women's weight change over 6y. *Am J Clin Nutr.* 2008;88(3):677–684.
21. Soriguer F, Moreno F, Rojo-Martínez G, et al. Monounsaturated n-9 fatty acids and adipocyte lipolysis in rats. *British J Nutr.* 2003;90(6):1015–1022.
22. Piers LS, Walker KZ, Stoney RM, et al. Substitution of saturated with monounsaturated fat in a 4-week diet affects body weight and composition of overweight and obese men. *British J Nutr.* 2003;90(3):717–727.
23. Massiera F, Saint-Marc P, Seydoux J, et al. Arachidonic acid and prostacyclin signaling promote adipose tissue development: a human health concern? *J Lipid Res.* 2003;44(2):271–279.
24. Chagnon YC, Rankinen T, Snyder EE, et al. The human obesity gene map: the 2002 update. *Obesity Res.* 2003;11(3):313–367.
25. Loos RJ, Bouchard C. Obesity – is it a genetic disorder? *J Intern Med.* 2003;254(5):401–425.
26. Zhang Y, Proenca R, Maffei M, et al. Positional cloning of the mouse obese gene and its human homologue. *Nature.* 1994;372(6505):425–432.
27. Montague CT, Farooqi IS, Whitehead JP, et al. Congenital leptin deficiency is associated with severe early-onset obesity in human. *Nature.* 1997;387(6636):903–908.
28. Willer CJ, Speliotes EK, Loos RJ, et al. Six new loci associated with body mass index highlight a neuronal influence on body weight regulation. *Nature Genet.* 2009;41(1):25–34.
29. Zellner DA, Loaiza S, Gonzalez Z, et al. Food selection changes under stress. *Physiol Behav.* 2006;87(4):789–793.
30. Dallman MF, Pecoraro N, Akana SF, et al. Chronic stress and obesity: A new view of “comfort food”. *Proc Natl Acad Sci.* 2003;100(20):11696–11701.
31. Doll HA, Petersen SEK, Stewart-Browan S. Obesity and physical and emotional well-being: associations between body mass index, chronic illness, and the physical and mental components of the SF-36 Questionnaire. *Obesity Res.* 2000;8(2):160–170.
32. Johannsen DL, Johannsen NM, Specker BL. Influence of parents' eating behaviours and child feeding practices on children's weight status. *Obesity.* 2006;14(3):431–439.
33. Blissett J, Meyer C, Haycraft E. Maternal and paternal controlling feeding practices with male and female children. *Appetite.* 2006;47(2):212–219.
34. Adam Wysokiski, Iwona Koszewska. Mechanisms of Increased Appetite and Weight Gain Induced by Psychotropic. *Journal of Advanced Clinical Pharmacology.* 2014;1:12–33.
35. Hil JO, Peters JC. Biomarkers and functional foods for obesity and diabetes. *Br J Nutr.* 2002;88(2):213–218.
36. Monika Choudhary, Kiran Grover. Development of functional food products in relation to obesity. *Functional Foods in Health and Disease.* 2012;2(6):188–197.
37. Rolls B, Barnett RA. *Volumetrics.* USA: Harper-Collins; 2000.
38. Grunwald GK, Seagle HM, Peters JC, et al. Quantifying and separating the effects of macronutrient composition and non-energetic food components on energy density. *Br J Nutr.* 2001;86(2):265–276.
39. Pereira MA, Ludwig DS. Dietary fiber and body weight regulation: observations and mechanisms. *Pediatr Clin North Am.* 2001;48(4):969–980.
40. Ludwig DS. Dietary glycemic index and body weight regulation. *Nutr Soc Aust.* 2000;24:286–293.
41. Yoshioka M, Doucet E, Drapeau V, et al. Combined effects of red pepper and caffeine consumption on 24h energy balance in subjects given free access to foods. *Br J Nutr.* 2001;85(2):203–211.
42. Wang H, Wen Y, Du Y, et al. Effects of catechin enriched green tea on body composition. *Obesity.* 2009;18(4):773–779.
43. Kubota K, Sumi S, Tojo H, et al. Improvements of mean body mass index and body weight in preobese and overweight Japanese adults with black Chinese tea [Pu-Erh] water extract. *Nutr Res.* 2011;31(6):421–428.
44. Nakai M, Fukui Y, Asami S, et al. Inhibitory effects of oolong tea polyphenols on pancreatic lipase in vitro. *J Agric Food Chem.* 2005;53(11):4593–4598.
45. Thielecke F, Boschmann M. The potential role of green tea catechins in the prevention of the metabolic syndrome—a review. *Phytochemistry.* 2009;70(1):11–24.
46. Rumpler W, Seale J, Clevidence B, et al. Oolong tea increases metabolic rate and fat oxidation in men. *J Nutr.* 2001;131(11):2848–2852.

47. Kao YH, Hiipakka RA, Liao S. Modulation of endocrine systems and food intake by green tea epigallocatechin gallate. *Endocrinology*. 2000;141(3):980–987.
48. Bell SJ, Goodrick GK A. Functional Food Product for the Management of Weight. *Crit Rev Food Sci Nutr*. 2002;42(2):163–178.
49. Diepvens K, Westerterp KR, Plantenga MS. Obesity and thermogenesis related to the consumption of caffeine, ephedrine, capsaicin, and green tea. *AJP – Regu Physiol*. 2007;292(1):77–85.
50. Zemel MB, Shi H, Greer B, et al. Regulation of adiposity by calcium. *FASEB Journal*. 2000;14(9):1132–1138.
51. Davies KM, Heaney RP, Recker RR, et al. Calcium intake and body weight. *JCEM*. 2000;85(12):4635–4638.
52. Bahadori B, Wallner S, Schneider H, et al. Effect of chromium yeast and chromium picolinate on body composition of obese, non-diabetic patients during and after a formula diet. *Acta Medica Austriaca*. 1997;24(5):185–187.
53. Kaats GR, Blum K, Pullin D, et al. A randomized, double-masked, placebo controlled study of the effects of chromium picolinate supplementation on body composition: A replication and extension of a previous study. *Curr Ther Res*. 1998;59(6):379–388.
54. Mahat MY, Kulkarni NM, Vishwakarma SL, et al. Modulation of the cyclooxygenase pathway via inhibition of nitric oxide production contributes to the anti-inflammatory activity of kaempferol. *Eur J Pharmacol*. 2010;642(1–3):169–176.
55. Myoung HJ, Kim G, Nam KW. Apigenin isolated from the seeds of *Perilla frutescens britton var crispa* (Benth.) inhibits food intake in C57BL/6J mice. *Arch Pharm Res*. 2010;33(11):1741–1746.
56. da-Silva WS, Harney JW, Kim BW, et al. The small polyphenolic molecule kaempferol increases cellular energy expenditure and thyroid hormone activation. *Diabetes*. 2007;56(3):767–776.
57. Stewart LK, Soileau JL, Ribnicky D, et al. Quercetin transiently increases energy expenditure but persistently decreases circulating markers of inflammation in C57BL/6J mice fed a high-fat diet. *Metabolism*. 2008;57(7 Suppl 1):S39–S46.
58. Fischer-Posovszky P, Kukulus V, Tews D, et al. Resveratrol regulates human adipocyte number and function in a Sirt1-dependent manner. *Am J Clin Nutr*. 2010;92(1):5–15.
59. Picard F, Kurtev M, Chung N, et al. Sirt1 promotes fat mobilization in white adipocytes by repressing PPAR- $\gamma$ . *Nature*. 2004;429:771–776.
60. Chen S, Li Z, Li W, et al. Resveratrol inhibits cell differentiation in 3T3-L1 adipocytes via activation of AMPK. *Can J Physiol Pharmacol*. 2011;89(11):793–799.
61. Vigilanza P, Aquilano K, Baldelli S, et al. Modulation of intracellular glutathione affects adipogenesis in 3T3-L1 cells. *J Cell Physiol*. 2011;226(8):2016–2024.
62. Ejaz A, Wu D, Kwan P, et al. Curcumin Inhibits Adipogenesis in 3T3-L1 Adipocytes and Angiogenesis and Obesity in C57/BL Mice. *J Nutr*. 2009;139(5):919–925.
63. Zhao J, Sun X-B, Ye F, et al. Suppression of fatty acid synthase, differentiation and lipid accumulation in adipocytes by curcumin. *Mol Cell Biochem*. 2011;351(1–2):19–28.
64. Kim CY, Le TT, Chen C, et al. Curcumin inhibits adipocyte differentiation through modulation of mitotic clonal expansion. *J Nutr Biochem*. 2011;22(10):910–920.
65. Wang H, Wen Y, Du Y, et al. Effects of catechin enriched green tea on body composition. *Obesity*. 2010;18(4):773–779.
66. Basu A, Sanchez K, Leyva MJ, et al. Green tea supplementation affects body weight, lipids, and lipid peroxidation in obese subjects with metabolic syndrome. *J Am Coll Nutr*. 2010;29(1):31–40.
67. Nagao T, Meguro S, Hase T, et al. A Catechin-rich Beverage Improves Obesity and Blood Glucose Control in Patients With Type 2 Diabetes. *Obesity*. 2008;17(2):310–317.
68. Kim H, Sakamoto K. (-)-Epigallocatechin gallate suppresses adipocyte differentiation through the MEK/ERK and PI3K/AKT pathways. *Cell Biol Int*. 2011;36(2):147–153.
69. Ueda M, Furuyashiki T, Yamada K, et al. Tea catechins modulate the glucose transport system in 3T3-L1 adipocytes. *Food Funct*. 2010;1(2):167–173.
70. Osam Kajimoto, Yoshitaka Kajimoto, Mitsuharu Yabune, et al. Tea Catechins with a Galloyl Moiety Reduce Body Weight and Fat. *J Health Sci*. 2005;51(2):161–171.
71. Nagao T, Komine Y, Soga S, et al. Ingestion of a tea rich in catechins leads to a reduction in body fat and malondialdehydemodified LDL in men. *Am J Clin Nutr*. 2005;81(1):122–129.
72. Nagao T, Hase T, Tokimitsu I. A green tea extract high in catechins reduces body fat and cardiovascular risks in humans[ast]. *Obesity*. 2007;15(6):1473–1483.
73. Wu CH, Lu FH, Chang CS, et al. Relationship among Habitual Tea Consumption, Percent Body Fat, and Body Fat Distribution. *Obesity*. 2003;11(9):1088–1095.
74. Hsu C-L, Huang S-L, Yen G-C. Inhibitory Effect of phenolic acids on the proliferation of 3T3 L1 preadipocytes in relation to their antioxidant activity. *J Agric Food Chem*. 2006;54(12):4191–4197.
75. Nagasaka R, Chotimarkorn C, Shafiqul IM, et al. Anti-inflammatory effects of hydroxycinnamic acid derivatives. *Biochem Biophys Res Commun*. 2007;358(2):615–619.
76. Hsu CL, Lo WH, Yen GC. Gallic acid induces apoptosis in 3t3-L1 pre-adipocytes via a fas- and mitochondrial-mediated pathway. *J Agric Food Chem*. 2007;55(18):7359–7365.
77. Ohara K, Uchida A, Nagasaka R, et al. The effects of hydroxycinnamic acid derivatives on adiponectin secretion. *Phytomedicine*. 2009;16(2–3):130–137.
78. Son MJ, Rico CW, Nam SH, et al. Effect of oryzanol and ferulic acid on the glucose metabolism of mice fed with a high-fat diet. *J Food Sci*. 2011;76(1):7–10.
79. Flachs P, Horakova O, Brauner P, et al. Polyunsaturated fatty acids of marine origin upregulate mitochondrial biogenesis and induce  $\beta$ -oxidation in white fat. *Diabetologia*. 2005;48(11):2365–2375.
80. Pérez-Matute P, Pérez-Echarri N, Martínez JA, et al. Eicosapentaenoic acid actions on adiposity and insulin resistance in control and high-fat-fed rats: role of apoptosis, adiponectin and tumor necrosis factor- $\alpha$ . *Br J Nutr*. 2007;97(2):389–398.
81. Gorąca A, Huk-Kolega H, Piechota A, et al. Lipoic acid – biological activity and therapeutic potential. *Pharmacol Rep*. 2011;63(4):849–858.
82. Cho KJ, Moon HE, Moini H, et al. Alpha-lipoic acid inhibits adipocyte differentiation by regulating pro-adipogenic transcription factors via mitogen-activated protein kinase pathways. *J Biol Chem*. 2003;278(37):34823–34833.
83. Prieto-Hontoria PL, Pérez-Matute P, Fernández-Galilea M, et al. Lipoic acid inhibits leptin secretion and Sp1 activity in adipocytes. *Mol Nutr Food Res*. 2011;55(7):1059–1069.
84. Fernández-Galilea M, Pérez-Matute P, Prieto-Hontoria P, et al. Effects of lipoic acid on apelin in 3T3-L1 adipocytes and in high-fat fed rats. *J Physiol Biochem*. 2011;67(3):479–486.
85. Prieto-Hontoria PL, Pérez-Matute P, Fernández-Galilea M, et al. Lipoic acid prevents body weight gain induced by a high fat diet in rats: effects on intestinal sugar transport. *J Physiol Biochem*. 2009;65(1):43–50.

86. Salinthon S, Yadav V, Schillace RV, et al. Lipoic Acid Attenuates Inflammation via cAMP and Protein Kinase A Signaling. *PLoS ONE*. 2010;5(9):1–10.
87. Barnes PM, Powell-Griner E, McFann K, et al. Complementary and alternative medicine use among adults: United States, 2002. *Adv Data*. 2004;343:1–19.
88. Bondiolotti G, Bareggi SR, Frega NG. Activity of two different polyglucosamines, L11 2o and FF45o, on body weight in male rats. *European journal of pharmacology*. 2007;567(1–2):155–158.
89. Kang SA, Hong K, Jang KH, et al. Altered mRNA expression of hepatic lipogenic enzyme and PPAR $\alpha$  in rats fed dietary levan from *Zymomonas mobilis*. *J Nutr Biochem*. 2006;17(6):419–426.
90. Martins F, Noso TM, Porto VB, et al. Maté tea inhibits in vitro pancreatic lipase activity and has hypolipidemic effect on high-fat diet-induced obese mice. *Obesity*. 2009;18(1):42–47.
91. Okuda H, Han L, Kimura Y. Anti-Obesity Action of Herb Tea. (Part 1). Effects of Various Herb Teas on Noradrenaline Induced Lipolysis in Rat Fat Cells and Pancreatic Lipase Activity. *Japanese Journal of Constitutional Medicine*. 2001;63(1–2):60–65.
92. Koo SI, Noh SK. Green tea as inhibitor of the intestinal absorption of lipids: potential mechanism for its lipid-lowering effect. *J Nutr Biochem*. 2007;18(3):179–183.
93. Hsu TF, Kusumoto A, Abe K, et al. Polyphenol-enriched oolong tea increases fecal lipid excretion. *Eur J Clin Nutr*. 2006;60(11):1330–1336.
94. Ahn J, Lee H, Kim S, et al. Curcumin-induced suppression of adipogenic differentiation is accompanied by activation of Wnt/ $\beta$ -catenin signaling. *Am J Physiol Cell Physiol*. 2010;298(6):C1510–C1516.
95. Klein G, Kim J, Himmeldirk K, et al. Antidiabetes and anti-obesity activity of *Lagerstroemia speciosa*. *Evid Based Complement Alternat Med*. 2007;4(4):401–408.
96. Maeda H, Hosokawa M, Sashima T, et al. Fucoxanthin and its metabolite, fucoxanthinol, suppress adipocyte differentiation in 3T3-L1 cells. *Int J Mol Med*. 2006;18(1):147–152.
97. Ambati S, Yang JY, Rayalam S, et al. Ajoene exerts potent effects in 3T3-L1 adipocytes by inhibiting adipogenesis and inducing apoptosis. *Phytother Res*. 2009;23(4):513–518.
98. Smyth S, Heron A. Diabetes and obesity: the twin epidemics. *Nat Med*. 2006;12(1):75–80.
99. Kim JH, Hahm DH, Yang DC, et al. Effect of Crude Saponin of Korean Red Ginseng on High Fat Diet-Induced Obesity in the Rat. *J Pharmacol Sci*. 2005;97(1):124–131.
100. Lei F, Zhang XN, Wang W, et al. Evidence of anti-obesity effects of the pomegranate leaf extract in high-fat diet induced obese mice. *Int J Obes*. 2007;31(6):1023–1029.
101. Pasman WJ, Heimerikx J, Rubingh CM, et al. The effect of Korean pine nut oil on in vitro CCK release, on appetite sensations and on gut hormones in post-menopausal overweight women. *Lipids Health Dis*. 2008;7:10.
102. Yun JW. Possible anti-obesity therapeutics from nature—a review. *Phytochemistry*. 2010;71(14–15):1625–1641.
103. Datau EA, Wardhana, Surachmanto EE, et al. Efficacy of *Nigella sativa* on serum free testosterone and metabolic disturbances in central obese male. *Acta Med Indones*. 2010;42(3):130–134.
104. Li Z, Song R, Nguyen C, et al. Pistachio nuts reduce triglycerides and body weight by comparison to refined carbohydrate snack in obese subjects on a 12-week weight loss program. *J Am Coll Nutr*. 2010;29(3):198–203.
105. Pal S, Khossousi A, Binns C, et al. The effect of a fibre supplement compared to a healthy diet on body composition, lipids, glucose, insulin and other metabolic syndrome risk factors in overweight and obese individuals. *Br J Nutr*. 2011;105(1):90–100.
106. Lenon GB, Li KX, Chang YH, et al. Efficacy and safety of a chinese herbal medicine formula [RCM-104] in the management of simple obesity: a randomized, placebo-controlled clinical trial. *Evid Based Complement Alternat Med*. 2012;2012:435702.
107. Genta S, Cabrera W, Habib N, et al. Yacon syrup: beneficial effects on obesity and insulin resistance in humans. *Clin Nutr*. 2009;28(2):182–187.
108. He RR, Chen L, Lin BH, et al. Beneficial effects of oolong tea consumption on diet-induced overweight and obese subjects. *J Chin Integr Med*. 2009;15(1):34–41.
109. Abidov M, Ramazanov Z, Seifulla R, et al. The effects of Xanthigen in the weight management of obese premenopausal women with non-alcoholic fatty liver disease and normal liver fat. *Diabetes Obes Metab*. 2010;12(1):72–81.
110. Razquin C, Martinez J, Martinez-Gonzalez M, et al. A 3years follow-up of a Mediterranean diet rich in virgin olive oil is associated with high plasma antioxidant capacity and reduced body weight gain. *Eur J Clin Nutr*. 2009;63(12):1387–1393.
111. Li Z, Song R, Nguyen C, et al. Pistachio nuts reduce triglycerides and body weight by comparison to refined carbohydrate snack in obese subjects on a 12-week weight loss program. *J Am Coll Nutr*. 2010;29(3):198–203.