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Effect of different plant parts, as hypolipidemic agents on weight management and their mechanisms of action: A review

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ABSTRACT

Obesity is a major health problem worldwide and globally has reached epidemic Proportions. More than one billion over weight adults are detected with at least 300 million of them clinically considered obese. Obesity is associated with dyslipidemia and dietary intervention is one of the main aspects in the management of this epidemic. Thousands of biologically active phytochemicals have been identified in different plant parts with marked effects on body weight reduction and hypolipidemic action. The objective of this article is to present some animal and human experimental studies that examine the effect of different plant parts and families, and their nutrients on body weight reduction and some biomarkers of hyperlipidemic factors. The article is extended to explain the mechanisms of action by which these constituents could modulate biological processes related to obesity and hyperlipidemia in both animal and human studies.These phytochemicals can have complementary and overlapping mechanisms of action such as modulation of detoxification enzymes, stimulation of the immune system, reduction of platelet aggregation, modulation of cholesterol synthesis, hormones metabolism and antioxidant effects. So, plants whish human consumed daily could be used in body weight management, body fat reduction and decrease using drugs and chemicals which damage health.

***Keywords*: Obesity, hyperlipidemia, plant parts, phytochemicals, mechanisms of action.**

Introduction

Obesity is one of today's most visible-yet most neglected public health problems. Obesity is associated with a number of metabolic disorders including coronary heart disease, hypertension, stroke, certain cancers, non–insulin diabetes mellitus, gallbladder disease and dyslipidemia (AIHW, 2003). [1]. The World Health Organization (WHO) estimates that currently around one in every three in the world's adult is overweight, while nearly one in every ten is obese. According to the WHO Statistics, Egypt is the fattest African country and also is the 14th fattest country in the world with nearly 35% of its adult population, around 19 million Egyptians are obese. Such pattern is the highest rate across the globe. Among Egyptians, above the age of 15, overweight and obese females (76%) are more than males (64.5%). The rate of obesity in Egypt has markedly risen over the past 30 years. Egypt had the highest 26.3 average body mass index in the world and 1.6% of 2-6 year olds, 4.9% of 6-10 year olds, 14.7% of 10-14 year olds and 13.4% of 14-18 year olds were obese (WHO, 2015).

Dietary intervention is one of the main aspects in the management of obesity. Studies have shown that dietary fats are associated with obesity and a low fat diet was effective in weight loss in some people. However, the steady increase in the obesity rate in spite of the apparent decrease in fat consumption suggests that other dietary factors may be involved (Bray *et al.,* 2004). Thousands of biologically active phytochemical components have been identified in plant foods, e.g., grains, seeds, nuts, legumes, leaves, vegetables and fruit. In a Western diet alone, plant parts including roots, leaves, stems, fruit and seeds from more than 40 botanical families have the potential to contribute significant variety and complexity to the human diet. An extensive study on phytochemicals in cell-culture systems and animal models has provided a wealth of information on the mechanisms by which a diet rich in different plant parts may lower the risk of chronic diseases including obesity and hyperlipidemia in humans.

The objective of this article is to present some animal and human experimental studies that examine the effect of different plant parts on body weight reduction and some biomarkers of hyperlipidemic factors and show the mechanisms of action by which these plant parts could modulate

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biological processes related to obesity that may reduce the hyperlipidemic biomarkers in both animal and human studies.

Effect of different plant parts and their mechanisms of action:

1. Plant leaves:

1.1. Red cabbage *(Brassica oleracea):*

A study in 2013 revealed that there was a significant reduction in body weight of obese aged rats orally administered with red cabbage leaves anthocyanin rich extract by about 16.98% compared with control rats. Feeding obese aged rats with this extract showed a significant reduction in triglyceride level, total cholesterol, low density lipoprotein cholesterol (LDL) and very low density lipoprotein cholesterol (VLDL) compared with obese aged control rats (Nematallah, 2013). Anthocyanin fraction (cyanidin-3-glucoside) significantly increased the phosphorylation of adenosine monophosphate-activated protein kinase (AMPK) and acetyl-coenzyme A carboxylase (ACC) in the liver, suggesting a potential target for the prevention of obesity (Wu *et al.,* 2013). In hypercholestrolemic individuals, endothelial function can be impaired by dyslipidemia and mild chronic inflammation represented as increased total cholesterol or LDL-cholesterol concentrations. Supplementation with in anthocyanin rich diets or pure anthocyanin-rich extracts resulted in a decrease in serum triglyceride, total and LDL-cholesterol and an increase in serum high density lipoprotein cholesterol (HDL-C) in different animal models (Rogers and Fuke, 2006).

1.2. Parsley leaves *(Petroselinum crispum):*

Parsley leaves extracts caused a significant reduction in body weight of rats from zero time to the end of the experimental period (30 days) and the reduction in body weight reached 13.98% compared with zero time. Parsley leaves significantly reduced serum total cholesterol, LDL, VLDL and triglycerides levels compared with control rats (Nematallah *et al.,* 2007). The reduction in body weight caused by parsley leaves may be a result of the diuretic effect of parsley. The hypolipidemic effect of parsley may be attributed to inhibition of oxidative damage of hepatic tissues due to its antioxidant effects. The essential oil contents of parsley plays a significant role in the scavenging effect on free radicals as well as the flavonoid rich components (Darias *et al*., 2001; Ozsoy-Sacan *et al.,* 2006).

Positive changes in serum total and LDL–C levels at the end of a trail of feeding hypercholesterolemic rats on parsley leaves (30%) were observed. Parsley food fragment is devoted as the most effective potential agent against cholesterolemia, promoting mechanisms of liver protection against oxidative stress induced by cholesterolemia and thus protecting liver from hypercholesterolemia complications (Ahmed *et al*., 2010).

1.3. Spinach leaves *(Spinacia oleracea):*

Feeding obese rates on 10% spinach leaves powder in the diet caused a significant reduction in body weight compared with negative and positive control rats and the reduction reached 26.83%. It was found that spinach leaves powder caused a more body weight loss than other diets. There were a significant reduction in the levels of lipids profile (Total cholesterol, LDL and VLDL) as a result of feeding on spinach leaves compared with positive control obese rats (fed on high fat diets). Feeding obese rats on spinach leaves powder caused an increase in serum lipase enzyme activity by 11.13% compared with negative control obese rats at zero time (Sahar *et al.,* 2013). Lipase enzyme activity is important because of its ability to hydrolyze triglycerides. The metabolic activities of human adipocytes has focused on plasma triacylglycerol hydrolysis and the uptake of fatty acids in adipose tissue by lipase enzyme. Consistent with the reduction of postprandial insulinemia and triacylglycerol, after a low glycemic index diet (spinach leaves), there was a significant reduction in lipase enzyme expression in adipose tissue and an increase in serum levels, which could have induced a reduction in fat depot (Kallio *et al.*, 2007).

2. Plant roots:

2.1. Red radish roots *(Raphanus sativus):*

It could be shown that no significant differences were found among the tested rat groups fed on different red radish parts (leaves, roots, seeds and whole plant) for lipids profile at zero time. The rat group fed on red radish roots was the most effective for the reduction of total lipids, triglycerides, total cholesterol and LDL-C levels which improved lipids profile especially the cholesterol components. Feeding on red radish roots increased the relative ratio of liver, kidney and brain weights compared to body weight of rats, while no effect was found for heart, spleen and lung weights (Dalia *et al.,* 2007). It was observed that radish lowered plasma cholesterol in mice fed on cholesterol-enriched diet. It is conceivable that the cholesterol lowering action of red radish could be due to the interference with exogenous cholesterol absorption and the effect of peroxidase on hyperlipidemia which may be a contributing factor in the prevention of hyperlipidemia (Balasinska *et al.,* 2005). Red radish roots contained also, anthocyanins (pelargonidin –3–glucoside) which had hypolipidemic effects through an enhancement of LDL-R gene expression and the clearance ability of LDL and a decrease in the lipid biosynthesis (Duchnowicz *et al.,* 2012).

2.2. Echinacea roots *(Echinacea purpurea):*

Administrating Echinacea ethanolic and water extracts orally to rats caused a significant decrease in body weight from zero time till the end of the experiment. The reduction in body weight was 10.37% and 14.89% for water and ethanolic extracts of Echinacea roots, respectively, compared with control aged rats at the end of the experiment. Echinacea ethanolic extract was more effective in weight loss compared with water extract. Administration of aged rats with Echinacea ethanolic extract lowered their triglycerides levels from 273.47 to 153.60 mg/dl (43.83%), while the Echinacea water extract caused a 39.10% reduction value in triglycerides levels compared with control aged rats. When aged rats dose was 6 mg of thier Echinacea ethanolic or water extracts, the levels of total cholesterol, LDL and VLDL were significantly reduced compared with control aged rats. Ethanolic extract caused the highest reduction in lipids profile followed by water extract (Nematalla *et al.,* 2011). It was found that Echinacea root extracts suppressed the oxidation of human low density lipoprotein (LDL) as evaluated by reduced agarose electrophoretic mobility following oxidative modification by Cu^{2+}. The mechanisms of antioxidant activity of Echinacea extracts included free radical scavenging and transition metal chelating. Antioxidant activity was found to delay the formation of conjugated diene hydroperoxide and extend the lag phase of peroxidation (Hu and Kittsw, 2000).

2.3. Ginger roots *(Zingiber officinale):*

The loss in body weight as a result of orally administration of the ginger roots water extract (2 ml) for rats once daily before meal reached 15.92% reduction compared with control rats. Ginger root extract, also, caused a significant reduction in the levels of serum total, LDL-C, VLDL-C and triglycerides compared with control rats (Nematallah *et al.,* 2007). Consumption of ginger roots extract may be proven beneficial in attenuation of atherosclerosis development, since it as associated with reduced macrophage-mediated oxidation of LDL, reduced uptake of oxidized LDL by macrophages, reduced oxidative state of LDL and reduced LDL aggregation. All these effects lead to a reduced cellular cholesterol accumulation and foam cell formation and this may be related to the fact that ginger roots extract can act as a free radical scavenger which reduced LDL oxidative state (Fuhrman *et al.,* 2000).

3. Plant fruits:

3.1. Bitter orange fruits *(Citrus aurantium):*

Bitter orange extract caused a significant body weight loss (1.4 kg) and body fat (an average change of 2.9%) in overweight adults. Adrenergic amines extracted from bitter orange induced an increase in metabolic rate and enhanced the thermic response to the meal. The epinephrine excretion increased by 2.4 folds when bitter orange was added to the meal. Bitter orange extract is a rich source of vitamin C (an important water soluble antioxidant), polyphenols, flavonoids, chlorogenic acids and other cinnamates nature. These antioxidants have an influence on lipids metabolism and lipids oxidation in hypercholesterolemic rats as a group of metabolic protective agents (Gougeon *et al.,* 2005 ; Leontowicz *et al.,* 2002).

3.2. Blueberry fruits *(Vaccinium angustifolium):*

It was found that mice fed on the high fat diet plus purified anthocyanins from blueberries in drinking water had a lower body weight gain and a body fat than that fed on the high fat (controls). Anthocyanins feeding (as the whole blueberry) did not prevent, and may have actually increase obesity. However, administration of purified anthocyanins from blueberries or strawberries reduced obesity. Consumption of purified anthocyanins can significantly inhibit body weight gain, lower the size of adipocytes, attenuate lipid accumulation and decrease leptin secretion (Luke *et al.,* 2008 ; Hwang *et al.*2011). Anthocyanin prevents or reverses hypercholesterolemia-induced endothelial dysfunction by inhibiting cholesterol and 7-oxysterol accumulation in the aorta of mice fed on anthocyanins compared with mice fed on a high cholesterol diet. The cholesterol oxidation product, 7-ketocholesterol, increased to 180.1 µg/ml in the control emulsion, while it was only 15.4 and 39.0 µg/ml in the emulsions containing 1 µg/ml of the anthocyanin and tocol extracts, respectively. Anthocyanin extract was relatively greater than tocol extract in stabilizing cholesterol (Zhang *et al.,* 2013).

4. Plant seeds:

4.1. Fennel seeds *(Foeniculum vulgare):*

Aqueous extract (350 mg/kg b. w.) of fennel seeds administered to diabetic rats increased final body weight, body weight gain (25.1±7.5%) and food efficiency ratio value compared with diabetic control rats. In diabetic rats, lipids profile were significantly increased, while the diabetic group which received fennel seeds extract had significantly lower levels of serum total cholesterol (35.9%), triglycerides (43.4%) and LDL–C levels (41.8%) compared with diabetic control group. The phytochemicals found in fennel seeds extract which were responsible for its effect were tannins, resins, terpenes, flavonoids and carbohydrates. So, it is advised to give an aqueous extract of fennel seeds to the patients with hyperlipidemia (El-Badrawy *et al.,* 2010).

4.2. Soybean seeds *(Glycine max):*

The fact that must be kept in mind is that, excess fat in diet is the main causative agent for relatively massive body weight gain as well as lipidemia. Normal rats make 1.11fold increase in final to initial body weight in a month and half period according to dietary pattern used, meanwhile, an increase to almost 1.40 fold for positive control rats fed on hypercholesterolemic diet was recorded. There were a significant reduction in total cholesterol, triglycerides and LDL-C levels at the end of the experiment relative to initial time or positive control rats as a result of feeding on soybean seeds (defatted soybean extrudate). The reduction of blood cholesterol by soybean seeds may be in part due to the higher plant protein content with high quality amino acids. Therefore, triglycerides levels and related VLDL-C value were less in rats fed on soybean protein than that fed on casein. The higher VLDL–C uptake could be responsible for the hypotriglyceridemia in rats fed on soybean protein. There is no doubt that dietary protein affect plasma cholesterol concentration, this effect is variable but is generally greater in hypercholesterolemic than in normocholesterolemic subjects (Maha *et al.,* 2008) [25]. It was found that rats fed on casein led to significant higher values in body weight gain than rats fed on soy protein. Total and LDL cholesterol levels were 18% lower in soybean rats group compared to casein group. Serum and hepatic cholesterol and triglyceride levels as well as LDL and VLDL-C were significantly lower in rats fed on soybean seeds protein than in rats fed on casein diet up to 160 days (Tovar *et al.*, 2005). Soy protein intake significantly decreased triglyceride levels by 43.1% in hyperlipidemic subjects as a result of high isoflavones intake from soybean seeds besides soy protein which led to a greater decrease in serum LDL-C than low isoflavones intake, demonstrating that isoflavones in soy seeds have LDL cholesterol-lowering effects independent of soy protein (Chen *et al.,* 2005).

4.3. Flaxseeds *(Linum usitatissimum):*

It was proposed that the cholesterol-lowering effect of flaxseeds meal is more likely due to lignan content which combined with bile acids and prevented cholesterol reabsorption. It was found that, 10% flaxseed diet did not affect serum lipids but 20% and 30% flaxseed diets lowered plasma total cholesterol by 21% and 33%, respectively. Plasma triglyceride concentration in obese rats was reduced, also, by 37% in rats fed on flaxseed meal and by 19% in rats fed on soy protein compared to those fed on casein (Bhathena *et al.,* 2003).

4.4. Fenugreek seeds *(Trigonella foenum-graecum):*

Rats were administered fortified bread with fenugreek seeds which decreased feed intake and body weight gain (%). The percent liver weight to body weight was decreased, serum cholesterol, triglycerides, LDL and VLDL cholesterol were, also, decreased as compared to the positive control group. Oral administration of aluminum chloride ($Alcl_3$) to rats during 5 months enhanced the levels of lipid peroxidation in brain, liver and plasma together with lactate dehydrogenase activity, total cholesterol, triglycerides and LDL-C levels. All these parameters were decreased as a result of fenugreek seeds supplementation either as fenugreek seed powder (5%) or fenugreek seed extract (100 mg/kg) (Mohamed, 2013; Yosra *et al.,* 2012). It was observed that fenugreek can ameliorate dyslipidemia in diabetic obese rats fed a control, a high fat diet or a high fat diet containing 0.5% or 2% fenugreek for 4 weeks. Hepatic and plasma triglycerides and mRNA expression levels of lipogenic genes were lower in the 2% but not changed in the 0.5% fenugreek group than in the control group. The hydrolyzed saponin fraction (diosgenin) in fenugreek inhibited the accumulation of triglycerides in hepatic cells. The inhibitory effect of fenugreek on the mRNA induction of lipogenic genes in the liver caused the suppression of lipid accumulation in the liver and decreased the plasma triglycerides concentration in mice fed high fat diet. It is likely that the decrease was due to the fenugreek-dependent decrease in the hepatic triglycerides levels (Uemura *et al.,* 2011). Several mechanisms in addition to various components have been suggested to explain the lipid-lowering effect of fenugreek seeds. These include a direct effect on cholesterol metabolism by inhibiting the key enzymes involved in cholesterol and fatty acids synthesis. Precipitable protein/peptide or associated factors could be responsible for improvement in serum lipid profile through hypolipidemic effect on adipocytes and liver cells leading to decrease triglycerides and cholesterol synthesis in addition to enhanceLDL receptor-mediated LDL uptake (Vijayakumar *et al.,* 2010).

4.5. Sweet lupin seeds *(Lupinus albus):*

Sweet lupin seeds and therapeutic lifestyle changes were suggested as therapeutic interventions for the management of metabolic syndrome in human subjects for 6 months. The body weight, body mass index, blood pressure, total cholesterol, LDL, triacylglycerol, uric acid and alanine transaminase were markedly decreased by 26.85%, 26.95%, 13%, 53.84%, 57.84%, 36.14%, 47.58% and 61.62%, respectively, compared to those at baseline. In a randomized, parallel, double-blind, single study of 50 subjects for 12 weeks intervention: half of the participants consumed a sweet lupin seeds protein concentrate (30 g/day of protein), the other half consumed a lactose-free skimmed milk powder, both into a mixed low lipid diet. At the end of intervention, both groups showed similar reductions of total cholesterol against baseline (-6.7% and -7.2%, respectively) but the reduction of LDL cholesterol (-8.0%), non-HDL cholesterol (-7.5%) and proprotein convertase subtilisin/kexin type9 (PCSK9) (-12.7%) levels were statistically significant only after the sweet lupin diet (Harisa and Alanazi, 2015 ; Pavanello *et al.,* 2017). The intake of lupin concurrent with low carbohydrate diet induced body weight reduction as sweet lupin seeds has a low glycemic index due to the presence of anti-nutritional factors that may decrease the digestion and absorption of foodstuff. Body weight reduction was associated with reduction of triacylglycerol and LDL-C as well as increase in HDL–C, sweet lupin seeds up-regulates LDL receptors and down regulates cholesterol biosynthesis genes. Lupin interferes with cholesterol, also, enterohepatic circulation and decreases the accumulation of fat in the liver (Fontanari *et al.,* 2012).

4.6. Oat seeds *(Avena sativa):*

Three oat products were supplemented into high fat diets and fed to obese rats for 8 weeks. Each oat product decreased body weight, epididymal fat accumulation and serum inflammatory factor levels and significantly regulated serum lipid levels. Oat bran significantly reduced mean adipocyte size and tumor necrosis factor α-mRNA expression levels. The oat components shifted the overall structure of gut microbiota in obese rats which significantly correlated with total cholesterol, triacylglycerol, endotoxin and tumor cell necrosis factor α–levels in serum and mRNA expression levels. Oat products attenuated obesity and related metabolic disorders while modifying the gut microbiota composition and increased the total short-chain fatty acids concentration in colonic digesta (LinDong *et al.,* 2016). It was found that the high fat diet with 5% oat β-glucan significantly reduced body weight, epididymal and subcutaneous adipose tissue weights compared with high fat diet fed mice. Supplementation with β-glucan from oat seeds for 8 weeks also decreased fasting glycemia, area under glucose curve and triglyceride in serum. Dietary high fat diet with 5% oat β-glucan decreased lipid accumulation in hepatocytes and adipocyte size compared with mice from high fat diet group (Zhong *et al.,* 2015). In high fat diet fed rats, oat effectively reduced body weight and fat, and decreased food efficiency but not appetite. Oat lowered serum glucose, free fatty acid, triacylglycerol, cholesterol, LDL-C/HDL-C ratio and dose-dependently reduced hepatic triglycerides and cholesterol. 30% oat markedly reduced lipid synthesis biomarkers, while 15% and 30% oat stimulated expressions of oxidation markers and phosphorylated adenosine mono-phosphate protein kinase (AMPK). Oat increased LDL receptor, being beneficial for serum lipid-lowering (HueiPeng *et al.,* 2013).

5. Plant wastes:

5.1. Pea husks *(Pisum sativum):*

Diabetic control rats recorded food intake value lower than the normal control group fed on basal diet. A significant decrease of the mean value of food intake was observed in all diabetic rats fed on different levels of pea husks (4, 8 and 12%) as compared to the normal control group. Body weight gain in all treated groups which were fed on different levels of fibers from pea husks was decreased significantly. On the other hand, diabetic groups fed on 8 or 12% of pea husks showed a significant decrease in feed efficiency ratio as compared to the normal and diabetic control groups. Total serum cholesterol, triglyceride, low and very low density lipoprotein cholesterol levels showed a significant increase in control diabetic group compared with normal control rats, while these values recorded a significant decrease in diabetic groups fed on 8% and 12% pea husks as compared to both normal and diabetic control groups (Eman, 2008). The consumption of insoluble fiber-rich fraction diet relative to cellulose diet could effectively decreased the levels of serum total cholesterol, triglyceride and liver cholesterol, and increased the levels of total lipids, cholesterol and bile acids in feces. Fiber is recommended for weight loss on the basis of delayed gastric emptying and increased satiety thus caused a weight reduction and a dispose fat from the body. The marked cholesterol and lipid-lowering effects of insoluble fiber might be partly attributed to its ability to enhance the excretion of lipids and bile acids *via* feces (Chi and Ya, 2005).

5.2. Grape pomace *(Vitis vinifera):*

The industrial processing of grapes generates a high quantity of by-products called pomace which includes skins, seeds and rachis of grapes. Some preclinical *in vivo* studies on the capacity of grape pomace to prevent LDL oxidation has shown that, a 15% grape pomace in a cholesterol diet (0.3%) is able to reduce the rat liver and serum levels of cholesterol by half, while increasing high density lipoprotein by 26%. Grape pomace might be also used as a treatment to limit dietary fat absorption and the accumulation of fat in adispose tissue, through its activity on inhibition of the fat-metabolizing enzymes (pancreatic lipase and lipoprotein lipase). Thus, grape pomace have been promoted as a source of polyphenols (flavonoids, stilbenes and phenolic acids) which significantly ameliorated plasma lipid levels, the concentration of cholesterol-standardized tocopherol and the antioxidant capacity of plasma were significantly increased, while oxidized LDL and levels of LDL-cholesterol were significantly reduced (Dohadwala and Vita, 2009 ; Castilla *et al.,* 2006).

Conclusion

Obesity is a problem faced by many societies and it constitutes the main cause of metabolic syndrome. In most communities unhealthy diets and sedentary lifestyle are the main risk factors for the development of obesity. On the contrary, balanced diets, regular exercise and body weight control are essential for health quality. Diet and lifestyle are a major modifiable of hypertension, dyslipidemia, diabetes and obesity. Epidemiologic, animal models and human studies support the association between several plant parts intake and low risk of chronic diseases including hyperlipidemia, hyperglycemia and obesity. Plants are rich sources of a variety of nutrients including vitamins, trace minerals, dietary fiber and many other classes of biologically active compounds. These phytochemicals can have complementary and overlapping mechanisms of action such as modulation of detoxification enzymes, stimulation of the immune system, reduction of platelet aggregation, modulation of cholesterol synthesis, hormones metabolism and antioxidant effects. Elevated serum total cholesterol, LDL cholesterol and triacylglycerol levels as well as reduced HDL cholesterol level are identified risk factors for obesity and related diseases. Treatment of hypercholesterolemia has focused on increasing fecal excretion of cholesterol and bile acids and reducing hepatic cholesterol synthesis through diet modification and use of pharmacologic agents. The hypocholesterolemic effects and body weight reduction of several plant parts and their constituents have been discussed in the current article besides their mechanisms of actions.

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