Review

Medicinal plants and phytochemicals with anti-obesogenic potentials: A review

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**ABSTRACT**

Human mortality has been significantly increased in last few decades due to the increased prevalence of obesity and associated chronic disorders such as type 2 diabetes, non-alcoholic fatty liver disease, coronary heart disease and atherosclerosis. Apart from genetic and medicine or drug related side effects, nearly 90–95% people became obese due to the imbalanced calorie intake and lack of nutritional knowledge. The anti-obesogenic drugs, Orlistat and Sibutramine, which have been duly approved by Food and Drug Administration (FDA), USA, work very well on diet-induced obesity however they are not getting popular to the people with overweight/obesity due to the higher cost and severe side effects. In contrast, plant based drugs have been considered as a better alternative due to their lower cost and negligible side effects. A number of medicinal plants and their bioactive constituents have received attention from scientists not only for their anti-obesity activity in vitro and in vivo but also in clinical trials. However, there is no systematic review of data available in the scientific domain in order to guide researchers to conduct further in depth research. In our present review, we differentiated the anti-obesogenic effects of various medicinal plant extracts, fractions and their bioactive compounds at in vitro, in vivo and clinical conditions. During our review, we could also identify the most effective plants with strong anti-obesogenic effects at in vitro or in vivo studies with lack of clinical trials when no one tried to isolate pure bioactive compounds from these plants. Hence, scientific community, government agencies/pharmaceutical industries should work together not only to isolate pure bioactive compounds but also to conduct clinical trials including toxicity to develop better alternative anti-obesity drugs.

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**Abbreviations:**
AGT7, aquaporin 7; aP2, apo protein 2; Apo-A, apolipoprotein A; ATGL, adipose triglyceride lipase; Aebp1, adipocyte enhancer binding protein 1; ALT, alanine transaminase; AST, aspartate transaminase; AMPPK, AMP-activated protein kinase; CAT, catalase; ACC, acetyl-CoA carboxylase; AUC, area under the curve; CSL2, C5a like receptor 2; CPT-IL, carnitine palmitoyl transferase; CYP7A1, cholesterol 7a-hydroxylase; C/EBPα, CCAAT/enhancer-binding protein α; CPT-1, carnitine palmitoyl transferase-1; DGAT, diacylglycerol acyltransferase; FAS, fatty acid synthase; FABP2, fatty acid binding protein 2; FGF-2, fibroblast growth factor 2; G6PDH, glyceraldehyde 3-phosphate dehydrogenase; GLUT4, glucose transporter type 4; GPx, glutathione peroxidase; HDL, high density lipoproteins; HSL, hormone sensitive lipase; HMG-Co A R, 3-OH-3-methylglutaryl coenzyme A reductase; Lep, leptin; LDL, low density lipoproteins; LPL, lipoprotein lipase; IL6, interleukin 6; MCP-1, monocyte chemoattractant protein-1; MDA, malonaldehyde; MMP-2, matrix metalloproteinase 2; NF-κB, nuclear factor-kappa-B; OGTT, oral glucose tolerance test; PDE, phosphodiesterase; PGC-1α, peroxisome proliferator-activated receptor-gamma coactivator-1α; TGF, triglyceride hydrolyase; PPAR, peroxisome proliferators activated receptor γ; PPARγ, peroxisome proliferator-activated receptor γ; ROS, reactive oxygen species; SREBP 1c, sterol regulatory element-binding protein 1c; SOD, superoxide dismutase; TSP, thrombospondin; TNF, tissue inhibitors of metalloproteinases; TNFα, tumor necrosis factor α; UCP3, uncoupling protein 3; VLDL, very low density lipoproteins; VEGF-A, vascular endothelial growth factor A.

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1. Introduction

Obesity is a severe metabolic disorder and well known risk factor for a number of life style related chronic diseases. Usually it develops due to the imbalance of energy consumption versus energy expenditure, lack of nutritional knowledge and characterised by the accumulation of excess fat in adipose tissue, which is associated with a number of chronic diseases such as type 2 diabetes, hypertension, coronary heart disease, hyperlipidemia, cancer and so on [1,2]. On a global scale, obesity is an epidemiological problem and a major contributor to the global burden of non-communicable chronic diseases and disability.

According to the recent data from World Health Organization (WHO), more than 1.9 billion adults worldwide are overweight and at least 600 million of them are clinically obese [3]. Obesity will be a cause of major global medical expenditures over the next 25–50 years since the numbers of global overweight people have been tripled in last 30 years [4]. The prevalence of obesity and overweight individuals is highest in the USA (26% obese and 62% overweight in both sexes) when lowest rate of obesity (3%) and overweight (14%) has been observed in south–East Asia [4]. Over 50% people are either overweight or obese in India, Indonesia, Pakistan, Russia, Mexico, Brazil, Egypt, South Africa, Europe, the Eastern Mediterranean, and Americas [5]. Nearly half to quarter of the women are obese in South Africa, Europe, the Eastern Mediterranean and USA (42%, 23%, 24% and 2% respectively) [4,5].

According to recently and previously published epidemiological studies [6,7], genetic, metabolic, social, behavioural and cultural factors are involved in the rapidly increasing prevalence of obesity [8,9]. Although medical community is aware of the various health risks concerning obesity [10], every year, the number of people with obesity is increasing around the world for past few decades. The obesity has been observed in the people those who consume more daily calories compared to their requirement [11]. Over consumption of calories causes the rapid growth of adipocytes in humans and animal systems by impairing the function of neural palpation (brain) and causing leptin resistance [12]. It is very well known that the number and size of adipose tissue can be regulated by the inhibition of adipocyte generation from precursor cells and inhibition of adipocyte development to control the adipocyte size. Obesity is usually induced by the increased size of adipocytes and by recruiting new adipocytes from precursor cells. These two processes are fully dependent on the regulation of the adipocytes differentiation [13] and most of the anti-obesogenic drugs are developed based on these mechanisms.

Mainly two different types of anti-obesogenic drugs are currently available in the market [14]. One of these is orlistat, which reduces intestinal fat absorption through inhibition of pancreatic lipase activity [15–18] (Table 1) and the other one is sibutramine, which is an anorectic or appetite suppressing drug [19–21]. Both drugs have been reported to have side-effects including blood pressure induction, dry mouth, constipation, headache, and insomnia [22–24,18] and these drugs are not affordable for the people particularly in the developing countries. Although a number of new anti-obesity drugs are currently under clinical trial, including centrally-acting drugs (e.g. radafaxine and oleyolestone), drugs targeting peripheral episodic satiety signals (e.g. rimonabant and APD356) and drugs blocking fat absorption (e.g. cetilistat and AO9604) [25] (Table 1), they still need to be approved by FDA based on the results of clinical trials. Hence, the demand of natural anti-obesity drugs has been increased in the recent years not only due to their lower side effects but also for their lower cost. A huge number medicinal plant parts and their extracts, fractions and isolated pure compounds have been investigated to examine their anti-obesity activity and possible mode of actions (Figs. 1 and 2). However, there is no intensive review is written in order to further evaluate and summarise their anti-obesity efficacy.

Hence, the principle aim of the present review was to evaluate the anti-obesity efficacy of various medicinal plant parts and their extracts, fractions and isolated pure compounds which have been published in last decay or during January 2006–May 2016.

2. Literature review method

PubMed, Science direct, Medline, Scopus, Google scholar, Iran Medex, Web of Science databases were searched from January 2006 to May 2016 to collect relevant data for this review study. The search terms or keywords obesity: high fat diet; medicinal plants; anti-obesity; bioactive compounds; folk medicines for obesity: traditional medicines; anti hyperlipidemic; and hypolipidemic were used either alone or in combination to search the articles. The publications with available abstract and/or full text were reviewed for this study along with few existing reviews. The anti-obesity

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Mechanism of action</th>
<th>Example</th>
<th>Side effects</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>HMG-Co A Reductase enzyme inhibitor Fibrates</td>
<td>Lowering total LDL by inhibiting cholesterol biosynthesis</td>
<td>Lovastatin, Atorvastatin</td>
<td>Congestive cardiac failure.</td>
<td>Halford [25]</td>
</tr>
<tr>
<td>Nicotinic acid Derivative</td>
<td>Inhibit lipolysis within adipocytes</td>
<td>Niacin</td>
<td>Upper gastrointestinal disturbance, headache, myalgia.</td>
<td>Halford [25]</td>
</tr>
<tr>
<td>Bile acid Sequestrants (Resin)</td>
<td>Bind with bile acid and promote bile acid excretion</td>
<td>Cholestipol, Colestyramine</td>
<td>Hyperglycemia, increase uric acid.</td>
<td>Halford [25]</td>
</tr>
<tr>
<td>Lipase</td>
<td>Reduces intestinal fat absorption through inhibition of pancreatic lipase</td>
<td>Orlistat</td>
<td>Abdominal fullness, constipation</td>
<td>Halford [25]</td>
</tr>
<tr>
<td>HMG-Co A Reductase enzyme inhibitor</td>
<td>Central: Inhibits synaptic reuptake of nor epinephrine and serotonin</td>
<td>Sibutramine</td>
<td>GI symptoms (oily spotting, flatus with discharge, fecal urgency, oily stools incontinence)</td>
<td>Thurairajah et al. [18], Karamadoukis et al. [23]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Dry mouth, constipation, headache, insomnia, increased blood pressure</td>
<td>De et al. [22], Slovacek et al. [24]</td>
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