Journal Of Harmonized Research (JOHR)

Journal Of Harmonized Research in Pharmacy
2(1), 2013, 01-33

ISSN 2321 – 0958

Review Article

# A REVIEW ON HERBAL MEDICINAL PLANTS FOR THE TREATMENT OF OBESITY

**Neeraj Kumar Sharma*, Dheeraj Ahirwar**

[1]School of Pharmacy, Chouksey Engineering College, Bilaspur-495004, India

,

**Abstract:**
This study is for the effects of some Indian medicinal plants that are claimed to be useful in the treatment of obesity are reviewed. Research studies are being carried out to detect and confirm the action of drugs and natural products that yield better and long-lasting results in terms of weight reduction. In this field, medicinal plants play a pivotal role. The statins inhibit 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase and, thereby, suppress cholesterol biosynthesis.

**Keywords:** Obesity, Herbal medicines, lipid lowering, anti-obesity

## 1. Introduction:

Obesity is known to be a social problem and has become the focus of much attention by public and especially health-related institutions, whose aim is to provide as much information as possible to reduce its prevalence. Both statistics and the observation of people that we commonly meet are evidence to the fact that many of these attempts fail. Taking advantage of the strong impact it has on the audience, the mass media have taken hold of this topic, but do not necessarily deal with it with due seriousness; at the same time, food and drug industries continue to propose and advertise new weight-lowering products. Obesity is a disease in which excess body fat has accumulated to such an extent that health may be negatively affected. It is commonly defined as a weight divided by height squared 30 kg/m2 or higher. This distinguishes it from being overweight as defined by a BMI of between 25-29.9. As a result, obesity has been found to reduce life expectancy. With rates of obesity increasing among both adults and children, authorities view it as a serious public health problem. Attempts to address it include population-wide measures to improve dietary choices.

**For Correspondence:**
nhbiii@gmail.com
Received on: December 2013
Accepted after revision: March 2013
Downloaded from: www.johronline.com

Problem related to obesity therapy

- Motivations
- Lifestyle
- Underestimation of psychological problems
- Working activity
- Availability to carry out adequate and constant physical activity
- Pressure from advertisements
- Do-it-yourself solutions
- Long-lasting results
- Lack of acceptable level of information and education related to eating behavior
- Insufficient sleep

- Genetics
- Medical illness
- Microbiological
- Neurobiological mechanisms
- Endocrine disruptors - food substances that interfere with lipid metabolism
- Decreased variability in ambient temperature\
- Decreased rates of smoking, which suppresses appetite
- Increased use of medication that leads to weight gain
- Increased distribution of ethnic and age groups that tend to be heavier
- Pregnancy at a later age
- Intrauterine and intergenerational effects.
- Positive natural selection of people with a higher BMI

Why have all of the campaigns organized by health organizations failed? Why is this topic the object of so much attention by the mass media, and why is it so appealing? Why is this problem along with other pathologies with a strong social impact, such as diabetes hardly ever dealt with?

Obesity itself is a disease and is a serious risk factor for many other chronic complications, such as diabetes, hypertension, dyslipidemia, and cardiovascular diseases. People become obese when the body takes in more calories than it burns off and those extra calories are stored as fat. Due to its direct stimulatory effect on the catabolism of fat, fibrates have been used as primary or adjunct therapy for several years to control obesity.

Therefore, the challenge is to maintain cholesterol or lipid homeostasis in lipid-independent disorders after the use of lipid-lowering drugs, in order to minimize side effects, and that may not be an easy task. Alternatively, specific targeting of the biological molecule/process but not an unrelated one such as lipid/cholesterol may be another option to achieve a better therapeutic outcome under these conditions.

Literature revealed that a lot of plant and their formulation are being used as for the treatment of obesity. But still lots of scientific evaluations are remaining on medicinal plants for antiobesity aspect. Therefore in this review work to give an introduction about antiobesity property of some medicinal plants.

**Medicinal plants**

It is possible to find on the market medicinal plant products formulated as dry extracts for the preparation of decoction; as total or oil concentrates; tablets and opercles with total phytocomplexes, and less often as hydroalcoholic extracts and tinctures. The products available on the market have been evaluated in relation to the indications, the active principles, the dosage and, therefore, the quantity of active ingredients advised by the producer or the physician. We will deal with a necessarily partial list of the medicinal plants that are used either alone or in association, and sold as industrial preparations or by physiotherapists for the treatment of obesity. The acknowledged therapeutic indications of each are reported, as well as the pathologies for which they may be used. Some medicinal plants are not specific for the treatment of obesity, but are used in association with others.

Therefore, in this review, we surveyed natural products with anti-obesity potential and reviewed the scientific data, including experimental methodologies, active components, and mechanisms of action against obesity. A growing body of evidence indicates that natural products having anti-obesity effects can be arranged into five categories based on their distinct mechanisms; they produce

(1) Decreased lipid absorption,
(2) Decreased energy intake,
(3) Increased energy expenditure,
(4) Decreased pre-adipocyte differentiation and proliferation, or
(5) Decreased lipogenesis and increased lipolysis.

Therefore, in this review, we addressed naturally occurring compounds possessing anti-obesity activity by categorizing them as per these mechanisms. A wide variety of plants possess pancreatic lipase inhibitory effect shown in Table 1.1

Table 1.1 Anti-obesity biomaterial compounds showing inhibition of pancreatic lipase

| ***Source*** | **Active component** | **Experimental methods a (treated dose, subjects, duration of treatment)** | **Major activity** | **Reference** |
|---|---|---|---|---|
| *Juniperus communis (bark)* | Crude ethanol /water extract | Inhibitory activity of pancreatic lipase | $IC_{50}$ = 20.4 and 21.9 lg/mL, respectively | Kim and Kang, 2005 |
| *Panax japonicas (rhizomes)* | Chikusetsu saponins | 3%, ICR mice with HFD, 9 weeks | 22%* decrease in body weight gain | Han *et al*., 2005 |
| *Platycodi radix* | Platycodin saponins | 70 mg/kg, SD rats with HFD, 4 weeks | 13% decrease in body weight gain | Zhao *et al*., 2005 , Zhao and Kim, 2004, |
| *Platycodi radix* | Crude aqueous /ethanolic extract (saponin) | 5%, ICR mice with HFD, 8 weeks | 12%* decrease in body weight gain | Han *et al*., 2000 |
| *Acanthopanax senticosus* | stem bark | 10.6% ellagic acid 800 mg/kg, ICR mice with HFD,5 weeks | 54%* decrease in body weight gain | Lei *et al*., 2007; Han *et al*., 2000 |
| *Thea sinensis (oolong tea)* | Crude aqueous extract (caffeine) | 5%, ICR mice with HFD, 10 weeks | 10%* decrease in body weight gain | Han *et al*., 1999 |
| *Cassia mimosoides* | Proanthocyanidin | Inhibitory activity of pancreatic lipase; 2.5%, SD rats with HFD8 weeks | $IC_{50}$ = 0.11 mg/ml; 60%* decrease in body weight gain | Yamamoto *et al*., 2000 |
| *Kochia scoparia (fruits)* | Crude aqueous extract (saponins) | 3%, ICR mice with HFD, 9 weeks | 19%* decrease in body weight gain | Han *et al*., 2006 |
| *Afromomum meleguetta* | Spilanthes acmella | Crude ethanolic extract 2 mg/ml, inhibitory activity of pancreatic lipase | 90%, 40% lipase inhibition, respectively | Ekanem *et al*., 2007 |
| *Salacia reticulate* | (mixed with cyclodextrin) | Crude aqueous extract 0.5%, SD rats with HFD, 8 weeks | 27% decrease in body weight gain | Kishino *et al*., 2006 |

| ***Source*** | **Active component** | **Experimental methods a (treated dose, subjects, duration of treatment)** | **Major activity** | **Reference** |
|---|---|---|---|---|
| *Thea sinensis (leaf)* | Saponin | 0.5%, ICR mice with HFD, 11 weeks | 17%* decrease in body weight gain | Han *et al*., 1999. |
| *Nelumbo nucifera (leaf)* | Crude | ethanolic extract 5%, ICR mice with HFD, 5 weeks | 28%* decrease in body weight gain | Ono *et al*., 2006 |
| *Trigonella foenum graecum L. (seed)* | Crude ethanolic extract | 0.3%, ddY obese mice, 22 days | 14%* decrease in body weight gain | Handa *et al*., 2005 |
| *Salix matsudana (leaf)* | Poly phenol (PP) | 5% PP, Wistar King rats with HFD, 9 weeks | 20%* decrease in body weight gain | Han *et al*., 2003 |
| *Vitis vinifera* | Flavonoid glucoside | 5%, rats of ICR strain with HFD9 weeks | 19%* decrease in body weight gain | Han *et al*., 2003<br>Han *et al*., 2006 |
| | Crude ethanolic extract | 1 mg/ml, 3T3-L1 adipocyte, 8 days | Inhibitory effect on lipase activity = 80% | Moreno *et al*., 2003 |
| *Eriochloa villosa* | Crude methanolic extract | 0.2 mg/ml, inhibitory activity of pancreatic lipase | Inhibitory effect on lipase activity = 83% | Sharma *et al*., 2005 |
| *Orixa japonica* | Crude methanolic extract | 0.2 mg/ml, inhibitory activity of pancreatic lipase | Inhibitory effect on lipase activity = 81% | Sharma *et al*., 2005 |
| *Salvia officinalis L. (leaf)* | Methanolic extract | Inhibitory activity of pancreatic lipase | $IC_{50}$ = 36 lg/ml | Ninomiya *et al*., 2004 |
| *Setaria italic* | Crude methanolic extract | 0.2 mg/ml, inhibitory activity of pancreat lipase | Inhibitory effect on lipase activity = 80% | Sharma *et al*., 2005 |

| ***Source*** | **Active component** | **Experimental methods a (treated dose, subjects, duration of treatment)** | **Major activity** | **Reference** |
|---|---|---|---|---|
| *Acanthopanax Sessiliflorous* | Lupane-type saponins | 0.5%, ICR mice with HFD, 4 weeks | 40%* decrease in body weight gain | Yoshizumi *et al*., 2006 |
| *Aesculus turbinate (seed)* | Escin | Inhibitory activity of pancreatic lipase | $IC_{50}$ = 14 lg/ml with escin IIb | Kimura *et al*., 2006 |
| *Cyclocarya paliurus (Batal) Iljinskaja* | Crude aqueous extract | Inhibitory activity of pancreatic lipase | $IC_{50}$ = 9.1 lg/ml | Kurihara *et al*., 2003 |
| *Cassia nomame* | Flavan dimers | Inhibitory activity of pancreatic lipase | $IC_{50}$= 5.5 lM with (2S)-30,40,7-trihydroxyflavan-(4a?8)-catechin | Hatano *et al*., 1997 |
| *Gardenia jasminoides (fructus)* | Crocin, crocetin | Inhibitory activity of pancreatic lipase50 mg/kg/d, -induced hyperlipidermic mice, 5 weeks | $IC_{50}$ = 2.1 mg/ml with crocetin; 25%* decrease in body weight gain with crocin | Lee *et al*., 2005, Sheng *et al*., 2006 |
| *Dioscorea nipponica* | Crude methanolic extract | 5%, SD rats with HFD, 8 weeks | $IC_{50}$ = 5–10 lg/ml, 37% decrease in body weight gain | Kwon *et al*., 2003 |
| *Coffea canephora* | Caffeine, chlorogenic acid, | 0.5%, ddy mice with standard diet, 14 days | 157% decrease in body weight gain | Shimoda *et al*., 2006 |
| *Peptide* | e-Polylysine | 0.4%, C57BL/6 mice with HFD, 60 days | 29%* decrease in body weight gain | Tsujita *et al*., 2006 |
| *Glycyrrhiza* | uralensis Licochalcone | A Inhibitory activity of pancreatic lipase | $IC_{50}$ = 35 lg/ml, Ki = 11.2 lg/ml | Won *et al*., 2007 |
| *Chitosan* | Not specified | 3 g/day, human wt. 8 week | 22% decrease in body weight | Kaats *et al*., 2006 |

| ***Source*** | **Active component** | **Experimental methods a (treated dose, subjects, duration of treatment)** | **Major activity** | **Reference** |
|---|---|---|---|---|
| *Chitosan–chitin* | Chitosan (80%), chitin (20%) | 15%, ICR mice with HFD, 9 weeks | 143%* decrease in body weight gain | Han *et al*., 1999; Gades and Stern 2003, Gallaher *et al*., 2002. |
| *Manno-oligosaccharides* | | 1%, ICR mice with HFD, 12 weeks | oligosaccharides 40% decrease in hepatic triglyceride, no body weight change | Takao *et al*., 2006 |
| *Levan* | | 10%, SD rats with HFD, 4 week | 160% decrease in body weight | Kang *et al*., 2006 |
| *Fungus, Laetiporus Sulphureus* | Mycelia extract | 2 mg/ml fungal extract, lipase activity | Inhibitory effect on lipase activity = 83% | Slanc *et al*., 2004 |
| *Fungus, Tylopilus felleus* | Mycelia extract | 2 mg/ml fungal extract, lipase activity | Inhibitory effect on lipase activity = 96% | Slanc *et al*., 2004 |
| *Fungus, Hygrocybe Conica* | Mycelia extract | 2 mg/ml fungal extract, lipase activity | Inhibitory effect on lipase activity = 97% | Slanc *et al*., 2004 |
| *Basidiomycete, Boreostereum* | Vibralactone | Inhibitory activity of pancreatic lipase | $IC_{50}$ = 0.4 lg/ml | Liu *et al*., 2006 |
| *Streptomyces toxytricini* | Lipistatin | Inhibitory activity of pancreatic lipase | $IC_{50}$ = 0.14 lM | Weibel *et al*., 1987, Hochuli *et al*., 1987 |
| *Streptomyces sp. NR0619* | Panclicins | Inhibitory activity of pancreatic lipase | $IC_{50}$ = 0.89 lM with panclicin | D Mutoh *et al*., 1994, |
| *Actinomycetes sp. MG147-CF2* | Valilactone | Inhibitory activity of pancreatic lipase | $IC_{50}$ = 0.00014 lg/ml | Kitahara *et al*., 1987 |

**Suppressive effect on food intake:**

Body weight regulation through appetite control is a multifactor event resulting from neurological and hormonal interrelationships. A line of evidence indicates that serotonin, histamine, dopamine, and their associated receptor activities are closely associated with satiety regulation. These receptors may enable researchers to better target their searches for drugs that treat obesity through energy intake reduction (Chantre and Lairon, 2002). Agents that act via peripheral satiety peptide systems, alter the various hypothalamic neuropeptides' CNS levels, or alter the key CNS appetite monoamine neurotransmitters' levels may be suitable candidates for drugs that will suppress appetite (Halford and Blundell, 2000; Wynne et al., 2005). Any changes a potential appetite suppressant induces should be considered in terms of: (1) the psychological experience and behavioral expression of appetite, (2) metabolism and peripheral physiology, and (3) the CNS neural pathways' functioning (Halford and Blundell, 2000). In general, natural appetite suppressants are dietary supplements that aid in appetite control. Appetite suppressant mechanisms of action typically affect hunger control centers in the brain, resulting in a sense of fullness. However, in animals and humans, ghrelin secretion in the stomach may increase with decreased food intake, stimulating increased intake. Therefore, ghrelin antagonism may decrease or blunt the increased appetite that potentially occurs with decreased feeding, and, thus, may be a potential adjunctive treatment for obesity (Bays, 2004). MCH receptor antagonism may also prove an important target for obesity treatment through appetite regulation. One clear example of a natural appetite suppressant is Hoodia gordonii, a leafless, spiny, succulent plant growing in some South African countaries (van Heerden, 2008). Despite its popularity, there is insufficient clinical information on H. gordonii to prove its efficacy. However, the consensus now is that H. gordonii regulates appetite and can significantly reduce calorie intake and boost weight loss (Lee and Balick, 2007; MacLean and Luo, 2004; Van Heerden et al., 2007; Van Heerden, 2008). There are currently more than 20 international patents on compounds originating in H. gordonii, and many hoodia-containing commercial preparations are available on the market (Van Heerden, 2008).

Reportedly, other plant extracts and herbal supplements shown in table no. 1.2

Table 1.2: Anti-obesity biomaterials showing appetite-repression activity.

| ***Source*** | **Active component** | **Experimental methodsa (treated dose, subjects, uration of treatment)** | **Major activity** | **Reference** |
|---|---|---|---|---|
| *Panax ginseng (root)* | Crude saponins 200 mg/kg, | SD rats with HFD, 3 weeks | 37% decrease in body weight gain | Kim *et al*., 2005 |
| *Garcina cambogia* | (-)-Hydroxycitric acid (HCA) | 154 nmol HCA/kg, Zucker obese rats, 92 days | 8% decrease in body weight gain | Saito *et al*., 2005; Heymsfield *et al*., 1998. |
| *Camellia sinensis (leaf)* | (-)-Epigallo-cathechin gallate (EGCG) | 82 mg/kg SD rats (7 days),<br>81 mg/kg lean Zucker rats (8 days),<br>92 mg/kg obese Zucker rats (4 days) | 53% decrease in body weight gain,<br>32% decrease in body weight gain, | Kao *et al*., 2000; Moon *et al*., 2007; Dulloo *et al*., 1999; Wolfram *et al*., 2006 |
| *Caralluma fimbriata (cactus)* | Crude ethanolic extract (pregnane glycosides) | 1 g/day, overweight adult Indian men<br>and women, 60 days | 2.5% decrease in body weight gain K | uriyan *et al*., 2007. |
| *Coix lachrymajobi var. mayeun (seed)* | Crude aqueous extract | 500 mg/kg, SD rats with HFD,<br>4 weeks | 36%* decrease in body weight gain | Kim *et al*., 2004 |
| *Hoodia gordonii and*<br>*H. pilifera* | Steroidal glycoside (P57AS3) | Intracerebroventricular injection,<br>24 h | 40–60% reduction in food intake | MacLean and Luo 2004, Van Heerden 2008. |
| Not specified | Oleoyl-estrone | 4.4 lmol/g/day, Zucker lean rats with HFD, 12 days | 30% decrease in body weight gain | Remesar *et al*., 2000; Salas *et al*., 2007; Ferrer *et al*., 2007. |
| *Phaseolus vulgaris* | Lectins | 100 mg/kg, Harlan–Wistar rats, | 16 h 8.25-fold* decrease in food intake | Baintner *et al*., 2003 |
| *Pinus koraiensis (pine nut)* | Pine nut fatty acids | 3 g, obese women, 4 h | 60% increase in cholecystokinin -8 (satiety hormone) secretion | Pasman *et al*., 2008; Hughes *et al*., 2008. |

**Stimulatory effects on energy expenditure**

Abundant evidence indicates many rodent models of obesity show reduced energy expenditures, which contribute to the development of obesity, whereas the role of reduced energy expenditure in the promotion of human obesity is much less clear. Excessive adiposity results from an imbalance in energy homeostasis, in which the consequences of excessive food intake are not balanced by increased energy expenditure (Flatt, 2007; Redinger, 2009). Energy expenditure has many components. It can be separated into a number of different categories. The simplest scheme divides energy expenditure into three categories: (1) physical activity, (2) obligatory energy expenditure, and (3) adaptive thermogenesis.

To regulate body weight and energy expenditure, mammalian BAT establishes non-shivering thermogenesis through dissipation of excess energy as heat (Cannon and Nedergaard, 2004). BAT plays an important role in obesity control by controlling energy balance. The key player in this process is UCP1, which discharges the proton gradient generated in oxidative phosphorylation, thereby dissipating energy as heat. Thus, searching for substances that upregulate UCP1 gene expression may be a worthy strategy for achieving obesity control through increased energy expenditure (Kumar *et al*., 1999). One analogue of UCP1, UCP3, is also a potentially potent anti-obesity agent, because it mediates the thermogenesis regulated by the thyroid hormone, β3-adrenergic agonists, and/or leptin in some organs (Gong *et al*., 1997). Numerous naturally-occurring compounds have been proposed as treatments for weight loss via enhanced energy expenditure, including caffeine (Dulloo, 1993; Racotta *et al*., 1994) and capsaicin (Kawada *et al*., 1986; Rayalam *et al*., 2008). However, researchers attribute most of such putative effects on energy expenditure to green tea and its extract, where the catechins, such as EGC and EGCG, have received tremendous attention (Wolfram *et al*., 2006; Moon *et al*., 2007).

Table 1.3: Anti-obesity biomaterials promoting energy expenditure.

| ***Source*** | **Active component** | **Experimental methodsa (treated dose, subjects, uration of treatment)** | **Major activity** | **Reference** |
|---|---|---|---|---|
| *Pinellia ternata* | Crude aqueous Extract | 400 mg/kg, obese Zucker rats, 6 weeks | Slight decrease in body weight gain (data not shown) Increased UCP1 expression in BAT and PPARa in WAT | Kim *et al*., 2006. |
| *Nelumbo nucifera (leaf)* | Crude ethanolic extract (flavonoid) | 1%, A/J mice with HFD, 12 weeks | 15%* decrease in body weight gain, Activation of b-adrenergic receptor | Ohkoshi *et al*., 2007. |
| *Panax ginseng (berry)* | Crude ethanolic Extract | 150 mg/kg, ob/ob mice, 12 days | 13% decrease in body weight gain, Increased energy expenditure and body temperature | Attele *et al*., 2002. |
| *Glycine max (soybean)* | β -conglycinin, glycinin (globulins) | 23.7% b-conglycinin, and 21.9% glycinin, KK-Ay obese mice, 4 weeks | 10% decrease in body weight gain, Acceleration of b-oxidation, suppression of fatty acid synthesis | Moriyama *et al*., 2004; Ishihara *et al*., 2003. |
| *Undaria pinnatifida (sea weed)* | Fucoxanthin | 2%, KKAy mice with soybean oil diet, 4 weeks | 17% decrease in body weight gain UCP1 expression in WAT | Maeda *et al*., 2005. |
| *Not specified* | Medium-chain triglycerides (MCT) | Diet containing 64.7% MCT, 24 obese men, 28 days | 1.3% decrease in body weight gain, Increased energy expenditure | St-Onge *et al*., 2003; Papamand *et al*., 1998; Bourque *et al*., 2003. |
| *Fish oil* | EPA and DHA | C57BL/6 J mice with 60% fish oil diet containing 7% EPA and 24% DHA, 5 months | 58% decrease in body weight gain Upregulation of UCP2 in liver | Tsuboyama-Kasaoka *et al*., 1999. |

**Inhibitory effect on adipocyte differentiation**

Adipocytes play a central role in the maintenance of lipid homeostasis and energy balance, by storing triglycerides and releasing free fatty acids in response to changing energy demands. Because adipocyte tissue growth can be due to both hyperplasia and hypertrophy of adipocytes, several studies screening for antiobesity materials have focused on the processes of adipocyte proliferation and differentiation (Kim *et al*., 2006a). In this search, 3T3-L1 pre-adipocytes cells are currently used as an in vitro model for the study of obesity, because such cells accumulate triglycerides upon differentiating in culture (Cowherd *et al*., 1999; Green and Kehinde, 1975). This is due to the expression of adipocyte specific genes, such as PPARc and C/EBPa (Wu *et al*., 1999; Lefterova and Lazar, 2009). For this reason, natural products that specifically target adipogenesis inhibition had been considered promising with regard to their potential in treatment of obesity. However, current research suggests that inhibiting adipogenesis or adipose tissue expansion is unhealthy, leading to type 2 diabetes and other metabolic diseases, such as atherosclerosis (Lefterova and Lazar, 2009). Fatty acids, particularly polyunsaturated fatty acids (PUFA), act as signal transducing molecules in adipocyte differentiation. In adipocyte tissue, saturated and monounsaturated fatty acids are more readily acylated into triglycerides than PUFA are (Awad *et al*., 2000; Evans *et al*., 2000; Okuno *et al*., 1997). Thus, PUFA plays a central role in suppressing fatty acid synthesis and regulating adipocyte differentiation through suppression of late-phase adipocyte differentiation (Madsen *et al*., 2005; Okuno *et al*., 1997). Recent reports have demonstrated another interesting mechanism, in extract of macrofungus Cordyceps militaris mycelia, which suppressed 3T3-L1 adipocyte differentiation through activation of the aryl hydrocarbon receptor (Shimada *et al*., 2008). Table 2.4 lists the wide variety of natural products found to inhibit pre-adipocyte proliferation and/or the apoptotic effect.

In addition to showing inhibitory activity against adipocyte differentiation, several naturally-occurring compounds have displayed apoptotic effects on maturing pre-adipocytes. For example, some phytochemicals, such as esculetin, resveratrol, quercetin, genistein, EGCG, capsaicin, and conjugated linoleic acids induced apoptosis of maturing 3T3-L1 pre-adipocytes through suppression of ERK1/2 phosphorylation, activation of the mitochondrial pathway, AMPK activation, or anti-oxidant activity (Hargrave *et al*., 2002; Hwang *et al*., 2005; Hsu and Yen, 2006; Yang *et al*., 2008). Thus, inducing apoptosis in mature adipocytes may be important for treating obesity with naturally-occurring compounds.

The cell cycle is closely associated with adipocyte growth and proliferation and is thus an important factor to consider in targeting anti-obesity natural products. Recent evidence has indicated that certain phenolic compounds lead to cell cycle arrest at the G1 phase during 3T3-L1 adipocyte differentiation. Recent reports have shown that phenolic compounds also efficiently induce apoptosis in 3T3-L1 adipocytes through AMPK activation (Hwang *et al*., 2005; Lin *et al*., 2005). A combined treatment, of ajoene and conjugated linoleic acid, enhanced apoptosis in mature 3T3-L1 adipocytes through a synergistic

increase of expression in several proapototic factors (Rayalam *et al*., 2008). Sirtuin 1 is another target molecule for anti-obesity treatment. Decreased adipogenesis due to resveratrol correlated with increased expression of Sirtuin1, which promotes fat mobilization by repressing PPARc (Picard *et al*., 2004; Rayalam *et al*., 2008).

Table 1.4: Anti-obesity biomaterials inhibiting adipocyte differentiation.

| **Source** | **Active component** | **Experimental methodsa (treated dose, subjects, uration of treatment)** | **Major activity** | **Reference** |
|---|---|---|---|---|
| *Garcina cambogia* | (-)-Hydroxycitric acid (HCA) | 4 lg/ml, 3T3-L1 adipocyte, 8 days | 35% decrease in lipid accumulation | Kim *et al*., 2004. |
| *Pinus densiflora* | Crude aqueous extract 10 g/kg | SD rats with HFD, 6 weeks | 12% decrease in body weight gain | Jeon and Kim 2006. |
| *Cortidis rhizome* | Berberine | 5 mg/kg, db/db mice, 26 days | 13% decrease in body weight | Lee *et al*., 2006; Huang *et al*., 2006; Hu and Davies 2009. |
| Not specified (product of Sigma) | Esculetin | 200–800 lM, 3T3-L1 adipocyte, 48 h r | 200 lM, pre-adipocyte apoptosis 800 lM, inhibition of adipogenesis | Yang *et al*., 2006 |
| *Glycine max* (product of Gibco) | Genistein | 100 lM, 3T3-L1 adipocyte, 48 h | Inhibition of preadipiocyte differentiation by 60% | Harmon and Harp 2001, Harmon *et al*., 2002; Zhang *et al*., 2009; Kim *et al*., 2006; Naaz *et al*., 2003. |
| Not specified (product of Gibco) | Naringenin | 100 lM, 3T3-L1 adipocyte, 48 h | Inhibition of preadipiocyte differentiation by _40% | Harmon and Harp 2001. |
| Not specified (product of Sigma) | Quercetin | 250 lM, 3T3-L1 adipocyte, 48 h | Inhibition of preadipiocyte differentiation by 71.5%, $IC_{50}$ = 40.4 Lm | Hsu and Yen 2006. |
| Chili pepper (Capsicum) | Capsaicin | 3T3-L1 adipocyte, 72 h r | 1. Inhibition of population: $IC_{50}$ = 45 lM 2. Apoptosis percentage: 26.7% at 250 lM | Hsu and Yen 2007. |
| Deep sea water | Minerals (mainly Ca and Mg) | Hardness 1000, 3T3-L1 adipocyte,72 h | 27% decrease in lipid accumulation | Hwang *et al*., 2009 |

| **Source** | **Active component** | **Experimental methodsa (treated dose, subjects, uration of treatment)** | **Major activity** | **Reference** |
|---|---|---|---|---|
| Chitosan oligosaccharides | MW 1–3 kDa | 3T3-L1 adipocyte, 72 h | 90% decrease in lipid accumulation | Cho *et al*., 2008, Rahman *et al*., 2008. |
| Kochujang (fermented red pepper paste) | Not identified | 1 mg/ml, 3T3-L1 adipocyte, 24 h | 70–75% decrease in adipogenic transcription factors | Ahn *et al*., 2006 |
| Fish oil | Docosahexaenoic acid | 200 lM, 3T3-L1 adipocyte, 4 h | 90% increase in lipolysis | Kim *et al*., 1999; Parrish *et al*., 1990; Flachs *et al*., 2005. |
| Perilla oil (product of Ajinomoto Co., Japan) | Rich in a-linolenic acid | 12% dietary fat, SD rats, 12 weeks | 94% decrease in TG accumulation | Okuno *et al*., 1997. |
| Palm oil | c-tocotrienol | 24 lM, 3T3-L1 adipocyte, 21 days | 48% decrease in TG accumulation | Uto-Kondo *et al*., 2009. |
| Sterol (product of Sigma) | b-sitosterol | 16 lM, 3T3-L1 adipocyte, 72 h | 65% decrease in preadipiocyte Differentiation | Awad *et al*., 2000. |
| Scutellaria baicalensia (product of Sigma) | Baicalein | 100 lM, 3T3-L1 adipocyte, 48 h | 1.86-fold decrease in lipid Accumulation | Cha *et al*., 2006. |
| *Lagerstroemia speciosa L.* | Hot water extract (tannic acid) | 0.1–0.25 extract (20 mg/l tannic acid), 3T3-L1 adipocyte, 48 h | No differentiation | Liu *et al*., 2001; Bai *et al*., 2008; Klein *et al*., 2007 |
| *Undaria pinnatifida* (brown algae) | Fucoxanthin | 15 lM, 3T3-L1 adipocyte, 120 h | Inhibition of preadipiocyte differentiation by 70% | Maeda *et al*., 2006 |

| **Source** | **Active component** | **Experimental methodsa (treated dose, subjects, uration of treatment)** | **Major activity** | **Reference** |
|---|---|---|---|---|
| Conjugated linoleic acids | Trans-10, cis-12 CLA | 100 lM, 3T3-L1 adipocyte, 3 days | 36% decrease in TG accumulation | Evans *et al*., 2000; Joseph *et al*., 2009. |
| *Lithospermum Erythrorhizon* | Shikonin | 20 lM, 3T3-L1 adipocyte, 48 h | Inhibition of preadipiocyte differentiation: $IC_{50}$ = 1.1 lM | Lee *et al*., 2009. |
| *Panax ginseng* | Ginsenosides | 40 lM, 3T3-L1 adipocyte, 6 day | 40%* decrease in TG accumulation with gensenoside Rg3 | Hwang *et al*., 2009; Park *et al*., 2008; Kim *et al*., 2009. |
| *Brown algae* | Fucoidan | 100 lM, 3T3-L1 adipocyte, 24 h | Inhibition of preadipiocyte differentiation by 33% | Kim *et al*., 2009. |
| *Zizyphus jujuba (fruit)* | Extract of choroform Fraction | 50 lM, 3T3-L1 adipocyte, 24 h | Inhibition of GPDH activity by 80%* | Kubota *et al*., 2009. |
| *Silybum marianum* | Silibinin | 30 lM,, 2 days | 60%* decrease in TG accumulation | Ka *et al*., 2009. |
| Combined natural Compounds | Genestein (G), quercetin (Q), resveratrol (R) | 50 lM G, 100 lM Q, 100 lM R, 3T3-L1 adipocyte, 3 days | 92% decrease in lipid accumulation | Park *et al*., 2008. |
| Garlic | Ajoene | 100 lM, 3T3-L1 adipocyte, 24 h | Inhibition of preadipiocyte differentiation by 86% | Ambati *et al*., 2009. |
| *Humulus lupulus* | Xanthohumol | 75 lM, 3T3-L1 adipocyte, 24 h | Inhibition of preadipiocyte differentiation by 51% | Yang *et al*., 2007; Mendes *et al*., 2008. |
| *Lagerstroemia Speciosa (leaf)* | Ellagitannins | 0.04–0.5 mg/ml, 3T3-L1 adipocyte, 24 h | Inhibition of preadipiocyte differentiation by max. 100% | Bai *et al*., 2008. |

| **Source** | **Active component** | **Experimental methodsa (treated dose, subjects, uration of treatment)** | **Major activity** | **Reference** |
|---|---|---|---|---|
| *Ascophyllum nodosum* | Aqueous methanolic Extract | 75 lg extract, 3T3-L1 adipocyte, 8 days | Inhibition of GPDH activity by 20% | Uto-Kondo *et al*., 2009. |
| *Seabuckthorn* | Isorhamnetin | 50 lM, 3T3-L1 adipocyte, 3 days | 2.75-fold* decrease in TG Accumulation | Lee *et al*., 2009. |
| *Wasabia japonica* (leaf) | Not identified | 667 lg/ml, 3T3-L1 adipocyte, 6 days | Inhibition of GPDH activity by 36% | Ogawa *et al*., 2009. |
| Red yeast rice fermented by *Monoscus ruber* | Not identified | 2 mg/ml, 3T3-L1 adipocyte, 8 days | 86% decrease in TG accumulation | Jeon *et al*., 2004. |
| *Coriolus versicol* or mushroom fruit | (-) Ternatin | 1.3 lM, 3T3-L1 adipocyte, 9 days | 87% decrease in TG accumulation | Ito *et al*., 2009. |
| *Cordyceps militaris* | Mycelial extract | 0.2%, 3T3-L1 adipocyte, 12 days | 93.7% decrease in lipid accumulation | Shimada *et al*., 2008. |
| *Ipomoea batatas* (root) | Sporamin | 0.5 mg/ml, 3T3-L1 adipocyte, 5 days | Inhibition of preadipiocyte differentiation by 84% | Xiong *et al*., 2009. |
| *Rosmarinus officinalis* | Carnosic acid | 0–10 lM, 3T3-L1 adipocyte, 2 days | Inhibition of preadipiocyte differentiation: $IC_{50}$ = 0.86 lM | Takahashi *et al*., 2009. |
| *Curcuma longa* | Curcumin | 50 lM, 3T3-L1 adipocyte, 8 days | 2.4-fold* decrease in TG accumulation | Lee *et al*., 2009; Ejaz *et al*., 2009; Miller *et al*., 2008; Wang *et al*., 2009. |
| *Linum usitatissimum* | Secoisolariciresinol | 0.15 lM, 3T3-L1 adipocyte, 14 days | Almost 100%* decrease in TG Accumulation | Tominaga *et al*., 2009. |

| **Source** | **Active component** | **Experimental methodsa (treated dose, subjects, uration of treatment)** | **Major activity** | **Reference** |
|---|---|---|---|---|
| *Hibiscus sabdariffa* | Flower extract | 100 lg/ml, 3T3-L1 adipocyte, | 4 days 50% decrease in TG accumulation | Kim *et al*., 2003. |
| *Solanum tuberosum* | Ethanolic extract | 0–200 lg/ml, 3T3-L1 adipocyte, 24 h | Inhibition of preadipiocyte differentiation: $IC_{50}$ = 46.2 lg/ml | Yoon *et al*., 2008. |
| *Soy isoflavone* | Genistein | 200 lM, 3T3-L1 adipocyte | 90%* inhibition of adipocyte differentiation, 43%* decrease in cell adipocyte viability | Hwang *et al*., 2005. |
| *Undaria pinnatifida* | Neoxanthin | 20 lM, 3T3-L1 adipocyte | 64% reduction in lipid accumulation, 40% reduction in GPDH activity | Okada *et al*., 2008. |
| *Commiphora mukul* | Cis-guggulsterone | 200 lM, 3T3-L1 adipocyte, 24 h | 90%* decrease in adipocyte Differentiation | Yang *et al*., 2008. |
| *Rehmannia glutinosa* | Crude ethanolic extract | 1 mg/ml, 3T3-L1 adipocyte, 48 h | 2-fold* decrease in adipocyte Differentiation | Jiang *et al*., 2008. |
| *Eriobotrta japonica* | Corosolic acid | 45 lM, 3T3-L1 adipocyte | 4.17-fold* decrease in adipocyte Differentiation | Zong and Zhao 2007. |
| *Irvingia gabonesis (seed)* | Extract | 250 lM, 3T3-L1 adipocyte, 72 h | 81% decrease in TG accumulation | Oben *et al*., 2008. |

**Regulatory effect on lipid metabolism**

The pharmacological targeting of lipolysis can be envisaged in two different ways. The first strategy entails stimulating triglyceride hydrolysis in order to diminish fat stores, thereby combating obesity. This option requires the associated oxidation of the newly released fatty acids and led to the development of the β-3-adrenergic agonists (Langin, 2006). However, considering that excessive lipolysis contributes to high circulating fatty acid levels and development of dyslipidemia (as seen in metabolic syndrome), a blockade of such a fatty acid release may be of therapeutic interest (Langin, 2006). Some examples of the natural compounds involved in b-adrenergic receptor activation are the various flavonoids in the leaves of Nelumbo nucifera (NN). Through this pathway, NN extract dietary supplementation resulted in significant suppression of body weight gain in A/J mice fed a HFD (Ohkoshi *et al*., 2007).

PPARc is a transcription factor predominantly expressed in adipose tissue, and it activates adipocyte differentiation both in vivo and in vitro (Cornelius *et al*., 1994). When PPARc is overexpressed, 3T3-L1 pre-adipocyte induction begins. This suggests that PPARc suppression blocks adipogenesis and lipogenesis (Lefterova and Lazar, 2009). Thus, PPARc agonism leads to the amelioration of lipid abnormalities in dyslipidemic patients. Findings from a number of rodent studies have demonstrated that PPARc agonists can improve insulin resistance, as well as dyslipidemia. Concomitantly, rodent disease models have demonstrated that PPARc agonists prevented increased adiposity and body weight without any reduction in food intake (Kersten, 2002). Similarly, PPARa activation mediated the expression of genes that regulate lipid oxidation. Aqueous extract of Salacia oblonga root (active main component, magniferin) has demonstrated PPARa activator properties, which then improved postprandial hyperlipidermic and hepatic steatosis in a genetic-obesity animal model (Huang *et al*., 2006). Additionally, a mixture of three herbal extracts improved lipid metabolism by increasing hepatic mRNA levels of PPARa, the target enzyme responsible for fatty acid b-oxidation (Lee *et al*., 2008a). AMPK is an enzyme found in numerous tissues throughout the body. It has been characterized as a metabolic master switch that regulates the activities of a number of target proteins controlling metabolism. The role of AMPK in the exercising skeletal muscle has been studied extensively. In broad terms, AMPK activation in skeletal muscle appears to increase glucose transport (Hayashi *et al*., 2000) and fatty acid oxidation (Winder and Hardie, 1999; Ruderman *et al*., 1999).

There, the fatty acids can be oxidized or converted to ketone bodies (in the liver) for use as fuel in other organs (Flier, 2004). Thus, the net result of this chain of events is that an increase in muscle AMPK leads to an increase in CPT-1 and in fatty acid oxidation. Table1.5 summarizes the many natural AMPK activators that have been found.

Table 1.5: Anti-obesity biomaterials promoting lipid metabolism.

| **Source** | **Active component** | **Experimental methods (treated dose, subjects, uration of treatment** | **Major activity** | **Reference** |
|---|---|---|---|---|
| *Salacia oblonga* (root) | Mangiferin | 900 mg/kg, ZDF rats, 28 days | 40% decrease in liver/body weight ratio Hepatic PPARa activator | Rong *et al*., 2008; Huang *et al*., 2006. |
| *Ilex paraguariensis* | Crude water extract | 0.24%, SD rats with HFD, 60 days | 11% decrease in body weight gain Down regulation of adipose tissue | Pang *et al*., 2008. |
| *Cortidis rhizome* | Berberine | 5 mg/kg, db/db mice, 26 days | 13% decrease in body Weight AMPK activation | Lee *et al*., 2006; Huang *et al*., 2006. |
| Mixture of *Morus alba*, *Melissa officinalis*, *Artemisia capillaries* | Crude aqueous extract | 0.2%, C57BL/6 J mice with HFD, 12 weeks | 7% decrease in body weight Gain Hepatic PPARa activator | Lee *et al*., 2008. |
| *Nelumbo nucifera* (leaf) | Crude ethanolic extract (flavonoid) | 1%, A/J mice with HFD, 12 weeks | 15%* decrease in body weight gain Activation of badrenergic receptor | Ohkoshi *et al*., 2007. |
| *Curcuma longa* L. | Curcumin | 3%, ob/ob mice with HFD, 4 weeks | 7%* decrease in body weight gain Reversal of inflammatory and metabolic derangements | Weisberg *et al*., 2008. |
| | Curcuminoids | 0.2%, SD rats with HFD, 2 weeks | 11% decrease in body weight gain Alterations in fatty acid Metabolism | Asai and Miyazawa 2001. |
| *Eucommia ulmoides* (leaf) | Crude aqueous extract | 1%, db/db mice, 6 weeks | No data Down regulation of lipogenic enzymes | Park *et al*., 2006. |
| *Arachis hypogaea* (shell) | Crude ethanolic extract | 1%, Wistar rats with HFD, 12 weeks | 12% decrease in body weight gain Inhibition of fat absorption, activation of lipid metabolism | Moreno *et al*., 2006. |
| *Coix lachrymajobi var. mayeun* (seed) | Crude aqueous extract | 500 mg/kg, SD rats with HFD, 4 weeks | 36%* decrease in body weight gain Modulation of leptin | Kim *et al*., 2004. |

| **Source** | **Active component** | **Experimental methods (treated dose, subjects, uration of treatment)** | **Major activity** | **Reference** |
|---|---|---|---|---|
| *Salacia reticulate* (root) | Aqueous extract (polyphenolic Compounds) | 125 mg/kg, Zucker fatty rats, 27 days | 7%* decrease in body weight gain Inhibition of lipid metabolizing enzymes and stimulation of lipolysis | Yoshikawa *et al*., 2002. |
| *Glycyrrhiza glabra* L. (root) | Licorice flavonoid oil (LFO) | 2% LFO, KK-Ay obese mice, 4 weeks | 30% decrease in body weight gain PPARc agonistic activity | Nakagawa *et al*., 2004. |
| *Diospyros kaki* (leaf) | Crude methanolic extract | 5%, SD rats with HFD, 6 weeks | 11% decrease in body weight gain, Modulation of leptin and lipogenic enzymes | Lee *et al*., 2006. |
| *Morus alba* L. (leaf) | Crude aqueous extract | 0.5%, db/db mice, 12 weeks | 7% decrease in body weight Gain, PPARs agonistic activity | Park *et al*., 2005. |
| *Panax ginseng* | Crude aqueous extract | 0.5%, db/db mice, 12 weeks | 8% decrease in body weight Gain, PPARs agonistic activity | Park *et al*., 2005. |
| *Lagerstroemia speciosa* L.(leaf) | Crude aqueous extract | 0.5%, db/db mice, 12 weeks | 3% decrease in body weight Gain, PPARs agonistic | Park *et al*., 2005. |
| *Zea mays* L. | Purple corn color (PCC) (anthocyanins) PCC | 1.1%, C57BL/6J mice with HFD, 12 weeks | 21%* decrease in body weight gain AMPK activation | Tsuda *et al*., 2003; Kong *et al*., 2003. |
| *Glycyrrhiza uralensis* | Crude ethanolic extract (flavonoids) | 0.2%, C57BL/6 J mice with HFD, 4 weeks | 22% decrease in body weight gain PPARc agonistic activity | Mae *et al*., 2003. |

| **Source** | **Active component** | **Experimental methods (treated dose, subjects, uration of treatment)** | **Major activity** | **Reference** |
|---|---|---|---|---|
| *Aralia mandshurica* (AM) and *Engelhardtia chrysolepis* (EC) | Aralox | 150 mg/d AM and 150/d mg EC, 32 women, 15 weeks | 4% decrease in body weight Gain, Stimulation of hormone sensitive lipase | Abidov *et al*., 2006. |
| *Evodia rutaecarpa* (fruit) | Crude ethanolic extract (evodiamine) | 0.02%, SD rats with HFD, 21 days | 23% decrease in body weight | Kobayashi *et al*., 2001. |
| *Commiphora mukul* | E- and Z-guggulsterone | 4.5 g/d, 40 patients, 16 weeks | Reduction in cholesterol and triglyceride levels by 22, and 27%, respectively Antagonist of the bile acid receptor | Urizar and Moore 2003, Verma and Bordia 1988 |
| *Rhynchosia volubilis* (black soybean) | Tripeptide (Ile-Gln-Asn) | 10 mg/ml, 3T3-L1 adipocyte, 8 days | IC50 = 0.014 mg protein/ml AMPK activation | Kim *et al*., 2007. |
| Not specified | Ginsenoside | Rg3 40 lM, 3T3-L1 adipocyte | 40%* decrease in TG accumulation PPARc agonistic activity | Hwang *et al*., 2009. |
| Soybean | L-carnitine (soy Genistein+isoflavone | 0.2% genistein + 0.5% Lcarnitine, C57BL/6 J mice with HFD, 12 weeks | 254% decrease in body weight gain PPARs agonistic activity | Yang *et al*., 2006. |
| *Coffea canephora* | Caffeine, chlorogenic acid, neochlorogenic acid, feruloyquinic acids | 0.5%, ddy mice with standard diet, 14 days | 157% decrease in body weight gain Inhibition of fat absorption, activation of fat metabolism | Shimoda *et al*., 2006. |
| Soybean | b-conglycinin, glycinin (globulins) | 23.7% b-conglycinin, and 21.9% glycinin, KK-Ay obese mice, 4 weeks | 10% decrease in body weight gain Acceleration of β oxidation, suppression of fatty acid synthesis | Moriyama *et al*., 2004. |

| ***Source*** | **Active component** | **Experimental methods (treated dose, subjects, uration of treatment)** | **Major activity** | **Reference** |
|---|---|---|---|---|
| Phytochemicals | Resveratrol (R), Quercetin (Q) | R25 + Q25 lM (R100 + Q100 lM), 3T3- L1 adipocyte, 6 days | 69% decrease in lipid accumulation, 74% decrease in adipocyte viability | Yang *et al*., 2008; Ahn *et al*., 2007. |
| *Glycine max* (Soy) isoflavone | Genistein | 200 lM, 3T3-L1 adipocyte | 90%* inhibition of adipocyte differentiation. | Hwang *et al*., 2005. |
| *Fish oil* | Eicosapentaenoic acid (n- 3 polyunsaturated fatty acid) | 1 g/kg, Wistar rats with cafeteria diet, 5 weeks | 9%* decrease in body weight gain Down regulation of PPARc, apoptosis in WAT | Pérez-Matute *et al*., 2007. |
| *Phytochemicals* | Caffeine + arginine + soy isoflavones+L-carnitine (CASL) | CASL (250 mg, 6 g, 2 g, 1.5 g/kg) KK mice with HFD, 3 weeks | 5.4% decrease in body weight gain Inhibition of lipogenesis in liver | Murosaki et al., 2007. |
| *Rubus idaeus (raspberry)* | 4-(4-Hydroxyphenyl) butan-2-one (RK) | 2% RK, ICR mice with HFD, 10 weeks | 17%* decrease in body weight gain Increased lipolysis | Morimoto et al., 2005. |
| *Deep sea water* | Minerals (mainly Ca and Mg) | Deep sea water of hardness 1000, ob/ob mice, 84 days | 7% decrease in body weight Gain GLUT and AMPK Activation | Hwang et al., 2009. |
| *Chitosan* | Not specified | 3 g/day, human overweight adults, 8 weeks | 22% decrease in body weight gain, Decrease in fat absorption | Kaats et al., 2006. |
| *Chitosan oligosaccharides* | MW 125–145 kD | 2%, Wistar rats, 4 weeks | 9%decrease in body weight gain, Decrease in fat absorption | Bondiolotti et al., 2007. |
| *Not specified* | Oleoylethanolamide | 5 mg/kg, Wistar rats with HFD, 2 weeks | 3.6%* decrease in body weight change, PPARa agonistic activity | Guzmán et al., 2004; Fu et al., 2005. |

| | | | | |
|---|---|---|---|---|
| *Not specified* | PEGylated conjugated linoleic acid (PCLA) | 200 lM PCLA, 3T3-L1 adipocyte,72h | 80% increase in body lipolysis, PPARc agonistic activity | Moon et al., 2006. |
| *Not specified* | Conjugated linoleic acid (CLA) | 1.5% CLA, C57Bl/6 mice with HFD, 6 weeks | 52%* decrease in body weight gain Inhibition of FA uptake into adipose | Liu et al., 2007; Lin et al., 2001; Li et al., 2008. |
| *Solanum tuberosum* | Crude ethanolic extract | 200 mg/kg, SD rats, 4 weeks | 5%* decrease in body weight gain Down regulation of P38 MAPK | Yoon et al., 2008. |
| *Momordica charantia* | Crude ethanolic extract | 0.2 mg/ml, 3T3-L1 preadipocytes | 61% increase in glucose uptake with 0.5 nM insulin and 75% increase in adiponectin secretion. | Roffey et al., 2007. |

**Combined effect for obesity treatment:**

As mentioned above, many natural products show anti-obesity activities of varying mechanisms. Perhaps the recommended approach to researching more efficient obesity treatments and achieving the synergistic effects of natural products should be to seek treatments using multiple products or products having multiple activities (Rayalam *et al*., 2008). Some natural biomaterials possessing multi-functional antiobesity activities have been discovered. Green tea and Garcina cambogia are good examples. Researchers originally found green tea possessed higher anti-oxidant activity than anti-obesity activity, owing to its high concetration of catechins, including epicatechin, ECG, and EGCG. Subsequent research proved the antiobesity activity of catechins resulted from the combined actions of appetite reduction, greater lipolytic activity and energy expenditure, and less lipogenic activity and adipocyte differentiation (Boschmann and Thielecke, 2007; Chantre and Lairon, 2002; Dulloo *et al*., 1999; Hsu and Yen, 2006; Kao *et al*., 2000; Lin and Lin-Shiau, 2006; Moon *et al*., 2007; Nagao *et al*., 2005; Thielecke and Boschmann, 2009; Wolfram *et al*., 2006). G. cambogia is widely known for its anti-obesity activity (Heymsfield *et al*., 1998; Kim *et al*., 2004). Several polyunsaturated fatty acids also show combinations of anti-obesity actions, including upregulation of mitochondrial biogenesis, induction of b-oxidation, and suppression of adipocyte lipogenesis (Flachs *et al*., 2005). Taken together, combination therapies employing natural products that target different obesity genes and/or different stages of the adipocyte life cycle might prove beneficial in treating obesity.

Table 1.6: Other anti-obesity biomaterials, whose mechanisms are unidentified.

| **Source** | **Active component** | **Experimental methodsa (treated dose, subjects, duration of treatment)** | **Major activity** | **Reference** |
|---|---|---|---|---|
| *Hibiscus sabdariffa* | Anthocyanin | 120 mg/kg, ob/MSG mice, 60 days | 10% decrease in body weight gain | Aguilar *et al*., 2007. |
| *Panax ginseng (berry)* | Crude ethanolic extract | 150 mg/kg, ob/ob mice, 12 days | 11% decrease in body weight gain | Dey *et al*., 2003. |
| *Trigonella foenum graecum L. (seed)* | Crude ethanolic extract | 350 mg/kg, mice with HFD, 22 days | 14%* decrease in body weight gain | Handa *et al*., 2005. |
| *Acanthopanax senticosus (stem bark)* | Crude aqueous extract | 500 mg/kg, C57BL/6 J mice with HFD, 12 weeks | 4%* decrease in body weight gain | Cha *et al*., 2004; Park *et al*., 2006. |
| *Ginseng* | Crude ethanolic extract | 500 mg/kg, ICR mice with HFD, 8 weeks | 16% decrease in body weight gain | Yun *et al*., 2004. |
| *Cissus quadrangularis* | Standardized extract (phytosterols) | Two daily dose (514 mg each), obese persons, 8 weeks | 23% decrease in body weight gain | Oben *et al*., 2006. |
| *Panax quinquefolium L. (berry)* | Crude aqueous extract (Ginsenosides | 0.6 ml/kg (juice), ob/ob mice, 10 days | 250% decrease in body weight gain | Xie *et al*., 2007. |
| *Eucommia ulmoides (leaf)* | Crude aqueous extract | 10 mg/ml, hMSC adipocyte, 7 days | 1/12decrease in TG accumulation | Lee *et al*., 2004. |
| Carotenoid Pigment | Astaxanthin | 30 mg/kg, ddy mice with HFD, 60 days | 15%* decrease in body weight gain | Ikeuchi *et al*., 2007. |
| Fungi | Isaria sinclairii | 10%, Zucker mice, 17 weeks | 17% decrease in body weight gain | Ahn *et al*., 2007. |

**Conclusions**

Against this background, we may say that some medicinal plant preparations can be usefully associated to diet therapy, appetite-repression activity, inhibitory effect on adipocyte differentiation, effect on lipid metabolism, or by combined effect for obesity treatment. Although their characteristics should be underlined to avoid disappointment. Many other products are ineffective and their use generally supported by the mass media and industries must be countered to avoid a negative fall-out in the treatment for obesity and on the validity of phytotherapeutics.

**Reference**


1. Anonymous, 1986. African Pharmacopoeia. *General Methods for Analysis*. Africa: Organization of African Unity/ Scientific Technical and Research Commission (OAU/STRC), 1st ed. ISBN No.: 9782453080.
2. Anonymous, 1999. *The Ayurvedic Pharmacopoeia of India*. 1(2): 15-16.]
3. Anonymous, 2007. *The Wealth of India*, NISCAIR, CSIR New Delhi. 5th ed. ISBN No.: 81-85933-04-09.
4. Anonymous, About.com geography, "Population In India", http:// geography. about.com /od/obtainpopulationdata/a/ indiapopulation.html, (Browsing date: 4th January 2012)
5. Agrawal, S. S., and Paridhavi, M., 2007. Herbal Drug Technology. Hyderabad, India: Universities Prees Private Limited Hyderabad, 1st ed. ISBN No.: 8173715793.
6. Daniel M, Method in Plant Chemistry and Economic Botany. Kalyani publishers New Delhi, India. 1991. ISBN NO. 978-0-19-927735-3
7. Mohn A, Catino M, Capanna R, Giannini C, Marcovecchio M and Chiarelli F. 2005. *Increased oxidative stress in prepubertal severely obese children: effect of a dietary restriction-weight loss program*. J Clin Endocrinol Metab. 90: 2653–8.
8. Kalousová M, Zima T, Tesar V, Dusilová-Sulková S and Skrha J. 2005. *Advanced glycoxidation end products in chronic diseases—clinical chemistry and genetic background.* Mutat Res. 579: 37–46.
9. Piwowar A, Knapik-Kordecka M and Warwas M. 2007. *AOPP and its relations with selected markers of oxidative/antioxidative system in type 2 diabetes mellitus.* Diabetes Res Clin Pract. 77: 188–92.
10. Ahn, J., Lee, H., Kim, S., Ha, T., 2007. *Resveratrol inhibits TNF-a-induced changes of adipokines in 3T3-L1 adipocytes.* Biochem. Biophys. Res. Commun. 364: 972–977.
11. Ahn, M.Y., Jee, S.D., Lee, B.M., 2007. *Antiobesity effects of Isaria sinclairii by repeated oral treatment in obese Zucker rats over a 4-month period*. J. Toxicol. Environ. Health. 70: 1395–1401.
12. Asai, A., Miyazawa, T., 2001. *Dietary curcuminoids prevent high-fat diet-induced lipid accumulation in rat liver and epididymal adipose tissue*. J. Nutr. 131: 2932–2935.
13. Attele, A.S., Zhou, Y.P., Xie, J.T., Wu, J.A., Zhang, L., Dey, L., Pugh, W., Rue, P.A., Polonsky, K.S., Yuan, C.S., 2002. *Antidiabetic effects of Panax ginseng berry extract and the identification of an effective component.* Diabetes 51: 1851–1858.

14. Awad, A.B., Begdache, L.A., Fink, C.S., 2000. *Effect of sterols and fatty acids on growth and triglyceride accumulation in 3T3-L1 cells.* J. Nutr. Biochem. 11: 153–158.
15. Bai, N., He, K., Roller, M., Zheng, B., Chen, X., Shao, Z., Peng, T., Zheng, Q., 2008. *Active compounds from Lagerstroemia speciosa, insulin-like glucose uptakestimulatory/ inhibitory and adipocyte differentiation-inhibitory activities in 3T3-L1 cells*. J. Agric. Food Chem. 56: 11668–11674.
16. Baintner, K., Kiss, P., Pfüller, U., Bardocz, S., Pusztai, A., 2003. *Effect of orally and intraperitoneally administered plant lectins on food consumption of rats*. Acta Physiol. Hung. 90: 97–107.
17. Ballinger, A., Peikin, S.R., 2002. *Orlistat: its current status as an anti-obesity* drug. Eur. J. Pharmacol. 440: 109–117.
18. Bays, H.E., 2004. *Current and investigational antiobesity agents and obesity therapeutic treatment targets*. Obes. Res. 12: 1197–1211.
19. Birari R.B., Bhutani K.K., 2007. *Pancreatic lipase inhibitors from natural sources: unexplored potential*. Drug Discov. Today 12: 879–889.
20. Bitou N., Ninomiya M., Tsujita, T. and Okuda H., 1999. *Screening of lipase inhibitors from marine algae.* Lipids 34: 441–445.
21. Bondiolotti G., Bareggi S.R., Frega N.G., Strabioli S. and Cornelli, U. 2007. *Activity of two different polyglucosamines, L112_ and FF45_, on body weight in male rats*. Eur. J. Pharmacol. 567: 155–158.
22. Drew B.S., Dixon A.F. and Dixon J.B. 2007. *Obesity management: update on orlistat*. Vasc. Health Risk. Manag. 3: 817–821.
23. Dulloo A.G. 1993. *Ephedrine, xanthines and prostaglandin-inhibitors: actions and interactions in the stimulation of thermogenesis*. Int. J. Obes. Relat. Metab. Disord. 17: S35–S40.
24. Dulloo A.G., Duret C., Rohrer D., Girardier L., Mensi N., Fathi M., Chantre P. and Vandermander J. 1999. *Efficacy of a green tea extract rich in catechinpolyphenols and caffeine in increasing 24-h energy expenditure and fat oxidation in humans*. Am. J. Clin. Nutr. 70: 1040–1045.
25. Ejaz A., Wu D., Kwan P. and Meydani M. 2009. *Curcumin inhibits adipogenesis in 3T3-L1 adipocytes and angiogenesis and obesity in C57/BL mice*. J. Nutr. 139: 919–925.
26. Ekanem A.P., Wang M., Simon J.E. and Moreno D.A. 2007. *Antiobesity properties of two African plants (Afromomum meleguetta and Spilanthes acmella) by pancreatic lipase inhibition.* Phytother. Res. 21: 1253–1255.
27. M. Geigerman, C. Cook, J. Curtis, L. Kuebler and B. McIntosh. 2000. *Conjugated linoleic acid suppresses triglyceride accumulation and induces apoptosis in 3T3-L1 preadipocytes.* Lipids 35: 899–910.
28. Feltrin K.L., Little T.J., Meyer J.H., Horowitz M., Rades T., Wishart J. and Feinle-Bisset C. 2008. *Comparative effects of intraduodenal infusions of lauric and oleic acids on antropyloroduodenal motility, plasma cholecystokinin and peptide YY, appetite, and energy intake in healthy men*. Am. J. Clin. Nutr. 87: 1181–1187.

29. Ferrer-Lorente R., Cabot C., Fernández-López J.A. and Alemany M. 2007. *Effects of combined oleoyl-estrone and rimonabant on overweight rats*. J. Pharmacol. Sci. 104: 176–182.
30. Flachs P., Horakova O., Brauner P., Rossmeisl M., Pecina P., Franssen-van Hal N., Ruzickova J., Sponarova J., Drahota Z., Vlcek C., Keijer J., Houstek J., and Kopecky J. 2005. *Polyunsaturated fatty acids of marine origin upregulate mitochondrial biogenesis and induce b-oxidation in white fat*. Diabetologia 48: 2365–2375.
31. Flatt J.P. 2007. *Differences in basal energy expenditure and obesity*. Obesity (Silver Spring) 15: 2546–2548.
32. Fleming R.M. 2007. *The effect of ephedra and high fat dieting: a cause for concern! A case report*. Angiology 58: 102–105.
33. Flier J.S. 2004. *Obesity wars: molecular progress confronts an expanding epidemic*. Cell 116: 337–350.
34. Fu J., Oveisi F., Gaetani S., Lin E. and Piomelli D. 2005. *Oleoylethanolamide, an endogenous PPAR-a agonist, lowers body weight and hyperlipidemia in obese rats*. Neuropharmacology 48: 1147–1153.
35. Gades M.D. and Stern J.S. 2003. *Chitosan supplementation and fecal fat excretion in men*. Obes. Res. 11, 683–688.
36. Green H and Kehinde O. 1975. *An established preadipose cell line and its differentiation in culture. II. Factors affecting the adipose conversion.* Cell 5: 19–27.
37. Guzmán M., Lo Verme, J., Fu J., Oveisi F., Blázquez C and Piomelli D. 2004. *Oleoylethanolamide stimulates lipolysis by activating the nuclear receptor peroxisome proliferator-activated receptor a (PPAR-a).* J. Biol. Chem. 279: 27849–27854.
38. Hadváry P., Lengsfeld H and Wolfer H. 1988. *Inhibition of pancreatic lipase in vitro by the covalent inhibitor tetrahydrolipstatin*. Biochem. J. 256: 357–361.
39. Hadváry P., Sidler W., Meister W., Vetter W and Wolfer H. 1991. *The lipase inhibitor tetrahydrolipstatin binds covalently to the putative active site serine of pancreatic lipase*. J. Biol. Chem. 266: 2021–2027.
40. Halford J.C. 2006. *Obesity drugs in clinical development.* Curr. Opin. Invest. Drugs 7: 312–318.
41. Halford J.C and Blundell J.E. 2000. *Pharmacology of appetite suppression*. Prog. Drug Res. 54: 25–58.
42. Han L.K., Kimura Y., Kawashima M., Takaku T., Taniyama T., Hayashi T., Zheng Y.N and Okuda H. 2001. *Anti-obesity effects in rodents of dietary teasaponin, a lipase inhibitor*. Int. J. Obes. Relat. Metab. Disord. 25: 1459–1464.
43. Han L.K., Kimura Y and Okuda H. 1999. *Reduction in fat storage during chitin– chitosan treatment in mice fed a high-fat diet*. Int. J. Obes. Relat. Metab. Disord. 23: 174–179.
44. Han L.K., Kimura Y and Okuda H. 2005. *Anti-obesity effects of natural products*. Stud. Nat. Prod. Chem. 30: 79–110.
45. Han L.K., Nose R., Li W., Gong X.J., Zheng Y.N., Yoshikawa M., Koike K., Nikaido T., Okuda H and Kimura Y. 2006. *Reduction of fat*

*storage in mice fed a high-fat diet long term by treatment with saponins prepared from Kochia scoparia fruit*. Phytother. Res. 20: 877–882.

46. Han L.K., Sumiyoshi M., Zhang J., Liu M.X., Zhang X.F., Zheng Y.N., Okuda H and KimuraY. 2003. *Anti-obesity action of Salix matsudana leaves (part 1). Antiobesity action by polyphenols of Salix matsudana in high fat-diet treated rodent animals*. Phytother. Res. 17: 1188–1194.
47. Han L.K., Sumiyoshi M., Zheng Y.N., Okuda H and Kimura Y. 2003. *Anti-obesity action of Salix matsudana leaves (Part 2). Isolation of anti-obesity effectors from polyphenol fractions of Salix matsudana*. Phytother. Res. 17: 1195–1198.
48. Hwang H.S., Kim S.H., Yoo Y.G., Chu Y.S., Shon Y.H., Nam K.S and Yun J.W. 2009. *Inhibitory effect of deep sea water on differentiation of 3T3-L1 adipocytes*. Mar. Biotechnol. (NY) 11: 161–168.
49. Hwang J.T., Lee M.S., Kim H. J., Sung M. J., Kim H.Y., Kim M.S and Kwon D.Y. 2009. *Antiobesity effect of ginsenoside Rg3 involves the AMPK and PPAR-c signal pathways*. Phytother. Res. 23: 262–266.
50. Hwang J. T., Park I. J., Shin J. I., Lee Y. K., Lee S. K., Baik H.W., Ha J and Park O.J. 2005. *Genistein, EGCG, and capsaicin inhibit adipocyte differentiation process via activating AMP-activated protein kinase*. Biochem. Biophys. Res. Commun. 338: 694–699.
51. Ikeuchi M., Koyama T., Takahashi J and Yazawa K. 2007. *Effects of astaxanthin in obese mice fed a high-fat diet*. Biosci. Biotechnol. Biochem. 71: 893–899.
52. Ishihara K., Oyaizu S., Fukuchi Y., Mizunoya W., Segawa K., Takahashi M., Mita Y., Fukuya Y., Fushiki T and Yasumoto K. 2003. *A soybean peptide isolate diet promotes postprandial carbohydrate oxidation and energy expenditure in type II diabetic mice*. J. Nutr. 133: 752–757.
53. Ito M., Ito J., Kitazawa H., Shimamura K., Fukami T., Tokita S., Shimokawa K., Yamada K., Kanatani A and Uemura D. 2009. *Daisuke uemura (_)-ternatin inhibits adipogenesis and lipid metabolism in 3T3-L1 cells*. Peptides 30: 1074–1081.
54. Jeon T., Hwang S.G., Hirai S., Matsui T., Yano H., Kawada T., Lim B.O and Park D.K. 2004. *Red yeast rice extracts suppress adipogenesis by down-regulating adipogenic transcription factors and gene expression in 3T3-L1 cells*. Life Sci. 75: 3195–3203.
55. Jeon J. R and Kim J.Y. 2006. *Effects of pine needle extract on differentiation of 3T3-L1 preadipocytes and obesity in high-fat diet fed rats*. Biol. Pharm. Bull. 29: 2111–2115.
56. Kim H.K., Della-Fera M., Lin J and Baile C.A. 2006. *Docosahexaenoic acid inhibits adipocyte differentiation and induces apoptosis in 3T3-L1 preadipocytes*. J. Nutr. 136: 2965–2969.
57. Kim H.K., Nelson-Dooley C., Della-Fera M.A., Yang J.Y., Zhang W., Duan J., Hartzell D.L., Hamrick M.W and Baile C.A. 2006. *Genistein decreases food intake, body weight, and fat pad weight and causes adipose tissue apoptosis in ovariectomized female mice.* J. Nutr. 136: 409–414.

58. Kim H.M., Hong S.H., Yoo S.J., Baek K.S., Jeon Y.J and Choung S.Y. 2006. *Differential effects of chitooligosaccharides on serum cytokine levels in aged subjects.* J. Med. Food 9: 427–430.

59. Kim H.Y and Kang M.H. 2005. *Screening of Korean medicinal plants for lipase inhibitory activity.* Phytother. Res. 19: 359–361.

60. Kim J.H., Hahm D.H., Yang D.C., Kim J.H., Lee H.J and Shim I. 2005. *Effect of crude saponin of Korean red ginseng on high-fat diet-induced obesity in the rat.* J. Pharmacol. Sci. 97: 124–131.

61. Kim M.J., Chang U.J and Lee J.S. 2009. *Inhibitory effects of fucoidan in 3T3-L1 adipocyte differentiation*. Mar. Biotechnol. 11: 557–562.

62. Lee, I.A., Lee, J.H., Baek, N.I., Kim, D.H. 2005. *Antihyperlipidemic effect of crocin isolated from the fructus of Gardenia jasminoides and its metabolite Crocetin*. Biol. Pharm. Bull. 28: 2106–2110.

63. Lee J., Chae K., Ha J., Park B.Y., Lee H.S., Jeong S., Kim M.Y., Yoon M. 2008. *Regulation of obesity and lipid disorders by herbal extracts from Morus alba, Melissa officinalis, and Artemisia capillaris in high-fat diet-induced obese mice*. J. Ethnopharmacol. 115: 263–270.

64. Lee J., Jung E., Lee J., Kim, S., Huh S., Kim Y., Kim Y., Byun S.Y., Kim Y.S and Park D. 2009. *Isorhamnetin represses adipogenesis in 3T3-L1 cells*. Obesity (Silver Spring) 17: 226–232.

65. Lee J.S., Lee M.K., Ha T.Y., Bok S.H., Park H.M., Jeong K.S., Woo M.N., Do G.M., Yeo J.Y., Choi M.S., 2006. *Supplementation of whole persimmon leaf improves lipid profiles and suppresses body weight gain in rats fed high-fat diet*. Food Chem. Toxicol. 44: 1875–1883.

66. Lee M.S., Kim C.T., Kim I.H and Kim Y. 2008. *Inhibitory effects of green tea catechin on the lipid accumulation in 3T3-L1 adipocytes*. Phytother. Res. 23: 1088–1091.

67. Lee R.A and Balick M.J. 2007. *Indigenous use of Hoodia gordonii and appetite suppression*. Explore (NY) 3: 404–406.

68. Lee Y.K., Lee W.S., Hwang J.T., Kwon D.Y., Surh Y.J and Park O.J. 2009. *Curcumin exerts antidifferentiation effect through AMPKa-PPAR-c in 3T3-L1 adipocytes and antiproliferatory effect through AMPKa-COX-2 in cancer cells*. J. Agric. Food Chem. 57: 305–310.

69. Lee Y.S., Kim W.S., Kim K.H., Yoon M.J., Cho H.J., Shen Y., Ye J.M., Lee C.H., Oh W.K., Kim C.T., Hohnen-Behrens C., Gosby A., Kraegen E.W., James D.E and Kim J.B. 2006. *Berberine, a natural plant product, activates AMP-activated protein kinase with beneficial metabolic effects in diabetic and insulin-resistant states.* Diabetes 55: 2256–2264.

70. Lefterova M.I and Lazar M.A. 2009. *New developments in adipogenesis.* Trends Endocrin. Met. 20: 107–114.

71. Lei F., Zhang X.N., Wang W., Xing D.M., Xie W.D., Su H and Du L.J. 2007. *Evidence of anti-obesity effects of the pomegranate leaf extract in high-fat diet induced obese mice*. Int. J. Obes. (Lond.) 31: 1023–1029.

72. Lei T., Xie W., Han J., Corkey B.E., Hamilton J.A and Guo W. 2004. *Medium-chain fatty acids attenuate agonist-stimulated lipolysis, mimicking the effects of starvation*. Obes. Res. 12: 599–611.

73. Li J.J., Huang C.J and Xie D. 2008. *Anti-obesity effects of conjugated linoleic acid, docosahexaenoic acid, and eicosapentaenoic acid*. Mol. Nutr. Food Res. 52: 631–645.
74. Li Y., Huang T.H and Yamahara J. 2008. *Salacia root, a unique ayurvedic medicine, meets multiple targets in diabetes and obesity*. Life Sci. 82: 1045–1049.
75. Lin J., Della-Fera M.A and Baile C.A. 2005. *Green tea polyphenol epigallocatechin gallate inhibits adipogenesis and induces apoptosis in 3T3-L1 adipocytes*. Obes. Res. 13: 982–990.
76. Lin J.K and Lin-Shiau S.Y. 2006. *Mechanisms of hypolipidemic and anti-obesity effects of tea and tea polyphenols*. Mol. Nutr. Food Res. 50: 211–217.
77. Lin Y., Kreeft A., Schuurbiers J.A and Draijer R. 2001. *Different effects of conjugated inoleic acid isomers on lipoprotein lipase activity in 3T3-L1 adipocytes*. J. Nutr.Biochem. 12: 183–189.
78. Liu D.Z., Wang F., Liao T.G., Tang J.G., Steglich W., Zhu H.J and Liu J.K. 2006. *Vibralactone: a lipase inhibitor with an unusual fused beta-lactone produced by cultures of the basidiomycete Boreostereum vibrans*. Org. Lett. 8: 5749–5752.
79. Liu F., Kim J., Li Y., Liu X., Li J and Chen X. 2001. *An extract of Lagerstroemia speciosa L. has insulin-like glucose uptake – stimulatory and adipocyte differentiation inhibitory activities in 3T3-L1 cells*. J. Nutr. 131: 2242–2247.
80. Liu L.F., Purushotham A., Wendel A.A and Belury M.A. 2007. *Combined effects of rosiglitazone and conjugated linoleic acid on adiposity, insulin sensitivity, and hepatic steatosis in high-fat-fed mice*. Am. J. Physiol. Gastrointest. Liver Physiol. 92: G1671–G1682.
81. Liu X., Kim J.K., Li Y., Li J., Liu F and Chen X. 2005. *Tannic acid stimulates glucose transport and inhibits adipocyte differentiation in 3T3-L1 cells*. J. Nutr. 135: 165–171.
82. MacLean D.B and Luo L.G. 2004. *Increased ATP content production in the hypothalamus may be a signal for energy-sensing of satiety: studies of the anorectic mechanism of a plant steroidal glycoside*. Brain Res. 1020: 1–11.
83. Ninomiya K., Matsuda H., Shimoda H., Nishida N., Kasajima N., Yoshino T., Morikawa T and Yoshikawa M. 2004. *Carnosic acid, a new class of lipid absorption inhibitor from sage. Bioorg.* Med. Chem. Lett. 14: 1943–1946.
84. Oben J., Kuate D., Agbor G., Momo C and Talla X. 2006. *The use of a Cissus quadrangularis formulation in the management of weight loss and metabolic syndrome*. Lipids Health Dis. 5: 24.
85. Oben J.E., Enyegue D.M., Fomekong G.I., Soukontoua Y.B and Agbor G.A. 2007. *The effect of Cissus quadrangularis (CQR-300) and a Cissus formulation (CORE) on obesity and obesity-induced oxidative stress.* Lipids Health Dis. 6: 4.
86. Oben J.E., Ngondi J.L and Blum K. 2008. *Inhibition of Irvingia gabonensis seed extract (OB131) on adipogenesis as mediated via down regulation of the PPARgamma and leptin genes and up-regulation of the adiponectin gene*. Lipids Health Dis. 7: 44.

87. Ogawa T., Tabata H., Katsube T., Ohta Y., Yamasaki Y., Yamasaki M and Shiwaku K. 2009. *Suppressive effect of hot water extract of wasabi (Wasabia japonica Matsum.) leaves on the differentiation of 3T3-L1 preadipocytes.* Food Chem. 4: 43–46

88. Ohia S.E., Opere C.A., LeDay A.M., Bagchi M., Bagchi D and Stohs S.J. 2002. *Safety and mechanism of appetite suppression by a novel hydroxycitric acid extract (HCASX).* Mol. Cell. Biochem. 238: 89–103.

89. Ohkoshi E., Miyazaki H., Shindo K., Watanabe H., Yoshida A and Yajima H. 2007. *Constituents from the leaves of Nelumbo nucifera stimulate lipolysis in the white adipose tissue of mice*. Planta Med. 73: 1255–1259.

90. Okada T., Nakai M., Maeda H., Hosokawa M., Sashima T and Miyashita K. 2008. *Suppressive effect of neoxanthin on the differentiation of 3T3-L1 adipose cells*. J. Oleo. Sci. 57: 345–351.

91. Okuno M., Kajiwara K., Imai S., Kobayashi T., Honma N., Maki T., Suruga K., Goda T., Takase S., Muto Y and Moriwaki H. 1997. *Perilla oil prevents the excessive growth of visceral adipose tissue in rats by down-regulating adipocyte differentiation*. J. Nutr. 127: 1752–1757.

92. Ono Y., Hattori E., Fukaya Y., Imai S and Ohizumi Y. 2006. *Anti-obesity effect of Nelumbo nucifera leaves extract in mice and rats*. J. Ethnopharmacol. 106: 238–244.

93. Orci L., Cook W.S., Ravazzola M., Wang M.Y., Park B.H., Montesano R and Unger R.H. 2004. *Rapid transformation of white adipocytes into fat-oxidizing machines.*Proc. Natl. Acad. Sci. USA. 101: 2058–2063.

94. Pang J., Choi Y and Park T. 2008. *Ilex paraguariensis extract ameliorates obesity induced by high-fat diet: potential role of AMPK in the visceral adipose tissue*. Arch. Biochem. Biophys. 476: 178–185.

95. Papamandjaris A.A., MacDougall D.E and Jones P.J. 1998. *Medium chain fatty acid metabolism and energy expenditure: obesity treatment implications.* Life Sci. 62: 1203–1215.

96. Park H.J., Yang J.Y., Ambati S., Della-Fera M.A., Hausman D.B., Rayalam S and Baile C.A. 2008. *Combined effects of genistein, quercetin, and resveratrol in human and 3T3-L1 adipocytes.* J. Med. Food 11: 773–783.

97. Sheng X., Zhang Y., Gong Z., Huang C. and Zang Y.Q. 2008. *Improved insulin resistance and lipid metabolism by cinnamon extract through activation of peroxisome proliferator-activated receptors*. PPAR Res. 1–9.

98. Shimada T., Hiramatsu N., Kasai A., Mukai M., Okamura M., Yao J., Huang T., Tamai M., Takahashi S., Nakamura T. and Kitamura M. 2008. *Suppression of adipocyte differentiation by Cordyceps militaris through activation of the aryl hydrocarbon receptor*. Am. J. Physiol. Endocrinol. Metab. 295: E859–E867.

99. Shimoda H., Seki E. and Aitani M. 2006. *Inhibitory effect of green coffee bean extract on fat accumulation and body weight gain in mice.* BMC Complement. Altern. Med. 6: 9.

100. Slanc P., Doljak B., Mlinaric A. and Strukelj B. 2004. *Screening of wood damaging fungi and macrofungi for*

*inhibitors of pancreatic lipase*. Phytother. Res. 18: 758–762.

101. Slovacek L., Pavlik V. and Slovackova B. 2008. *The effect of sibutramine therapy on occurrence of depression symptoms among obese patients*. Nutr. Metab. Cardiovasc. Dis. 18: e43–e44.
102. Sørensen L.B., Cueto H.T., Andersen M.T., Bitz C., Holst J.J., Rehfeld J.F. and Astrup A. 2008. *The effect of salatrim, a low-calorie modified triacylglycerol, on appetite and energy intake*. Am. J. Clin. Nutr. 87: 1163–1169.
103. Van Heerden F.R., Marthinus Horak R., Maharaj V.J., Vleggaar R., Senabe J.V. and Gunning P.J. 2007. *An appetite suppressant from Hoodia species*. Phytochemistry 68: 2545–2553.
104. Verma S.K. and Bordia A. 1988. *Effect of commiphora mukul (gum guggulu) in patients of hyperlipidemia with special reference to HDL-cholesterol*. Indian J. Med. Res. 87: 356–360.
105. Wang S.L., Li Y., Wen Y., Chen Y.F., Na L.X., Li S.T. and Sun C.H. 2009. *Curcumin, a potential inhibitor of up-regulation of TNF-alpha and IL-6 induced by palmitate in 3T3-L1 adipocytes through NF-kappaB and JNK pathway*. Biomed. Environ. Sci. 22: 32–39.
106. Wang Y.W. and Jones P.J. 2004. *Conjugated linoleic acid and obesity control: efficacy and mechanisms*. Int. J. Obes. Relat. Metab. Disord. 28: 941–955.
107. Weibel E.K., Hadvary P., Hochuli E., Kupfer E. and Lengsfeld H. 1987. *Lipstatin, an inhibitor of pancreatic lipase, produced by Streptomyces toxytricini. I. Producing organism, fermentation, isolation and biological activity*. J. Antibiot. (Tokyo) 40: 1081–1085.
108. Fugh-Berman A. and Myers A. 2004. *Citrus aurantium, an ingredient of dietary supplements marketed for weight loss: current status of clinical and basic research*. Exp Biol Med (Maywood), 229(8): 698-704.
109. Carnat A., Carnat A. P., Fraisse D. and Lamaison J. L. 1999. *Standardization of the sour orange flower and leaf*. Ann. Pharm. Fr. 57(5): 410-414.
110. Malhotra S., Bailey D. G., Paine M. F. and Watkins P. B. 2001. *Seville orange juice-felodipine interaction: comparison with dilute grapefruit juice and involvement of furocoumarins*. Clin Pharmacol Ther. 69(1): 14-23.
111. Penzak S. R., Acosta E. P., Turner M., Edwards D. J., Hon Y. Y., Desai H. D. and Jann M. W. 2002. *Effect of Seville orange juice and grapefruit juice on indinavir pharmacokinetics*. J Clin Pharmacol. 42(10): 1165-1170.
112. Naganuma M., Hirose S., Nakayama Y., Nakajima K. and Someya T. 1985. *A study of the phototoxicity of lemon oil*. Arch Dermatol Res. 278(1): 31-36.
113. Bui L. T., Nguyen D. T. and Ambrose P. J. 2006. *Blood pressure and heart rate effects following a single dose of bitter orange*. Ann Pharmacother. 40 (1): 53-57.
114. Song D. K., Suh H. W., Jung J. S., Wie M. B., Son K. H. and Kim Y. H. 1996. *Antidepressant-like effects of p-synephrine in mouse models of immobility tests*. Neurosci Lett., 214(2-3): 107-110.