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Obesity and Natural Products

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Abstract Obesity in adults is characterized when the Body Mass Index (BMI) is greater than or equal to 30. It is estimated that 1.7 billion people in the world are overweight or obese, and more than one third of U.S. adults (35.7%) are obese. There are a variety of factors that play a role in obesity, such as behavior, environment, and genetic factors. Usual countermeasures include adequate physical activity, avoidance of calorie-dense foods, and use of certain drugs for promoting weight loss. Surgery is an extreme measure and anyone considering it must have failed consistently in losing weight through lifestyle changes and less invasive methods. The main drugs currently employed in obesity treatment present dangerous side effects, namely: elevation of blood pressure, insomnia, constipation, headaches, among others. For this reason, a wide variety of natural materials have been explored for their obesity treatment potential. Considering that natural anti-obesity products have different mechanisms, the recommended approach to research a more effective obesity treatment, reaching the associated synergistic effects, must involve the combination of natural products and/or products with multiple activities. This chapter describes several natural products with anti-obesity activity, and active components and mechanisms of action to combat obesity.

Keywords: *anti-obesity activity, metabolic syndrome, natural products, obesity*

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1. Introduction

The obesity is a universal chronic disease defined as the excessive accumulation of body fat resulting in weight gain, above the ideal, which prevalence has grown rapidly and reached epidemic proportions around the world, representing one of the most public health problems in the beginning of this century [1,2]. Patients with obesity have increased risk of developing many diseases; especially type 2 diabetes mellitus (T2DM), dyslipidemias, arterial hypertension, sleep apnea, cardiovascular diseases and neoplasm, with significant increase in mortality [3,4].

2. Definition and Epidemiology

Calculating body mass index (BMI), also known as quetelet index is defined by dividing the mass (Kg) by the square of the height (m) – it is the epidemiological indicator for the diagnosis of overweight and obesity. According to the adapted classification by the World Health Organization (WHO), obesity is defined by a BMI greater than or equal to 30 Kg/m2 [5]. The presence of overweight or obesity increases the risk of comorbidities, there is an association between BMI and mortality or chronic diseases (Table 1) [6].

Table 1. Classification of obesity according to BMI (Kg/m2) and the risk of disease

BMI (Kg/m2)	Classification	Class of obesity	Risk of disease
<18,5	Underweight	-	High
18,5-24	normal weight	-	Normal
≥25	Overweight	-	little high
25-29,9	class I obesity	I	moderate risk
35,0-39,9	class II obesity	II	high risk
≥40	class II obesity	III	very high risk

*Adapted from Pischon et al., 2008.

The definition of infant obesity it´s more complicated and the IMC also change with height and age. Obesity is

considered when the percentage above 95% of BMI for age and sex [7].

Excess fat can be located in the abdominal area, which is defined as *android-type obesity*, central obesity, abdominal obesity or apple shaped, showing a high risk of cardiovascular complications when compared to gynecoid obesity, inferior obesity, peripheral obesity, gluteal-femoral (i.e. the *pear shape*) which the fat is concentrated in the region of the hips [8].

The measurement of waist circumference (WC), made at the midpoint between the lower costal and the iliac Crest, is the anthropometric method that reflects indirectly the contents of visceral fat. However, the abdominal waist values that determine the cardiomethabolic risk vary depending on the population studied. The first North American recommendations established the values of 102 cm for men and 88 cm for women, as cut-off points 5. In other populations, smaller levels – 94 cm for men and 80 cm for women – have been considered more suitable [4,9,10]. The combination of WC measurement with the IMC offers a good alternative to the determination of risks and helps decrease the limitations of each of the individual evaluations [11].

The measurement of waist circumference virtually overrides the relationship waist-hip ratio (WHR), defined by division of waist circumference and hip circumference (at the level of the great trochanter of the femur). Relation >0,8 in woman and >0,9 in men defines the central fat distribution and statistically correlate with the most amount of visceral fat by imaging methods [12,13].

There are other techniques for assessing body fat, the more accurate are the computed tomography and magnetic resonance imaging, methods, generally, costly and of little clinical applicability. The electrical bioimpedance, which evaluates the tissue resistance offered by the passage of electric current, is highly accurate, easy to use, allowing you to evaluate the lean body mass and adipose with precision [10].

The epidemic of obesity is now recognized as one of the most important public health issues facing the world [14]. Tragically, adult obesity is more common worldwide than malnutrition. There are about 475 million obese adults and about 1,5 billion overweight adults [15]. More than 200 million children of school age are overweight [16]. The prevalence of obesity among adults has increased dramatically during the 1990s and early 2000s. The proportion of those who were classified as obese increased from 13% of men in 1993 to 26% in 2010 and from 16% of women in 1993 to 26% in 2010 (HSE) [16,17]. World Health Organization (WHO) projected that by 2015 the world population will be 2,3 billion overweight people and 700 million obese. It indicates an increase of 75% in cases of obesity in 10 years [18].

The prevalence of obesity in the United States increased during the last decades of the 20 Century. According to the *National Health and Nutrition Examination Survey*, 2009-2010, more than 35% of Americans are obese. In General, adults over 60 years old are more prone to obesity than young adults. And, 16.9% of American children are obese. The prevalence of obesity was higher among teenagers than among preschool children [19].

In Europe, about 60% of adults and more than 20% of schoolchildren are overweight or obese. This equates to about 260 million adults and more than 12 million children [20].

The survey of Family Budgets (POF) 2008-2009, carried out in partnership between the IBGE and the Ministry of health, showed that obesity and excess weight have increased significantly in recent years, in all ages. In Brazil, 50% of men and 48% of women are overweight, with 12,5% of men and 16,9% of women have some degree of obesity [21].

Obesity is associated with health problems including type 2 diabetes, cardiovascular disease and cancer. The costs attributable to overweight and obesity are projected to reach £9.7 billion by 2050, with wider *costs* to society estimated to reach £49.9 per year. These factors combine to make obesity prevention a public health problem [22].

3. Pathophysiology and Etiology

The body weight is a result of the complex interaction between physiological and psychological factors that control food intake and energy expenditure. Food intake is governed by hunger, satiety and appetite. The first two are genetically controlled, getting blood glucose levels stimuli, opiates, esplacnicos neurons, neurotransmitters and several cytokines, such as leptin, adiponectin, interleukin 6, tumor necrosis factor and resistin. The appetite has cultural influences and psychological control, reflecting a response to learning from prior contact with food [23].

The total energy expenditure comprises the energy expenditure at rest, thermogenesis induced by diet and physical exercise. Increased body fat is a result of the imbalance between energy intake and energy expenditure. Exercise influences the law of thermodynamics, intrauterine factors, sex hormones, adrenal hormones, growth hormone and slimming effect prior [24].

It is estimated that genetic factors may respond by 24% to 40% of the variance of the weight gain, for determining differences in factors such as basal metabolism rate, satiety and appetite, among others. It is believed that changes in food and sedentary lifestyle pattern acting on susceptibility genes are the main determinant of growth of world obesity. It is likely that obesity has polygenic origin and multifactorial, associated with an obesogenic environment [23].

The global epidemic of obesity should have its explanation focused on the identification of environmental factors involved [25]. In modern societies, the dietary intake is represented by processed foods, high energy content, rich in lipids and carbohydrates. The westernization of life style habits characterized by the unlimited offer of low-cost food palatable, practical and high-calorie [26].

Allied to this factor there is the increased sedentarism, with a decrease in physical activity practice in developed countries and mainly among lower income populations [26]. The urbanization increased the car traffic, combined with the lack of safety of suburban neighborhoods, lower income populations are more vulnerable to physical inactivity and obesity [27].

4. Non-pharmacological Treatment

The success in the treatment of obesity depends on the magnitude of weight loss and obesity-related comorbidities reduction at the beginning of the treatment [28].

A therapeutic intervention for weight loss is effective when there is a reduction greater than or equal to 1% of body weight per month, reaching at least 5% in 3 to 6 months. The literature supports that the decrease of 5 to 10% of weight reduces the risk factors for diabetes and cardiovascular diseases [29,30].

The treatment of obesity is based on interventions for lifestyle modification in the dietotherapy orientation, increasing physical activity and behavioral changes. However, the number of patients who obtain satisfactory results with non-pharmacological measures is low [31].

Most of the dietary treatments of obesity involves reducing caloric intake, encourage the consumption of foods low in fat and high in fiber. Although it seems simple, in practice, most patients present difficulty of long-term maintenance [31].

Physical exercise is an important strategy for the prevention of obesity, guaranteed an additional weight loss diet. Aerobic activities can promote weight loss and fat mass; resistance exercises increase lean body mass [31].

The cognitive-behavioral treatment is also part of obesity treatment, aiming to control the feeding stimulus, or triggers that trigger the early food intake, as well as evaluate and adjust the patient's motivation and the misfits of feeding behavior [31].

5. Pharmacological Treatment

Considering that chronically overweight and obesity lead to complications and high mortality, when there is no weight loss with the adoption of non-pharmacological measures, the use of drugs should be considered.

The use of medicines in the treatment of obesity and overweight are indicated when there are failure in lifestyle change, in patients with a BMI greater than or equal to 30 kg/m²; and with a BMI equal to or greater than 25 kg/m2 is associated with other risk factors such as hypertension, Hyperlipidemia, 2 DM, sleep apnea, osteoarthritis, gout; or with a waist circumference greater than or equal to 102 cm (males) and 88 cm (females) [31].

In this context we can mention the modulating pharmacological agents of energetic homeostasis, such as: Amfepramone, Fenproporex and Mazindol.

The amfepramone (*diethylcathinone*) is the oldest catecholaminergic agent used in the treatment of obesity [32]. It acts on the central nervous system (CNS) by increasing the release of norepinephrine into the synaptic cleft of *hypothalamic neurons*, stimulating the noradrenergic receptors and inhibiting hunger. The main side effects of amfepramone are related to noradrenergic action. The most frequent are: dryness in the mouth, insomnia, migraine and constipation; more rarely, irritability and euphoria [33].

The fenproporex is an inhibitor of appetite of catecholaminergic action, which acts in the CNS, being used in the treatment of obesity since the 70´s decade. There are few controlled studies published about its use, with variations of the doses used and criteria for assessment of weight loss. The most frequently reported side effects are: dry mouth (38-52%), insomnia (15-37%), irritability (13-19%), euphoria (11%) and tachycardia (19%-21%) [31,34].

The mazindol is a tricyclic derived, non-amphetaminic, which has action on the SNC, by blocking the reuptake of noradrenaline in the *pre-synaptic* endings. It was approved as anorexigenic drug in 1973 (51). The major side effects observed were: dry mouth (25%), constipation (22%), nausea (10%), sleep disorders (9%) and dizziness (8%) [35].

Beyond this drug class, we still the Serotonergic drugs (sibutramine) and the Analogs of lipstatin (orlistat).

The sibutramine is a serotonin reuptake inhibitor of noradrenaline in the nerve endings of CNS, and this action has anorexigenic and satiety effects is effective in improving metabolic syndrome parameters such as fasting glucose, triglycerides and HDLc [36]. The sibutramine is contraindicated in patients with a history of cardiovascular disease, including coronary artery disease, stroke or transient ischemic attack, cardiac arrhythmia, congestive heart failure, peripheral arterial disease or uncontrolled hypertension [37].

In SCOUT (Sibutramine Cardiovascular Outcome Trial), there was an increase of 16% in the risk of non-fatal cardiovascular events with sibutramine, this occurred only and so only in obese (diabetes or not) with documented coronary disease (or equivalent of cerebrovascular disease or peripheral blood). Approximately 2,700 diabetics with another risk factor, an average age of 65 years were randomized to receive placebo or sibutramine for five years and the incidence of events was identical in both groups [38]. This documents that sibutramine is contraindicated in patients with heart disease (which was already known), but documents that was safe in patients without heart disease. In January 2010, the European Medicines Agency (EMA) has suspended the license of commercialization of medicine sibutramine [39], and in early October 2010 has been suspended in the United States [40].

The orlistat has intestinal action, acts by inhibiting pancreatic lipase, reducing in 30% the absorption of ingested fats, which are eliminated by fecal excretion. Less than 1% of the drug is absorbed and there is no action in the CNS. Compared with placebo, the orlistat reduced waist circumference, BMI, systolic and diastolic blood pressure, fasting blood glucose, glycated hemoglobin, total cholesterol and LDL cholesterol (LDLc) in patients with type 2 DM [41]. The most common symptoms are loose stool, presence of oil in the feces, fecal urgency, fecal incontinence, flatulence and, less frequently, abdominal pain and rectal pain [42].

The medications that eventually are used for weight loss, but that aren't officially approved for the treatment of obesity, including metformin, fluoxetine, sertraline, topiramate, liraglutide.

Among the SSRIS, fluoxetine and sertraline have been evaluated in patients with overweight, but without formal indication in the treatment of obesity. Its indication is the treatment of depression and bulimia nervosa [43].

The bupropion is an atypical antidepressant noradrenaline-dopamine reuptake inhibitor and a smoking cessationaid, it´s also demonstrated decreased food intake and dose-dependent weight loss [44].

Topiramate enhances the activity of gamma-aminobutirato acid (GABA); blocks sodium channels dependents, antagonizes glutamate receptors and inhibits

carbonic anhydrase. Second used in epilepsy, mood stabilizer, prophylaxis of migraine and in weight loss [45].

The liraglutide is a synthetic drug that has action similar to the hormone glucagon-like peptide (GLP-1). Stimulates insulin release and inhibits the production of glucagon, aiding in the treatment of type 2 Diabetes Mellitus. In addition to these effects, has *satietogenic* acting both in the central nervous system and the digestive tract, delaying gastric emptying and intestinal motility.

Thus, diabetics in using medicine lose weight because decrease caloric intake. This drug was launched in Brazil for the treatment of type 2 Diabetes [46]. Studies in non-diabetic obese of phase I and II showed that the drug has few side effects: migraine, nausea and vomiting in the first few weeks of use, these effects diminish with time. Weight loss is significant (7 Kg on average). Phase III studies are being conducted in 27 countries, including in Braz. Patients with overweight and without co-morbidities were excluded from the study. New studies are being conducted in an attempt to free the non-diabetic obese patient's medication [47].

6. Surgical Treatment

The unsatisfactory results of treatment with diet, exercise or physical pharmalogical therapy reflect the difficulty of the obese patient in changing the lifestyle. With these non-surgical methods often cannot be a significant and sustained weight loss (> 5 years), with many recurrences [48]. In 1991, The *National Institutes of Health* (NIH) demonstrated safety and the long-term success of several anti-obesity surgeries, and that mortality rates are relatively low. Meet potential criteria to bariatric surgery, patients with BMI ≥ 40 Kg/m^2 or BMI ≥ 35 Kg/m^2, associated with clinical co-morbidities, such as cardiovascular diseases, diabetes, hypertension, osteoarthritis or psychological disorders [49]. Bariatric Surgery should never be the first treatment for patients with severe obesity. The procedure should only be indicated when clinical treatment fails (with at least 2 years of specialized medical follow-up) or when the patient cannot keep within a therapeutic plan established [50].

7. New perspectives

The *Food and Drug Administration* (FDA) has not approved any anti-obesity medication since 1999 and 2010 withdrew from the market the drug sibutramine that was approved in 1997. There is a concern of the medical profession and, truly, what will fill this gap in the absence of any firm guidance from the FDA on drugs [40].

Despite the vote by an Advisory Committee of the Agency, in December last year, have been in favor of the release of the new drug, Contrave®, an Association of the antidepressant bupropion and naltrexone, used in the treatment of drug addiction in recent months, 69, was the third weight loss drug rejected by US authorities, joining the Qnexa® and the Lorqess® [40].

The FDA from The USA, approved recently the Belviq® (lorcaserin hydrochloride) for the treatment of obesity, as an adjunct to a low-calorie diet associated with regular practice of physical activities. The new drug was approved for use in adults with a BMI ≥ 30 kg/ m² or with a BMI ≥ 27 kg/m² (overweight) and who have at least a related condition, such as hypertension, dyslipidemia or 2 DM [51].

The greater consequence, however, is the impact that the lack of treatment options causes on the American people and the world's population. More than a third of American adults are obese and vulnerable to devastating consequences of obesity, and increasing numbers are severely affected and without treatment options. The recent withdrawal of drugs from the market, as well as the limited effectiveness and numerous adverse effects, form a set of reasons for new drugs for the treatment of obesity are operated. Thus emerges the need of new therapeutics to monitor the progression of the epidemic of obesity [52] and among these new possibilities, natural products occupy an area of active research and promising, with significant development in the treatment of this pathology, the obesity.

8. Combined Effect in the Treatment of Obesity: the Natural Products Anti-obesity

Traditional Medicine can be appropriately defined as a medical system based on beliefs of certain people and as an important cultural element with its knowledge scope built and settled in daily life, making totally part of what is defined and known as popular wisdom. Therefore, it is noteworthy that the health-disease binomial and the way to understand it is related to historical organization of communities, covering their cultural characteristics and their knowledge. Considering this aspect, is appropriate to consider the use of natural resources for the treatment of diabetes.

Many natural products show a better anti-obesity activity when attached to a balanced diet and even with the use of allopathic medicines. However, the combined effect with herbal medicines and natural products is increasing its offer on the market, because they are products with less toxicity and besides having greater viability for future anti-obesity drugs. Several natural products have a *hipolipemic* activity, which we can observe both in products derived from plants as well as of animal origin [53].

Examples of lipid-lowering substances derived from natural products such as statins and fibrates, help improving a lipid profile, as well as anorexigenic drugs on the market that operates in an attempt to control appetite, reducing obesity and its complications, such as sibutramine and orlistat, combining with a balanced diet and the practice of physical exercises [53,54].

To emerge new researches about substances coming from plants, it is necessary the characterization of active principles where, Pharmacology enters in the context of the pharmacological effects of extracts and isolated chemical constituents and ethnobotany, seeking information from knowledge of different peoples [54].

With the use of natural products by several people, and reported satisfactory results, the need to deepen the knowledge and enrich the pre-clinical and clinical studies performing Pharmacopoeia with natural products for the treatment of obesity.

The treatment of obesity brings good points to the patient, because it reduces the risk of morbidity and mortality. One of the main effects were studied with natural products, they were the thermogenic effect of several potential natural compounds such as caffeine, ephedrine, ephedra, capsaicin and catechins present in green tea [55,56,57].

The thermogenesis is the energy generated in the form of heat in living tissue. To evaluate the amount of heat produced, is the sum of all heat produced in a State of rest, fasting (12 hours) and room temperature. This is directly proportional to basal metabolism rate [58]. To get a Thermogenic outcome through diet, studies were carried out with edible natural products that have such activity. Unless that they are foods which have difficulty in being digested by the body by consuming as many calories to digest them. These foods also have the capacity to increase body temperature by speeding metabolism and consequently burning fat [59].

Examples of thermogenic foods are the red pepper, ginger, mustard, Apple Cider vinegar, spinach, asparagus, cabbage, broccoli, orange, kiwi, caffeine, guarana, ice water, linseed, vegetable fats, coconut oil and cocoa products. In addition to the thermogenic effect, there are also in several literatures a wide variety of plants and other products derived from animals that have positive activity for the hypolipidemic effect, that can cite the *Garcina cambogia* Roxb., *Camellia sinensis* (L.) Kuntze – green tea, *Panax ginseng* A.C. Meyer, *Phaseolus vulgaris* L., *Caralluma fimbriata* Wall., *Citrus aurantium* L., *Ephedra sínica* Stapf., *Fucus vesiculosos* L., *Rhamnus purshiana* DC., Chitosan, Orlistat, capsaicin (Table 2).

Table 2. Species with positive activity for the hypolipidemic effect.

Species	Family/ Botanical Aspects	Part Plant	Chemicals-Related Effects	Reference
Camellia sinensisi Linnaeus	Theaceae/ Small tree or shrub branched	Leaves	Flavonoids, Flavonols predominate are catechins, epicatechin 3-gallate, epigallocatechin	Nagao et al., 2005[60]; Grove et al., 2010[61]
Capsicum annuum Linnaeus	Solanaceae/ Bush	Fruit	Capsaicin	Jeon et al., 2010 [62]
Caralluma fimbriata Wall.	Asclepiadaceae/ Bush	Leaves	Hexadecanoic acid and Oleic acid	Priya et al., 2011[63]; Kamalakkannan et al., 2010[64]
Citrus aurantium Linnaeus, Carl von	Rutaceae/ Herbaceous plant	Fruit	Synephrine	Kalluf,2008 [65]; Haaz et al., 2006[66]
Ephedra sinica Stapf.	Ephedraceae/ Bush	-	γ-terpinene	Wang et al., 2006[67]
Fucus vesiculosus Linnaeus	Fucaceae/ Alga	Stalk	Lodine, mucilage, phytosterols, tetraterpenes	Moro et al., 2000[68]; Souza et al., 2012[69]
Garcinia cambogia Linnaeus	Clusicaceae/ Bush	-	Hydroxycitric acid	Leonhardt et al., 2002[70]; Heymsfield et al., 1998[71]
Panax ginseng C.A. Meyer	Araliaceae/ Bush	Root and Berry	Ginsenosides	Kalluf,2008[65]; Dey et al., 2003[72]
Phaseolus vulgaris Linnaeus	Fabaceae/ Herbaceous plant, climber or not	Common bean	Fiber	Celleno et al., 2007[73]; Moro et al., 2000[68]
Rhamnus purshiana D.C.	Rhamnaceae/ Bush	-	Anthraquinonic (cascarosides)	Kalluf,2008[65]

A new paradigm in the treatment of obesity is a higher ingestion of food derived from plants, because of their amount of vitamins, proteins, minerals and bioactive compounds, where the junction of these substances are essential in the maintenance of health [74].

Various natural compounds have been shown to be effective in adipocyte differentiation and in thermogenesis which the capsaicin, derived from the red pepper (*Capsicum annuum* L.) is a bioactive compound that acts on the stimulation of appetite, helps in digestion and stands out from the others. Has increased salivation, engine produces a greater secretion and stimulates intestinal motility [75].

Clinical studies with capsaicin performed with human beings showed an increase in energy expenditure after meals. It was observed in pre-clinical and clinical trials that the thermogenic action of capsaicin is induced by Beta-Adrenergic receptors [76,77]. Also stimulates the sympathetic nervous system, which reduces lipid mobilization and decrease in breast adipose tissue [76]. Combined treatment with capsaicin can reduce body fat by increasing lipid oxidation, since these intracellular signaling pathways activate adaptive, which increases lipid oxidation by decreasing the oxidative stress [74].

The *Camellia sinensis* (L.) Kuntze is a plant rich in flavonoids, where the flavonols that predominate are catechins, among them the epicatechin 3-gallate, epigallocatechin. The epicatechin 3-gallate is the main bioactive compound present in *Camellia sinensis* (L.) Kuntze. The catechin is present at low levels in human plasma, where for the hypolipidemic effect, suggests the intake by several times a day [60]. Human studies show that green tea consumption increases by 4% the energy expenditure for thermogenesis, as compared to the group treated with placebo and caffeine, also improves the lipid profile in humans and in rats by decreasing the rates of triglycerides and total cholesterol [78,79]. The catechin epigallocatechin gallate is related to the improvement of conditions for the practice of exercises, favoring an improvement in lipid oxidation [78,80].

Other studies show that the natural antioxidants such as green tea are used for an effective correction index lipaemic specimen such as lowering cholesterol and triglycerides. The epigallocatechin regulates various enzymes involved in lipid catabolism and anabolism, as for example the acetyl CoA-carboxylase, fatty acid synthetase, pancreatic lipase, gastric lipoprotein, lipoprotein lipooxigenase. Its thermogenic effect occurs in

medication of β-adrenergic receptors such as caffeine, which is also present in composition of green tea [56,78,81].

The *Garcina cambogia* Roxb., native species from Asia, Africa, Tropical America and Polynesia Robx To the family Clusicaceae has as its major constituent hydroxycitric acid (HCA) that accelerates the thermogenesis and controls and reduces body fat. The HCA has in it action mechanism the reduction of acetyl-CoA, which will limit the availability of units of 2 carbons in fatty acid biosynthesis and cholesterol. It promotes the oxidation of fatty acids, increasing the release of serotonin (5-HT2a) and decreasing the concentration of leptin in human serum. The HCA also has anorectic effect, causing a decrease in food intake [82].

Clinical research with the dried bark extract of *Garcina cambogia* Roxb., reveal that reduces the intake of calories and have a feeling of satiety and HCA inhibits the conversion of carbohydrates into fat. Other clinical research show that there was apitite reduction of serum leptin in the groups treated with HCA, where several studies have assessed the potential effect of *Garcina cambogia* Roxb. dextract HCA associated with other substances with potential weight loss [83,84].

Rhamnus purshiana DC., popularly known as cascara, is a medicinal plant used in the treatment of obesity, has laxative effect, stimulating peristalsis and bowel motility, increasing the frequency of evacuationy, being recommended for occasional constipation [85,86]. Only a study related to the treatment for thinning in addition, can cause gastrointestinal disturbances and, its prolonged use (10 to 30 years), can be a risk factor for colorectal cancer [86,87]. Is a natural product that already exists for therapeutic use, can be administered in the form of drops, tablets or encapsulated extract [85].

The principal constituents found in cascara sagrada are the anthraquinonic, the cascarosides and the primary heterosides of higher pharmacological activity. The cascarosides C and D are isomers corresponding to *Chrysalin*. These cascarosídeos have increased pharmacological activity. The main use of cascara sagrada is for constipation *re-establishinq* the colon natural tone in humans. The hematotoxin, an albuminoid is the main active compound responsible for the emetic action [65].

The Ginseng (*Panax ginseng* A.C. Meyer) is a botanical species widely used in Chinese medicine, because the Eastern ancient peoples believe that increase longevity and improve quality of life. The root of *Panax ginseng* A.C. Meyer can increase muscle strength and aerobic work capacity [69]. The majority constituents of the plant are the ginsenosides, the main class of bioactive compounds from ginseng. It is generally indicated to cases of physical and mental fatigue [72]. Statistically significant benefits were found with the administration of doses greater than 2 g per day of standardized extract, for a period of more than 8 weeks. However, there is controversy. There were not results with smaller doses. Its effects are also more valid in athletes with 40 years or more [65].

In one study, which examined the supplementation of Panax ginseng on mice, using 150 to 300 mg of extract of leaves and stalk for 12h was demonstrated by a decrease in blood glucose (dose dependent) and glucose tolerance test, in addition to the weight loss [73]. In case of overdosage, it can lead to brain arthritis with intense headache, morning diarrhea, nausea and vomiting [74]. Ginseng can alter blood pressure, cause insomnia, nervousness, rash, euphoria and diarrhea when given for a long period of time [69,75].

The *Fucus vesiculosus* L. is a dark alga in the family fucaceae, very abundant in the rocky coast of the Atlantic Ocean, Pacific Ocean and the North Sea. Its main bioactive compounds are polysaccharides and mineral salts, which also contains alginic acid, algin or which is a mucilaginous fiber, which on contact with the stomach if it moisturizes and causes sensation of fullness and laxative effect because it is not absorbed by the intestine. It may be prescribed in pill or capsule form increases basal metabolism, stimulating the thyroid gland, due to the concentration of iodine. With this, his overdose can lead to hyperthyroidism, tachycardia and hypertension, in addition to interacting with other herbal medicines as: *Equisetum arvense* L., *Rhamnus purshiana* DC., *Passiflora* sp.; *Senna alexandrina* Mill. and *Ephedra sinica* Stapf. [85,88].

The *Ephedra sinica* Stapf. is a species well known in Asia in the Ephedraceae family also widely used for the treatment of obesity by Orientals. Its rich contents of ephedrine and caffeine also may have lipolytic action, increasing the basal metabolic rate. However, high doses of this extract may lead to tachycardia, increased heart rate and blood pressure when used in conjunction with compounds that have caffeine. Should not be used for extended period of time, because due to the presence of ephedrine consumption is associated to tolerance and dependence [85,89,90,91]. In an analysis, with the use of ephedra in humans, for a period of 8 weeks to 6 months, it was noted a small weight reduction (0.9 kg), as compared to the placebo group [91]. There are indications that aid in weight loss and improve physical capacity.

The *Citrus aurantium* L. popularly called bitter orange is a phytotherapeutic which aids in weight loss, without changing in body composition the physical activity of practitioners, the synephrine, bitter orange majority compound, can be a substitute for ephedrine, but without its side effects, such as increased heart rate and blood pressure [65]. There is a chemical complex of particular interest, where the bark contains flavones, synephrine alkaloids, octopamine, and N-methyltyramine, and carotenoids. In a survey it was demonstrated a metabolic increase when supplemented with the meal. Increase by 29% the energy expended by joining to food, while when administered alone increased only 4%. Also leads to an increase in fat burning and increases lipolysis. The bitter orange taken together with the *Caralluma fimbriata* Wall. and the phaseolamine can form a powerful compound slimming. Complete and extremely effective, because it contains several chemical compounds that can stimulate the metabolic rate which is possibly increase the burning of calories in the body. The *Citrus aurantium* L. increases metabolism by stimulating the beta-3 receptor, avoiding negative side effects on the cardiovascular system. In addition, as the administration of *Citrus aurantium* L. increases the availability of fat oxidation (cellular respiration), the body has access to larger amounts of energy [91,92]. It is recommended that 20 mg of Synephrine (bitter orange compound), being safe doses up to 60 mg for chronic use. Must be used doses up to 600 mg bitter orange a day, to increase lipolysis and thermogenic action, has slightly sedative action [85].

The *Caralluma fimbriata* Wall. it is an edible Cactus, very common in India, used by Indians of the tribe to suppress hunger and increase stamina. Its secondary constituents are the side pregnano glycosides, flavone, megastigmame, saponins and other flavonoids. This *phytoterapic* inhibits the action of the enzyme lipase citrate, Thus, inhibiting the absorption of fats, it also inhibits the appetite and increases lean body mass. The inhibition of appetites can be by the action of glycoside Perpignan which is common in plants of Asclepiadaceae family. They are recommended doses up to 1000 mg a day [65]. Kamalakkannan et al demonstrated in a study with rats fed with high calorie and high-fat diet, supplementation of The *Caralluma fimbriata* Wall. it is an edible Cactus, very anti-obesity effects obtained by decreasing the appetite (dose dependent). These effects are reflected on feed intake, body weight, abdominal fat, serum lipid profiles. In addition to the decrease of leptin resistance characteristics, being 50 mg/kg/day dose which appeared ideal for treating and preventing obesity and associated pathologies. The mechanism of action may be related to sensory function of the hypothalamus, amplifying the signal energy, also very similar to the effect found in the plant *Hoodia gordonii* (Masson) Sweet ex Decne [93].

In a study of men and women with a BMI greater than 25 kg/m2 getting 1 g of *Caralluma fimbriata* Wall. per day for 60 days, was shown a decreased appetite and abdominal circumference, also when compared to the control group (who received placebo) [94].

The White beans (phaseolamine - *Phaseolus vulgaris* L.) are very common in food legumes of Brazilians. It is an excellent food, providing essential nutrients for the human being, such as protein, iron, calcium, magnesium, zinc, vitamins (especially B-complex), carbohydrates and fiber. Also stands for improve the calorie intake by reducing the ingestion of calorie [95].

Studies carried out with products based on white bean extract (*Phaseolus vulgaris* L.), showed that the mechanism of action is inhibition of alpha-amylase, by preventing the digestion of carbohydrates, thus decreasing the calories ingested, promoting weight loss. This effect occurs primarily in reducing glucose absorption, in this way, can improve blood glycemy [96,97].

In a study with humans was used 1500 mg extract of white beans, twice a day, at lunch and at dinner, for 8 weeks, combined with a proper diet, It has been demonstrated that the group that received the phaseolamine obtained a 129% more weight loss than the control group, however, was a small sample study, where only 27 participants have followed the guidance until the end of treatment [96]. Celleno et al. [97], analyzed dietary supplementation of 450 mg extract of *Phaseolus vulgaris* L. on the body composition of 60 overweight volunteers, for 30 consecutive days, being administered before meals rich in carbohydrates. This study found that individuals who received the extract showed significantly better results regarding weight loss, BMI reduction, fat mass reduction, adipose tissue thickness and waist and hip ratio, and there was still a better maintenance of lean body mass when compared to the placebo group [97].

Found in various animals such as insects and crustaceans, chitin and Chitosan, polysaccharides and main constituent found in shells of shrimp and shells of crabs. Both polysaccharides are different in respect to solubility, the chitin is insoluble in most solvents and soluble Chitosan in aqueous solutions of inorganic and organic acids [98]. Lee et al., [99] considers the most important feature of Chitosan to its action as a chelator, where it binds the substances such as cholesterol, fats, proteins, tumor cells and metal ions, where this ability of Chitosan differs from chitin. This trait as quelant, helps in fat reduction and body weight reduction through the capture of fat ingested and its ability to reduce levels of LDL cholesterol without affecting HDL cholesterol levels. Studies suggest that the loads of cationic Chitosan bind to negative charges of bile acids and fatty acids, resulting in the *hypocholesterolemic effect* , increasing the excretion of cholesterol, phospholipids, monoglycerides and fatty acids associated with, leading to an increase in the oxidation of cholesterol in the liver. Several studies have attempted to establish the mechanism of action of Chitosan which consit in the emulsification of lipids in the stomach, with attraction of lipids into the duodenum.

Zahorska-Markiewicz et al., [100] concluded that Chitosan can be used as a drug, better security, and supporting as a valuable treatment for obesity in the long term, and that also lowers blood pressure along with weight loss, improving the risk and complications of cardiovascular disease, more common in obese.

With a variety of natural products that inhibit appetite, when taken together, Act on different targets, both in the obesity genes, and an *adipocyte differentiation.* Some natural products do not have their mechanism of action identified yet, what can be improved in further research, since obesity is a global health problem, where various allopathic medicines are being withdrawn from the market because of their harmful side effects to humans. With the use of natural products, it is considered a safe and effective method, which may improve the exploitation of natural sources to a safe pharmacological action in the treatment of obesity.

9. Conclusion

The obesity has become practically a pandemic which cause many health aggravations that became a major concern for Governments and health systems, besides great economic niche for pharmaceutical industries. Because of that numerous researches are carried out in search of new effective and safe drugs in the treatment against obesity, Since currently the regulatory agencies responsible for marketing authorization of medicines are very strict in the assessment for the release of such products, example of this is the Brazil that has only one medicinal product released to be marketed with indication of combating obesity.

So the natural products are at the forefront of these new researches if not for production of herbal medicines, for the discovery of new drugs that can be isolated or synthesized. It generates more effective and safe new drugs to combat obesity.

Conflicts of Interest

No conflict of interest in this work.

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