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Hoodia Gordonii a herbal plant: A Review

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Abstract— *According to statistics compiled by the World Health Organization (WHO), around one billion persons are overweight today, with another 300 million being obese. Based on these data, it is clear that obesity has become a huge international problem, impacting nations of all economic levels. Estimates predict that by 2025, Brazil would rank fifth in the world in obesity prevalence, up from its current rate of roughly 13%. Although certain herbal treatments are indicated for therapy, many other natural items are utilized without consideration to their safety or effectiveness in preventing or reducing weight gain. Notable among these is the African plant Hoodia gordonii, whose commercial powder was sold freely until it was banned in February 2007 by the Brazilian National Sanitary Surveillance Agency (ANVISA) due to a lack of scientific proofs of its efficacy and safety. Moreover, its putative association with leptin and insulin involved in neuroendocrine control of hunger and satiety is not well understood, nor is its method of action in suppressing desire and thirst.*

Keywords— Hoodia gordonii, obesity, herbal medicine, treatment.

I. INTRODUCTION

One billion persons are estimated to be overweight, with another 300 million being obese, according to figures from the World Health Organization (WHO, 2010). Based on these data, it is clear that obesity has become a huge international problem, impacting nations of all economic levels. It is estimated that by 2025 Brazil would rank fifth in the world in obesity rates (Brasil, 2009; Ogden et al., 2006), with 13% of the population already classed as obese.

Obesity is a complex disease with many contributing causes, including but not limited to cultural, genetic, psychological, metabolic, endocrine, and environmental influences. A team of specialists trained in different areas should provide any necessary treatments or therapies.

Numerous natural compounds are used without discrimination to prevent, decrease, or postpone weight gain, despite the lack of research evaluating their therapeutic effectiveness and safety. Hoodia gordonii (Apocinaceae, sub-family Asclepiadaceae) powder, a plant native to Africa, was widely available until it was banned by the National Sanitary Surveillance Agency (ANVISA) in 2007 due to a lack of scientific evidence supporting its efficacy and safety (Anvisa, 2007). Commercial goods based on H. gordonii have been appearing in a variety of forms due to expanding interest in the plan in recent years. Unfortunately, the plant's low availability in contrast to the high demand has led to an uneven market, raising concerns about the likelihood of manipulation, notably in the case of the cactus Opuntia ficus, often referred to as cactus.

There have been no research conducted on the effectiveness or toxicity of H. gordonii commercial powder or its chemical components (nutrients and anti-nutrients). More research is required to determine its

method of action in reducing hunger and thirst, as well as any potential links to the satiety-inducing hormones insulin and leptin.

II. LITERATURE REVIEW

Obesity

Concept

Excessive amounts of fat in the body are the hallmark of obesity. The body mass index (BMI) is the most often used diagnostic indicator in adult patients. The body mass index (BMI) is found by dividing one's weight by the square of their height. According to the World Health Organization's (WHO) (WHO, 2010) definition, a healthy weight ranges from a body mass index (BMI) of 18.5 to 24.9. A body mass index of 30 or above defines obesity. Abeso, Sbem, and WHO (2010).

So, "a weight that is above what is considered healthy for a specific height" (CDC, 2010) is the current definition of overweight and obesity in the public.

Etiology

Obesity may have a variety of root causes. It has been suggested that endocrine abnormalities, poor eating habits, and heredity all have a role in obesity (Sbem, 2010). Since there is no way that humankind's genetic legacy could have changed much in the span of a few decades, environmental influences must be to blame. However, various predisposing genetic variables may be playing a substantial part in determining energy imbalance of overweight (Coutinho, 2007), which must be taken into account when assessing a clinically obese patient

Furthermore, it is now recognized through studies of physiology and the neuroendocrine control of hunger and satiety that the obesity pandemic is caused by the obesogenic environment, which is the product of the interaction of racial characteristics, genetics, and culture (Apovian, 2010)..

Prevalence and progression

More than a billion persons are overweight, and another 300 million are clinically obese; this worldwide disease has reached epidemic proportions. North America, the United Kingdom, Eastern Europe, the Middle East, the Pacific Islands, Australia, and China have all seen a tripling of their respective obesity rates since 1980. In contrast to wealthy nations, however, emerging nations are increasing at a quicker pace (Opas/OMS, 2003).

Obesity rates in the United States are 32.2% in men and 35.5% in women, according to the most recent data (Flegal et al., 2010) from the National Health and Nutrition Examination Survey (NHANES). Recent data suggests that other countries have already surpassed U.S. rates, including China among children and Australia and the UK among women (Popkin, 2010). Previous studies have shown that the United States has the highest rates of obesity among the population (Fabricatore et al., 2008; Houston et al., 2008; Ogden et al., 2006).

About 18 million individuals in Brazil are regarded to be overweight. When the number of obese and overweight people is added together, it doubles from 30 years ago to 70 million now (Sbem, 2010).

Current estimates place the percentage of obese adults in Brazil at about 13%, with the prevalence being higher among women (13.6%) than males (12.4%). Since the initial evaluation in 2006, annual increase rates have been recorded (Brasil, 2009), indicating serious cause for alarm.

Problems associated

The metabolic impacts of obesity and excess weight include increased blood pressure, cholesterol, and triglyceride levels, as well as insulin resistance. Problems with health are not lethal, but they are quite incapacitating. According to a 2002 World Health Organization research (Opas/OMS, 2003), an estimated 2.5 million individuals worldwide die annually from obesity-related causes.

Some of the most common illnesses in today's culture have a connection to obesity, including a higher chance of developing diabetes mellitus. For obese adults who also smoke, the chance of death rises even more (Francischi et al., 2000). Obesity has also been linked to biliary illnesses, osteoarthritis, cardiovascular disease, and some types of cancer (Bray, 2004; Thande et al., 2008).

Economic impacts

Between 2% and 7% of health care spending in low-income nations is attributable to obesity-related conditions. Since not all diseases related to obesity are included in these numbers (Opas/OMS, 2003), the actual costs of this pandemic are certainly substantially greater.

Obesity-related healthcare costs in the United States were around $78.5 billion in 1998 (Finkelstein et al., 2009), and are projected to rise to $147 billion in 2008 (both figures are for inpatient and outpatient care and prescription drugs).

When it comes to nations with obesity concerns, Brazil ranks sixth worldwide. Approximately 12% of the overall yearly expenditures of Unified Health Services (SUS) with hospitalizations (Gigante et al., 2009) may be attributed to the direct costs connected with this condition. These costs include hospitalizations, medical consultations, and medicines.

Treatments to reduce obesity

Dietary changes, regular exercise, medication, and behavioral modifications are all part of the treatment plan (Francischi et al., 2000). Public health initiatives, medical programs, and community-supported reforms in the food sector are all proposed as means of combating the obesity pandemic by encouraging healthier diets and more physically active lifestyles. Programs in the community that encourage exercise both before and after work, as well as on weekends, may help people lead healthier lives (Apovian, 2010).

Different medicines that encourage weight reduction are available as treatments for these people. Studies have focused on a number of medications for weight loss, including serotonin reuptake inhibitors like sibutramine and lipase inhibitors like orlistat, as well as catecholaminergic agents like amfepramone diethylpropion, fenproporex, mazindol, and ephedrine-caffeine combinations, serotoninergic drugs like fenfluramine and fluoxetine, and other medications like metformin.

In addition to these, it is considered that there has been a significant rise in the usage of "natural products" for weight loss among the general public in recent years. Artichoke (Cynara scolynmus), aloin (Aloe vera), boldo (Peumus boldus), coot (Baccaharis sp), cascara sagrada (Rhamnus purshiana), Centella asiatica, citrin extract (Garcinia sp), chlorella (Chlorella pyrenoidosa), Maytenus (Maytenus ilicifolia), spir However, there is a lack of scientific evidence regarding the usefulness and safety of products like Hoodia gordonii, which have also been used for the same reason.

The current understanding of fat cells as an endocrine organ, along with contributions from the intestine and pancreas, sheds light on the neuroendocrine regulation of appetite and satiety by substances like leptin, insulin, and ghrelin, opening up a range of therapeutic options for treating obesity (Apovian, 2010; Bays, 2004).

Hormones involved in neuroendocrine regulation of appetite and satiety

Leptin

Adipose tissue, which regulates feeding by acting on cells in the hypothalamus of the central nervous system, is the primary source of leptin (Greek mites = thin), a protein consisting of 167 amino acids with a structure similar to cytokines (Reseland et al., 2001). As well as modulating neuroendocrine function and energy meta-bolism, leptin's effect in the hypothalamus of mammals encourages lowering food intake and increasing energy expenditure (Auwerx and Staels, 1998; Friedman and Halaas, 1998).

Inhibiting the production of NPY and other appetite-related neuropeptides, leptin suppresses food intake and increases the production of anorexigenic neuropeptides like -melanocyte-stimulating hormone (-MSH), corticotropin-releasing hormone (CRH), and amphetamine- and cocaine-induced peptides (CART) (Elmquist et al., 1998; Friedman and Halaas, 1998). Therefore, elevated leptin levels suppress appetite, whereas decreased leptin levels cause overeating (Romero and Zanesco, 2006).

Hyperleptinemia, which is common in the obese population, may be indicative of leptin resistance, a disease analogous to insulin resistance in type 2 diabetes. High levels of leptin in this situation are linked to overeating and weight gain (Considini et al., 1996.

According to rat studies (Spanswick et al., 1997), leptin activates an ATP-sensitive potassium channel, suggesting that this channel may serve as a molecular target of the hormone in hypothalamus neurons.

Insulin

Insulin is a peptide hormone that consists of two polypeptide chains (A and B) joined together by two disulfide links; each chain has 21 amino acids. varying animals have somewhat varying amino acid compositions, yet all of their chains share the same 10 residues. In modest quantities (0.1 mM or 0.6 mg/mL), one individual

insulin molecule may be found. As a monomer, insulin performs its biological action under physiological settings by being maintained at concentrations between 10 and 3 mM. Insulin dimerization occurs at values greater than 0.1 mM (Chien, 1996).

It has a crucial role in glucose homeostasis, growth, and differentiation, and is the most anabolic hormone we know of. Specifically, insulin decreases glucose synthesis in the liver (by decreasing gluconeogenesis and glycogenolysis) and increases peripheral uptake of glucose, mostly in muscle and adipose tissue. In addition to increasing protein synthesis and decreasing protein breakdown, insulin also promotes lipogenesis in the liver and adipocytes (Carvalheira et al., 2002).

Beta cell insulin secretion and insulin concentration in the blood are inversely related to body fatness, as shown by Halpern et al. (2004). Insulin's anabolic impact boosts glucose absorption, and a drop in blood sugar levels stimulates hunger (Woods et al., 1998). The recently discovered insulin receptors in the brain have shown the critical role that insulin plays in the central nervous system, where it regulates the activity of leptin and promotes satiety and energy expenditure (Hallschmid and Schultes, 2009; Schwartz, 2000).

Ghrelin

One of the primary activities of the gastrointestinal hormone ghrelin (English grow = growth) discovered in the stomach of rats is to stimulate the production of growth hormone (GH) (Kojima et al., 1999; Kojima et al., 2001). Gr is a 28-amino-acid peptide that is mostly made by cells in the digestive system (Bednarek et al., 2000; Kojima et al., 1999).

One of the most essential flags to the top of food consumption, ghrelin is directly engaged in controlling short-term energy balance. Its levels are highest during fasting and before meals, and they drop after eating, pointing to neural regulation. It does more than just make you hungry; it also gets your stomach moving and increases digestive secretions (Konturek et al., 2004; Nakazato et al., 2001).

In the hypothalamic regions that control food intake and obesity, leptin signaling is crucial, according to research in animals (Nakazato et al., 2001; Romero and Zanesco, 2006).

following carbohydrate-rich meals, the plasma concentration of ghrelin drops as insulin rises; however, following animal protein- and lipid-rich meals, ghrelin levels rise somewhat along with insulin (Erdmann et al., 2004; Salbe et al., 2004).

Hoodia gordonii (Apocinaceae)

Taxonomic information

Hoodia belongs to the subfamily Asclepiadaceae of the plant family Apocinaceae, which is part of the Gentianales order. About 250 genera and 2000 species make up this family; most of them are medicinal plants (herbs) and shrubs with white sap; others have succulent stems and thorns like cactus with tiny leaves (University of Hawaii, 2007; Van Heerden, 2008). Among the many species in the genus Hoodia, H. gordonii, H.pilfera, H. lugardii, and H. ruschii have been the focus of a great deal of study (Archer and Victor, 2003; Chow et al., 2005; MacLean and Luo, 2004).

Hoodia gordonii, like other members of its genus, is succulent and squishy, with a flower-shaped crown of about 100 mm in diameter and many upright and cylindrical rods ranging in color from gray-green to gray-brown. The stems, which number 11–17 and are united in their bottom half at obtuse angles, culminate in thorns that are 6–12 mm in length and are highly sharp (Bruyns, 2005).The press often refers to H. gordonii as "cactus" or "cactus of the desert" due to the plant's spiky look; nevertheless, it is not a member of the family Cactaceae, which includes actual cacti (Van Heerden, 2008).

Thirteen species are currently of primary interest due to their anorectic properties (H. alstonii, H. currorii, H. Dreger, H. flava, H. gordonii, H. juttae, H. mossamedensis, H. officinalis, H. parviflora, H. pedicellata, H. pilifera, H. ruschii, and H. triebner.

Distribution

The deserts of Namibia and the Kalahari in southern Africa are natural habitats for the Hoodia plant. The San people, also known as Bushmen, are the original residents of South Africa, Namibia, Botswana, and Angola and are responsible for cultivating the plant Hoodia gordonii (Figure 1). Xhoba is what the Indians use to refer to this plant (WHO, 2003).

Hoodia species are protected in South Africa, thus collectors, growers, shippers, and exporters must get

permission from the appropriate authorities before doing any of those things. They are closely linked to slow-growing, finicky plants. As a result of their scarcity, commercial production of plants will become more important in the future (Van Heerden, 2008).

Export of H. gordonii is strictly regulated by the South African government and international agreements to safeguard plant species since it is now on the endangered species list (Avula et al., 2008).

History

The San are one of the oldest groups living in southern Africa, and they have been consuming H. gordonii bites for thousands of years. They used the plant to stave off hunger, reduce appetite, and preserve the supply for many days while they went on a hunting trip without food or water (WHO, 2003). According to research (Bruyns, 2005), the plant's sap may help with hunger pangs during extended journeys to remote locations in quest of native hunting.

This appetite-suppressing action piqued scientific curiosity, and in the 1960s of the 20th century, a chemical named P57, found in H. gordonii, was identified and trademarked by the Council for Scientific and Industrial Research (CSIR) in South Africa. The CSIR licensed the chemical P57 to the British company Phytopharm later in 1997. Initial testing showed promise for the medicine, and Phytopharm eventually parted ways with Pfizer for $21 million. The businesses believed the medicine would completely change the $9.5 billion slimming product industry. A protracted legal struggle ensued between business and the CSIR on one side and the San people on the other over the allocation of profits from the exploitation and marketing of Hoodia (WHO, 2003) after a complaint by foreign firms who were accused of biopiracy.

Pfizer gave up the rights to Hoodia in 2002, citing difficulties in synthesizing the compound and the discovery of P57-related adverse effects in mice as reasons for the decision components of the extract could not be easily removed (Bindra, 2005). Pfizer's hoodia research leader Jasjit Bindra said the supplement still needs a lot of work before it can win over the FDA in North America. People interested in the diet should refrain from using it until safer versions are created.

Fig.1. Hoodia gordonii (Hübner. and Tränkle, 2004).

After years of discussion, the two sides were able to settle their differences in March of 2003. Agreement rules provide that 8% of license fees paid to Phytopharm and 6% of royalties paid to the CSIR on drugs approved for commercial sale shall be distributed to the San people. The projected annual transfer amount for the future is $10–$12 million (WHO, 2006).

High demand for Hoodia-based goods may be attributed to the widespread fascination with the plant's appetite-suppressing effects in recent years. It is believed that more than a hundred various product forms (tablets, capsules, gels, juices, powders, teas, and others) containing the plant are commercially available for sale in the United States alone (Avula et al., 2008). The high demand and low supply have set the stage for possible product adulteration with O. ficus or even another species of Hoodia (Avula et al., 2007; Avula et al., 2008; Rader et al., 2007; Van Heerden, 2008).

Chemical composition of the extracts of Hoodia

Recent patents (Bronner, 2005; Gardiner et al., 2006; MacLean, 2006; Raskin et al., 2006; Rifkin, 2005; Van Heerden et al., 2004; Verdegem et al., 2008) demonstrate that CSIR researchers separated many active components. P57 (trirabinoside 14-hydroxy-12-tigloilpregnano) (MW = 1008), also known as the appetite-suppressing active component in H. gordonii extracts, as shown in Figure 2 (MacLean and Luo, 2004).

H. gordonii extracts include a trirhabinoside, 14-OH, 12-tigloyl pregnane steroidal glycoside (MW = 1008), which is thought to be the active component. It has certain

similarities with other cardenolides in its basic steroid structure (MacLean and Luo, 2004), most notably in its 14-OH substitution. However, H. gordonii isn't the only member of the genus to contain the 14-glucoside; additional members include H. currori, H. macranth, H. parviflora, and H. H.pilifera ruschii (Avula et al., 2007; Avula et al., 2008; Van Heerden et al., 2007).

Chloroform preparations of aerial H. gordonii have recently yielded ten novel C (21)-steroid compounds, dubbed gordonisides. 3-beta, 14-beta-hydroxy-pregn-5-en-17-.22 betaona was the starting point for the novel compounds. In a 2007 study (Dall'acqua and Innocenti).

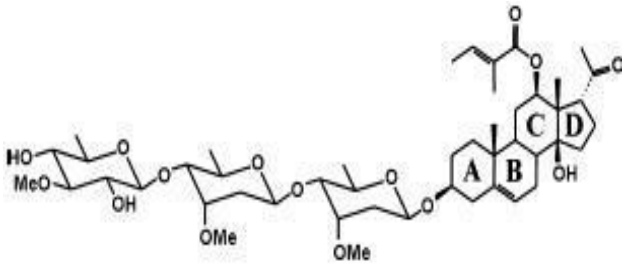

Fig.2. Structure of glicosyde P57. Steroidal glycoside trirabinosíde, 14-OH, 12-tigloilpregnane (Janssen et al., 2008).

Eleven novel oxipregnanos, glucosides with the basic structure 12-O-beta, named tigloil isoramanona hoodigosides, were also isolated from the shoots. Using chemical evidence and nuclear magnetic resonance, their structures were established (Pawar et al., 2007).

There is very little, if any, data available on the possible chemical components (proteins, carbs, lipids, vitamins, fiber, poly-phenols, nitrate, oxalic acid, lectins, saponins, and digestive enzyme inhibitors) of H. gordonii.

Pharmacological effects of extracts of Hoodia gordonii

Extracted from the dried sap of the plant, which included P57 among other components, these tests were undertaken over the course of many months using obese diabetic Zucker rats, but the results were never published by Phytopharm or Pfizer. The findings demonstrated sustained anorexic action and diabetes reversal upon dosing. In addition, several experiments show that the suppression of eating and weight loss occur in overfed animals consuming a very appetizing meal (MacLean and Luo, 2004). The extract of H. gordonii was also shown to be safe in short-term human tests, as reported by Phytopharm (MacLean and Luo, 2004).

In contrast to Trichoplusia ni larvae treated with a control diet, Trichoplusia ni larvae given a diet containing latex of H. gordonii (1,000 ppm) exhibited no suppression of development and reproduction.

Extracts of H. gordonii, which were isolated and purified to produce the steroidal glycoside P57AS3 (P57), were injected intracerebroventricularly into rats, demonstrating the compound's potential mode of action in the central nervous system. The substance reduced food intake by 60% within 24 hours, and the rise in ATP content in hypothalamic neurons was as high as 150% (MacLean and Luo, 2004).

Purified extracts of H. gordonii containing active glycosides were shown to be efficient in lowering weight in rats (Tulp et al., 2001; Tulp et al., 2002; Van Heerden et al., 2007) whether given in the food or by gavage.

The chemical P57 has been proven in studies with animals, including humans, to decrease gastric acid secretion, making it suitable for use in formulations for the treatment of illnesses and diseases associated with hypersecretion of stomach acid (Hakkinen et al., 2004). In addition, no difference in food intake was seen after supplementing the feed of broiler chickens with powdered H. gordonii at doses ranging from 0 to 500 mg/animal/day for 30 days (Mohlapo et al., 2009).

Therefore, Holt (2006) concluded that formulations including H. gordonii and other herbal medications may help regulate weight, reduce hunger, and treat metabolic abnormalities related to obesity. For thousands of years, the San have relied on H. gordonii for its purported ability to reduce appetite and thirst (WHO, 2006).

Scientific research

Despite the high economic value of H. gordonii, as shown by its widespread use as a capsule ingredient, very little is known about the plant. Others focused on the process of appetite suppression (Dall'acqua and Innocenti, 2007; MacLean and Luo, 2004), while yet others aimed to unravel the components of ativos (Pawar et al., 2007; Shukla et al., 2009).

Studies are currently focused on developing analytical methods, primarily utilizing high performance liquid chromatography for identification of glycosides characteristic and confirm the authenticity of commercial

samples (Avula et al., 2006; Avula et al., 2007; Avula et al., 2008; Janssen et al., 2008) due to the high possibility of fraud and adulteration of products marketed as H. gordonii.

No data on the adverse and long-term consequences of H. gordonii consumption can be found in the scientific literature. Given these facts, the Brazilian Sanitary Surveillance Agency (ANVISA) banned advertising and handling in 2007 (Anvisa, 2007).

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