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Review Article

Hoodia Gordonii, An Herbal Anti-Obesity Agent

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ABSTRACT

Hoodia gordonii is a spiny succulent plant commonly consumed for its claimed anti-obesity effects. Traditionally, the Khoi-San people of South Africa and Namibia used it to suppress hunger and thirst during extended hunting expeditions. However, the commercialization of this plant has been highly contentious, largely due to disputes over intellectual property rights and benefit-sharing, as well as the withdrawal of interest from several major pharmaceutical companies involved in its development. Scientific studies have focused heavily on quality control, given the limited availability of H. gordonii due to its restricted geographical distribution, slow growth rate, the need for permits to cultivate or export it, and high public demand, which has led to widespread product adulteration. Although many steroidal glycosides have been identified in H. gordonii, the primary emphasis has been on P57, a pregnane glycoside thought to be the active component and a marker for determining the quality of raw materials and products. Despite this, there is a lack of scientific publications addressing key issues such as in vivo biopharmaceutics, the biological activity of all its chemical components, clinical effectiveness, and, most importantly, safety. This raises significant concerns, as H. gordonii is among the most widely consumed natural products for weight loss. This review offers an up-to-date-overview of all the current available knowledge pertaining to H. gordonii achieved by systematic analysis of the available literature.

INTRODUCTION

According to data from the World Health Organization (WHO, 2010), approximately one billion people are considered overweight, with an additional 300 million classified as obese. These figures indicate that obesity has become a major global issue, affecting countries across all economic levels (1). Projections suggest that by 2025, Brazil will rank fifth globally in obesity rates (Brasil, 2009; Ogden et al., 2006), with 13% of its population already categorized as obese (2). Hoodia gordonii (Masson) Sweet ex Decne. is a spiny succulent plant traditionally used by the Khoi-San people of South Africa and Namibia to

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suppress hunger and thirst during long hunting trips or times of famine. Its potential anti-obesity properties have attracted significant research and commercial interest(3). Obesity has become a major modern health concern, with an estimated 1.6 billion adults worldwide being overweight and at least 400 million classified as obese by 2005. The number of obese teenagers and children has risen sharply, contributing to the recognition of obesity as a global epidemic. In 2005, at least 20 million children under the age of five were overweight(4). Obesity is linked to various health conditions such as type-2 diabetes, cardiovascular disease, hypertension, sleep apnea, and strokes, among others. Key aspects that should be examined before the commercialization of H. gordonii products, such as the bioavailability of its active ingredient, have been largely overlooked(6). Most research has focused on quality control due to the high rate of adulteration in commercially available H. gordonii products. This adulteration stems from several factors, including unethical companies driven by profit, the limited supply of H. gordonii, its slow maturation cycle, the requirement for a CITES (Convention on International Trade in Endangered Species) permit for cultivation and export, and high consumer demand. This review provides an up-to-date summary of H(7). gordonii, addressing key concerns related to its use in commercial products, as well as scientific studies that have explored various aspects of the plant and its phytochemical components. From a scientific perspective, while some studies have focused on the plant's active ingredient, P57, a pregnane glycoside thought to be responsible for its appetite-suppressing effects, there remains a significant gap in research regarding the bioavailability, efficacy, and safety of Hoodia-based products. This review aims to provide a comprehensive overview of Hoodia gordonii, including its traditional uses, the challenges associated with its commercialization, and the current state of scientific research on its potential as an herbal appetite suppressant(8).

Botanical Description :

- **Description and classification**:

Hoodia gordonii (Masson) Sweet ex Decne. is a spiny, succulent plant characterized by small thorns along its fleshy, grey-green to grey-brown stems. Initially, the plant has a single stem, but as it matures, it can develop up to 50 branches from a common base(9). The plant typically grows to about one meter in height and spreads to a similar width. Its large flowers, which bloom near the top of the plant, are generally flesh-colored, though some Namibian populations produce more intense purple-red flowers. Flower sizes range from 50 to 100 mm, with smaller flowers appearing later in the blooming season. The plant typically flowers in August or September, producing so many flowers that they almost hide the stems. The flowers emit an unpleasant odor, similar to rotting flesh, which attracts flies and blowflies for pollination(10). By October and November, the plant produces seed capsules that resemble antelope or goat horns. These capsules contain numerous flat, light brown seeds with silky hairs attached to one end. Hoodia gordonii belongs to the genus Hoodia, which is classified as stapeliads within the tribe Ceropegieae of the subfamily Asclepiadoideae, under the Apocynaceae family. The former classification of Trichocaulon is no longer recognized, as all species within Trichocaulon have been reclassified under Hoodia, which is no longer considered part of the Asclepiadaceae family(11). The full botanical name, Hoodia gordonii (Masson) Sweet ex Decne., reflects the contributions of several individuals. Hoodia pilifera was the first Hoodia species discovered by Carl P. Thunberg and Francis Masson in 1774. In 1779, Robert Gordon observed a species of Hoodia and created a drawing, which Masson later described as Stapelia

gordonii Masson. In 1830, Robert Sweet of England assigned Stapelia gordonii to a new genus, Hoodia, named after Mr. Hood, a renowned succulent cultivator in Britain. Finally, Hoodia gordonii was officially published by Joseph Decaisne in 1844 after the previous genus names were declared invalid(12).

- **Geographical distribution and habitat:**

Hoodia gordonii is widely distributed across South Africa and Namibia. It grows in regions like the western Cape, the northern and northwestern parts of the northern Cape extending as far as Kimberley, and the southernmost areas of the Free State, as well as southwestern Namibia. The plant has a broad tolerance for different habitats, able to withstand extreme heat (above 40°C) and relatively low temperatures (down to -3°C), though it is sensitive to frost. It primarily grows in areas with summer rainfall and can be found in various environments, including dry sandy soils, stony slopes, and flat, barren areas. Cultivating Hoodia gordonii from seeds is difficult, as it is slow-growing and requires significant care, attention, and protection(13).

Fig: Hoodia gordonii

- **Ethnopharmacology-**

Hoodia species are reported to have been consumed by the Khoi-San people of South Africa and Namibia to suppress appetite and thirst during long hunting trips or times of food scarcity. Typically, a small piece of the peeled stem is eaten fresh to remove the thorns. Hoodia species like H. currori, H. flava, H. gordonii, and H. pilifera were used in this way. Additionally, H. currori was used to treat indigestion, hypertension, diabetes, and stomachaches, while Hoodia officinalis subsp. officinalis was used to treat pulmonary tuberculosis. Among these, H. piliferum, known as “ghaap,” was consumed more frequently for its cool, watery taste. In contrast, H. gordonii, with its bitter flavor, was considered less desirable, earning it names like "muishondghaap" and "jakkalsghaap," implying it was fit only for animals. However, after good rains, the bitterness of H(14). gordonii diminishes, and its juicy stems were sometimes eaten raw or cooked. Adding to the confusion, several stapeliad species are also referred to as “ghaap” in vernacular terms. Many papers incorrectly state that H. gordonii was used to treat ailments such as abdominal cramps, diabetes, indigestion, and hypertension, but these medicinal uses are actually attributed to other Hoodia species. These general uses of Hoodia species, including H. gordonii, are outlined in a detailed ethnopharmacological account by Van Heerden.From this detailed ethnopharmacological account, H. gordonii was also used for the treatment of tuberculosis,

and the honey from the flowers could be used to treat cancer(15).

- **Commercialisation-**

The use of Hoodia species, particularly H. pilifera, by the Khoi-San people as a food source and water substitute was documented in 1932 and 1937. These records prompted the Council for Scientific and Industrial Research (CSIR) in South Africa to include Hoodia species in a 1963 study of edible wild plants. The CSIR also investigated the appetite-suppressing effects of Hoodia extracts, leading to a significant discovery in 1995 when the structure of compound P57 (P57AS3) was clarified and patented in South Africa. In 1998, a global patent for pharmaceutical compositions with appetite-suppressing properties was granted by the World Intellectual Property Organization. That same year, the CSIR signed a licensing agreement with the British pharmaceutical company Phytopharm to develop P57 further. Phytopharm then sublicensed the pharmaceutical giant Pfizer for additional research and commercialization (12). However, following Pfizer's merger with Pharmacia in 2003, the nutraceuticals division responsible for P57 development was closed, and Pfizer discontinued its research on H. gordonii. There were also unconfirmed reports that challenges in synthesizing the P57 molecule and the ineffectiveness of synthetic versions compared to natural ones contributed to the halt. In 2004, the patent was licensed to Unilever to incorporate H. gordonii extracts into functional foods. Despite significant investment, including building an extraction facility, Unilever abandoned these plans in December 2008 due to concerns over safety and efficacy. They terminated all Hoodia-related activities in South Africa as of 31 March 2009(13). Despite these setbacks, Phytopharm remains hopeful about the Hoodia program and aims to find new partners for further development, seeing its potential as a profitable industry. However, the San people, who claim ownership of the intellectual property regarding Hoodia's appetite-suppressant properties, have expressed disappointment with Phytopharm's slow progress in developing a commercial product (16).

- **Intellectual property rights-**

When the CSIR was awarded the patent for Hoodia in 1998, the San people were unaware of it and only found out through a Phytopharm press release. Feeling exploited, the San accused the CSIR and Phytopharm of biopiracy and began opposing the patent. Represented by the South African San Council, they filed a lawsuit against the CSIR and its licensees. This resulted in a settlement in March 2003, where both parties agreed to share any royalties from future sales of drugs or products derived from Hoodia. The agreement was based on the Convention on Biological Diversity (CBD), established in 1992 at the Earth Summit in Rio de Janeiro. The CBD, which includes 190 parties, focuses on three key objectives: conserving biological diversity, using its components sustainably, and ensuring fair and equitable benefit-sharing from the use of genetic resources (17). As part of the agreement, the CSIR committed to paying the San 8% of all payments it receives from licensees and 6% of all royalties once the drug is commercialized. The funds would be managed by a San-controlled trust, which would ensure fair distribution among the San people. The Hoodia case garnered international attention, not only for the plant's potential to suppress appetite but also because it was one of the first instances where holders of traditional knowledge were granted a share in the profits derived from it (18). The case raises important political, environmental, and ethical issues, especially regarding intellectual property law. Scholars like Martin and Vermeylen have analyzed whether intellectual property rights can be used to promote the development of indigenous peoples while also preserving their cultural and

natural knowledge. Additionally, Schroeder and Chennells have examined whether benefit-sharing agreements like this one could help the San, who suffer from extreme poverty, malnutrition, and inadequate access to essential health care, overcome these challenges (19).

- **Historical use of Hoodia as a source of food and water-**

Hoodia plants have long been used by the indigenous peoples of southern Africa as a source of food and water. The earliest recorded use dates back to the 19th century, when Hoodia pilifera (L.f) Plowes (previously known as Trichocaulon piliferum (L.f) N.E. Br.) was noted for being consumed by indigenous communities to quench thirst. This plant was also used as a substitute for both food and water (Marloth, 1932), and species of Trichocaulon were reported to be eaten raw or preserved in sugar (White and Sloane, 1937). H. pilifera, which has two subspecies—H. pilifera subsp. pilifera and H. pilifera subsp. annulata—is a small, spiny shrub found mainly in the southern regions of the Western and Eastern Cape Provinces of South Africa. It is commonly called ‘ghaap’, ‘guaap’, or ‘ngaap’ by the indigenous people. In contrast, Hoodia gordonii (Masson) Sweet ex Decne. is more widely spread across the summer rainfall regions of Namibia and into the Northern and Western Cape Provinces of South Africa. While H. gordonii often forms large colonies of robust, spiny shrubs (Bruyns, 2005), it is reportedly less commonly eaten than H. pilifera due to its bitter aftertaste, earning it names like ‘muishondghaap’ or ‘jakkalsghaap’ (Bruyns, 1993). However, due to its wider distribution, larger size, and faster growth rate, H. gordonii was chosen as the focus for further development(20).

- **Traditional use of Hoodia gordonii**:

Hoodia gordonii is a succulent plant native to the deserts of Southern Africa, particularly found in Namibia, Botswana, and South Africa. For centuries, the indigenous San (Bushmen) people of the Kalahari Desert have used Hoodia gordonii as a natural appetite suppressant and thirst quencher during long hunting expeditions in the harsh desert climate. Key aspects of its traditional use include:

1. Appetite Suppressant:

The San would chew on the fresh stems of the Hoodia plant to curb hunger, sustaining themselves during long hunts when food was scarce, a vital practice in the arid desert environment.

2. Thirst Quencher:

Besides suppressing hunger, Hoodia helped reduce thirst, allowing hunters to go extended periods without water.

3. Medicinal Uses:

While its main traditional use was for hunger and thirst, it is believed that the San also used Hoodia as a general health tonic, although specific medicinal applications are not well-documented.

4. Spiritual Significance:

Hoodia may have had cultural or spiritual importance, as the San people maintained a deep connection with the plants and animals in their environment, often incorporating them into their rituals and traditions. The plant's active compound, P57, has been isolated and studied for its appetite-suppressing properties, though its safety and effectiveness in modern pharmaceutical applications continue to be researched and debated(21).

- **Phytochemistry:**

The Van Heerden group was a pioneer in phytochemistry, isolating two steroidal glycosides, known as compounds 1 and 2, from Hoodia gordonii and Hoodia pilifera extracts. Compound 1, commonly referred to as P57AS3 or simply P57, gained particular attention. Since this initial discovery, many new structural analogs have been isolated from Hoodia gordonii(22). These include eleven oxypregnane glycosides (hoodigosides A-K), ten pregnane glycosides (hoodigosides L-U), ten steroidal glycosides

(gordonosides A-I and L), seven pregnane glycosides (hoodigosides V-Z and hoodistanalosides A-B), along with other compounds labeled as formulas 7, 8, and 12. The core chemical structures of these compounds, or their aglycones, include hoodigogenin A, calogenin, hoodistanal, dehydrohoodistanal, and isoramanone, which are formed through acid or enzymatic hydrolysis. The identification of these new compounds has opened avenues for exploring their biological activity and has also been instrumental in developing quality control methods for H. gordonii products(23)

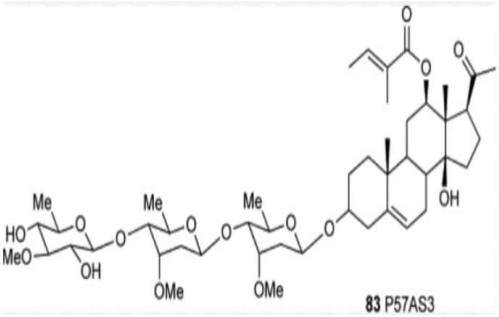

Fig: P57AS3

- **Effects, mode of action, clinical trials:**

The rise in popularity of Hoodia over the last decade is mainly due to its use as an appetite suppressant. Several patents have been filed covering H. gordonii extracts, constituents, and preparations for appetite suppression, anti-diabetic effects, and treatment of gastric acid secretion damage. However, there is limited information about Hoodia's mechanism of action, which would be of significant interest. Research has assessed the metabolic stability of P57AS3 in human liver microsomes and its interaction with drug-metabolizing enzymes. The transport of P57AS3 in the intestines was studied using the Caco-2 cell model, where it was found that its intestinal transport is mediated by P-glycoprotein and multidrug resistance-associated protein transporters. P57AS3 was metabolically stable and exhibited weak inhibition of CYP 3A4(24).

In rats, intracerebroventricular injection of P57AS3 (0.07 mg per injection) reduced food intake by 40–60% over 24 hours following administration. The effect was dose-dependent and suggested a likely central nervous system (CNS) mechanism of action for P57AS3. In a later study, oral administration of P57AS3 over three days (6.25–50 mg/kg) led to significant reductions in food consumption and body mass gain in rats, compared to those treated with either a vehicle or the appetite suppressant fenfluramine(25). These effects persisted during an eight-day monitoring perio Unilever recently filed a patent for polysaccharides derived from plants in the Asclepiadoideae subfamily (Hoodia, H. gordonii, Stapeli), which are claimed to have immunostimulating effects, though the specifics are not yet clear(26). To the author's knowledge, no peer-reviewed papers have been published on clinical trials involving Hoodia. The only available information comes from press releases by Phytopharm, reporting on a double-blind, placebo-controlled clinical trial with overweight male volunteers, which showed a statistically significant reduction in daily calorie intake and body fat(27). There is limited evidence of serious side effects in the literature, although a recent report from Italy mentioned Hoodia preparations being linked to one case of acute hepatitis and another of anticholinergic syndrome when taken with other medications. Additionally, VAN WYK has compiled a monograph on H. gordonii covering its general description, identity, quality, efficacy, and safety. This monograph is expected to be published in the African Herbal Pharmacopoeia by the third quarter of 2009(28).

- **Clinical studies of hoodia gordonii:**

Preparation of extract-

An organic solvent extract was prepared using a dichloromethane-methanol mixture in a 1:1 ratio, following the method by Corley and Miller (2009). To begin, 20 grams of dry powder were weighed

and mixed with 100 ml of the solvent mixture, then left overnight for extraction. The organic layer was separated from the raw plant material through centrifugation at 3000 ×g for 15 minutes at room temperature. This extraction process was repeated twice under the same conditions. The resulting supernatants were combined and dried at 40 °C. The final extract yield was 8.0% of the dry powder provided by the manufacturer(29).

Animals, treatment, monitoring of food intake and body weight-

Male Sprague Dawley rats, weighing between 200 and 250 g, bred and housed at the Experimental Animal Facility of the Institute, were used for this study. The rats were kept in a temperature-controlled environment at 22°±1 °C with 55–60% humidity in a light-regulated room (lights on from 6:30 am to 6:30 pm). Two weeks before the experiment, the rats were adapted to a restricted feeding schedule, where they were fed only during a 6-hour window in the light phase to monitor food intake. The rats were given a commercial rodent diet from M/S Golden Feed Pvt. Ltd., Delhi, along with water ad libitum. The study's protocols were approved by the Institute's Animal Care and Use Committee and followed the National Institute of Health's Guide for the Care and Use of Laboratory Animals. Before starting the experiments, the animals were randomly divided into control and experimental groups. Six groups of animals (n=6 per group) were initially treated with an oral crude alcoholic extract at doses of 50, 100, and 150 mg/kg body weight using a rodent feeding needle once daily for five days. The control groups received an equivalent volume of tap water administered in the same manner. The extract was administered in the morning, coinciding with the time food and water were provided. Based on results, the minimum effective dose of 100 mg/kg body weight was chosen for further biochemical tests. To assess if the extract had a continuous or progressive anorectic effect, food intake was measured every two hours (at 2 h, 4 h, and 6 h) using a digital balance. Additionally, food intake was monitored for three days after the treatment ended (over an eight-day period) to evaluate any residual effects. This part of the study was conducted on a separate batch of rats, split into control and treated groups (n=6 each). Body weight changes were recorded daily after treatment(30).

Sample collection for biochemical analysis-

Following the five-day treatment, the rats were fasted overnight, then anesthetized and sacrificed. Blood plasma was collected by centrifuging the blood at 1000 ×g for 10 minutes at 4 °C. The organs, including the liver, spleen, kidney, and brain, along with the gastrocnemius muscle and epididymal fat tissue, were weighed and recorded.

RESULTS AND DISCUSSION-

The effect of H. gordonii crude extract on food intake, body weight, and organ weights was examined at oral doses of 100 mg/kg and 150 mg/kg. The extract caused a dose-dependent reduction in food intake over the 6-hour period on all five days. No reduction in food intake was observed at the lower dose of 50 mg/kg body weight [Table 1].At doses of 100 mg/kg and 150 mg/kg, food intake decreased by 17.5% (range: 12.4%–22..3%) and 22.8% (range: 18.4%–26.7%), respectively ($p < 0.05$) (Table 1). In a separate experiment monitoring food intake at different time points, a 15% reduction was observed within 2 hours after administration, and this reduction persisted until the sixth hour. After the 100 mg/kg dose was discontinued on day 5, food intake returned to normal levels (comparable to the untreated group) between days 6 and 8, indicating that the extract has a transient effect rather than a lasting one. Body weight remained unaffected at the 50 mg/kg dose, with treated animals showing a 3.8% increase compared to 3.6% in the control group. Similarly, at the 100 mg/kg dose, no significant difference in body

weight was observed, with treated animals showing a 3.7% gain compared to 4% in the control group. However, at the 150 mg/kg dose, treated rats experienced a slower rate of weight gain (1.8%) compared to the control group (6%), suggesting a reduction in weight gain due to the treatment. No significant differences in organ weights were observed(31,32).

Table 1
Effect of crude *H. gordonii* extract on food intake.

Oral treatment (mg/kg body weight)		Day 1	Day 2	Day 3	Day 4	Day 5	Mean ± SD
50	C (g)	96.0	100.0	95.0	96.0	99.0	97.2 ± 2.4
	T (g)	97.0	101.0	94.9	96.0	100.0	97.7 ± 2
	Diff (g)	+1	+1	−0.1	0	+1	0.5 ± 0.6
	Diff (%)	1.04	1	2.7	0	1	
100	C (g)	97	101	100	95	97	98.0 ± 2.4
	T (g)	85	84	81.3	78.5	75.4	80.8 ± 4.0
	Diff (g)	−12	−17	−18.7	−16.5	−21.6	17.2 ± 3.5*
	Diff (%)	12.4	16.8	18.7	17.4	22.3	
150	C (g)	97	99	95	95.5	97.6	97.8 ± 1.4
	T (g)	74.5	78	77.5	72	71.5	74.7 ± 2.7
	Diff (g)	−22.5	−21	−17.5	−23.5	−26.1	22.1 ± 2.8*
	Diff (%)	23.2	21.2	18.4	24.6	26.7	

Values are mean ± SD (n = 6), C: Control, T: Treated, *p<0.05; + denotes an increase and − denotes a decrease in food intake in comparison to control.

Safety and Adverse Effects of Hoodia gordonii

1. Limited Research- Despite its widespread use in the weight loss industry, there is a lack of extensive clinical research on the safety and effectiveness of Hoodia gordonii Most available studies are either small in scale or provide inconclusive results. The active compound in Hoodia, P57, is thought to suppress appetite by acting on the hypothalamus, but its exact mechanism and long-term safety remain unclear.

2. Possible Side Effects- Increased Heart Rate and Blood Pressure: Some evidence suggests that Hoodia may raise heart rate and blood pressure, which could be risky for individuals with heart conditions. Gastrointestinal Issues: Some users have reported nausea, vomiting, and other digestive problems such as bloating and cramping. Liver Toxicity: There are concerns about potential liver damage linked to Hoodia, though the evidence remains inconclusive. Blood Sugar Changes: Since Hoodia influences appetite and possibly metabolism, it may also affect blood sugar levels, raising concerns for individuals with diabetes or those on medications that regulate blood sugar

3. Regulatory Concerns- Hoodia products are marketed as dietary supplements in many countries, which means they are not held to the same strict testing standards as pharmaceutical drugs. This can result in inconsistencies in product quality, dosage, and the potential presence of contaminants. Several countries have issued warnings or imposed bans on the importation of Hoodia-based products due to safety concerns and the risk of fraudulent or contaminated items being sold.

4. Drug Interactions- Appetite Suppressants: Hoodia may interact with other medications or supplements that suppress appetite, potentially intensifying their effects. Medications for Hypertension or Heart Conditions: Since Hoodia could affect heart rate and blood pressure, individuals on medications for these conditions should use caution. Blood Sugar Medications: Hoodia's possible influence on blood sugar levels may lead to unexpected changes in glucose control for those taking diabetes medications (33,34,35).

Future Directions and Challenges of Hoodia gordonii:

Hoodia gordonii is widely marketed as a natural appetite suppressant, numerous scientific, ethical, and regulatory issues remain unaddressed. To advance its potential applications and enhance its safety profile, focused research efforts will be necessary. The following outlines key future

directions and challenges that researchers and industry stakeholders may face.

Future Directions

1] Comprehensive Clinical Trials-Well-Designed Human Trials: Most current studies on Hoodia have been either limited in scale or conducted in animal models. To confirm the efficacy and safety of Hoodia gordonii in humans, larger, well-controlled clinical trials are needed. These should explore its long-term effects on appetite suppression, metabolism, and any potential side effects. Investigating P57's Mechanism: The active compound P57, thought to interact with the hypothalamus to reduce hunger, requires further research to gain a comprehensive understanding of its molecular mechanisms. This could lead to the development of more targeted appetite-suppressing therapies.

2] Bioavailability and Dosage Optimization-

Formulation Improvement: A significant challenge is enhancing the bioavailability of the active components in Hoodia, such as P57, to ensure effective absorption by the body. Advanced formulation methods, such as encapsulation or the use of nanoparticles, could improve efficacy and minimize adverse effects.

Standardized Dosing: Commercial Hoodia supplements frequently show inconsistencies in the content of their active ingredients. It is essential to establish standardized dosing protocols grounded in scientific research to ensure both safety and effectiveness.

3] Ethnopharmacological and Ethical Considerations- Sustainable Harvesting and Fair Trade: Hoodia gordonii is native to Southern Africa, and its commercial use raises ethical issues related to the rights of local communities, especially the San people. Future Hoodia research should emphasize fair trade practices, equitable benefit sharing, and sustainable harvesting techniques to safeguard the plant and local ecosystems.Integration of Traditional Knowledge: Working alongside indigenous communities to integrate their traditional knowledge and practices into Hoodia research could offer valuable insights into its safe and effective application.

4] Pharmaceutical Applications: Exploring Other Therapeutic Uses: In addition to appetite suppression, the bioactive compounds in Hoodia may have potential applications in other medical fields, such as metabolic syndrome, diabetes, or obesity-related conditions. Researching these wider therapeutic possibilities could enhance the plant's role in modern pharmacology (36).

Challenges

1] Regulatory Hurdles**:**

Inconsistent Regulation Across Markets: Hoodia supplements are frequently categorized as dietary supplements, allowing them to avoid strict pharmaceutical regulations. This lack of consistent regulation across different countries creates challenges in ensuring product safety and quality control. There is a need for more rigorous and harmonized global regulations to guarantee that consumers receive authentic and safe products.

Adverse Effect Monitoring: As the availability of Hoodia-containing products increases, there is an escalating need for comprehensive post-market surveillance to monitor adverse effects and potential interactions with medications, especially in vulnerable groups such as individuals with cardiovascular or metabolic conditions.

2] Sustainability and Conservation Issues:

Overharvesting Concerns: Hoodia gordonii is a slow-growing succulent currently at risk due to overharvesting for commercial use. To safeguard the species from depletion, sustainable cultivation practices and conservation initiatives need to be established. This includes creating cultivation programs and exploring alternative propagation techniques, such as tissue culture.

Climate Change Impact: Since Hoodia is indigenous to arid environments, climate change may alter its natural habitat, potentially affecting

both the wild populations and the communities that depend on its traditional usage.

3] Challenges in Commercialization:

Market Fraud and Product Adulteration: A significant number of Hoodia products available in the market may be adulterated or fraudulent, often containing minimal to no actual Hoodia gordonii. This situation not only diminishes consumer trust but also poses potential health risks. Future commercialization efforts should emphasize stringent authentication methods, such as DNA barcoding, to ensure product quality and integrity. Competition with Synthetic Alternatives: Recent advancements in biotechnology have opened the door to synthesizing P57 or other appetite-suppressing compounds, which could decrease dependence on the natural plant. However, these synthetic alternatives must undergo thorough testing for both efficacy and safety before they can effectively replace the natural product.

4] Health and Safety Concerns:

Potential Toxicity: Although initial studies have raised concerns regarding the potential hepatotoxicity and cardiovascular effects of Hoodia, these claims are still inconclusive. It is essential to conduct rigorous long-term safety studies to address these health concerns before Hoodia can be widely recommended for weight loss or other medical applications. Drug Interactions: Considering the possibility of interactions with medications (such as those impacting blood sugar or cardiovascular function), additional research is required to comprehensively understand the interaction profile of Hoodia and to ensure its safety when used alongside commonly prescribed medications(37,38).

CONCLUSION: In the past decade, Hoodia has garnered increasing interest due to its appealing indication profile. This plant is traditionally used by the San people of Southern Africa as a thirst and appetite suppressant. The South African Council for Scientific and Industrial Research (CSIR) and the British company Phytopharm have been working on developing Hoodia as a pharmaceutical or food supplement but have yet to achieve success. Nevertheless, numerous patents have been granted for extracts and compounds derived from Hoodia, highlighting its appetite-reducing, anti-diabetic, and gastro-protective properties. Agreements for benefit sharing with the San people have been established to ensure they receive profits from Hoodia cultivation and its potential commercialization. To prevent overexploitation of this slow-growing plant and to ensure a sustainable supply, Hoodia species have been listed under Appendix II of the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES). This classification enforces strict rules regarding the collection, cultivation, transport, and export of Hoodia, which must be adhered to by all countries that are signatories to the Convention on Biological Diversity (CBD). However, with obesity being a significant concern in developed countries and the limited availability of effective treatments, there is substantial market potential for successful weight loss solutions. Some institutions are attempting to capitalize on this opportunity by offering Hoodia preparations, ignoring the aforementioned patents and agreements, despite the lack of data supporting successful clinical studies. These preparations are available in Europe and the U.S. Valuable phytochemical investigations focusing on a specific class of compounds, the pregnane glycosides, have facilitated quality control for Hoodia-containing crude drugs and preparations. However, the results of these screenings raise serious concerns regarding the safety of these products, as many appear to contain little to no actual Hoodia. Even if Hoodia itself is safe, the absence of the claimed ingredient in weight loss products poses a risk to consumers. What alternative substances might these preparations

contain? This raises significant safety concerns that warrant critical evaluation. Consumers should be aware of the potential for adverse reactions caused by unspecified components with unknown chemical and pharmacological profiles. Who will take responsibility for such cases? In addition to this ethical dilemma, several other questions remain unanswered: Why did two major companies involved in its development abandon the project? What prevented them from publishing safety, toxicology, and clinical data? Does Hoodia have any actual effects? What other compounds are present in Hoodia, and what effects or side effects do they produce? Currently, these questions lack clear answers, but it is essential for suppliers, customers, and governments to remain mindful of the sensitive context surrounding this potential weight-loss agent.

REFERENCES

1. Glasl S. Hoodia: A herb used in South African traditional medicine – Apotential cure for overweight? Pharmacognostic review of history, composition, health-related claims, scientific evidence and intellectual property rights. Schweiz Z Ganzheitsmed 2009; 21: 300–306.
2. Van Heerden FR, Vleggaar R, Horak RM, Learmonth RA, Maharaj V, Whit-tal RD. Pharmaceutical compositions having appetite-suppressant activity. US Patent 6376657 B1; 2002.
3. Pawar RS, Shukla YJ, Khan SI, Avula B, Khan IA. New oxypregnane glyco-sides from appetite suppressant herbal supplement Hoodia gordonii. Steroids 2007; 72: 524–534.
4. Pawar RS, Shukla YJ, Khan IA. New calogenin glycosides from Hoodia gordonii. Steroids 2007; 72: 881–891.
5. Dall'Acqua S, Innocenti G. Steroidal glycosides from Hoodia gordonii. Steroids 2007; 72: 559–568.
6. Abrahamse SL, Povey KJ, Rees DD. Appetite suppressant compositions. US Patent 0207227 A1; 2007.
7. Avula B, Wang YH, Pawar RS, Shukla YJ, Schaneberg B, Khan IA. Determi-nation of the appetite suppressant P57 in Hoodia gordonii plant ex-tracts and dietary supplements by liquid chromatography/electro-spray ionization mass spectrometry (LC-MSD-TOF) and LC-UV meth-ods. J AOAC Int 2006; 89: 606–611.
8. Shukla YJ, Pawar RS, Ding Y, Li X-C, Ferreira D, Khan IA. Pregnane glyco-sides from Hoodia gordonii. Phytochemistry 2009; 70: 675–683.
9. van Wyk B-E, Wink M. Medicinal plants of the world. Pretoria: Briza Publications; 2004: 171.
10. Bruyns PV. Stapeliads of Southern Africa and Madagascar, Volume 1. Pretoria: Umdaus Press; 2005.
11. Olivier I. Hoodia gordonii (Masson) Sweet ex Decne. Available at http://www.plantzafrica.com/planthij/hoodgord.htm. Accessed February 5,2008.
12. Van Heerden F. Hoodia gordonii: A natural appetite suppressant.J Ethnopharmacol 2008; 119: 434–437.
13. Holt S, Taylor TV. Hoodia gordonii: an overview of biological and botanical characteristics: Part 1. Townsend Lett 2006; 280: 104–113.
14. Van Wyk B-E, Gericke N. People's plants. Pretoria: Briza Publications; 2000: 70.
15. Foden W. Information document on trade in Hoodia gordonii and other Hoodia species. Available at http://www.plantzafrica.com/planthij/hoodia.htm. Accessed June 29, 2010.
16. Wynberg R, Schroeder D, Chennels R. Indigenous peoples, consent and benefit

sharing. Lessons from the San-Hoodia case. London: Springer Publications; 2009: 11–26, 89–121.
17. Martin G, Vermeylen S: Intellectual Property, Indigenous Knowledge, and Biodiversity. Capital-ism Nature Socialism 2005;(16)3:27–48.
18. Anonymous: Protecting traditional knowledge: the San and hoodia. Bulletin of the World Health Organization 2006;84(5):345.
19. Schoeder D, Chennells R: Benefit sharing and access to essential health care: a happy mar-riage? Medicine and Law 2008;27(1):53–69.
20. Bruyns, P., 2005. Stapeliads of Southern Africa and Madagascar. Umdaus Press, Hatfield, South Africa, pp. 1–329.
21. Van Heerden, F.R., et al. (2007). "Phytopharmacology of Hoodia gordonii." Journal of Ethnopharmacology, 113(2), 230-235.
22. Van Heerden FR, Horak RM, Maharaj VJ, Vleggaar R, Senabe JV, Gunning PJ. An appetite suppressant from Hoodia species. Phytochemistry 2007; 68: 2545–2553
23. Avula B, Wang Y-H, Pawar, RS, Shukla YJ, Smillie TJ, Khan IA. A rapid method for chemical fingerprint analysis of Hoodia species, related genera, and dietary supplements using UPLC-UV-MS. J Pharm Biomed Anal 2008; 48: 722–731
24. Madgula VLM, Avula B., Pawar RS, Shukla YJ, Khan IA, Walker LA, Khan SI: In Vitro Metabolic Stability and Intestinal Transport of P57AS3 (P57) from Hoodia gordonii and its Interaction with Drug Metabolizing Enzymes. Planta Med 2008;74:1269–1275.
25. MacLean DB, Luo LG: Increased ATP content/ pro-duction in the hypothalamus may be a signal for energy-sensing of satiety: studies of the anorectic mechanism of a plant steroidal glycoside. Brain Res 2004;1020:1–11.
26. Abrahamse SL, Van Adrichem JA, Van Der Burg Koorevaar MCD, Koek JH: Edible product having an immunostimulating effect. 2009: patent; WO2009071425.
27. Menniti-Ippolito F, Mazzanti G, Santuccio C, Moro PA, Clapai G, Firenzuoli F, Valeri A, Ras-chetti R: Surveillance of suspected adverse reactions to natural health products in Italy. Pharmacoepidemiology and Drug Safety 2008;17:626–635.
28. Van Wyk BE. Hoodia gordonii. In: Eloff JN, Brendler T, Gurib-Fakim A, Phillips LD (Eds.). The African Herbal Pharmacopoeia. Association for African Medicinal Plants Standards (AAMPS), Reduit, Mauritius (in press).
29. Chidakel, A., Mentuccia, D., Celi, F.S., 2005. Peripheral metabolism of thyroid hormone and glucose homeostasis. Thyroid 15, 899–903.
30. Corley, D.G., Miller, J., 2009. Plant derived or derivable material with appetite suppressing activity. US7482028.
31. Cowley, M.A., Smith, R.G., Diano, S., Tschop, M., Pronchuk, N., Grove, K.L., Strasburger, C.J., Bidlingmaier, M., Esterman, M., Heiman, M.L., Garcia-Segura, L.M., Nillni, E.A., Mendez, P., Low, M.J., Sotonyi, P., Friedman, J.M., Liu, H., Pinto, S., Colmers, W.F., Cone, R.D., Horvath, T.L., 2003. The distribution and mechanism of action of ghrelin in the CNS demonstrates a novel hypothalamic circuit regulating energy homeostasis. Neuron 37, 649–661.
32. Cummings, D.E., Purnell, J.Q., Frayo, R.S., Schmidova, K., Wisse, B.E., Weigle, D.S., 2001. A preprandial rise in plasma ghrelin levels suggests a role in meal initiation in humans. Diabetes 50, 1714–1719.

33. Fouche, G., Cragg, G.M., Pillay, P., Kolesnikova, N., Maharaj, V.J., & Senabe, J. (2006). Investigation of the pharmacological activities of selected Hoodia species. Journal of Ethnopharmacology, 107(3), 422-427.
34. Van Heerden, F.R. (2008). Hoodia gordonii: a natural appetite suppressant. Journal of Ethnopharmacology, 119(3), 434-437.
35. Sliwoski, G., Kothiwale, S., Meiler, J., & Lowe, E.W. (2014). Computational methods in drug discovery. Pharmacological Reviews, 66(1), 334-395.
36. Van Heerden, F.R. (2008). Hoodia gordonii: a natural appetite suppressant. Journal of Ethnopharmacology, 119(3), 434-437
37. Vermaak, I., Viljoen, A.M., & Hamman, J.H. (2011). Hoodia gordonii: An up-to-date review of a commercially important anti-obesity plant. Planta Medica, 77(11), 1149-1160.
38. Lambert, J.D., & Kennett, M.J. (2013). Ethical considerations in the commercial development of Hoodia gordonii: The San people and benefits haring agreements. South African Journal of Science, 109(1-2), 45-50.

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