

INDIGENOUS USE OF *HOODIA GORDONII* AND APPETITE SUPPRESSION

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Say “weight loss” out loud in a public place and 65 or so of every 100 people present will pay attention—that is the general estimate of overweight people age 20 and above in the United States. Add to the statement “natural weight loss” and they will come over and ask where they can purchase your product. Americans spend \$30 billion dollars a year trying to lose weight¹ at a time when one of six inhabitants of the earth are faced with the suffering brought about by constant hunger and starvation.² And of course, we want to do it “naturally,” without pain. Enter botanicals—many plants have been used over the years for appetite suppression, engendering great interest from the public and private sector. Some of these plants have been used by indigenous cultures to stave off hunger during famine or journeys—such as a protracted hunting trip. However, only a handful of botanicals used for this purpose have been documented by ethnobotanists.³

Hoodia gordonii,⁴ described by the English botanist Robert Sweet in *Hortus Britannicus* in 1830, is one plant that has attracted a huge wave of interest.⁵ Contrary to the popular media, it is not a cactus, but a member of the Asclepiadaceae, the milkweed family. The geographical distribution of *H. gordonii* is South Africa and neighboring Namibia. The traditional uses of *H. gordonii* by the San people of Southern Africa have been as an appetite suppressant, thirst quencher, a cure for abdominal cramps, hemorrhoids, tuberculosis, indigestion, hypertension, and as an antidiabetic.⁶ This plant is very tolerant to harsh conditions, growing in extreme heat (>40°C) to low temperatures (−3°C) in dry sands, stony slopes, or under the protection of desert growing plants. *Hoodia gordonii*, an inhabitant of the Kalahari sands, is known to flower with blooms as large as 75 mm. Each bloom has an odor

that resembles rotten meat, as do the other *Hoodia* species. Thus, these blooms have earned the description of *carrion flowers*.⁷ Some experts suggest the odor was possibly an evolutionary strategy designed to attract its pollinators—flies that feed on rotten meat. There are 16 other *Hoodia* species,⁶ and some of these are used by indigenous peoples to suppress appetite.

Carl Peter Thunberg, the so-called Father of South African Botany, described the first species in this genus, *Hoodia pilifera*, in 1773. Under earlier classifications, *Hoodia pillansii* and other spiny-stemmed *Hoodia* species that have been used as appetite suppressants were in a different genus, *Trichocaulon*. In 1992, the species were regrouped into the genus *Hoodia*, with *Hoodia gordonii*, the most notable species from the standpoint of supplements, transferred from the genus *Stapelia*—where it was originally known as *Stapelia gordonii*.⁸

Sustainable harvesting is an important issue when assessing the risk of whether a botanical is endangered—especially if it becomes a widely exported species. The Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES) “is an international agreement between governments. Its aim is to ensure that international trade in specimens of wild animals and plants does not threaten their survival.”⁹ There are three categories in CITES: Appendix I lists species that are the most endangered among CITES. Appendix II lists species that are not necessarily now threatened with extinction but that may become so unless trade is closely controlled. Appendix III is a list of species included at the request of a party (member state) that already regulates trade in the species and needs the cooperation of other countries to prevent unsustainable or illegal exploitation.⁹ *Hoodia gordonii* is listed in Appendix II of CITES, denoting is fragile conservation status.

Hoodia plants, on average, live 15 years, but in cultivation can live up to 25 years. Unlike other succulents, *Hoodia gordonii* must be grown from seeds rather than cuttings, as the cuttings will not root and are ready for harvest in two to three years. Anyone wishing to cultivate or harvest wild *Hoodia* species outside of South Africa must register for a CITES permit.

In 1997, scientists from the South African Council for Scientific and Industrial Research (CSIR) isolated a group of steroidal glycosides from *Hoodia gordonii* and several other *Hoodia* species, *Hoodia lugardii* and *Hoodia currori*. A patent was filed citing these compounds as the responsible constituents for appetite suppression. The structure, 3-0-[-.beta.-D-thevetopyranosyl(.fwdarw.4)-.beta.-D-cymaropyranosyl-(1.fwdarw.4)-.beta.-D-cymoaropyranosyl]-12.beta.0-tigloyloxy-14,hydroxy-14.beta.-pregn-50-en-20-one(C.sub.47H.sub.740.sub15M.sup.+878) is the steroidal glycoside identified as the active principle.¹⁰ In June 1997, Phytopharm, a pharmaceutical company based in the United Kingdom, announced collaboration with CSIR to research the plant for its appetite-suppressant activity.¹¹ Phytopharm referred to the steroidal glycoside and its collective analogs as P57. The business arrangement was designed to take P57 into worldwide development while CSIR retained the marketing rights. Phytopharm was allowed to seek licensees for other markets.¹¹ By August of 1998, Phytopharm announced that it had signed a licensing agreement with Pfizer to develop and commercialize P57.¹² However, five years later, on July 2003, Pfizer returned its rights to Phytopharm and discontinued clinical development of P57.¹³ The reason for Pfizer’s move to discontinue clinical development of P57 was not entirely clear. Years later, in an April 26th, 2005 interview in *The New York Times*,¹⁴ Jasjit S. Binda, PhD, a former researcher on *Hoodia* at

Pfizer, stated that unwanted constituents from P57 could not be easily removed from the formulation and negatively affected liver metabolism. Today, Unilever, owner of Slim-Fast, holds the exclusive rights to the *Hoodia gordonii*'s appetite-suppressing compound (P57).¹⁵

The San are credited with the discovery of *Hoodia*'s use for appetite suppression. The San are Southern Africa's oldest human inhabitants—their existence is traced as far back as 20,000 years—possibly 40,000 years according to a National Geographic News report on this culture.¹⁶ When hunting and gathering were the predominant lifestyle of the San, *Hoodia* stems were chewed to stave off hunger and thirst during long hunting trips in the Kalahari desert.

Today, most San are working as farm laborers. In 1997, when *Hoodia* was undergoing the patenting process as an appetite suppressant, the San were struggling in communities with few resources. Although early agreements guaranteed royalties to these people should a pharmaceutical product be developed, the use of this plant by the supplement industry, unlicensed by the San and without materially acknowledging their intellectual contribution to this scientific discovery, has not, to the best of our knowledge, resulted in any significant royalties to the San. In addition, as we shall discuss, there is growing concern among knowledgeable experts that often there is little or no *Hoodia* in many of these diet products so common on store shelves. Thus, marketing the story of the San's discovery, rather than the ingredient itself, again produces no compensation for these people, and potentially some of these products join the ranks of those sold today that are a form of cultural "greenwashing,"¹⁷—in essence pretending to somehow help the environment or its people.¹⁸ We would encourage consumers to be much more aware of this practice that pervades our society, and react according to their conscience.

There is little data on *Hoodia*'s mechanism of action. The steroidal glycosides attributed with appetite suppressant activity affect the central nervous system pathways mediated by a variety of neuropeptides. Neuropeptides serve as messengers, facilitating communication between the brain and the rest of the body. There are over 100 of these small molecules with



A picture of *Hoodia gordonii* seeds taken at The New York Botanical Garden by Roberta Lee, April 28, 2007.

specific roles in regulating body processes such as mood, sleep, wakefulness, and hunger. (For those interested in learning more about the wonder of neuropeptides, Candace Pert's book *Molecules of Emotion* can serve as an easy-to-read reference.¹⁹)

The regulation of hunger is complicated. It involves a balance between energy intake (food consumption) and metabolic energy expenditure. Additionally, energy expenditure itself is a product of resting metabolism and physical activity. The act of eating triggers a cascade of sequential physiological reactions that help us digest and move our food through the gastrointestinal tract. Part of this process also involves signaling from a variety of sites within the brain (eg, hypothalamus), which sends signals of satiety, shutting down our desire to eat.²⁰

In animal trials, P57 injected in to the central nervous system of mice (brains) seemed to lower food intake by as much as 40% to 60% over the next 24 hours.²¹ To the best of our knowledge, despite press

releases indicating positive results, it appears that there are no publications in peer-reviewed journals involving human trials with *Hoodia* extract. However, a press release from Phytopharm indicated that in a phase I/II trial, 18 subjects were randomized to receive P57 or placebo under controlled diet conditions for 15 days. "Preliminary data indicated that there was a statistically significant reduction in the average daily calorie intake of the P57 group compared with the placebo group ($p=0.014$). Preliminary data also indicate a statistically significant reduction in body fat content in the P57 group compared with the placebo group at the completion of dosing ($p=0.035$). No serious adverse effects were experienced by any of the subjects, and the safety data were consistent with a satisfactory overall safety profile. The pharmacokinetic data confirm that the systemic exposure to biologically active constituents of P57 was consistent with the observed clinical effects."²² Mark Blumenthal, founder and executive direc-

tor of the American Botanical Council, in his recent article published in *Natural Health*, also verified the inaccessibility of clinical trial data.²³ Blumenthal noted that few adverse effects have been reported for *Hoodia*, but suggests judicious use of *Hoodia* supplements until the quality of products and more details on their safety are forthcoming.

Product testing has shown that not all *Hoodia* supplements have active ingredients. In our interview, Elan Sudberg, COO and lab manager for Alkemists Pharmaceuticals (an independent lab for third-party natural-product analysis), noted that several years back as little as 30% of the *Hoodia* products randomly tested contained adequate amounts of the botanical. However, he commented that in recent years, the percentage of products with adequate *Hoodia* has risen to 60% (Elan Sudberg, personal communication, April 2006). In light of this information, how can a consumer tell the difference between a quality product and one that is not? At present, it seems that the situation is one of caveat emptor, or buyer beware.

Botanists estimate that there are over 400,000 species of seed and cone-bearing plants on earth. The vast majority have yet to be thoroughly analyzed for their potential to improve healthcare and otherwise improve our society—for food, medicine, fiber, shelter, and to satisfy many of our other needs. One of these is the small milkweed, *Hoodia gordonii* and its related species. Tragically, many of these resources, and the knowledge of their value, are being lost very quickly. The fight to preserve nature is made all the more complicated by the predominance of the quarterly balance sheet that guides most human actions today, as well as what many of our species see as more immediate problems. No matter where we live however—in a large city or on a remote island—we are experiencing the results of a declining environment. It is time to wake up.

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