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Research Article
Toxicity of Candlenut Seed (*Aleurites moluccanus*), A Purported Herbal Weight Loss Supplement

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Abstract

This review examined the potential beneficial or toxic effects of a purported weight loss supplement commonly known as candlenut tree seed, "nuez de la India" and "semilla de Brasil" (*Aleurites moluccanus*), that is promoted throughout the world via the internet as a "safe" and "effective" option for the treatment of obesity as well as for a plethora of various health problems. An extensive internet search in peer reviewed medical journals and textbooks, as well as commercial websites was undertaken using the key words *Aleurites moluccanus*, "candlenut seed", "nuez de la India" and "semilla de Brasil". The parameters sought included clinical toxicity and safety in humans, as well as weight loss efficacy in clinical trials. No scientific journal articles were found support the use or efficacy of this seed for weight loss. Various documented cases from many countries around the world confirm both the seed's toxicity, as well as its potential lethality. Candlenut seed is a potentially dangerous product that should be avoided by people who are seeking an alternative treatment for obesity.

Key words: Dietary supplements, herbal medicine, *Aleurites moluccanus*, clinical toxicity, candlenut seed

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INTRODUCTION

A great diversity of species belonging to the plant kingdom has been employed for medicinal purposes by humans since the dawn of time. Various species of plants and fungi were undeniably the first curative agents known to humans[1]. From the Paleolithic era to modern times, medicinal plants have been used extensively by all world cultures as an integral part of healing therapies applied to both humans, as well as animals[2]. Due to the alarming increase in obesity rates around the world, many people in various countries seek a rapid solution to their weight problem. Unfortunately, some of these people oftentimes are victims of "natural" or "miracle" product marketing schemes that purportedly claim efficacy and safety for the herbal supplements they sell for weight loss but often lack any scientific evidence to substantiate their claims.

Obesity as a worldwide health concern: A person is considered to be obese when she/he has a body mass index (BMI) of 30 or greater. This affliction is directly or indirectly related to a host of health issues and is an important risk factor for various diseases, such as Type 2 diabetes, certain types of cancer and cardiovascular disease, among many others[3]. Obesity is not only an important and rapidly growing health problem in many industrialized countries but is also becoming increasingly prevalent in various developing nations as well. For example, in the United States (US) and Mexico more than two-thirds of the adult population is both overweight and obese, compared to 29% of adults in China[4,5].

Regulation of herbal supplements in the united states: The US Congress passed the Dietary Supplements Health Education Act (DSHEA) in October of 1994, classifying herbal and nutritional supplements as food not drugs, thus not requiring prior approval by the Food and Drug Administration (FDA) or a medical prescription for their purchase. One of the mandates of the DSHEA is that manufacturers of herbal products may not make unsubstantiated health claims regarding their products[6]. Unfortunately, certain websites do indeed state or openly imply that their herbal products are both safe and effective in the treatment of various diseases but do so without citing any scientific peer reviewed clinical studies.

Herbal product identity, efficacy and safety

Bedlam in the cyber marketplace: Many people around the world are still under the erroneous and romanticized impression that herbal products are "natural" and hence automatically considered to be both safe, as well as lacking in any negative side effects. Unfortunately, factual information is often lacking regarding certain herbal supplements employed for weight loss. An additional caveat is the practice of mislabeling some herbal supplements, thus making the use of these supplements confusing, risky, or simply ineffectual in curing any ailment. The lack of adequate quality control practiced by some herbal product companies around the world is conducive to a great variability in both the quantity as well as the quality in the content of the herbal supplement sold to the public. If the preceding situation were not concerning enough, a portion of the information available on the internet regarding certain herbal weight loss supplements may be both exaggerated as well as misleading. This misinformation may lead to intoxications among the unwary public[7-10].

With regard to the above, a study assessed the quality as well as the quantity of information on the internet, regarding certain herbal supplements available to consumers in the US. The authors evaluated 32 websites that advertised and sold herbal-based supplements for weight loss. The websites they chose were assessed for the presence of the names of active or inactive ingredients, recommended dose, as well as other Food and Drug Administration (FDA) requirements for labeling. The data mentioned in each of the selected websites regarding supplement safety for the most common herbal ingredients in the products evaluated were compared to the available standard herbal supplement information references. The results of the study led the researchers to conclude that the potential health risks related to certain herbal products advertised and marketed for weight loss may not be adequately stated on certain internet websites[10].

Lack of quality control and mislabeling of certain herbal products: The scientific literature has recorded various instances of serious (and sometimes fatal) intoxications around the globe due to the mislabeling of herbal products, the intentional or non-intentional adulteration of certain products with heavy metals or drugs, for example, as well as the erroneous identification of various medicinal plant species. A simple mistake regarding the precise identification of an herb or the incorrect use of a certain part of a plant can have serious or even fatal results. This important issue is exemplified by the so-called "Chinese herb nephropathy", caused by the adulteration of a weight loss supplement with a very toxic and carcinogenic plant from China (*Aristolochia fangchi*), which contains a hazardous compound known as aristolochic acid. The supposed weight loss supplements containing this plant caused hundreds of serious intoxications in Europe and some in the US, which prompted the FDA to ban its use and sale

within the US.[11]. A great diversity of herbal products originating in Asia, Africa or South America, for example, are continually imported into the US as well as many other Western countries. Oftentimes, however, some of these products have not been thoroughly tested for purity, safety or efficacy in their countries of origin, prior to their importation[9,12-14].

Anecdotal "evidence" versus clinical studies: Anecdotal "evidence" by means of clients' testimonials regarding the supposed efficacy and safety of various herbal supplements abounds on a swath of internet sites, as well as in magazines, pamphlets and brochures distributed by certain supplement companies in order to promote their products. However, this type of information is very subjective and therefore unreliable. Only controlled studies with human participants, especially clinical studies, are a trustworthy source of evidence for the safety and efficacy of any herbal or nutritional supplement. Unfortunately, not all herbal products advertised on the internet have undergone rigorous and well designed clinical trials. Additionally, through their misleading advertising, certain manufacturers of herbal or "natural" weight loss supplements tend to encourage self-medication and self-diagnosis, which can be potentially hazardous to the unwary consumer[15-17].

Herbal product use in the largest US-Mexico border: The extensive border between the United States and Mexico comprises a unique area of research regarding the traditional use of medicinal plants and herbal remedies. Studies made in the bordering cities El Paso, Texas and Ciudad Juarez, Mexico have shown that approximately 70% of their combined populations use diverse types of herbal products for both medicinal as well as aesthetic purposes[18,19]. Due to their popularity in Mexican traditional/folk medicine, the use of medicinal herbs along the border has a tendency to be considerably higher compared to the rest of the US[20-23]. Many herbal products obtained in Ciudad Juarez and other Mexican border cities are often imported into the US[19]. One example is the candlenut tree seed, which is sold in Mexico under the common names of "nuez de la India" (India nut) or "semilla de Brasil" (Brazil seed). The seed is available for purchase as a crude drug (raw seed) or in capsules. This product is available for sale in various markets in Mexico, as well as via the internet in the US[24].

Candlenut tree seed: The seed of this Asian tree (*Aleurites moluccanus-Euphorbiaceae*) is commonly known around the world by a wide variety of common names in various languages including Avellano, Candleberry, Indian walnut, Jamaican walnut, Kukui, Lumbang oil, Magic Nuez, Magic nut, Tuitui, Árbol de Indias, Nuez de la India, Nogal de la India, Otaheite walnut, Palo de la India, Palo de nuez, Semilla de Brasil, Singapore nut and Varnish tree[24-29].

Weight loss and other unsupported health claims regarding candlenut tree seeds: The seeds are advertised worldwide through various venues in the media but especially on the internet. They are touted as having "fat burning" and other weight loss properties, among many other unsubstantiated health claims. However, there are no known controlled clinical trials undertaken in humans to assess any of the purported beneficial effects, especially during prolonged treatments[30,31].

Certain ads on the internet state that the seeds can help to lose weight and lower cholesterol. Additionally, some websites state (without citing a single clinical study to support their claims) that ingesting the seed can be beneficial for the treatment of a plethora of diverse health conditions including arthritis, alopecia (baldness), cellulite, constipation, hemorrhoids, skin conditions, as an anorexic (to suppress appetite), as well as to stop tobacco addiction. Certain companies marketing candlenut seed state that it is feasible to lose up to 10 kg (22 lbs), in just a few weeks after ingesting the seed. Some companies and individuals who sell and advertise candlenut seeds on the web mention that a very small portion (approximately 1/8 to ¼) of the seed should be decocted (boiled) in water prior to ingesting it at night, before retiring. This may pose a problem for some consumers, as no exact dose has been specified, making it difficult to measure the exact quantity of the seed that will actually be ingested. Additionally, the method of taking the seed varies according to the indications mentioned by various commercial sites on the internet. This situation only augments the confusion and misinformation for the unwary consumers who may be desperate to lose weight, placing them more at risk for intoxication[24,30,31].

Toxic properties of related *Aleurites* species: Various closely related species to the candlenut tree, including *Aleurites fordii* (commonly known as "Tung nut tree") are also known to contain irritant toxins especially affecting the skin as well as the gastrointestinal tract. These plants have few medicinal uses, but been implicated in cases of poisoning, in both humans as well as animals[32-36]. The spurge family is known to possess various bioactive phytochemicals, of which the phorbol esters seem to be the most prominent with regard to their potential toxicity[34,37].

Toxicity of phorbol esters: Phorbol esters are toxic diterpene compounds that are present within the Euphorbiaceae and Thymelaceae botanical families. The phorbol moiety is comprised of one or two long-chained esters. In this way, it bears resemblance to diacylglycerol, which acts as a substrate of protein kinase C (PKC). The PKC is activated by phorbol esters and this causes a strong inflammatory response. The PKC is an important regulatory enzyme involved in signal transduction at the cellular level. Furthermore, phorbol esters of the tigliane type are very strong cathartics (purgatives) and also act as powerful tumor promoters due to their co-carcinogenic action. Phorbol esters can also be very irritating to the skin and eyes. The seeds may cause vomiting, gastrointestinal pain and diarrhea if ingested in quantity. The fruit of the candlenut tree also contains potentially toxic compounds (saponins)[27,34,37].

Symptoms and effects of poisoning: According to various sources, the ingestion of candlenut tree seeds causes a sensation of discomfort and nausea a few minutes after ingestion. These symptoms are followed by vomiting, abdominal pain (cramping), diarrhea, dehydration, as well as an imbalance in electrolytes. Due to its chemical components, the seed possesses a strong cathartic action and may cause diarrhea, dehydration and loss of electrolytes. The chronic ingestion of the seeds may affect the gastrointestinal system, causing intestinal muscle atony. Additionally, there are reports of alterations in heart rate due to the ingestion of the seeds[26,31,34,37].

Inaccurate information and another case of mistaken identity: In spite of all the documented evidence that the seed has strong irritating effects upon the gastrointestinal system, one internet site mentions in Spanish that the candlenut seed ("nuez de la India") is "a gentle laxative and diuretic" and "not a stimulant laxative". Furthermore, the site also states that the seed is "one of the rare excellent sources of naturally occurring GLA (gamma linolenic acid) in the world". To add to the confusion, this site mentions that the candlenut seed is the same as "semilla de Brasil" or "Brazil seed"[24]. This only augments the bemusing situation, as some people may mistake the so-called "Brazil seed" with the well known "Brazil nut", (*Bertholletia excelsa*) a very different, edible and nutritious species, belonging to a distinct botanical family (*Lecythidaceae*)[29].

Management of poisoning: A person poisoned by the seeds should receive intravenous hydration, anti-emetics, as well as electrolyte replacement therapy, especially for people with severe gastrointestinal symptoms. Proper hydration is of primordial importance in children poisoned by the seeds[26]. The application of activated charcoal and sodium sulfate may also be necessary in some cases, along with gastric lavage[34,37].

Reported intoxications: A medical case report from Spain mentioned the intoxication of a 33 year old woman who was hospitalized in the province of Navarra after ingesting a whole candlenut seed as a laxative for weight loss. The woman was semi-conscious and presented with hypotension and bradycardia. Approximately 24 h after ingestion, the patient presented nausea, vomiting and copious watery diarrhea, after which she had syncope, preceded by dizziness. Upon physical examination, the patient showed a cardiac frequency (CF) of 45, with discrete hypotension (90/60) but without neurological deficits. The electro cardiogram showed sinus bradycardia with 1st grade auriculo-ventricular blockage. The woman was taken to the hospital's emergency observation unit and started on dopamine (5 μg kg^{-1} min^{-1}), her CF decreasing to 28-30 pulses min^{-1} and her blood pressure dropping to (65/40). Her digoxinemia was 0.3 μg L^{-1}. Dopamine administration was continued for 24 h. The patient's CF progressively returned to normal and she was discharged 7 days after being admitted to the hospital[38]. This and other related events prompted the Spanish government to ban the use of the seed due to its toxic properties[39].

An Argentine internet news agency stated that in the city of Paraná, at least 4 women were admitted to the intensive care unit (ICU) of 2 different hospitals after ingesting the seed with the expectation of losing weight. One of the patients, 28 years of age mentioned, she experienced headaches as well as digestive pain and "having to go the bathroom many times". The symptoms persisted for at least 5 days after having suspended taking the seed. The other patient, 33 years old, stated she took the seed for a weeklong treatment as part of a weight loss regimen. She mentioned feeling nauseous and wanting to vomit. Additionally, she experienced fatigue, bone pain and expelled bloody stools. The two other cases involved a 5 days stay at the hospital's ICU, due to the symptoms exhibited by the patients. One of the women exhibited liver impairment and pancreatitis, while on the other presented cardiac problems. One of the attending physicians mentioned that ingesting the seed causes abundant diarrhea and acts a strong diuretic. For this reason, affected patients lose abundant electrolytes via the feces and urine, which originates an imbalance at both the cellular as well as the blood levels.

With regard to the heart, the seed produces changes in the electrocardiogram (EKG), including arrhythmias, heart blocks and potentially cardiac arrest[40].

Various governmental health agencies prohibit the use of candlenut seed: As mentioned above, the health ministry of Spain banned the use of the seed[39]. Various countries in South America have also prohibited the sale and / or importation the seed. The Argentine government's regulatory agency for medications, foods and medical technology, (officially known as Administración Nacional de Medicamentos, Alimentos y Tecnología Médica) or Anmat, prohibited the use of candlenut seed in 2014, due to its potential lethality. The agency also banned its importation, as a means to curb its availability to the public. However, the product is still available for sale by clandestine vendors as well as via certain websites on the internet[41].

The Chilean government's pharmacovigilance agency also prohibited the use of candlenut seed in February of 2017, due reports of intoxications within that country[42]. Additionally, the Brazilian government banned the ingestion of the seed in 2016 due to 3 reported deaths associated with the ingestion of the seeds for weight loss[43].

Unsubstantiated health claims and confirmed toxicity of candlenut seed: There are no known clinical studies in humans to verify the various unsubstantiated claims regarding weight loss (or any other health benefits) made by some commercial companies which market candlenut tree seeds. The seeds' bioactive ingredients possess a drastic purgative effect as well as co-carcinogenic (tumor-promoting) action. Certain individuals may also be allergic to the plant's components. For this reason, the ingestion of any part of the plant, especially the seeds, is not a safe option for weight loss and should be avoided during pregnancy and lactation, as well as in children and in the elderly. Persons suffering from various pre-existing health conditions, such as heart or kidney disease, gastroenteritis, colitis and irritable bowel syndrome (IBS), for example, could also be more at risk for intoxication[26,37,44,45].

CONCLUSION

Even though many people seek "natural" or "alternative" solutions for weight loss, they should be aware that not all herbal products available for sale, especially on the internet, are safe and that self-medication with these supplements can be very hazardous or even lethal. The active ingredients in the seed of the candlenut tree ("nuez de la India" or "semilla de Brasil") possess a drastic purgative action, as well as potential tumor-promoting activities. Due to the fact that no known clinical studies exist to support the plethora of supposed health benefits claimed by companies that market the seeds as a "safe and efficacious" weight loss supplement, along with their confirmed toxicity, it is highly inadvisable to ingest them in any quantity.

SIGNIFICANCE STATEMENTS

This literature review investigated the potential toxicity of the candlenut tree seed (*Aleurites moluccanus*) also known in Spanish as "nuez de la India". This seed is a purported weight loss supplement sold in markets as well as via the internet around the globe. The extensive review not only revealed that there are no clinical studies to confirm its safety or efficacy, it also shows that various reports from diverse countries around the world document the seed's toxicity and potential lethality. The information contained herein will assist biomedical practitioners in augmenting their knowledge regarding the dangers of ingesting the seed, as well as the adequate prophylactic procedures to follow in case of intoxication.

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