

# The Depilatory and Cytotoxic Action of "Coco De Mono" (*Lecythis ollaria*) and its Relationship to Chronic Seleniosis

FRANCISCO KERDEL-VEGAS<sup>1</sup>

In Venezuela, the term "coco de mono" ("monkey's coconut") is used to designate two plants completely different from each other. On the one hand are species of the genus *Lecythis*, characterized by a woody urn-or-pot-shaped pericarp covered by an operculum inside of which the seeds are found. On the other hand, is *Couroupita guianensis*, known popularly as "coco hediondo" ("foul coconut") in reference to the disagreeable odor of its rounded, hard-shelled but fleshy fruit and of the plant's sap. This paper deals only with species of the genus *Lecythis*. The toxicity of these plants and their depilatory effects are herein described.

## History

The Lecythidaceae are composed of nearly 45 species in tropical South and Central America, distributed over a vast area running from Brazil to Costa Rica. Pittier (1) reports that *Lecythis* species was first described in Venezuela by the botanist Loefling around 1754-1755, in the vicinity of Barcelona (Eastern Venezuela). The reference is as follows: *Lecythis ollaria* Loefl. Ites. Hisp. 159, 1758. Syn: Olla del mono, olleto. According to information supplied by Ernst, the same species grows also in the States of Guárico and Portuguesa (Central Venezuelan flatlands).

The bark of this large tree is reddish yellow, very hard and heavy, and the oil extracted from the seeds is considered to be a powerful hemostatic agent. Related species identified in Venezuela are:

<sup>1</sup>Professor of Dermatology, Hospital Vargas and Universidad Central de Venezuela, Caracas, Venezuela.

Received for publication April 26, 1965.

*Lecythis minor* Jacq. Stirp. Am. 1: 168, t. 109. 1788.

*Lecythis longifolia* H.B.K. gen. sp. 7: 26. 1825.

*Eschweilera cordata* Miers. Trans. Linn. Soc. 30: 270. 1873.

*Couroupita guianensis* Aubl.

*Jugastron christii* Pittier. 1925.

*Lecythis hipartita* Pittier, Arb. y. arb. nuev. Ven. 39. 1923.

Pérez Arbeláez of Colombia (2) applies the term "olla del mono" to *Lecythis ollaria*, *L. elliptica* H.B.K., and *L. curranii* Pitt., which are also called kaberali and sapucaiapilao (Brazil). He describes the fruits as pot-shaped, dry pericarps with thick edges, provided with a lid. The nuts, which he claims are edible, are found inside and have a brown covering and a yellowish, oily meat. He insists that these trees could well be a valuable element in forest repopulation because of their easy growth, the structure of their trunk and the favorable characteristics of the wood. He also maintains that the sap may be mixed into a very agreeable drink and that the seeds produce edible oil.

Menninger (3) reports that the *Lecythis* species have always been considered outstanding due to the delicious flavor of the sapucaya nuts produced by the same species, especially *L. zabucayo* Aubl., in their odd-looking seed pods (some as large as a human head). He also mentions that the flowers are large, generally red or yellow, and that they would be conspicuous if they were not hidden by the dense foliage which prevents their being seen until they fall on the ground. In relation to its pharmacological action, there is good information dating back two centuries, and Jacquin wrote in 1763: "Unicum semen integrum assumpsi,



Fig. 1. In the central part of the photograph, a coco de mono (*Lecythis ollaria*) tree is seen in a forested region of Portuguesa State, Venezuela.



Fig. 2. In this photograph, the width of the tree can be appreciated by comparison with the man climbing it. Notice the rough bark and the numerous fruits hanging from the branches.

quod sapore gratissimo deprehendi; sed post median horam nausea, anxietate magna, capitisque titubatione praetes consuetudinem fui vexatus; an ab hoc nucleo" (I took a single seed and found it very tasty, but half an hour later felt nausea, great anxiety and dizziness).

Lisandro Alvarado (4) describes *Lecythis* species as large trees of the lowlands and Guayana, so named because of the fruit's ellipsoidal structure which opens through a lid or operculum at one of its poles. Monkeys open the fruit easily in order to eat the nuts inside, but country people know their effect and do not eat them.

F. Vélez - Salas (5) comments on the testimony of a man who, after eating the fruit, experienced hair loss and mentions that the Indians used the latex of the pericarp as a depilatory. Prof. Castelhanos (6) of the Botanical Section of the National Museum of Brazil, stated that in Brazil there are about 27 species of *Lecythis*, in a region extending from the northern part of the country to the parallel which crosses Rio de Janeiro. The sapucaia, or chestnut of Pará, which is consumed as food in Brazil and other countries to which it is exported (i.e., Europe, United States), is *L. paraensis* Ducke (21, 22). In northern Brazil, there is a popular saying that eating sapucaia leads to hair loss. We know of no scientific or medical reports from Brazil.

Prof. Lair Renno (7) from Belo Horizonte (Brazil) maintains that according to "Flora Brasiliensis" Vol. XIV, Part I, there are 47 species of *Lecythis* in tropical and subtropical zones of the western hemisphere, the great majority in northern Brazil (Amazonas, Pará, etc.). He relates that the edible fruits of *Gustavia speciosa* DC. (Lecythidaceae) of Colombia, "rapidly produce an odd yellow coloration of the hair which generally disappears within 48 hours." The fruit of *Gustavia brasiliiana* DC. has emetic properties.

### Botanical Description

Dr. Tobias Lasser (8) informs me that in Venezuela, trees of the genus *Lecythis* are found in the States of Sucre, Anzoátegui, Guárico, Portuguesa, Lara, Bolívar, etc., covering therefore a vast expanse of the central, eastern, western, and southern zones of the country. At least four species have been

determined: *Lecythis longifolia*, *L. minor*, *L. ollaria* and *L. vernusta*. *Lecythis ollaria*, the causative agent of toxic syndromes and subsequent hair loss, is described by Lasser as follows:

*Lecythis ollaria* L. Sp. Pl. (Ed. 2)1 (1762) 734. Large tree with warty branches. Leaves sessile or subsessile, alternate, chartaceous, ovate to oblong-ovate, apex obtuse to subcordate, subserrate, reticulate venation not prominent, 5.2-9 cm long and 2.5-5 cm wide. Wood reddish yellow to dark brown, very strong. Spiked terminal inflorescence with ovate deciduous bracts; flowers variable, sepals six, oblong, uneven, with rounded margins, concave, persistent; petals six, larger than sepals, spatulate, subequal, oblong to subrounded, concave, with a reflex margin, white. Ovary inferior, four, four-locular with a depressed vertex, small style, obtuse stigma. Large pyxidium, rounded, with a six-lobed, ring-shaped, obtuse zone. Pericarp woody. Use: strong wood, insect resistant. Oil from seeds considered a powerful hemostatic agent.

### Clinical Observations

In the lowlands of Venezuela, where this plant is found, there is a popular belief among the natives that the seeds of this tree cause hair loss from scalp and other parts of the body. According to observations in the literature, all the individuals who have suffered from intoxication and subsequent hair loss were strangers to the zone and, in at least two instances the potential victims were warned that hair loss might result from eating these nuts.

The cases published in Venezuela are as follows:

1. Observation by M. Vegas (9): In 1936, he examined a 50-year-old Caucasian engineer of North American nationality, who, while doing exploratory work for an oil company, was in the lowlands of the State of Guárico on March 15, 1936. He ate 10 raw and 10 boiled nuts of the type called "coco de mono." After 48 hours he ate 20 more, also boiled, suffering on the next day an acute intoxication with nausea, vomiting and cephalalgia. One week later, he developed a marked hypersensitivity of the scalp upon combing which lasted for four days.

Between the 10th and 12th day after the first ingestion, he noticed abundant hair loss while combing; this became accentuated in the following days and spread to the body hair. Subsequently, there were marked changes of the nail plates in both hands. After a few weeks, there appeared a grayish transversal band which, as described by the patient on July 1, 1936, was located approximately in the middle part of the nail limbus with lack of adherence between the plates and their base, leading to total loss of the nail on his right small finger. There was no pain, but there was an increase in sensitivity. He also felt pains in his neck muscles beginning three weeks after the ingestion of the nuts and continuing for several months. Re-growth of hair and nails led to a normal state after a period of time.

2. Observations by F. Vélez-Boza (10): In 1941, he was called to attend four patients who presented signs of acute intoxication with nausea and vomiting, after having ingested "coco de mono" nuts in the vicinity of San Joaquin, State of Anzoátegui. The patients were: a 12-year-old boy, a 17-year-old female and two males of 19 and 25 years, respectively. They had recently arrived in the region and had not been warned of the potential dangers of these nuts. The 12-year-old boy ate about seven nuts. Shortly thereafter, he felt nauseated, vomited the nuts and presented no further disturbance. The 19-year-old male also vomited an hour after the ingestion of 14 nuts but remained dizzy for another day. Romberg sign was positive. On the third week, he experienced hair loss, although in small quantities. The 25-year-old male and the 17-year-old female ate a large amount of the nuts, presenting, after a short time, nausea, and vomiting a small amount of what they had ingested. They complained of a strong burning sensation along the esophagus and in the stomach, marked dizziness, and they presented Romberg signs. There were no tendinous nor ocular disturbances. No other cardiac, renal nor circulatory relevant symptoms were observed, and there was no fever. Both patients had foul breath reminiscent of decomposed seaweed or phosphorus. On the next day, they developed diarrhea. The dizziness persisted for several days. At the end of the third week, there was abundant hair loss

from the scalp, leaving the patients almost bald. The hair fell out when gently pulled, but there was no pain. The ends of the hair when observed under the microscope did not show the bulbous portion. Loss of hair on other parts of the body was not observed. New hair started to grow before the loss was complete. The author considers the effect of "coco de mono" proportional to the amount of nuts ingested and to the time that the nuts were present in the digestive tract, since those that vomited thoroughly did not suffer any damage.

3. Observations by F. Kerdel-Vegas (11, 12, 13): The first patient was examined on May 5, 1962. He was a 54-year-old Caucasian, born in Italy but living in Caracas for many years. He came to consult because of abundant hair loss, which he claimed was caused by the ingestion of "coco de mono." On April 20, 1962, disregarding his guide's warning, he ate 70 to 80 nuts while on a hunting excursion in southern Portuguesa. That same afternoon, he felt nervousness and anxiety, and, during the night, he had strong chills followed by fever and delirium. Simultaneously, he developed diarrhea of approximately eight liquid bowel movements with no blood, mucus nor pus, which persisted—as did the fever—for 36 hours. Even after the fever and diarrhea had subsided, the marked nausea lasted without vomiting but with pronounced anorexia and arthralgia of all his joints. He also developed pain on the left side of his back towards the base of the thorax. On the eighth day after he ate the nuts, there was sudden and marked scalp and body hair loss, which increased in the following days. On May 3, he noticed a purple streak in the proximal part of his nail plates which gradually disappeared in the next three days. In the first few days, he lost much hair from the axillae, chest, pubis and thighs; he also lost his mustache, eyebrows and eyelashes and noticed, upon shaving, a decrease of beard growth. General medical examination, laboratory tests and a biopsy of his scalp showed results within the normal levels. From May 28 on, there was considerable hair re-growth and, on June 11, his appearance had returned completely to normal. Two other patients, with the same phenomenon of hair loss following the ingestion of "coco de mono" nuts, were ob-

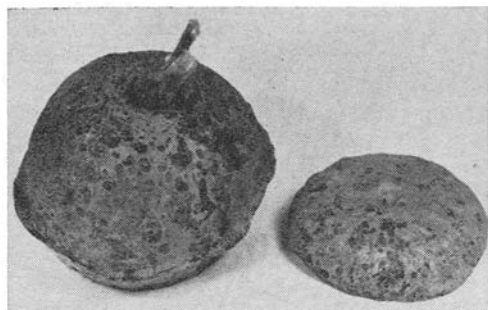


Fig. 3. External appearance of the fruit that contains the nuts and gives its name to the tree. On the right, the operculum, which is normally located at the bottom of the fruit.

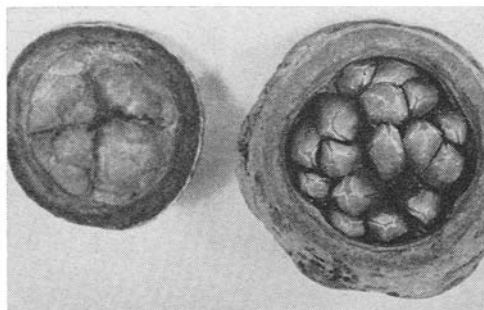


Fig. 4. Internal appearance of the fruit with 16 nuts inside. These fall to the ground after the operculum (on the right) falls off.

served on June 17, 1964. They had suffered acute intoxication on February 11, 1964, in southern Guárico near San Fernando de Apure.

One of them was a 24-year-old Caucasian female, born in Germany, laboratory technician by profession, who, on that day, ate 22 "coco de mono" nuts (she specified that 20 of the nuts were picked from the ground and 2 were extracted from a fruit picked from the tree and were, therefore, "fresh"). Three hours after eating them, she started to vomit, first the ingested food and later bile-like material, for nearly seven hours. She suffered convulsions and cephalgia. The night of that same day, she was taken to the local hospital where they treated her symptomatically, and she left next morning. After five days, she developed nocturnal muscular spasms in her calves which lasted two weeks. On February 18, seven days after the acute intoxication, her hair started to fall in great patches, first in the right temporal region and later diffusely over her scalp. On the eighth day, she was completely bald, except for a few isolated hairs in the parietal region. From that time on, she was forced to wear a wig. She did not suffer loss of eyelashes, eyebrows, pubic hair, axillae nor hair on the rest of her body. After the third day, she noticed a transversal white streak in all her fingernails which advanced towards the distal part of the nails as they grew; when it reached the free border, the nail broke along the streak line. This phenomenon was absent in the toenails.

On the same day and at the same site, a friend of the patient, a 38-year-old Caucasian male, born in Switzerland but living in Venezuela for 17 years and a photographer by profession, ingested 15 to 20 "coco de mono" nuts picked up from the ground and one "fresh" seed extracted from the fruit. Two hours later, he felt gastric disturbances and on the ninth hour developed mild diarrhea with soft stools and intense colic pains, which put him in a state of semi-consciousness. He also felt heaviness of the limbs, marked disorientation, blurred vision and loss of the notion of time, remaining thus for 12 hours. On the second and third days, he started to feel nightly heat flashes and muscular spasms in his calves, ankles and soles. On the same day as his companion (February 18), he noticed loss of hair, first from his beard (the patient normally has a heavy beard and mustache but marked hypochromatic baldness) and then from his scalp, chest, abdomen, pubis, axillae and, to a lesser degree, from the extremities. It is estimated that he presented 98% alopecia of his head and beard and 70% of the pubis; there was no *defluvium capillorum* of his eyelashes nor eyebrows. There was slight nail fragility, weeks after the acute intoxication. The hair loss process was completed in one week and re-growth was noticed immediately, so that his normal aspect was recovered in three months. Clinical and laboratory tests gave normal results.

4. Observation by P. Oropeza (14): On February 13, 1964, a two-year-old boy was

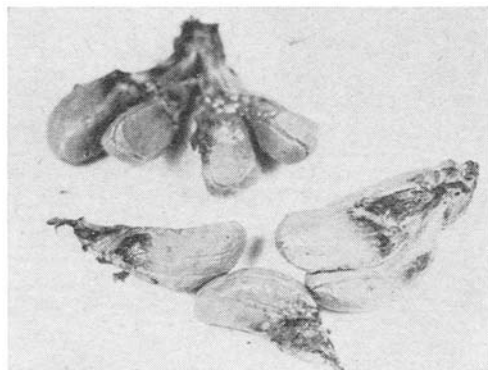


Fig. 5. Morphology of coco de mono nuts, immediately after being extracted from the fruit.

hospitalized in the Pediatric Department of the Hospital Universitario de Caracas. He weighed 10.3 kg., was very sick due to continuous vomiting and had a history of having ingested "coco de mono" nuts. He was treated symptomatically for severe dehydration and, although therapy was applied and proper medical attention given, he died on the afternoon of February 16. Autopsy was not performed. Subsequently, it was established that, although the boy had not left Caracas, he had eaten "coco de mono" nuts brought from Valle de la Pascua (State of Guárico, central plains of Venezuela).

#### Depilatory Effects on Animals

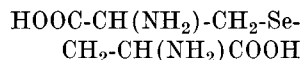
In multiple experiments carried out in mice, rats and hamsters (13), "coco de mono" has been administered by mouth at 5% concentration and intraperitoneally (aqueous fraction 1:1000 ml per kg) in order to study the inhibitory properties of these nuts on hair growth. A rounded zone of 1.5 cm in diameter on the dorsal region of the animal was depilated with tweezers, thus allowing the pilosebaceous follicles to enter the active growth phase (anagen) which was determined in the control animals by complete re-population of the depilated area in a seven-day lapse. During the same period, there was observed a complete inhibition of the hair growth in animals subjected to the action of "coco de mono" administered raw as well as in aqueous fraction or purified saline.

#### Histopathologic Study

After prolonged exposure to raw "coco de mono" or active extracts, a variety of histopathological alterations were found in the sacrificed animals, besides the hair growth inhibition. Among them: atrophy and disappearance of the sebaceous glands, marked atrophy of the epidermis, edema and intralveolar hemorrhage of the lungs, necrotic foci of the liver and spleen and intense sinusoidal congestion of the adrenals (13).

#### Isolation of the Active Principle

In a recent study by Kerdel-Vegas *et al.* (15), the procedure used in isolation of the active principle and the determination of its chemical structure are described. The active pharmacological factor turned out to be a hydrosoluble substance, thermostable, dialyzable (and, therefore, of low molecular weight), adsorbable by certain exchange resins (Dowex 1 and Dowex 50), and finally it was determined that it was the selenium-containing analog of the sulfur amino acid, cystathionine, the formula of which is:



#### In Vitro Cytotoxic Effects

Studies made by Aronow and Kerdel-Vegas (16) demonstrated a powerful cytotoxic effect *in vitro* of raw "coco de mono" as well as of its purified fractions and pure seleno-cystathionine. Based on the hypothesis that many cytotoxic substances now used in the treatment of leukemia and other forms of cancer produce extensive hair loss as a secondary effect, we have been able to demonstrate in a satisfactory manner that this substance which is capable of producing hair loss likewise possesses cytotoxic properties.

#### Comments

The possible mechanism of the activity of "coco de mono" in relation to alopecia could be related to inhibition of mitosis. It may perhaps be more closely related to inhibition of the action of cystathionine which represents an intermediate step in the transformation of methionine to l cystine. Cystine is an indispensable amino acid in the mech-

anism of keratinization, since it has been established that its disulfide cross-linkages (S-S) allow association of neighboring polypeptide chains between them, giving the hard keratin of hair and nails its characteristics. When the sulfur of cystathionine is replaced by selenium, giving seleno-cystathionine, it is possible that the new amino acid loses the properties of the original amino acid, thus affecting the process of normal keratinization.

Scientists from the Instituto Nacional de Nutrición (17), after noticing toxic problems in their experimental animals, established that these symptoms were due to a food factor. After some investigation, it was established that the causative factor was the sesame cake, an important component of the concentrate fed daily to these animals. Analysis demonstrated that the concentrate contained a high amount of selenium, and it seemed that the sesame utilized came from Turén, State of Portuguesa, located in the western plains of Venezuela, where cases of intoxication by "coco de mono" have been observed.

Recent analyses carried out on our request by the Union Carbide Corporation Nuclear Division reveal the following significant data:

- 1) Dried de-fatted nuts (*Lecythis ollaria*)  
2.23% Se by weight
- 2) Whole de-shelled nuts (*Lecythis ollaria*)  
0.58% Se by weight
- 3) Rat diet (commercial concentrate)  
0.0035% Se by weight

Since it has been established that any selenium level above 10 parts per million constitutes a toxic level (18), we can conclude that these findings are of more than academic interest.

In Venezuela, there is no information on the selenium content of the soil in different zones of the country. A study of this kind would be of interest, since it is now known that the toxic phenomena caused by "coco de mono" seeds are due to a selenium-containing amino acid. It is probable that large zones of the Venezuelan plains have a high selenium content. Data on these problems might influence, for example, certain agrarian reform plans pursued by the government, since it would be necessary to impose cultivating restrictions on plants capable of

"accumulating" selenium in those zones. It might be assumed that this accumulation does occur with sesame [Jaffé *et al.* (17)], and there is evidence that corn also accumulates selenium in Colombia (18, 20).

The problem of chronic seleniosis affects both humans and domestic animals. Since 1857, it has been described in the scientific literature as a disease of cattle: "alkali disease" producing loss of the long hairs of the tail and mane and such pain in the hoof that it interferes markedly with movement. This disease was originally reported in South Dakota. The acute form of this intoxication was later described as "blind staggers," a name indicating two of the common symptoms of the disease, which ends generally in paralysis and death. Selenium was not thought to be associated with these diseases before 1931 (18).

In 1560, in Colombia, Father Pedro Simón (19) described diseases similar to the alkali disease in domestic animals, malformation of children and of chickens and loss of hair and nails in humans. Father Simón wrote that corn and other vegetables grew well in certain regions, but that whenever man or animal ate of these there was hair loss. He mentioned also in his chronicle that Indian women gave birth to monsters that were abandoned by their parents. The naturalists (18) associated this disease with the soil rather than to any given species of fruit, vegetable, or cereal, from the simple fact that, when the crops were grown in other areas, they did not have toxic properties. The phenomenon was registered in zones called "peladeros" (barren spots) with the following signs: loss of the hair and hoofs in the cattle, malformation of lips and legs, abortions in a large number of animals, high percentage of infertility in chickens and even loss of hair and nails in human beings. Although these phenomena were recognized for centuries in Colombia, it was not until 1936 that the cause was determined to be selenium. In 1955, it was pointed out that, in a district of Colombia where "toxic corn" was cultivated, there were streams that had no animal life; that men and animals using the streams for drinking water showed loss of hair; small mammals became sterile; and horses suffered hoof damage (18).



### Conclusion

The observations of clinical cases of temporary alopecia (*defluvium capillorum*) after the ingestion of "coco de mono" nuts (*Lecythis ollaria*), associated with symptomatology of acute intoxication, fever and diarrhea and various neurological manifestations, preceded the experimental study of the active principle contained in these seeds. The marked cytotoxic effect of "coco de mono" has been determined *in vitro* in mice fibroblasts; the active principle has been isolated and has been identified as the selenium analog of the sulfur amino acid, cystathionine.

This discovery has led to great interest in the mechanism of inhibition of mitosis by the amino acid, to the experimental study of its toxicity and finally to the study of selenium found in the ground of different parts of Venezuela as well as in different pastures and cultivated areas.

The implications are obvious, not only for the public health point of view but also for the country's economy, since these studies can provide the basis for condemning for agricultural purposes vast zones of Venezuela flat lands.

### Literature Cited

- Pittier, H. 1926. Plantas Usuales de Venezuela. Lt. del Comercio, Caracas.
- Pérez Arbeláez, E. 1956. Plantas Útiles de Colombia. Suc. de Ricadeneyra, Madrid.
- Menninger, E. A. 1962. Flowering Trees of the World. Hearthsides Press, Inc., New York.
- Alvarado, L. 1921. Glosario de Voces Indígenas. Manrique & Ramírez Angel, Caracas.
- Vélez-Salas, F. 1959. Plantas medicinales de Venezuela. Edit. Las Novedades, Caracas.
- Castelhanos. Personal communication.
- Renno, L. Personal communication.
- Lasser, T. Personal communication.
- Vegas, M. 1936. Acción depilatoria del "Coco de Mono." Rev. Pol. Caracas, 27: 1843-1845.
- Vélez-Boza, F. 1943. Cuatro observaciones clínicas de los efectos producidos por la ingestión de las semillas de "coco de mono." Mem. Soc. Cienc. Nat. La Salle, 3(8); 28.
- Kerdel-Vegas, F. 1963. Caída del pelo generalizada debida a la ingestión de "coco de mono" (*Lecythis ollaria*). Bol. Acad. Cienc. Fis. Mat. Nat. 23, (64): 9-28.
- Kerdel-Vegas, F. 1964. Generalized hair loss due to the ingestion of "Coco de Mono" (*Lecythis ollaria*). J. Invest. Dermat., 42: 91-94.
- Kerdel-Vegas, F. y Aronow, L.: Efectos depilatorio y citotóxico del "Coco de Mono" (*Lecythis ollaria*). Dermat. Venez., in press.
- Oropeza, P. Personal communication.
- Kerdel-Vegas, F., Wagner, F., Russell, P. B., Grant, N. H., Alburn, H. E., Clark, D. E., and Miller, J. A. 1965. The structure of a pharmacologically active factor in the seeds of *Lecythis ollaria* ("Coco de Mono"). Nature, in press.
- Aronow, L. and Kerdel-Vegas, F. 1965. Cytotoxic and depilatory effects of extracts of *Lecythis ollaria* ("Coco de Mono"). Nature, in press.
- Jaffé, W., Chávez, J. F. and Koifman, B. 1964. Estudios preliminares sobre la toxicidad de muestras de ajonjolí con alto contenido de selenio. Arch. Venez. Nutrición 14: 7-23.
- Rosenfeld, I. and Beath, O. A. 1964. Selenium. Academic Press, New York.
- Simón, Fray Pedro. 1953. Noticias históricas de las conquistas de tierra firme en las Indias Occidentales, año 1560, 4: (Biblioteca Autores Colombianos) 222. Editorial Kelly, Bogotá.
- Benavides, S. T. and Silva-Mojica, F. 1959. Seleniosis. Instituto Geográfico de Colombia "Agustín Codazzi," Departamento Agrológico.
- Record, S. J. and Hess, R. W. 1948. Timbers of the New World. Yale Univ. Press, New Haven.
- Le Cointe, P. Arvores e Plantas Uteis. 2nd ed. Amazonia Brasileira III. São Paulo, 1947.