# Chaulmoogra oil as scientific knowledge: the construction of a treatment for leprosy

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The article investigates how knowledge of medicinal plants and related treatment practices are assimilated and transformed. Taking as its focus the use of chaulmoogra oil to treat leprosy, it examines how information on this plant was incorporated and transformed into scientifically validated knowledge when 'Brazilian chaulmoogra' came onto the scene. Pointing to the addition of chaulmoogra byproducts to the Instituto Oswaldo Cruz's production agenda in the 1920s, the study establishes links between productive processes and relates these to the period's scientific context. From the late nineteenth century until the 1940s, chaulmoogra oil was the great hope in efforts to cure leprosy. During this period, chaulmoogric treatment earned a place as scientific knowledge thanks to research studies conducted in laboratories throughout the Western world.

Keywords: chaulmoogra oil; leprosy; scientific translation; medicinal plants; Instituto Oswaldo Cruz.

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Up until the 1930s, diseases the world over were treated using medicine produced from substances found in nature, some of which were chemically and biologically prepared at pharmaceutical laboratories. The use of plants and other natural elements is an age-old practice common to all cultures and societies; indeed, it lies at the foundation of medical knowledge in today's Western societies. Starting in the 1940s, the evolution of techniques for synthetically producing chemical substances and molecules transformed the manufacture of medicine in the industrialized countries boasting more advanced chemical and pharmaceutical industries (Fernandes, 2004).

It was in this context that sulfones appeared and began to be used as specifics in the treatment of leprosy.[1] Derived from sulfonic acids by replacing hydroxyl with alkyl radical or aryl, development of these organic compounds followed from research by German biochemist Gerhard Johannes Paul Domagk (1895-1964), who was looking for an effective drug against meningitis, pneumonia, and other bacterial illnesses (IBGE, 2006). After Domagk published his research in 1935, Prontosil was put to use fighting bacterial infections.[2] Later research provided different variations, all from the sulfa group, which resulted in a gamut of products for controlling infections.

In 1941, Faget, Johansen, and Hillary Ross introduced treatment of leprotic infections using sulfanilamides at the National Leprosarium laboratory, in Carville, United States, marking the dawn of a new age in treatment of the disease (Faget, Johansen, Ross, 1942).[3] Two years later, Faget and group announced that intravenous administration of sodium salt of diaminodiphenylsulfone (DDS) could arrest the progress of leprosy. Their findings represented a remarkable advance in treatment of the illness, soon followed in 1946 by Robert Cochrane in India and in 1947 by John Lowe in Nigeria. The latter demonstrated that DDS was the most active, least toxic form against the leprosy bacilli, as well as the easiest to synthesize, and it could be administrated orally. In 1964, the bacillus demonstrated resistance to the drug, reaching as much as 50% (primary resistance) in countries where it was most commonly used (Rodríguez, n.d.).

In 1960, when sulfones were already being used on a wide scale, Orestes Diniz, discussing the question of leprosy prophylaxis in Brazil, stated that "sanitary policy had necessarily to entail isolation of the sick, since the precarious treatment then in fashion, using chaulmoogra oil, was not able to cure, save in a few scant cases of no statistical significance" (Diniz, 1960, p.87). Diniz saw a relation between the policy of isolating the ill in the large network of leprosaria built in Brazil and the previous therapeutic use of chaulmoogra as the main element of treatment. According to this argument, before sulfones appeared, the known therapeutic procedures offered no way of eliminating the bacilli from the bodies of the ill; moreover, what was known about the disease cycle and forms of contagion did not point to any ways of controlling them. Therefore, between the late nineteenth and mid-twentieth centuries, medical science had no way of establishing a scientific critique of the isolation system.

Before the advent of synthetic compounds, the fight against leprosy was based primarily on treatment with chaulmoogra oil and its derivatives. Many physicians and researchers were involved in the effort to translate "chaulmoogric" treatment – first observed in Hindu society – to the West, in the hopes of achieving a cure. Based on this research, which developed chaulmoogra oil as a scientific technique for treating leprosy around the world, scientists began to believe the disease could be cured.

In this article, we do not intend to discuss the efficacy of this oil as a form of treatment, since we are not interested in ascertaining whether it really cured the disease or merely attacked its symptoms. Clinical observations from that day point in both directions. Our goal is to consider the role the oil played in treating leprosy in Brazil for nearly five decades, prior to the advent of synthetic drugs. According to Laurinda Maciel (2004), "physicians paid close attention to other possible ways of treating Hansen's disease" and also tried employing other medications in conjunction with chaulmoogra derivatives (p.111). She states that "chaulmoogra oil, in the form of injections, capsules, or applied to the skin, was the least aggressive method of treatment with fewer complications for patients, and for this reason its use had attained a consensus among physicians" (p.111).

Our goal is to understand how scientific medicine incorporated chaulmoogra – originally a Hindu treatment, lying outside Western parameters – into a remedy seen as capable of combating leprosy. This process of transforming and integrating an object whose therapeutic qualities originally lacked any scientific recognition into a medicine validated by Western-style medical standards was by definition collective and prolonged. The development of such a process means that the object in question (in this case, chaulmoogras) comes to be defined through association with elements already employed by Western medicine and through its inclusion in scientific classifications with appropriate nomenclature. This constitutes its translation into the context of the new network of knowledge and practices.

This article focuses on part of the process, that is, the development of research and the production of chaulmoogra oil in Brazil and, more specifically, in the laboratories of the Instituto Oswaldo Cruz (IOC), where initiatives were headed by Dr. Heráclides Cezar de Souza Araújo.[4] We start from the premise that the routines intended to validate non-scientific elements against Western medical standards result in processes of 'scientific translation'. These processes emphasize actions essential to building networks that conjoin technical contexts – consonant with the routines and concepts defining scientific practice – with social contexts, led by the researchers engaged in these routines, who must recruit their allies and establish the boundaries of their work.

This leads us to understand that the scientific context of the elements in question (in our case, chaulmoogra oils) is transformed during scientific translation.[5] This process occurred during the transfer of knowledge between different systems of medicine, that is, between Indian and Western medicine. The present article explores the construction of chaulmoogric treatment as a scientific fact within the framework of norms and assumptions from Brazilian scientific knowledge between the late nineteenth and mid-twentieth centuries.

## Chaulmoogra oil as scientific knowledge

Plants known as chaulmoogras belong to the family *Flacourtiaceae*. Their oil contains hydnocarpic and chaulmoogric acids, considered responsible for the oil's therapeutic action in treating leprosy. These tropical plants are angiosperms – that is, they have both flowers and fruit – and usually grow to the height of a bush or medium-sized tree. Within this family, the genera known as chaulmoogra comprise *Hydnocarpus, Carpotroche, Caloncoba, Oncoba, Lindackeria* and *Mayna*, the latter two never used much in the treatment of leprosy. The genus

*Hydnocarpus* encompasses the bulk of the chaulmoogras, including the most valuable species in treating leprosy. Of these, the most frequently used were *H. anthelmintica*, *H. laurifolia (H. wightiana)*, and *H. kurzii (Takaktogenos kurzii)*, which were acclimated in various regions including Brazil. A number of specialists believed the species *H. kurzii (Takaktogenos kurzii)* was the legitimate chaulmoogra. The oil extracted from *H. laurifolia (H. wightiana*) seeds was the most commonly used in India and was considered a substitute for oil extracted from *Takaktogenos kurzii* (Possolo, 1945). However, since it was cheaper on the market, it was used more often around the world (Holmes, Aug. 1923).

The information we surveyed indicates that oil from chaulmoogra seeds has been used for many centuries to treat skin diseases in Asia, including leprosy. According to Helena Possolo, the first record of the oil's use comes to us from the oral tradition of Hindu peoples. Legend says that a king of Burma contracted leprosy, gave up his throne, and hid in the forest, where he cured himself by eating seeds of *Kalaw* fruit, which is what the Burmese and Siamese call chaulmoogra *Taraktogenos kurzii* (Possolo, 1945). Another legend attributes the discovery of chaulmoogra to Rama, the first king of the Indian city of Benares, who abdicated his throne in favor of his son after getting leprosy. He then hid away in the jungle, where he lived off nothing but herbs and roots; this included the fruit and leaves of the *Kalaw* tree, which cured him of the disease (Parascandola, 2003). Stellfeld (1940) asserts that the term 'chaulmoogra' comes from Hindu.

Starting in the sixth century, chaulmoogras can be found cited in some important compendia, such as the Burmese book *Maha-win-vatthu*; the Chinese pharmacopeia *Pê-ts'ao-kang-mu* (1552-1578); a book by the Dutchman Henricus Van Rheede Tot Draakenstein, entitled *Hortus Indicus Malabaricus* (1678), which describes *H. wightiana*, although it does not refer specifically to its use in treating leprosy; the Japanese-Chinese encyclopedia *Wakan Sansai Zuye* (1713); the Arab medical dictionary *Makhzan-al-Adwiya* (1771); and India's first pharmacopeia, called *The Bengal Dispensatory* (1841). The fourth edition of the *British Pharmacopeia* and the first edition of the *Farmacopéia Venezuelana* (1898) mark inclusion of chaulmoogra in the pharmacopeias of Western countries (Possolo, 1945).

When Western scientists and physicians learned about the use of chaulmoogra oil to treat skin ailments, laboratories and clinics began verifying the oil's therapeutic effect, inaugurating the process that ultimately led to its inclusion in the norms of Western-style therapeutics. This took place around the mid-nineteenth century, when the British Empire was defining policies on the establishment of medical institutions in India with an eye to exploring the potential of traditional uses of medicinal plants and bringing this information together in pharmacopeias and practices that could be used by the British doctors working in those colonial areas (Wujastyk, 2004).

Transforming something whose therapeutic qualities are not recognized by scientific medicine into a drug requires that it be separated out from the historical and social context in which it was first observed. Construction of a new network of knowledge then begins, socially connected both to the new context where the element will be located and, technically, to the set of practices and information that constitute medical science. This means that for chaulmoogra to be recognized as a remedy that could be prescribed by Western medicine, it would have to be evaluated according to the era's reigning scientific standards and thus

dissociated from its traditional network of knowledge – a network that encompassed not only practices intrinsic to the Indian medical system but also the cultural and social web of which the system was a part. It was only fully assimilated once a new network had been created, grounded on Western values and underpinning knowledge concerning its use.

Construction of the network began around the mid-nineteenth century, when British physician Frederic John Mouat published an article in *Indian Annals of Medical Science*, where he described successful treatment of a classic case "of the worst form of leprosy" through external application of chaulmoogra oil (cited in Parascandola, 2003). He pointed out that the oil and its cutaneous use had first been described in 1815 by surgeon and naturalist William Roxburgh, who identified it by the erroneous botanical name *Chaulmoogra odorata* (Parascandola, 2003).[6] Throughout that century, it was believed that *Gynocardia* was the source of the seeds used to produce chaulmoogra oil, which was already available in the West. But in 1901, Sir David Prain researched chaulmoogra seeds found both at the bazaar in Calcutta and at markets in London and Paris and determined they were from the *Taraktogenos kurzii* tree, which is native to Burma and northeastern India (Parascandola, 2003).

This was confirmed by Frederick B. Power, director of the Wellcome Chemical Research Laboratories, who had decided to undertake a thorough investigation of fresh chaulmoogra seeds from a London market and had confirmed they came from the species *Taraktogenos kurzii* (Parascandola, 2003). He noted that the seeds of the plant indicated by Roxburgh displayed no optical activity and had no hydnocarpic or chaulmoogric acids, two of the principle traits of the chaulmoogra group. *Gynocardia odorata* then became known as "false chaulmoogra" and it was concluded that the oil used in the West came from plants of the genus *Hydnocarpus*, mainly *Hydnocarpus kurzii*.

In brief, this process marked the development of new knowledge in Western medicine. The main assumption was that chaulmoogra oil possessed therapeutic properties which could be used to combat leprosy, then a serious public health problem throughout the world. Indian knowledge was thus modified by physicians and researchers in tune with the interests and needs of the era's technical and social contexts; it was further mediated by the technology and ways of thinking about scientific therapeutic practices prevalent at that time. The chaulmoogra oil treatments developed by Western scientists back then were associated solely with leprosy; there were no efforts to produce chaulmoogra-based drugs to treat, for example, tuberculosis – whose bacillus is similar to leprosy's – or other skin ailments.

Just as treatment with chaulmoogra oil changed over time, so did international trade in the oil and its derivatives. Chaulmoogra oil was at first purchased directly from India. Later, many leprosaria began ordering seeds and oil from India, then using them to produce the medications needed to treat the ill and even selling them to foreign sanitation services. This was the case, for instance, of the Culion Leper Colony on Palawan Island in the Philippines, which ordered *Hydnocarpus wightiana* seeds and oil from Ernakulam Trading & Co.; its chemistry department would then prepare about 20 liters per day of ethyl esters derived from chaulmoogra oil to supply the Manila hospital and Cebu colony, and also sell them to sanitation services abroad (Araújo, 1926).

In Brazil, the IOC also imported some *Hydnocarpus wightiana* oil in 1927 from the same company in southern India, which was well positioned in the trade and supplied seeds and

chaulmoogra oil to a number of countries. The purchase was to supply the IOC's recently established Leprology Laboratory, headed by Dr. Souza Araújo, so it could manufacture the ethyl esters needed to treat the sick people who went to Manguinhos for free testing and treatment (Araújo, 1957). At the same time, different species of Indian chaulmoogra were being acclimatized in other countries, including Brazil. A number of seeds planted in Brazil were donated by the United States (Araújo, fev. 1937).

## Chaulmoogric treatment

In order to prepare the oil, seeds were placed in an oven and then crushed. The light yellow oil was extracted from the powder using sulfuric ether. Our research indicated that at the same time the scientific community used this oil, it also endeavored to develop new ways of utilizing its active principle more efficiently. So it was that chaulmoogra oil was transformed from a plant product used by the Indian population into a drug produced in Western pharmaceutical laboratories.

The oil was first administered externally, being applied directly to ulcers, replicating its traditional use in the East. But in the 1850s, Mouat tested its use internally, with his patients taking pills produced from seeds beat into a pulp (Parascandola, 2003). The results of external application proved of limited help in treating the disease; although internal use was more effective, it was not well tolerated by the organism, causing vomiting, diarrhea, and gastric problems. In other words, the medicine's effectiveness was limited by the patient's digestive tolerance, prompting physicians, chemists, and pharmacists to refine remedies derived from chaulmoogra oil; they tested ointments for external use, along with pills, drops, or capsules for internal use.

In the final decade of the nineteenth century, the oil began to be administered via intramuscular or subcutaneous injections; these caused veritable panic among patients since they were very painful and caused local reactions and fever as well, although they did eliminate the nausea associated with oral administration. The following decade, Dr. Victor Heiser, of the U.S. Public Health Service, discovered a way of diminishing the pain and irritation caused by the injections; hypodermic use of the oil was modified by adding a camphor-based compound that increased absorption of the chaulmoogra (Parascandola, 2003). Around fifteen years later, chemical research led to the production of ethyl esters derived from chaulmoogra oil, which were used quite often because they were easier both to tolerate and to administer and, in the eyes of many doctors, more effective (Araújo, 1931). They were obtained after chaulmoogra oil, ethyl alcohol, and sulfuric acid underwent an esterification process (Araújo, 1928).

The International Leprology Congress, held in Manila in 1931, corroborated this process. It reached the following conclusion regarding the treatment of leprosy:

> The use of special therapeutic agents is aimed at curing lesions. To this end, the most regularly used drugs are oils from the chaulmoogric group (*Hydnocarpus wightiana* and *H. Anthelminthica*) and its derivatives. It has been found that these oils and their derivatives have the same effects, but at large leprosy treatment centers, esters are preferred over oils not only because they are a stable product that can be manufactured in repeated, uniform batches but also because they are less irritating and easier to absorb. … Depending upon

> the nature of the chaulmoogric product, it can be administered orally or intramuscularly, subcutaneously, or intravenously. The congress condemns the intravenous use of oils and esters; intravenous application should be reserved for sodium soaps. Dosing of these different preparations is not arbitrary; it should be determined in accordance with individual tolerance and the appropriateness or inappropriateness of intensive treatment. (Araújo, 1931, p.3)

The doctors gathered there felt it impracticable to establish a standard treatment, although they recommended hypodermic (or intradermic) treatment, especially when combined with the intramuscular method:

> For this treatment the congress recommends either esters or sodium soaps of Chaulmoogra, injected once weekly, with a dose of 5cc each time, 0.1cc of the chosen product being introduced with each puncture. The lesion to be treated should be completely infiltrated with the medication; if it is so small that it will not hold the entire dose indicated above, the remainder of the medicine should be injected intramuscularly. A combination of intradermic and intramuscular administration is preferred. The interval between injections of the same lesion will depend upon the degree and duration of the local inflammatory reaction. (Araújo, 1931, p.3)

The treatment was painful and protracted, as we can see in the account of a patient with Hansen's disease who was confined to a sanatorium in Aimorés, in the municipality of Bauru, São Paulo, in the 1940s:

> I went through the various exams and learned about the treatment program: intramuscular creosoted Chaulmoogra on Mondays and Wednesdays; infiltration with Chaulmoogra on Tuesdays and Fridays. ... The empty days hurried by. The weeks went by all alike. Every Monday and every Wednesday, the horror of the extremely painful injections, a thick inassimilable oil hardening my muscles uselessly. Every Tuesday and every Friday, one terrible infiltration after the other, one inflammation altering when another had not even disappeared, as part of the program to cover my body with needle-pricks, re-cover it, and continue indefinitely on this way of the cross. (Mancuso, 1996)

It should be pointed out that as scientific knowledge developed, the new information did not spread in a linear fashion, so the less painful hypodermic treatment, with fewer side effects, was not one of the forms mentioned in the case of patients at the São Paulo colony. Despite the recommendation by the world's top specialists ten years earlier, the injections prescribed were still intramuscular, in conjunction with infiltration with chaulmoogra oil derivatives. As we will see later, the decision not to use hypodermic shots was not taken throughout the country, for Brazil's foremost authority in the matter included them in his therapeutic repertoire.

Based on his extensive experience in treating leprosy, Dr. Souza Araújo, head of the IOC's Leprology Laboratory, advocated a type of treatment that he believed was more efficacious in curing Hansen's disease, one he called 'eclectic' since it involved the association of chaulmoogra derivatives with other substances. Souza Araújo recommended the internal use of two to eight pills of sodium salts, prepared from the total acids of *Hydnocarpus whigtiana* oil; two or three hypodermic injections of ethyl esters of chaulmoogra oil per week; three to four applications per month of galvanocautery on ulcers, infiltrations, and lepromas; and solutes

of trichloroacetic acid to be brushed over all lesions treated with galvanic current and on all others. As a supplementary treatment, he suggested the use of tonics like arsenic, creosoted cod-liver oil, and others, in addition to the periodic use of laxatives and diuretics. A steady regimen of a hearty diet, exercise, and periods of rest should also be followed (Araújo, 1930).

Heráclides Cezar de Souza Araújo had maintained ties with the IOC ever since his 1913 graduation from its specialization course (Curso de Aplicação). His work focused on leprology, and he headed the Leprology Laboratory from 1927 to 1956. His education was completed with courses in public health, at John Hopkins University in 1926, and in dermatology, at the London School of Dermatology, from 1930 to 1931. A researcher of national and international renown, he played a key role in creation of the International Leprosy Association, of which he was vice-president from 1932 to 1956. Devoting himself to research on Hansen's disease and its prevention and treatment, he was active in Brazil not only as a policymaker but also as a critic of public policies and initiatives in the field (COC, 1995). When it comes to understanding both the development of chaulmoogric therapy in Brazil as well as that era's thoughts about prevention, diagnosis, and treatment, and hypotheses about causality and cure, he is thus an important piece of the puzzle.

Based on information gathered during his voyages, Sousa Araújo wrote papers describing therapeutic practices around the world. Through this information, we could accompany the development of medical practices and knowledge about the treatment of leprosy. From his writings, we learned that up until the 1940s, the treatment of leprosy was based on chaulmoogra derivatives, with some variations. In 1926, he wrote that the specific treatment in the Philippines consisted solely of ethyl esters of *Hydnocarpus wightiana* oil, with a half percent of iodine, administered intramuscularly. In Japan, they used purified oil, also via intramuscular shots (Araújo, 1926). However, various treatments might be used in one same colony, with differing doses, chaulmoogra species, or ways of preparing the derivatives (salts, esters, esters with iodine), depending upon the clinical presentation of the disease (Araújo, 1926).

As the process of scientific translation of chaulmoogras took root, many preparations appeared on the market, developed by scientists around the world.[7] Despite the emergence of these new drugs and the praise they won – especially ethyl esters – many physicians continued to use pure oil or formulas considered less effective, due to high prices or problems obtaining large amounts of these products.

Although chaulmoogra oil and its derivatives offered the last hope in the attempt to cure this horrible illness, there were still controversies about its therapeutic effects. Believing the oil cured leprosy once and for all, many physicians considered it a specific; others had no confidence in the cure and felt the drugs were merely a palliative. The development of scientific knowledge about chaulmoogra oil in the treatment of leprosy was grounded first and foremost in the discovery that its therapeutic action derived from chaulmoogric and hydnocarpic acids. Yet even today, their underlying mechanism is not known. Three explanations have been advanced: bactericidal action; some influence in the immunological sector; and secondary immunizing action (with the oils acting on the liver to increase the amount of lipase in the blood, destroying the microbacteria's covering of fat and leaving them unprotected and easier for antibodies to attack) (Pupo, ago. 1926). In 1920, Professor Adolpho Lindenberg stated that "whoever has tried chaulmoogra oil in a large number of cases will reach the conclusion that

definitive results can be achieved in terms of recovery and the cure of leprosy" (Araújo, 1956, p.303).

In 1923, Dr. Emílio Gomes, a Brazilian bacteriologist, stated that he had observed treatment with chaulmoogra oil from a bacteriological standpoint and had not found the Hansen bacillus to disappear at any point (Araújo, 1956, p.463). Uncertainty regarding the oil's curative action is evident in the conclusions of the 1931 International Leprology Congress, mentioned earlier. Although the congress recommended use of chaulmoogra derivatives, it condemned the use of the term 'cure':

> The congress condemns the use of any term that indicates cure, in order to avoid misunderstandings, preferring instead the [English] term 'arrested' …, by which it is understood that the leprosy has been halted in its evolution. … It likewise condemns the term 'negative', widely applied to cases that no longer present bacilli in consequence of the treatment, simply because a small percentage relapsed. (Araújo, 1931)

On the other hand, key specialists had no lack of praise for the treatment. In a 1941 article summarizing her book *As Flacourtiaceas Antilepróticas*, which garnered the São Lucas award from Brazil's Academia Nacional de Medicina, Helena Possolo underscored the importance of chaulmoogra oils in treating people infected with the leprosy bacilli:

> Our country, which is throwing itself with all its might into the fight against leprosy, needs to make utmost use of the means our generous nature offers us. In the botanical gardens of many states, native or alien chaulmoogra already bear the weight of fruit that enclose the beneficial seeds. But it is necessary to multiply infinitely the efforts undertaken so far, so that many millions of chaulmoogra plants at experimental stations throughout the Fatherland line up as the armies they are, in defense of the Brazilian man. (Possolo, mar. 1941)

As we have seen so far, chaulmoogric therapy did not establish a foundation solid enough to warrant its recommendation as a treatment for eliminating the bacilli that caused the disease. Within this context, we can understand the questioning found in the conclusions of the Manila congress, as well as the controversy waged among Brazilian physicians regarding the results of this type of treatment.

## Production and research into chaulmoogra oil and its derivatives at the Instituto Oswaldo Cruz

In Brazil, the IOC was an important place for the production of oil derivatives and for research and teaching about chaulmoogric treatment. In our view, the institute was a place where the results of the scientific translation of chaulmoogra were incorporated, where this knowledge was disseminated, and where development of scientific knowledge about this therapeutic alternative continued. The IOC was born out of the Instituto Soroterápico Federal (Federal Serum Therapy Institute), which had been created in 1900 with the responsibility of producing sera and vaccines against the bubonic plague. In 1903, the IOC became an institution devoted to scientific research. During the first decades of the twentieth century, its activities ranged from research into the various diseases then afflicting the capital of the Republic to the production of immunizers for humans and animals, some of which were derived from studies

conducted by IOC researchers. The institute also played an important role in disseminating information about the different branches of microbiology, through its courses. Its organizational structure remained true to the framework established by Oswaldo Cruz during the Old Republic, based on the trio of research, production, and teaching, as well as on the autonomous administration of the resources generated through the production of biological preparations used for immunization. The by-laws approved in 1926 established six scientific divisions: Bacteriology and Immunity; Medical Zoology; Mycology and Phytopathology; Pathological Anatomy; Hospitals; and Applied Chemistry (Benchimol, 1990).

It was only starting in 1920 that the institute produced a significant number of studies and articles making reference to leprosy. We also found no reference to the production of drugs for treating leprosy prior to this time. But in 1918 the picture began to change as the reform of sanitation services, with much urging from the Liga Pró-saneamento (Pro-sanitation League), pushed public health in Brazil in new directions. Under Decree 13.159 of August 28, 1918, the IOC was made responsible for the Serviço de Medicamentos Oficiais (Official Medication Service), in turn requiring the establishment of an Applied Chemistry Division at the institute. According to the IOC's 1919 activities report, the division would be responsible for

> not only aiding and refining, to the extent possible, the State's drug services; also among its goals are chemotherapy studies, which are of great interest to human and veterinary medicine; chemistry matters applied to industries, especially those that require fermentation processes; the study of toxic and medicinal plants; and other issues of science, where clarification would be of utmost value to our land. (IOC, 1919)

Creation of the Serviço de Medicamentos Oficiais in 1918 and creation of the applied chemistry laboratory in 1919 later allowed the IOC to produce chaulmoogra oil derivatives. In 1920, the chemistry division still lacked a laboratory or the materials needed for carrying out its services (IOC, 1920). In 1922, the building that would house the Serviço de Medicamentos Oficiais was finished, and only then was the Applied Chemistry Division actually set up (IOC, 1922). In 1923, the chemistry division was undertaking work in chemotherapy and fermentation, and in 1924, for the first time the IOC's list of products included esters of chaulmoogra produced by this division (IOC, 1924).

From that point on, the Applied Chemistry Division produced chaulmoogric derivatives, which later were supplied to other IOC divisions, to the Departamento Nacional de Saúde Publica (National Department of Public Health), and to businesses (IOC, 1927). The Inspetoria de Profilaxia da Lepra e Doenças Venéreas (Inspectorship for the Prevention of Leprosy and Venereal Diseases) and the Serviço Sanitário de São Paulo (São Paulo Sanitation Service) placed a large part of the orders for chaulmoogra oil and its derivatives.[8] We also found invoices indicating that Rio de Janeiro's Faculdade de Medicina was supplied with the oil, while the Minas Gerais Secretary of Public Health also received oil and its derivatives.[9] Orders were also placed by private laboratories, which manipulated chaulmoogric preparations and gave them new names.[10]

Starting in the 1920s, research into leprosy was being conducted not only in the Chemistry Division but also in other of the institute's divisions. The Bacteriology and Immunology Division undertook a number of studies on the leprosy bacillus, treatment, transmissibility,

possibilities of a cure, and so on. This was mainly true following the 1927 creation of the Leprology Laboratory, headed by Dr. Souza Araújo, as mentioned earlier. According to him, right from the start, the laboratory published papers on various topics, such as prevention and treatment of leprosy, its bacteriology, clinical presentation, etiology, epidemiology, immunity and biochemistry, and experimental transmission of the bacillus. Some of these even explored the culture of chaulmoogra, leprosaria, *dispensários* (clinics), and *preventórios* (institutions for the mandatory isolation of children whose parents had leprosy) (Araújo, 1957). Other products from this laboratory included derivatives of chaulmoogra *Hydnocarpus wightiana* oil. Years later, Dr. Souza Araújo had this species of chaulmoogra planted in the IOC garden; according to him, the first harvest (1936) yielded an oil equal to the imported product (Araújo, 1957).

The institute's reports from the 1930s inform that the studies undertaken at the IOC were concerned in particular with the etiopathogeny, diagnosis, and treatment of yellow fever, tuberculosis, leprosy, and other regional diseases. In addition to this research, IOC scientists were responsible for routine services like the manufacture of sera, vaccines, and other chemical and biological products, such as remedies derived from chaulmoogra oil derivatives (sodium salts of chaulmoogra and ethyl esters of chaulmoogra). When Brazil was hit by the 1930s financial crisis, volume sales fell but demand for these derivatives remained high.

During the same period, in addition to conducting bacteriological and therapeutic research, the Leprology Laboratory continued to make drugs from chaulmoogra derivatives, like esters of chaulmoogra and Aleprol. Many of these were distributed free to institutions such as Rio de Janeiro's Hospital dos Lázaros and to the leprosaria in the states of Paraná, Pará, and Acre; they were also provided to the ill who had consultations at the institute (IOC, 1932). Souza Araújo's work describes his activities at the Leprology Laboratory, which encompassed bacteriological experiments and experiments involving the various drugs produced at or imported by the IOC, which he tested on his patients. In 1920, for instance, describing an experiment at the IOC with drugs prepared there by Astrogildo Machado, the eminent leprologist noted that only one drug produced notable improvement, while the others resulted in only insignificant improvements. He concluded by stating that "any drug treatment produces subjective improvements in all lepers, and for them, continuous medical assistance encourages happiness and hope, which consequently has a notable moral benefit" (Araújo, maio 1920, p.94).

For him, many charlatans were consequently able to advertise the sale of a specific to cure leprosy, which helps explain the large number of remedies on the market. In 1934, founded under the sponsorship of the League of Nations, the International Center for the Study of Leprosy began operations as an annex of the IOC; it was funded by the Brazilian government, by the League of Nations, and by Brazilian Maecenas Guilherme Guinle. Directed by a committee whose members included the director-general and technical director of the IOC, "most of [the Center's] work was entrusted to staff at the Instituto Oswaldo Cruz itself, under conditions that would allow for the achievement of the institution's high goals in the near future" (IOC, 1934).[11]

## Testing new substances: *sapucainha* and other Brazilian plants

The late 1920s saw the first large-scale production and sale to businesses of oil of *sapucainha*, known among scientists as the Brazilian chaulmoogra. This was one of the last preparations that IOC quit producing when chaulmoogric therapy was replaced with sulfonic treatment. In October 1929, the institute provided five kilograms of seeds from the plant (*Carpotroche brasiliensis*) to the Argentine Biological Institute.[12] Under Departamento Nacional de Saúde Pública (1921-1930), the Inspetoria de Profilaxia da Lepra recommended studies of esters extracted from oils of Brazilian medicinal plants and closed an agreement under which the IOC would prepare these esters. Studies focused primarily on *Carpotroche brasiliensis*, since its action in treating leprosy was in the spotlight (Possolo, 1945). *Carpotroche brasiliensis* is also known by the common names *canudo-de-pito*, *pau de lepra* (leprosy stick), and *fruta da lepra* (leprosy fruit).[13] Its main habitat is the Atlantic Rainforest in the states of Rio de Janeiro, Minas Gerais, Espírito Santo, Bahia, Piauí, and São Paulo. The properties of the oil extracted from its seeds are quite similar to those of *Taraktogenus kurzii*, which for some time was considered the true chaulmoogra.

The first analysis of the plant's oil was conducted by the German Theodore Peckolt between 1861 and 1869. Peckolt recommended that this oil be used to replace Indian chaulmoogra oil; he described it as a fruit with an edible pulp, containing from sixty to ninety seeds, which possessed excellent comburent properties. According to him, the plant loses its leaves in July, recovering them in December and January. Its fruit ripens in June, with an average of 140 fruit on heavier trees. The oil of its seeds contains oleic, palmitic, carpotrochic, carpotrochinic, and carpotrolenic acids.[14] It also contains a crystallized substance called *carpotrochina*.

According to his studies, native peoples and those living in rural inland areas used the fruit as an insecticide; furthermore, after undergoing a process of fermentation, the pulp became a bubbly beverage, much like a sparkling wine (Peckolt, 1868). Other research also tells of people using the pulp as an expectorant, the shell as an insecticide, and the oil to combat mange (Araújo, 1946). Even today, *sapucainha* ointments are sometimes used to treat skin rashes or parasitic dermatitis.

In the 1920s, we found many articles on *Carpotroche brasiliensis* published in magazines. On April 15, 1924, for example, *Chácaras e Quintaes* featured an article entitled "To cure morphea, let's raise foreign plants like Chaulmoogra; for the same purpose, the Cubans, however, want to raise a genuinely Brazilian plant: Canudo de Pito" (in Port.; emphasis from the original), by Gustavo Edwall (15 abr. 1924). Brazilian hospitals treated the ill with Indian chaulmoogra, but this meant Brazil had to face the problems of acclimatizing the plants as well as the high costs of importing the oil. It was therefore curious when the Cuban government asked Brazil for Brazilian chaulmoogra seeds, since that country had found that the oil from this plant was as useful as oil from the Indian chaulmoogra. During this period, a number of analyses of the oil from this species of chaulmoogra were published, and some Brazilian researchers began encouraging its use to replace foreign oil.[15]

In 1925, the IOC's chemistry division prepared 38,330cc of esters of chaulmoogra in addition to conducting scientific research, such as examining the plant oils from 46 Brazilian botanical species that might be applicable in treating leprosy (IOC, 1925). For this reason, in October

1925, the IOC director sent a communiqué to the Federal District Chief of Police, advising that the botanist Dr. João Kuhlmann had been assigned to visit fields and woodlands in the Federal District to collect specimens of regional flora for study at the institute.[16] That same year, the IOC director asked the Minister of Justice and Internal Affairs (to which the institute was subordinated) to intercede on its behalf with the Ministry of Foreign Relations to obtain seeds and herbarium material from Chile from the following plants: *Berberidopsis corallina*, *Azara lanceolata*, *Azara microphila*, and other species of the genus *Azara*. Although these were not chaulmoogra plants, they belonged to the family *Flacourtiaceae*, which is why scientists at Manguinhos were interested in studying them. The material would be used in researching the composition and medicinal properties of botanical species, with the main concern being possible application in treating leprosy.[17] It may have been because of this research that the IOC produced a larger number of preparations for therapeutic studies of leprosy.

In the 1926 activities report, Carlos Chagas described the routine activities of the institute's technical divisions and noted that 22,910 doses of esters of chaulmoogra oil had been produced: "In addition to these, 3,120gr. of soaps of chaulmoogra oil, 2,000cc of oil of *Carpothoche*, 2000cc of esters of the same oil were produced for therapeutic studies of leprosy" (IOC, 1926).

We also found that oil from *Carpotroche brasiliensis* was prepared and tested at that time (IOC, 1926). In the 1927 report on the Applied Chemistry Division, José Carneiro Felippe wrote that the following substances were prepared for the Comissão de Estudos de Terapêutica da Lepra (Committee on Studies of Leprosy Treatment): 2,340cc of oil of *Carpotroche*; 8,735cc of esters of *Carpotroche* oil; 11,800cc of sodium salts of chaulmoogra oil; and 8,000cc of esters of chaulmoogra oil. In addition, 18,350cc of esters of chaulmoogra oil were produced for the National Public Health Department. For other institute divisions, the figures were 140cc of esters of chaulmoogra oil and 860 pills of sodium salts of chaulmoogra oil (IOC, 1927).

To ensure good research progress and to further refine treatment and production of chaulmoogra oil derivatives, attention had to be paid to new discoveries and research development around the world, as well as to the importing of up-to-date equipment. The IOC imported apparatuses and glass ampoules, especially from Germany, with a good share of this material going to the Applied Chemistry Division.[18] The United States was another major supplier of laboratory equipment.[19] In addition, some IOC researchers went abroad for internships, where they undertook further specialization in their areas. In 1924, Souza Araújo took a study trip to the U.S. and a number of European countries at the invitation of the Rockefeller Foundation, where he observed developments in leprosy and cancer. According to a letter sent to him by Carlos Chagas, Souza Araújo was supposed to undertake general studies on leprosy, aimed not only at prevention but treatment as well.[20] In 1927, Dr. Nicanor Botafogo Gonçalves traveled to Germany to conduct research on plant chemistry, "equipping himself to explore the still obscure question of the nature and properties of the products of [Brazilian] flora, usable in treatment and in industry" (IOC, 1927). Returning in 1928, he carried out studies on Brazilian plants.

In 1929, when the services of the Applied Chemistry Division were expanded, its duties came to include the study of alkaloids and other components of Brazilian plants that might be utilizable in treatment or industry. Using its own funds, the institute hired a German specialist in plant chemistry, the chemist Fritz Unger, from the Pharmazeutischen Institut at

the Universität Berlin. His contract stated he was to conduct research into organic and plant chemistry, act as an advisor to institute staff, and hold courses in his specialty.[21] That same year, the institute signed a scientific exchange agreement with the Bacteriological Institute of Chile, which was also to include the exchange of preparations when possible.[22]

In the 1930s, the institute ran into problems importing material and periodicals, which hampered its efforts to make further progress in chaulmoogric treatment. In the 1931 report, Carlos Chagas complained about sparse funds for purchases of material, since a number of 'subconsignments' had been eliminated from the Lei de Despesas (Expenditures Law). He nonetheless stated in conclusion that "the Department's technical and administrative activities maintained a high level" (IOC, 1931, p.1). The same problem was mentioned in subsequent reports, since, according to Chagas, an unexpected devaluing of the Brazilian currency raised import prices substantially; as a result, it was harder to buy lab materials as well as books and periodicals for the library, which in turn obstructed services (IOC, 1932). In 1934, the new Director of the IOC, Dr. Antonio Cardoso Fontes, likewise complained about the lack of financial resources and called attention to the need to replace scientific apparatuses, machines, and facilities, for they were out-of-date and showing the wear of thirty years' worth of use (IOC, 1934).

Historians have pointed out that as of World War I, there was a movement to replace imports with equipment manufactured or repaired at the institute's own shops (Benchimol, 1988). Starting in the 1940s, the IOC decreased its production of chaulmoogra derivatives. In 1950, the institute was no longer exporting it, but still produced iodated *sapucainha* oil and chaulmoogra oil for use by its specialized divisions. From late 1951 on, we found no further information on the production of chaulmoogra derivatives on the list of IOC products.

## Conclusion

Research efforts to enhance leprosy treatment using chaulmoogra derivatives failed to achieve unequivocal acceptance among physicians. The side-effects of this type of treatment raised many problems. Furthermore, the treatment was prolonged and of questionable efficacy, since there was no consensus about its healing powers – that is, about its ability to eliminate Hansen's bacillus from the body, despite countless reports of such cases. Many physicians and researchers believed that chaulmoogra derivatives were mere palliatives. Advocates of this position felt any observed clinical improvements – e.g., healed lesions – did not necessarily mean that the leprosy bacillus had been eliminated. Further, according to the accepted bacteriological understanding of the day, it was only appropriate to speak of a cure or of a specific treatment if the causal agent could be eradicated.

In 1942, a major attack against the use of chaulmoogras was launched by the director of the U.S. National Institute of Health, George McCoy. He argued that many experienced scholars of leprosy were expressing ever more serious doubts about the value of the oil and its derivatives (Parascandola, 2003).

The ultimate demise of chaulmoogra oil therapy was brought by the introduction of sulfones to treat leprosy, a technique that was disseminated around the globe following World War II. In 1947, the Public Health Service Hospital in Carville, Louisiana – the most important U.S.

center for the treatment of leprosy – officially abandoned the use of chaulmoogra derivatives (Parascandola, 2003). In Brazil, although the oil continued to be used for some years, the introduction of sulfones made it possible to change the policy on isolating the ill, who could be treated on an outpatient basis. This not only established a new therapeutic practice but also initiated a new scientific discourse regarding the disease.

The medical community took its first official stance against the mandatory isolation of lepers in 1953, reported in the minutes of the 6th International Leprology Congress, held in Madrid. The gathering stated it was necessary to take selective caution when it came to isolation. The 7th Congress, held in Tokyo in 1958, would definitively endorse new types of public initiatives against leprosy, underscoring the administration of drugs over isolationist hospitalization (Cunha, 2005).

The event's recommendations were embraced by Brazil's Juscelino Kubitschek administration, through its policies, which made an effort to adopt recommendations concerning educational, medical, social, and legal matters, "with isolation no longer an official preventive policy" (Cunha, 2005). As Vívian Cunha recalls, "although the appearance of sulfones in the 1940s called into question the validity of policies towards leper sufferers adopted by the government, isolation was still heavily used throughout the country for another twenty years" (Cunha, 2005). On May 07, 1962, Decree 968 put an end to the mandatory isolation of the ill in Brazil. Nevertheless, São Paulo's Department of Prevention continued to isolate people with the disease until 1967 (Cunha, 2005; Monteiro, 2002; Monteiro, 2003).

## NOTES

[1] We have chosen to use the term *lepra* (leprosy) in this article because it was the name used to refer to this disease during the period under study (1890-1940), as found in the documental sources consulted during our research. The term *hanseníase* (Hansen's disease) was adopted in Brazil in the wake of Decree 165, dated May 14, 1976.

[2] This scientist developed the medication Prontosil, which proved quite effective in combating infections caused by streptococci in laboratory rats. He tested it on his own daughter, who was on her deathbed because of a streptococcal infection. Thanks to the drug, she made a full recovery. See Holmes, Aug. 1923).

[3] Sulfanilamides are broad-spectrum bacteriostatic synthetic antimicrobials, which act against a wide variety of microorganisms; they form the basis of the group of sulfonamides that are still in use today (Sánchez-Saldaña et al., sept.-dic. 2004).

[4] The scientist's personal archive contains a large number of studies on the topic. Stored and managed by the Casa de Oswaldo Cruz's Archive and Documentation Department, it was of inestimable value in the present research project.

[5] This definition is based on Sean Lei's critique of the concept of socio-technical network, originally proposed by Bruno Latour. On this topic, see Latour, 1988; Lei, 1999; and Roque, 2004.

[6] According to Parascandola, Roxburgh, in his catalog of plants found in the East India Company's botanical garden, had erroneously identified the seeds of the *Kalaw* tree as coming from the species identified botanically as *Gynocardia odorata*.

[7] Of special note were preparations of ethyl esters, Aleprol and Chaumoogrol, Antileprina, Mercado-Heiser mixture (600g. genuine chaulmoogra oil, 600g. camphorated oil, and 40g. resorcin for hypodermic application), Roger's formula (3g. *Hydnocarpus* of sodium, 97g. distilled water, 1g. phenol acid, and 1g. sodium citrate), Unna's formula, and Chaumoogric colloid from the Casa de Dausse (Araújo, 1928).

[8] SAG/Minutas de Ofícios, *ofícios* 685, 731 (1924) and *ofícios* 5, 604, 646, 856 (1925).

[9] SAG/Minutas de Ofícios, *ofícios* 593 (1931) and *ofícios* 17, 106, 365, 488 (1932).

[10] SAG/IOC – Thesouraria. Invoices and forms received during 1925, 1927, 1930, 1931.

[11] The Society of Nations, also known as the League of Nations, was an international organization created under the Treaty of Versailles on July 28, 1919, headquartered in Geneva, Switzerland. On April 18, 1946, the organization dissolved itself and transferred its responsibilities to the newly created United Nations. On scientific patronage in Brazil, see Sanglard, 2005.

[12] SAG/Cópias de Ofícios, *ofício* 656 (Oct. 9, 1929).

[13] Other names were *pau-de-caximbo*, *fruta de cotia*, *fruta de macaco*, *canudeiro*, *fruta-de-babado*, *papo-de-anjo*, *beribá do mato*, *ruchuchu* (Possolo, 1945).

[14] These last three terms are the nomenclatures first used by Peckolt, and maintained by Antenor Machado in his 1924 study. In 1926, Rodolfo Albino Dias da Silva analyzed the oil and declared that the acids obtained by Peckolt were merely mixtures of fatty acids in different proportions, but he stated there was a large amount of chaulmoogric and hydnocarpic acids, supposedly responsible for the oil's observed therapeutic action (Araújo, Jan.-Mar. 1935)

[15] Helena Possolo and J. Aguiar Pupo, for example, point to the high price of imported oil and the problems encountered in acclimatizing the Indian species, suggesting Brazilian chaulmoogra as an alternative. See Possolo, mar. 1941, p.192-195; e **Pupo, 1926b), p.1-9.**

[16] SAG/Minutas de Ofícios, *ofício* 694 (Oct. 10 1925).

[17] SAG/Minutas de ofícios, *ofício* 767 (Nov. 16 1925).

[18] SAG/Minutas de ofícios, *ofícios* 525 (1928) and 325 (1929).

[19] SAG/Cópias de ofícios, *ofícios* 598, 622, 740 (1930).

[20] SAG/Minutas de Ofício, *ofício* 498 (July 1924).

[21] SAG/Cópias de Ofícios, *ofícios* 43 and 44 (Jan. 21 1929).

[22] SAG/Cópias de Ofícios, *ofício* 37 (Jun. 12 1929).

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