



CINCHONA IN PORTUGAL - THE CONSUMPTION OF CINCHONA, DRUG RESEARCH AND INDUSTRIAL PRODUCTION (18th-20th CENTURIES) *

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ABSTRACT

The authors briefly trace the significant stages of the issue related to cinchona in Portugal, namely with the research carried out at the University of Coimbra as a platform. They exemplified the consumption of cinchona by executing a case study on the production of medication in the Pharmacy of the University of Coimbra's School Hospital (XVIII-XIX centuries). They divulge the main authors and main works that studied cinchona in Portugal (XVIII-XX centuries). They look back on the controversy between Coimbra and Lisbon, concerning the isolation of the cinchonine of Gomes (1810) Finally they cover the period of industrial investment in cinchona plantations in Portuguese colonies and the implantation of a quinine extraction industry and its relationship with the colonial issue.

CONSUMPTION OF CINCHONA IN PORTUGAL: CASE STUDY OF THE UNIVERSITY OF COIMBRA'S SCHOOL HOSPITAL AND ITS PHARMACY

In 1772 the University of Coimbra's new statutes, the only University in Portugal until 1911, accompanying innovation felt in several European countries, founded two new Universities (Mathematics and Philosophy) and several establishments destined for the teaching and research of experimental sciences: The School Hospital, Anatomical Theatre, Pharmaceutical

Dispensary, Chemical Laboratory, Botanical Garden, Physics Cabinet, Natural History Cabinet and the Astronomic Observatory.

The Pharmaceutical Dispensary was the School Hospital's pharmacy. It had three general objectives: to support the practical teaching of pharmacy to the students of medicine; to graduate chemists; to prepare medication for the patients of the Hospital; to prepare medication for the population, in its role as a public pharmacy(1).

The Pharmaceutical Dispensary depended on the University of Coimbra's Faculty of Medicine and at the end of the XVIII century and in the beginning of the XIX century it became a pharmacy of great dimension in Portugal. In 1850 the Pharmaceutical Dispensary prepared approximately 200 types of magistral medication a day.

Therefore, evaluating the consumption of cinchona in the Pharmaceutical Dispensary is a significant factor for the Portuguese Pharmacy(2).

Between the end of the XVIII century and in the first twenty years of the XIX century cinchona was the most used drug at the University of Coimbra's School Hospital.

The study carried out with a sample of about 2000 prescriptions (1954)(3) from the University of Coimbra's School Hospital between 1772 and 1836 reveal the following results:

TYPE OF DRUGS	Var.	% Var.	Quant.	% Quant.
Drugs of animal origin	11	7,2	81	3,3
Drugs of mineral and chemical origin	22	14,4	475	19,2
Drugs of vegetable origin	120	78,4	1915	77,5
TOTAL	153	100	2471	100

Key:

Type of Drugs — drugs of different origin

Var. — variety of drugs on prescriptions

% Var. — percentage of the variety of drugs on prescriptions

Quant. — quantity of drugs on prescriptions

% Quant. — percentage of the quantity of drugs on prescriptions

GEOGRAPHICAL ORIGIN OF THE DRUGS	Var.	% Var.	Quant.	% Quant.
Europe and Mediterranean basin	78	65	697	36,4
Africa and Orient	21	17,5	439	22,9
America	21	17,5	779	40,7
TOTAL	120	100	1915	100

Key:

Type of Drugs — drugs of different origin

Var. — variety of drugs on prescriptions

% Var. — percentage of the variety of drugs on prescriptions

Quant. — quantity of drugs on prescriptions

% Quant. — percentage of the quantity of drugs on prescriptions

The most prescribed American drugs	Quant.
Cinchona	434
Jalap	98
White Sugar	50
Ipecacuanha	47
Salsaparrilha	33
Other Drugs	117

Key:

The most prescribed American drugs — different drugs that are found on prescriptions

Quant. — the number of times they appear on prescriptions

Amongst the druggists that supplied drugs to the pharmacies many of them were Spanish, and emphasis is put on American drugs sold. The druggists outside of Coimbra, or even the Spaniards, supplied better quality drugs and at the lowest price. The names of the following Spanish druggists were found: António Pastor (date?, end of the XVIII century); Francisco Rodriguez Zimenez (1779); Josef Rodico Machado (1798); Francisco Rodriguez Sanchez (1801).

Cinchona was an object that generated scientific, medical, pharmaceutical interests etc. but it also fed strong commercial interests.

In the XVIII century, *Água de Inglaterra* became famous, as a very popular secret medicine in Portugal with Cinchona. Amongst the Portuguese producers of *Água de Inglaterra* one can



refer João Curvo Semedo (1635-1719), Jacob de Castro Sarmiento (1691-1762) and Fernando Mendes(4).

PORTUGUESE INNOVATION: THE DISCOVERY OF CINCHONA

At the beginning of the XIX century the Portuguese Government had the objective to verify if Brazil had Cinchona or other plants with antifebrile properties; commercial, economic and scientific issues were at stake(5).

The University of Coimbra, the School Hospital, the Academy of the Sciences of Lisbon and the Hospital of the Navy were entrusted to study the subject. In Lisbon the works were under the responsibility of doctor Bernardino António Gomes (1768-1823) and in Coimbra one of the main protagonists in the analysis of the cinchona was Tomé Rodrigues Sobral (1759-1829), a chemistry professor at the University of Coimbra(6).

B.A. Gomes reached conclusions before Sobral. He isolated a product - the cinchonino - that was the first alkaloid extracted from the cinchona. Gomes was able to isolate the cinchona from an alcoholic extract of gray cinchona. He obtained small cinchonino crystals(7).

In order to obtain the product, Gomes subjected cinchona's watery extractive solutions to a treatment with potash that he had prepared. The precipitate he obtained was recrystallized in the alcohol. He later isolated the crystals obtained (the cinchonine) that were soluble in the acids and that precipitated in the potash. The first cinchona alkaloid was isolated - the cinchonine.

His discovery led to enormous controversy. However, in spite of having discovered the new compound, Gomes did not immediately verify that it was a compound with alkaline properties, following the belief that there weren't acid and neutral components in the



vegetable kingdom For Gomes the alkalinity of the new compound was due to the potash that took part in the chemical work.

At the University of Coimbra, José Feliciano de Castilho (Professor at the University of Coimbra's Faculty of Medicine) did not accept the discovery arguing that it was impossible for Bernardino António Gomes to have reached such conclusions. The controversy arose between these two teachers.

It seems that what was at stake was more a conflict of power than a conflict of knowledge because the discovery had been made outside the University which was the only one that existed in Portugal at the time and therefore fought for leadership in scientific research.

The *Jornal de Coimbra* ("Coimbra Newspaper")(8) is a significant witness of that controversy. It would be diminished after B.A.Gomes moved to France where he showed the results to French scientists that told him they were valid. Laubert and Houton of Labillardière were two scientists that recognized the validity of the Gomes' work and results thus decisive in the acceptance of the discovery in Portugal.

Bernardino António Gomes discovered the appearance of crystals - the cinchonine - and of other crystalline like formations that had adhered to the walls of the containers, different from the previous ones, and that he did not identify. Hence, these crystals that Gomes did not identify were later identified, in 1820, by Pelletier (1788-1842) and Caventou (1795-1877), in Paris - it was the quinine(9).

Bernardino António Gomes was one step away from the largest discovery; indirectly, it seems that he obtained the quinine and was unable to identify it! The quinine would have antifebrile properties that were outstandingly more effective than the cinchonine.

Scientific and Industrial Investment

The success attained with the isolation of quinine and the preparation of medicine based on quinine salts was decisive to increase the investment in the cinchona plantation for the industrial exploration of. In the course of the second half of the XIX century studies were done on cinchona and quinine(10).

The colonial empires began to establish plantations outside South America with the objective of guaranteeing sufficient raw materials to obtain the product on an industrial level. In the first half of the XX century the industry of the quinine was, in some countries, source of enormous wealth. Plantations were established in the Far East - Ceylon, India and Islands of Java - there were attempts to establish plantations in Congo, in the Formosa, in Brazil and in S. Tome and Príncipe, Cabo Verde and Angola. The explorations executed by the English in India guaranteed about 2,5% of the total value. French established plantations in Algeria and in Madagascar. Belgium established plantations in Congo. The Germans planted cinchona in Tanganyika. The explorations implemented by the Dutchmen in the beginning of the XX century in Java and Samatra became famous. In the beginning of the XX century their plantations at times guaranteed the industry about 97% of the cinchona.

Under the protection of the Government of Holland the Cinchona Convention was established that provided the Holland with the monopoly of the cultivation of cinchona, setting prices and the provisioning of to underprivileged areas of the world.

Portugal tried to plant cinchona as well. Let us see some important dates:

—1864: Mendes Leal, Minister of the Navy whom obtained 30.000 seeds of *C.Pahudiana* in Java, a species that did not provide any guarantees. The results of the sowings were insignificant.

—1867: Bernardino António Gomes (Son) offered the University of Coimbra's Botanical Garden a cinchona (*Cinchona succirubra*) with a greater content of quinine. B.A.Gomes ordered seeds of various species from an array of countries: India, Ceylon, Java, Australia, France, etc. Other seeds of different species came to enrich the collection of The University of Coimbra's Botanical Garden.

—1869: Cinchona was introduced in Portuguese territory, through the colony of Cabo Verde, after extending the plantations to Madeira and S. Tome and in 1871, to S. Tome and Príncipe. The Portuguese Government sent recommendation letters to the governors of those territories on the value and interest of cinchona cultivation. The species introduced were: *C. calisaya*, *C. calisaya* var. *ledgeriana*, *C. succirubra* and *C. Officinalis*.

Júlio Augusto Henriques, the University of Coimbra's Botanical Garden's professor and director was the great promoter in the expansion of cinchona plantations in the Portuguese colonies in Africa, having carried out several studies on the quality of the plants.

During the course of over ten years, encouraged by J.A.Henriques, the University of Coimbra's Botanical Garden sent 1.183 plants and enormous amounts of seeds to the colonies, namely to Cabo Verde and São Tome.

A proposal was made that declared Portugal as having privileged conditions to plant cinchona, in Madeira, in the Azores, Cabo Verde and in São Tome because the peels would be more easily transported to German, English and French industries than if the plantations were in the middle east or in South America.

— 1872: J.A.Simões de Carvalho refers to the expedition of cinchonas to the Algarve

— 1874: Joaquim dos Santos e Silva chemically analyzes cinchona from Cape Verde sent by Jacinto de Sousa Ribeiro.



— 1880: Júlio Henriques warns that there is a need to carry out a pondered study of the species to be cultivated to attain the most profit with quinine.

The settlers in the Portuguese colonies were not especially interested in the cultivation of cinchona but rather other products such as coffee, receiving incentives and dividends from the government.

With the coffee crisis the peasants, looking back at the importance of the cultivation of cinchona and of the extraction of quinine, invested in their plantation.

Between 1875 and 1887 in São Tomé, the cinchona plantations increased from 31 to 1.600.000. It was there that the cultivation of cinchona, in national territory, acquired the best results allowing the supply to the national market and guaranteeing reasonable exportation.

However, the income in quinine was weak and the industry of quinine extraction in Portugal did not flourish, having disappeared after the First World War.

Three factors were decisive in that disastrous investment:

- a) Having fostered cinchona plantations in Portugal on a great scale at the same time that it was very powerful at an international level;
- b) Not having undergone a detailed study on the species to plant and having opted for the *C.succirubra* species that grew more quickly but was not the richest in quinine;
- c) The growth of several hybrid species(11).

SOME WORKS AND PORTUGUESE AUTHORS

In Portugal there were several authors and scientists that showed interest in the cinchona and its plantations as well as in botanical, pharmaceutical, therapeutic, clinical, chemical studies

etc. Between the end of the XVIII century and the middles of the XX century the following works are worthy of mention:

- José Mariano da Conceição Veloso, *Quinografia portuguesa* (1799)
- José Ferreira da Silva, *Observações sobre a propriedade da quina do Brasil* (1801)
- Francisco Tavares, *Observações e reflexões sobre o uso proveitoso e saudável da quina na gôta* (1802).
- Bernardino Barros Gomes, *A cultura das plantas que dão a quina* (1864)
- Júlio A. Henriques, *Instruções práticas para a cultura das plantas que dão a quina* (1880)
- Júlio A. Henriques, *Instruções práticas para culturas coloniais* (1884)
- Fausto Landeiro, *A quina e os seus derivados* (1936)
- Aloísio Fernandes Costa, *A introdução da cultura das quinas nas nossas províncias ultramarinas e a coparticipação dos portugueses no seu estudo químico* (1940)
- Aloísio Fernandes Costa, *A cultura das quinas* (1941)
- José Cardoso do Vale, *Dosagem dos alcalóides das quinas* (1941)
- Aloísio Fernandes Costa, *O problema das quinas* (1944)

Cinchona was included in the Portuguese pharmacopeias from very early on. The first Portuguese pharmacopoeia, the *Pharmacopea Lusitana* (1704)(12) whose author was Caetano de Santo António (?-1730,?) did not include a monograph on cinchona but included medicine with cinchona.

The first official Portuguese pharmacopoeia, the *Pharmacopea Geral* (1794)(13) whose author was Francisco Tavares (1750-1812)(14) included medication constituted of cinchona(15).

CONCLUSIONS

Just as in other European countries, cinchona was a drug of great importance in medical therapeutics. In addition, it was object of deep botanical and chemical studies and of commercial and industrial investments.

The work that is currently presented constitutes the systemization of four great chapters on the history of cinchona and quinine in Portugal which are being developed by the authors.

MANUSCRIPTS

Arquivo da Universidade de Coimbra, Portugal (A.U.C.):

—Documentos diversos relativos ao Dispensatório Farmacêutico e Laboratório Químico. Aquisição de drogas, rol de devedores, etc.), séc. XVIII-XIX. IV - 2^oE- 7 - 4 - 39 (Caixa).

—Dispensatório Farmacêutico - Folhas de Receita e Despesa. Despesa com obras. Guias de remessa de dinheiro para o cofre académico de géneros. Requisição de verbas (1784-1881). IV - 2^oE- 7 - 4 - 41 (Caixa).

—Dispensatório Farmacêutico-correspondência e outros dados relativos à aquisição de drogas, contas correntes e administração geral (1801-1868). IV - 2^oE - 7 - 4 - 44 (Pasta).

—Dispensatório Farmacêutico - Entrada e saída de drogas 1819-1822. IV - 2^oE- 7 - 4 - 46 (Livro).

NOTES

(1)See *Estatutos da Universidade de Coimbra* (1772), vol. III, Coimbra, Universidade, 1972; João Rui Pita, *Farmácia, medicina e saúde pública em Portugal* (1772-1836), Coimbra, Minerva, 1996.

(2)See João Rui Pita, *A Farmácia na Universidade de Coimbra (1772-1836). Ciência, ensino e produção de medicamentos no Dispensatório Farmacêutico*, 2 vols. and appendix, Coimbra, Tese de doutoramento, 1995.

(3)See João Rui Pita, *A Farmácia na Universidade de Coimbra (1772-1836). Ciência, ensino e produção de medicamentos no Dispensatório Farmacêutico*, vol. 2 and appendix.

(4)See J.P. Sousa Dias, A “Água de Inglaterra” no Portugal das Luzes. Contributo para o estudo do papel do segredo na terapêutica do século XVIII, Lisboa, 1986.

(5)See Ana Leonor Pereira; João Rui Pita, “Bernardino António Gomes, Pai (1768-1823). O isolamento do cinchonino”, *In Vivo. Revista Mensal de Saúde*, 2(6)2001, pp. 44-45. A. M. Amorim da Costa A química no I Colóquio sobre a origem e desenvolvimento da ciência em Portugal. III. Alcalóides e polímeros. *Boletim da Sociedade Portuguesa de Química*. 2ª Série, 23, 1986, pp. 37-39. Bernardo Jerosh Herold, "Bernardino António Gomes, Pai e Agostinho Lourenço, precursores Portugueses da Química dos Alcalóides e dos Polímeros Sintéticos", in *História e Desenvolvimento da Ciência em Portugal*, vol.1, Lisboa, Academia das Ciências de Lisboa, 1986, pp. 417-433.

(6)See Tomé Rodrigues Sobral, "Memoria sobre o principio febrifugo das quinas", *Jornal de Coimbra*, 14(82)1819, pp. 126-153.

(7)See Bernardino António Gomes, " Extracto do ensaio sobre o Cinchonino, e sobre sua influencia na virtude da Quina, e de outras cascas", *O Investigador Portuguez em Inglaterra*, 2(5) 1811, pp. 36-43; "Observações Botanico-Medicas sobre algumas Plantas do Brazil", *Memorias de Mathematica e Physica da Academia Real das Sciencias de Lisboa* , 3(1) 1812, pp. 1-104; "Ensaio sobre o Cinchonino e sobre sua influencia na virtude da Quina, e de outras cascas", *Memorias de Mathematica e Physica da Academia Real das Sciencias de Lisboa* , 3 (1) 1812, pp. 202-217; "Resultados das observações que se tem feito sôbre as virtudes da casca ' Portlandia hexandra ' chamada Quina do Brasil", *Arquivos do Instituto de Farmacologia e Terapêutica Experimental*, 1, 1931, pp. 77-85.

(8)See *Jornal de Coimbra*, Coimbra , 1812-1820.

(9)See P. Rossignol, “Les travaux scientifiques de Joseph Pelletier”, *Revue d’Histoire de la Pharmacie*, 281-282, 1989, 1989, pp. 135-152.

(10)See Louis Henri Destouches, *A quina na terapeutica*, Amsterdam, Repartição para o fomento do uso da quinina, 1931.

(11)See Aloísio Fernandes Costa, *O problema das quinas*, Lisboa, Cosmos, 1944. Aloísio Fernandes Costa, “A introdução da cultura das quinas nas nossas províncias ultramarinas e a participação dos portugueses no seu estudo químico”. In *Congresso do Mundo Português*, vol. 13, Lisboa. Comissão Executiva dos Centenários, 1940, pp. 327-352.

(12)Caetano de Santo António, *Pharmacopea Lusitana*, Coimbra, Impressão de Joam Antunes, 1704.

(13)*Pharmacopeia Geral para o reino e dominios de Portugal*, Lisboa, Regia Officina Typografica, 1794.

(14) Ana Leonor Pereira; João Rui Pita, “Francisco Tavares”, *In Vivo. Revista Mensal de Saúde*, 1(2) 2000, pp. 42-43.

(15)See, “Plantas medicinais da primeira farmacopeia oficial portuguesa (Pharmacopeia Geral, 1794)”, *Munda*, 30, 1995, pp. 57-68.

BIBLIOGRAPHY

—COSTA, Aloísio Fernandes — *Farmacognosia*, vol. 2, 2^a ed., Lisboa, Fundação Calouste Gulbenkian, 1978.

—FERRAZ, Márcia Helena Mendes — “Los estudios sobre las quinas en la literatura química-médica portuguesa de los inicios del siglo XIX”. In ACEVES PASTRANA, Patricia (Ed.) — *Estudios de Historia Social de las Ciencias Químicas y Biológicas*, nº 3 — *Farmacia, historia natural y química intercontinentales*, Villa Quietud, México, Universidad Autónoma Metropolitana, Unidad Xochimilco, 1995, pp. 189-202.

—FERRÃO, José E. Mendes — *A aventura das plantas e os descobrimentos portugueses*, Lisboa, Instituto de Investigação Científica e Tropical / Comissão Nacional para as Comemorações dos Descobrimentos Portugueses / Fundação Berardo, 1992.

—LOPES, Sandra; CARREIRA, Maria Teresa — “Bernardino António Gomes and the isolation of cinchonine in the early 19th century — a polemic work”. In: MALAQUIAS, Isabel; HOMBURG, Ernst; CALLAPEZ, M. Elvira — 5th International Conference on History of Chemistry - "Chemistry, Technology and Society" - Proceedings, SPQ-Sociedade Portuguesa de Química, 2006, pp. 637-641.

—PITA, João Rui — *Farmácia, medicina e saúde pública em Portugal (1772-1836)*, Coimbra, Minerva, 1996.

—PITA, João Rui — “A quina e outras drogas americanas na produção medicamentosa do Hospital da Universidade de Coimbra nos finais do século XVIII”, *Mare Liberum*, 17, 1999, pp. 197-228.

— PITA, João Rui; PEREIRA, Ana Leonor — “A Europa científica e a farmácia portuguesa na época contemporânea”, *Estudos do Século XX*, 2, 2002, pp. 231-265.

—PITA, João Rui — *História da Farmácia*, 3^a ed., Coimbra, MinervaCoimbra, 2007.

—PUERTO SARMIENTO, F.J. — *El mito de Panacea. Compendio de historia de la terapéutica y de la farmacia*, Madrid, Ediciones Doce Calles, 1997.

—PUERTO SARMIENTO, F.J.; DEL CASTILLO, Benito — “Presentation”. In: Hipolito Ruiz, *Compendio Historico-Medico Comercial de las quinas*, Burgos, Caja de Ahorros Municipal de Burgos, 1992.

*Research project: *História Ecológico-Institucional do Corpo (1900-1950). O caso português / Public and private ecological-institucional history of the body (1900-1950) – The Portuguese case* (Fundação para a Ciência e a Tecnologia, F.C.T.—POCTI/HAR/49941/2002) and *Farmácia, medicamento e terapêuticas em Portugal no século XX / Pharmacy, medicines and therapeutics in Portugal (20th century)* (Fundação para a Ciência e a Tecnologia, F.C.T.—CEIS20)