

## Malaria management in the 18th and 19th century India: role played by Madras Presidency

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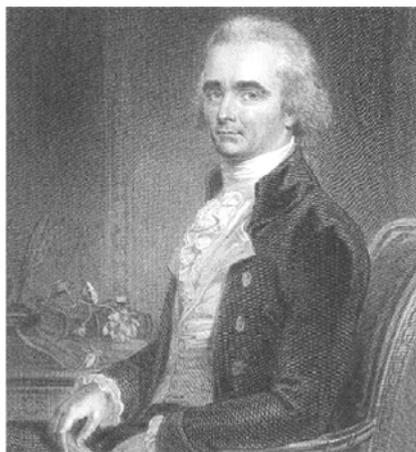
From the 17th century, *Cinchona* figured prominently in European pharmacopiae. Many European countries were frantically after *Cinchona* in the early 18th century. In the 18th century, a search for this tree occurred consistently. The usefulness of the bark of *Cinchona* in treating fevers was established and the European medical personnel were exploring for substitutes, driven by the following reasons: trade monopolies necessitated the search for species that had similar chemical properties, and a substitute for *Cinchona* bark would help reducing pressure on *Cinchona* production and its alkaloids. Medical personnel in India were no exception to this trend. A reference to the French explorer, geographer and mathematician Charles-Marie de la Condamine (1701–1774) would not be out of place here. He went to South America in 1735 to establish the diameter of the earth by measuring the meridian arc at Quito, Ecuador and to search for *Cinchona*. He found this tree near Loxa in Peru<sup>1</sup>. Because the British had no colonies in South America, they were initially searching for *Cinchona* substitutes within their colonies.

### Efforts to manage malaria in the 18th century India: search for substitutes

William Roxburgh (1751–1815), while supervising the Samalkottah botanical garden (Samalkot, c. 480 km north of Madras), searched for substitutes and found a native species of mahogany (*Swietenia febrifuga*, Meliaceae) in 1793. He studied the chemical properties of the bark of *S. febrifuga* by testing with chalybeate, limewater, vitriolic acid, vinegar, vegetable alkalis and magnesia. Roxburgh concluded that the greater the chemical contents in *S. febrifuga* bark, the bitterer it was. He concluded that *S. febrifuga* bark included several alkaloids not found in the bark of *Cinchona*, and the active chemicals in the bark of *S. febrifuga* were more readily water soluble and water extracts remained stable for a longer period of time than those extracted from *Cinchona*. Details of this

work are outlined by Roxburgh in a letter published by order of the Directors of the East India Company. This work is entitled<sup>2</sup>:

‘A botanical description of a new species of *Swietenia* (mahogany), with experiments and observations on the bark thereof, in order to determine and compare its powers with those of Peruvian Bark, for which it is proposed as a substitute [formally addressed], to the Honourable Court of Directors of the United East-India Company, by their most obedient, humble servant W. Roxburgh (1793).’



William Roxburgh (Source: [http://en.wikipedia.org/wiki/William\\_Roxburgh](http://en.wikipedia.org/wiki/William_Roxburgh)).

Mabberley<sup>2</sup> further remarks that this (*sic* letter) is an apparently completely overlooked publication, although two copies exist in the British Library, belonging to Sir Joseph Banks and to Robert Thornton.

Roxburgh’s notes on *S. febrifuga* listed as five points occur in volume 1 of the *New England Journal of Medicine and Surgery and the Collateral Branches of Science* of 1812 (section Intelligence, p. 199) as a notice, which the *New England Journal of Medicine and Surgery* claims as a material republished from an earlier issue of the *Journal of Natural Philosophy, Chemistry, and the Arts* edited by William Nicholson.

A recent article by Pradip Chakrabarti<sup>3</sup> provides excellent insights into the work

and travails of Roxburgh in the Madras Presidency in this specific context. For reasons of contextual flow, I provide here some details from Chakrabarti:

To verify the efficacy of the bark of *S. febrifuga*, Roxburgh sent samples of the mahogany bark to Christopher Samuel John (Tranquebar–Halle Mission) for trials in the Tranquebar–Mission hospitals. Surgeons T. L. F. Folly and J. G. Klein in Tranquebar tried the mahogany-bark decoctions on patients and on the Mission staff, including Johann Peter Rottler. Rottler, who suffered intermittent fever, was saved from death, treated with bark extracts of *S. febrifuga*. In a note, Rottler remarked to Roxburgh:

‘Your Bark *Swietenia Febrifuga* gets here the highest reputation by Dr Klein and Dr Folly.’

Upon Rottler’s insistence, 80 bark samples of *S. febrifuga* were shipped to Copenhagen. Charles Oakley (President of the Madras Council of the English East-India Company–EEIC) recommended that Roxburgh should obtain the endorsement of the Madras-Hospital Board for the recognition of *S. febrifuga*; Roxburgh sent the bark materials to James Anderson M D (Physician-General and President of the Madras Medical Board). In spite of several positive trials in the Madras Presidency, Roxburgh was keen on its recognition in Europe, which was hardly forthcoming. EEIC did nothing to encourage the scientific findings of its enterprising Madras staff. In disgust, in 1791, Roxburgh lodged a complaint with the Madras Government on its failure to promote the useful discoveries made by its own officers and in its own territories. Worse as it would be, Roxburgh’s work on mahogany bark suffered plagiarism by his British colleagues. Alexander Dalrymple (1737–1808) published Roxburgh’s notes on *S. febrifuga* bark under his name without acknowledging Roxburgh. Joseph Banks, a leading name in the then British botany, was skeptical of Roxburgh’s *S. febrifuga* study in Madras and offered only conditional support.

**Efforts to manage malaria in the 19th century India: introduction of *Cinchona***

*Cinchona* bark (Jesuit's bark, Peruvian bark) that includes many alkaloids was widely used in treating malaria – a disease of high-priority management in India in the 1850s (refs 4 and 5). Every possible effort to manage the disease was considered worthwhile. Pierre Joseph Pelletier (1788–1842) had isolated quinine and Jean Bienaimé Caventou (1795–1887) had isolated cinchonine in France in 1820 from the bark of *Cinchona*<sup>6</sup>. A member of the coffee family, *Cinchona* is native to tropical South American Andes. In the 19th century, cinchona was introduced and cultivated in India, Ceylon (Sri Lanka) and Indonesia, because of its medicinal value. Carolus Linnaeus named *Cinchona* after the Countess of Cinchón, wife of the Viceroy of Peru in 1742. The French, English, and Dutch frantically tried to introduce cinchona for cultivation in their respective colonies in the early 1800s. John Forbes Royle (1799–1858; Superintendent, Saharanpur 'Company' Gardens [now in Uttar Pradesh]) recommended to the Government of India to cultivate *Cinchona* in either the Khasias (25°40'–25°21'N; 90°15'–91°16'E) or the Nilgiris (11°08'–11°37'N; 76°0'–77°15'E) in 1835. Thomas Anderson (see Note 1) (1832–1870; Superintendent, Calcutta Botanic Garden, 1861–1868) emphasized the importance of introducing *Cinchona* into India in 1855, which was brought to the attention of the Government of Madras and William Graham McIvor (Superintendent of Government Garden, Ootacamund) in the same year<sup>7</sup> (see Note 2). George Robert Harris (1810–1872), Governor of Madras, initiated the discussion on introducing *Cinchona* in southern India – in Madras in particular – with the British Government. Charles Wood (1800–1885), Secretary of State for India in 1859, nominated Clements Robert Markham (see Box 1) to undertake the mission of bringing *Cinchona* to India from South America. William Jackson Hooker, the first Director of Kew Royal Botanic Gardens (KRBG), and Hugh Algernon Weddell, an authority on *Cinchona* supported Markham's deputation to Peru to collect *Cinchona* for India. Nonetheless, not everyone was supportive of Markham's nomination; a note in the *Gardeners' Chronicle* criticized that

Markham's efforts would fail because of his lack of knowledge of botany and science<sup>8</sup>. However, McIvor<sup>7</sup> states in his report (p. 107):

'This gentleman (*sic* Clements Markham) was selected, being conversant with the Spanish and Peruvian languages, and possessing an intimate knowledge of the various species of cinchona.'

The role played by the KRBG in Markham's South-America mission was immense. The Secretary of State for India, Charles Wood reckoned that an appropriate housing facility be got ready to raise *Cinchona*, since it was the function of the KRBG to receive and transmit large numbers of seedlings, to nurse the young stock in case those despatched to India should fail, and to recommend competent gardeners to take charge of the plantations in India<sup>8</sup>.

**Establishment of *Cinchona* in the Nilgiris**

*Cinchona* saplings shipped from England were to be sent to the Nilgiris via Calicut. CRM had chosen the Nilgiris as the destination because of certain similarities in climate with regions in Peru, where *Cinchona* grew naturally<sup>9</sup>.

Williams<sup>8</sup> refers to the establishment of the first stock of *Cinchona* in the Nilgiris as follows (p. 436):

'When they arrived at Bombay on 27 September 1869, there was further delay. The steamer for Calicut had left and for several days the plants suffered in the "very pernicious climate". ... At Ootacamund, the chief hill station, W. G. McIvor, Superintendent of the Government gardens, assisted in establishing the first plants. By December 1860 all the plants had died. ... The prophecy of the *Gardeners' Chronicle* seems to have been fulfilled.'

The McIvor report<sup>7</sup> states (pp. 107–108): 'In the early part of 1860, Mr Markham started on his important mission, having previously arranged the details of the expedition with an intelligence and forethought seldom equalled; so perfectly were his plans formed that failure was rendered

almost impossible, and the result has been an unequalled success, in the importation of plants and seeds. From this expedition we now possess upwards of 5,000 plants at Kew, a number of plants in the West Indies, 840 in Ceylon, on the 28th September last; about 80 plants in Calcutta, and at Ootacamund, on the Neilgherries (Nilgiris), about 9000 plants.' McIvor (p. 108) lists the following species that have been introduced (into the Government Botanical Gardens, Ootacamund: *Cinchona succirubra* (red bark), *C. calisaya* (calisaya bark), *C. nitida* (genuine grey bark), *C. micrantha* var. *provinciana*, *C. peruviana* (Potade Jallinizo), *C. lucumnaefolia* (Pahudiana of Howard from Java), and one unnamed species, and the values of dry bark in London market.

Williams<sup>8</sup> does not cite the McIvor report. Substantially valid information on *Cinchona* establishment in the Nilgiris occurs in this report<sup>7</sup>, which is summarized here:

McIvor at Ootacamund had received 463 plants from Peru, which he says were in an unhealthy state at the time of their arrival (8 April 1861). This McIvor statement somewhat matches with Williams's remark that the 'plants were dead', which I consider an assumption. The McIvor report continues to say that in two months he could resuscitate them to life. Quoting McIvor's words:

'... those plants are now in the most luxuriant state of health, being from 3 to 4 feet in height and some of their leaves measuring as much as 12 inches by 18.' (p. 109, line 4).

In the remainder of the McIvor report, detailed notes on different trials McIvor made on the germination of different taxa of imported *Cinchona* occur; he also refers to the errors that were committed at the Government Gardens, Ootacamund, based on experiences with growing *Cinchona* seeds that came from Java previously. This report also refers to the different secondary compounds that occur in the barks of different species of *Cinchona*.

A valuable report had gone unnoticed.

Before Markham's voyage to South America, McIvor had selected a site

**Box 1.** Clements Robert Markham

Clements Markham (at 24)  
(Source: en.wikipedia.org)

Clements Robert Markham (CRM) was born as the second son of the Reverend David Markham, the Vicar of Stillingfleet, Yorkshire, on 20 July 1830. At 14, a chance introduction to the Rear-Admiral George Seymour, changed CRM's life. Impressed by CRM's pleasing disposition, the admiral offered a cadetship to CRM enabling him to join Seymour's Flagship *HMS Collingwood*. CRM travelled to the Pacific Ocean in *HMS Collingwood*, which lasted four years. During this voyage *HMS Collingwood* halted in Chilean and Peruvian ports for long spells of time, and CRM used this time and opportunity to learn Spanish and Peruvian. He subsequently joined John Franklin on his Arctic voyage in 1850–1851. In 1853, on the death of his father, CRM badly needed a fulltime employment. He quit seafaring and secured a junior clerk's job at Legacy Duty Office, which grew into 'India Office' in 1857. At the India Office, CRM reported to the Indian Government on the need for the introduction of Peruvian cotton into Madras, on the growth of *Carapichea ipecacuanha* (Rubiaceae) in Brazil and the possibilities for cultivating *C. ipecacuanha* in India, and on the future of the pearl industry at Tirunelveli. CRM was also involved in an ambitious plan for

the transplanting of Brazilian rubber trees (*Hevea brasiliensis*, Euphorbiaceae), claiming that he would 'do for the India-rubber or caoutchouc-yielding trees what had already been done with such happy results for the cinchona trees'<sup>11</sup>. At 24, he was elected to the fellowship of the Royal Geographical Society; in 1888, he was its President. From an early age, he was passionate on being a geographer and explorer; he vetted this intellectual appetite by travelling extensively. CRM died in England on 29 January 1916. He will be remembered for innumerable contributions to both science and arts. He wrote close to 30 books. One of them was *Peruvian Bark: A Popular Account of the Introduction of Cinchona Cultivation into British India*<sup>13</sup>.

From England, CRM sailed to Peru in December 1859. He was accompanied by four assistants and one of them was John Weir, an eminent gardener and horticulturist of that period. The aim was to collect seeds and young plants of *Cinchona calisaya* (Figure 1) from Bolivia and Peru. *Cinchona officinalis* and *C. succirubra* were to be obtained by Richard Spruce and Robert Cross from Ecuador (see Note 3).



**Figure 1.** *Cinchona calisaya*. Source: Franz Eugen Köhler's *Medizinal-Pflanzen in naturgetreuen Abbildungen* (1888–1893). Chromolithography plate (from public domain).

along the Dodabetta stream for raising seeds and saplings of *Cinchona* that would arrive in the near future. Markham decided that a site in Naduvattam was better suited for *Cinchona* than the Dodabetta stream site due to microclimatic conditions. Plantations were established following Markham's decision. Government-run cinchona plantations expanded and prospered along Paikara (e.g., Wood and Hooker plantations) and Kundah until 1873.

In the 1870s, labour to work in the Niligiri *Cinchona* plantations was scarce. The Government, therefore, utilized prisoners and some of them were Chinese, who had been moved to Madras

from the British Straits Settlements ([BSS]: Singapore, Penang and Malacca) because of lack of prison space at BSS. These Chinese labourers, after serving their sentence, settled in Naduvattam working as market gardeners and dairy-men, and raised families marrying local women. Obviously they never returned to BSS. The Malay Chinese in Naduvattam established a Chinese village<sup>10</sup>.

### Quinine production in the Nilgiris

The Government sent *Cinchona* bark samples harvested from the Nilgiri plantations to England for chemical analysis.

John Broughton was the Government quinologist to manage the *Cinchona* plantations at the Niligiris, quinine quality control and for manufacturing quinine cost-effectively, thus making it affordable to all. After several experiments, Broughton launched the 'amorphous quinine' – a combination of different cinchona alkaloids. This product existed for three years and was abandoned in 1874; Broughton resigned in disgust. Price of cinchona products spiralled and extraction efforts in the Nilgiris suffered a setback until 1884. With the appointment of D. Hooper, production of cinchona alkaloids re-commenced in the Nilgiris in the new Naduvattam factory; in 1889, the

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first batch of quinine sulphate rolled out. The process of extraction involved use of caustic soda and shale oil, steaming and agitation. During agitation, the hot oil separated the alkaloids from the crushed bark; caustic soda enabled the oil to pick up the alkaloids<sup>10</sup>.

The Naduvattam factory received improved machinery in 1901, the cost of production of cinchona alkaloids halved in 1905–1906, and the quinine sulphate output was 16,300 lb, which was distributed throughout India, including Burma. For climate and soil reasons, subsequent plantations were raised in the Anamalais, where a locality by name ‘Cinchona’ (pincode: 642 106) exists today.

### Conclusion

Cinchona alkaloids, especially quinine, were used in the treatment of malaria for ages. With changes in human lifestyle and environment, *Cinchona* alkaloids are no more effective, because of resistance developed by the parasite. We have moved to use synthetic products such as mefloquine, doxycycline and combinations of atovoquone and proguanil hydrochloride; however, it is fascinating to see how the British Government and its different employees strived hard to

generate new knowledge and information. The *Cinchona* story illustrates that effort.

### Notes

1. Thomas Anderson went to Java in 1861 to collect plants and seeds of *Cinchona calisaya* for plantations in India; he established this species in Darjeeling. He managed the first cinchona plantations in India, but the results were disappointing<sup>12</sup>.
2. William Graham McIvor is referred as ‘W. E. McIvor’ in the paper<sup>7</sup> I consulted. I have no explanation of this omission.
3. Spruce’s efforts to introduce *Cinchona succirubra* into India need to be remembered, because *C. succirubra* flourished in India. According to CRM<sup>13</sup>: ‘India owes a considerable debt to the indomitable spirit of a very sick man (*sic* Richard Spruce)’.

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13. Markham, C. R., *Peruvian Bark: A Popular Account of the Introduction of Cinchona Cultivation into British India, 1860–1880*, John Murray, London, 1880, p. 550.

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