Quinine: A bark with a serious bite

Steve Ainsworth

A man, a plan, a canal. Panama! Ah, what a delight a simple palindrome is. Yet, had it not been for drugs and medical science, that famous palindrome would never have been written, and we wouldn’t be celebrating the 100th anniversary of the Panama canal opening this year.

Ferdinand de Lesseps (1805–1904), a French civil engineer who had built the Suez canal, began work on the Panama canal in 1880. Eight years later, the bankrupt project was abandoned. De Lesseps was arrested, shipped back to France, and sentenced to five years in gaol. It was all rather unfair, as the problem was not professional incompetence but disease.

Of de Lesseps’ workforce of 86 800, 52 800 were laid low by malaria and yellow fever. Over 5000 died. And no one knew what caused these diseases. The death toll would have been worse had it not been for the bark of a South American tree and a drug extracted from it.

That drug was quinine. It was the first effective treatment for malaria. The disease has been responsible for more human deaths than any other, and thus quinine is arguably the most important drug ever found. Its story is one of legend and adventure, of fortunes made and of empires gained.

Quinine is a large, complex molecule: it was synthesised in 1944, but its common source is the bark of the South American Cinchona tree.

It was in 1820 that two French scientists, JB Caventou and PJ Pelletier, first isolated the active ingredient in Cinchona bark. They named it quinine from ‘quinquina’, or ‘bark of barks’—the name that it had been given by South American Indians.

However, Cinchona was not an Indian word but the name of a Spanish Countess. Four centuries ago, the church bells in Lima, Peru were tolling to mark the last hours of Leonor, the Countess of Chinchon, who lay dying of a malarial fever in her husband’s palace. But a miracle arrived in the shape of a Jesuit priest, who saved her life by his prayers—and an infusion of a previously unknown tree bark.

Well, that’s the legend. Although ‘Jesuit’s bark’ was brought back to Spain during her husband’s time in Peru, in fact Leonor died in Spain without ever having set foot in South America. However, one century later, the story (invented in 1663 in a book by Sebastiano Bado) was swallowed whole by the Swedish botanist Linnaeus, who in 1742 gave the Cinchona tree its official name.

Nevertheless, Jesuits were involved. Jesuit Barnabé de Cobo (1582–1657), who explored Mexico and Peru, is credited with bringing Cinchona bark to Europe. Its efficacy was hailed as a miracle by Catholics. However, suspicious Protestants called it ‘powder of the devil’. In 1658, Oliver Cromwell, who suffered from recurrent malaria, refused to take Jesuit’s bark and died for fear that it was part of a Catholic plot to poison him.

Charles II was not so dogmatic. In 1679, an apothecary named Robert Tabor supplied the King with ‘Jesuit powder’. Tabor also cured King Louis XIV of France’s son of malaria using the drug. The French king rewarded Tabor with 3000 crowns, a pension, and a title.

As a result of royal endorsement, demand soared. And so did the price: at one point the value of the bark equalled its weight in gold. Fortunes could be and were made—not only by supplying Cinchona bark but also by faking it, by substituting dogwood bark.

By the close of the 18th century, over 25 000 Cinchona trees were being chopped down annually in Peru to meet demand, pushing the species towards extinction. By the mid-19th century, Peru was eventually forced to ban the export of Cinchona bark.

That was bad news, as it was quinine only that made it possible for Europeans to hold and extend their malaria-infested colonies.

It was the Dutch who first broke Peru’s monopoly. In 1854, Dutch secret agents paid $20 for a pound of Cinchona seeds— from which they grew 12 000 trees on their island of Java.

British secret agents were not far behind. In the late 1850s, a former naval officer, Clements Robert Markham, and Richard Spruce travelled to Peru, where they secretly acquired 600 plants and 100 000 seeds. By 1867, twelve hundred acres in British India were under Cinchona cultivation.

The British Empire was saved, but no one knew what caused malaria. It was not until 1895 that Ronald Ross of the Indian Medical Service first demonstrated its association with mosquitoes.

The Panama canal was finished by American engineers, with death rates only 3% of the figure previously encountered thanks to the introduction of vigorous antimosquito measures.

Quinine remained the only available treatment for malaria until the early 1920s. During the First World War, German scientists developed the first synthetic antimalarial compound—atabrin—and this was followed by resochin and sontochin, derived from 4-aminoquinoline compounds. American forces, upon capturing Tunisia during the Second World War, acquired, and then modified the drugs to produce chloroquine. Other compounds, such as proguanil, mefloquine, and doxycycline, would follow.

However, despite the emergence of newer drugs, quinine is still remembered as the bark that boasts a serious bite.

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