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Cinchona and its Product--Quinine

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The bark of cinchona produces several alkaloids. The most important alkaloid, quinine, has certain febrifuge properties. Quinine was used in the battle against malaria since the 1630's. Of 38 species of cinchona, four species have economic value for the production of quinine: C. calisaya, C. legeriana, C. officianalis and C. succirubra.

Cinchona, of the family Rubiaceae, is native to the South American Andes. It thrives best on steep mountain slopes in rich volcanic soils and an annual rainfall of 1,500 cm.(9) The cinchonas flower in 3-4 years. The flowers form small fragrant yellow, white or pink clusters at the end of branches, and are similar to lilacs. The fruits are 1-3 cm oblong capsules with numerous small, flat, winged seeds. The bark of wild species may yield a quinine content of as high as 7%, whereas cultivated crops yield contents up to 15%.(l)

HISTORY

Malaria has been credited to bringing down whole civilizations. Alexander the Great, in 323 B.C., was afflicted with the fevers which rendered him lifeless and crushed his dream of uniting the regions of his world. The fevers, heavy set in Rome, instilled such fear in the Catholic Church that the Vatican fled to Avignon, France for 68 years. Commoners with malaria were left too listless to work. Field hands and farmers neglected the crops. The fevers may well have been a hindrance to the progress of agriculture.

Consequently the search for a cure was intense. Countless theories on causes were put forth. Cures ranged from logical to the ridiculous. Physicians mixed herbs for medicine. Some bled patients to achieve a balance of blood and bile. One physician, determining the blood was bad, tied off the arteries of the patient. And yet another physician realized the hopelessness of a cure and prescribed a reading of the Iliad.

It is not certain who discovered the febrifuge properties-of the bark. The Indians knew of it as a cure for fevers. Although after the Spaniards began its use it was noted that many of the natives refused to use it. It is possible the bark may -have been reserved for royalty. Other natives learned to use powdered bark

with lemon juice.

Jesuits also have a claim on discovering the bark. Their method of finding new medicines was by chewing barks. The bark of cinchona is bitter and, therefore, labeled as a medicine. Father John de Lugo took an interest in the bark and undertook the propagation of its use. Because of the Jesuits interest it became known as the Jesuits Powder.

Yet the most famous story behind the discovery involves the wife of a Viceroy of Peru, Countess Ana of Chinchon. In 1638 the Countess contracted malaria while in Peru. She was given a powder that cured her of the fevers. Impressed by this new cure she collected the bark and gave it to others who needed it. However, it is widely disputed that the Countess was responsible for spreading the bark, or that she even had malaria. Nevertheless, Linnaeus named the genus Cinchona in her honor. It is regrettable though that there was an error in the spelling that in 1866 the International Botanical Congress opted to keep.

DOMESTICATION

Acceptance of the cinchona bark was not as immediate as would be expected for an otherwise incurable malady due to past failures with other claims to "cures". Physicians where uncertain of dosage size and frequency of administering the drug. Other reasons for the slow acceptance involved the Jesuit priests.

The bark, sometimes referred to as Jesuits Powder, was believed to be used in a plot against the King and all protestants of England. The commoners dubbed it the Jesuit's Poison. Nevertheless the importance of the bark was realized and intense harvesting in Loxa, the main source, left a large number of trees dead. Many were adding other barks and cinchonas with low quinine content. As a result the diluted -shipments were less useful as a cure. The demand for the bark fell. Alarmed at the scarcity of the cinchonas and the contamination of exports, expeditions were sent out to find cinchonas in other parts. Men such as Clements Markham, J. C. Hasskarl, and Charles Ledger in the mid 1800's began to collect young plants and seeds for crops. Hasskarl and Markham's early attempts to grow cinchonas in India and Java failed due to difficulties with transporting young trees, low quinine yield and/or crop failure.

Markham continued to experiment in India and shared his results with others. With the help of Richard Spruce he was able to collect trees and seeds of C. succirrubra and transported them to India successfully in 1860. The red cinchonas thrived the best. By 1867 India plantations covered 1,200 acres.

Plantations of the red cinchonas in Java did riot fair as well. The quinine content was of a low yield. In 1865 Ledger and his Indian servant, Manuel, had collected seeds of C. calisaya. A pound of seeds were sent to Java and cultivated. The quinine content was found to be high and the following generations gave an even higher yield. By 1876 yields were "the proportion of 13.25 per cent of quinine."(7)

South America, British India and Java traded varieties of cinchonas to achieve more variation. The species initially_ cultivated included C. lancifolia C. cordifolia. C. Trianae. C. succirubra, C. Officinalis

C. micrantha, C. Pahudiana, C. calQWra, C, Josephiana, and C. calisaya.

Java quickly became the largest producer accounting for 95% of the worlds commercial supply. Today other better antimalarial drugs exist. Still, in addition to its medicinal use quinine is used as a tonic, an antiseptic, and lotions against the sun and insects.(9)

CULTIVATION, MANAGEMENT AND HARVEST

Seeds, cuttings or grafting, may propagate cinchona. Seeds are sown in a rich sandy soil and kept mist till seedlings are 2 inches. Mercurial fungicides and careful watering controls seedling fungus.(9) Young plants are thinned and kept shaded and protected from wind. As the plants grow shading is slowly removed. When approximately 9 inches they are transplanted to permanent fields. Young trees are planted 2 feet apart. The closeness offers wind protection and prevents undergrowth competition. Organic fungicides keep branch canker in check.

In the 10th year, when quinine content is the highest, the trees are harvested. Trees may be partially stripped and bound with moss for protection. The moss also facilitates the growth of new bark. The replacement bark normally gives a higher yield of quinine.

Barks from trunks, roots and branches are all used. Removing the bark is done by beating the trees with sticks to loosen it. It is then stripped away with a knife and rolled. The barks from the roots, trunk and branches are separated and rapidly dried. The roots contain the highest quinine content with the trunk coming in second.

Bark from pruned branches is also used. Extensive cutting back on the older tree promotes growth of new branches, which helps increase the yield of each tree.

CONCLUSION

In early days infusions of powdered barks were prepared with lime or wine by boiling. Today other methods provide pure extracts that allow safer more precise prescriptions.

Malaria still exists today in both the Old and New Worlds. In the late 1970's over 500 cases were reported in the U.S., over 200,000 in South America and over 500,000 in Indonesia.(11) In the mid 1800's a parasite of the blood, Plasmodium vivax, was discovered as the cause of malaria. The cause of malarial spread, anopheles, was found in the early 1900's. Precautions against the mosquito help in controlling the spread of malaria but the anopheles is a sturdy family. As long as anopheles thrives the parasite and its disease will thrive. Studies done on the effects of quinine on P. vivax facilitated the development of new medicines. It is easy to see how important quinine had become the the medical world.

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