

International Journal of PharmaO2

ISSN: 2582-4708

Journal Home Page: http://www.ijpo.in/

(IJPO: A Peer-reviewed Bi-monthly online journal)

Review Article

Cinchona: A Crude Drug

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ARTICLE INFO

Article history: Received: 28/01/2021; Revised: 08/04/2021 Accepted: 15/04/2021; Available online: 01/05/2021.

Key Words: Cinchonine, Hydroxychloroquine, Malaria, Quinine.

Please cite this article as: Maniyar, R.M., et al. (2021). Cinchona: A Crude Drug. 3(3), 0130-0134.

ABSTRACT

Traditional medicines have occupied a huge space in our life because it helps us to treat different life threatening diseases with fewer side effects. As we all know that 56 percent geographical area of India is covered by a plant life, hence itself it is a treasure of crude drugs. There are many examples of crude drugs like curcuma, margosa, basil, vasaka, vinca, cinchona etc. In this pandemic of Covid-19 several countries are using Hydroxy-chloroquine (HCQ) to save many lives which are obtain from very well known crude drug that is Cinchona. It is a dried bark of cultivated trees of Cinchona officinalis belonging to family Rubiaceae. Its quinidine, cinchonine, chemical constituents are quinine, cinchonidine. It is used as anti-malarial, anti-pyretic, anti-asthmatic, cardio depressant, oxytocics and in neuralgia.

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Introduction

Cinchona is native to eastern slopes of the Andes at high altitude. The bark was first used as an antipyretic in 1630 by Jesuits, which is discovered in 1513 in Peru. The efforts of viceroy of Peru count cinchona it was shown as a drug in Europe in 1655. It was reported as an infusion in London Pharmacopoeia in 1677. In the viceroy, the genus was described by Linnaeus as cinchona in 1742. In 1860, *C. calisaya*, *C. micrantha*, *C. succirubra were* introduced in India by Markham. The former

importance of cinchona bark and its alkaloids in the treatment of malaria, has been lessened by the introduction of synthetic drugs but it remains of great economic important and salts of quinine and quinidine are included in most pharmacopoeias. In India owing to the antimalarial and antipyretic use of this drug; right from 1880, a large area was taken for cultivation of cinchona in West Bengal, which eventually shifted to South India. Importantly, either the cinchona bark or its extract cannot be utilized in the specific preparations (Evans,

ISSN: 2582-4708

WC. 2008). Comprising the Fe-salts, since the presence of 'cinchotannic acid' shall combine with these salts to cause precipitation unavoidably. Thus, 'cinchotannic acid' serves as pharmaceutically active constituent. The BP and EP recognize C. succirubra and its varieties and hybrids containing not less than 6.5% of total alkaloids, 30-60% of which consists of quinine-type alkaloids. According to recent study of the Count's diary, it appears that the Countess never suffered from malaria or other fever during her stay in Peru, and although the Count himself did so, there is no record of his having been treated with cinchona bark. The remedy, which become known as 'Pulvo de la Condesa' acquired a considerable reputation and was known in Spain in 1639.

The further distribution of the bark was largely due to the Jesuit priests, and the drug become known as Jesuit's Powder or Peruvian Powder. It first appeared in the London Pharmacopoeia in1677 under the name of 'Cortex Peruanus' (Wallis TE., 2005). The bark was originally obtained by felling the wild trees, which were exterminated in many districts. Ruiz (1792) and Royle (1839) suggested the cultivation of cinchonas in other parts of the world, Weddell germinated seeds in Paris in 1848, and the plant were introduced into Algiers in the following year but without much success. A further attempt by the Dutch was made in 1854, seeds and plants being obtained from Peru by Hasskarl and introduced into Java. (Somavilla NS. 2018).



Fig.1: Cinchona

Synonyms

Jesuit's bark, Peruvian bark **Biological source** (Michael J., 2020).

It is a dried bark obtained from *Cinchona* officinalis species of cinchona like *cinchona* succirubra, cinchona calisaya belonging to family *Rubiaceae*.

Geographical area

Nilgiris and Annamalai hills of Tamil Nadu and also grown in Darjeeling (West Bengal) **Cultivation and collection** (Kar, A.2013).

The cultivation and collection of cinchona bark is very specialized of tropical agriculture. There are some important factors like acid soil, rainfall and altitude are all important in cinchona cultivation. Cinchona tree height is about 1000 to 3000 meters. Low height of trees of cinchona contains low amount of quinine. Rainfall condition should be constant from 250-380 cm in a year. Very good growth is done in the temperature of 60°C to 75°F. Cinchona need light and required forest soil

which is rich lode in organic matter. 4.2 to 5.6 ph that means having acidic soil and small amount of nitrogen are establish to be most favorable for growth. Cinchona wants slopping situation, high steam and defense from wind. One gram of cinchona seeds carries 3500 seeds. The cinchona bark is collected by coppicing method. In coppicing method vertical incision is made on branches, trunk of tree and these incisions are connected by horizontal circle. The bark is then stripped off and dried in sun light and further by artificial heat. The drying of cinchona is done below 175°F.while drying the bark loses up to 70% of its weight. From 1985 to 1986 the cultivation had goes up to 10 lakhs kg of bark and about 26,000 kg of quinine salts. India sends out quinine and its salt of Rs 299.0 lakhs during 1995 to 1996.

Extraction method (Rangari VD. 2014).

Microwave Integrated Extraction and leaching

Microwave Integrated Extraction and leaching is use for the extraction of quinoline alkaloids from the bark of Cinchona succirubra. This method is performed in four steps which ensure complete, rapid and accurate extraction of the drug.

Conventional Soxhlet's extraction

The fat extraction is known as Conventional Soxhlet extraction it is use for extraction

process. This fat extraction uses the receiver reflux and siphon principle to do extract the solid matter of pure solvent.

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Altitude

1000 to 3000 meters above sea level. It also grows satisfactorily below 1000 metres, but it has been found to contain low quinine.

Hemoglobin Globin utilized by malaria parasite

Heme (highly toxic for malaria parasite)

Quinine and Chloroquine Prevent this conversion



Hemozoin (non toxic to parasite)

Fig.2: Mechanism of action of Cinchona (Vinod, VD. 2014)

Table 1: Comparison of cinchona (Gokhale, SB. 2007)

C. succirubra	C. calisaya	C. ledgeriana	C. officinalis
Frequently 20-40 mm diameter and 2-6 mm thick	Diameter 12-25 mm and 2-5 mm thick	Diameter 12-25 mm and 2-5 mm thick	Up to 12 mm diameter and 1 mm thick
Well marked longitudinal wrinkles, relatively few transverse cracks.	Broad longitudinal fissures; Transverse cracks about 6-12 mm apart	Similar to C. calisaya, but cracks more numerous and less deep.	Transverse cracks, very numerous, often less than 6 mm apart
Some pieces , but by no means all show reddish wart		Some pieces show longitudinal wrinkle sand reddish warts	
Powder reddish – brown	Powder cinnamon - brown	Powder cinnamon - brown	Powder yellowish

ISSN: 2582-4708

Macroscopic characters (Kokate, C.K. 2007) Cinchona exhibits the typical histological character of the bark. The cork cell are thinwalled, followed by phelloderm. The cortex consists of several secretary channels and phloem fibres. Medullary rays with radially arranged cells are present. Idioblast of calcium

oxalate is the specific characteristic of cinchona bark. Starch grain and present in a parenchymatous tissues. Stone cells are rarely present in the structure.

A few of a cork cells are lignified. Medullarys are 2 to 3 cells wide.

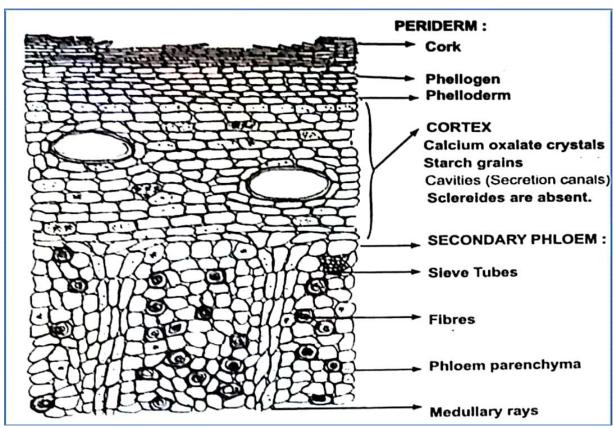


Fig.3: Microscopy of Cinchona bark

Chemical constituents (Ferroni, E., 2017) It consist 25 alkaloids mainly belongs to Quinine and Quinidine group. the main alkaloids are:

Quinine, Cinchonine, Cinchonidine, and Quinidine.

It also consist Starch, Tannins, Glycosides and Protein.

Table: Chemical tests of cinchona

Tests	Observation	Inference
Heat the powdered drug in a dried test tube with little glacial acetic acid	Purple vapors are produced at the upper part of test tube	Complies
Thalleoquin test	Green colour with bromine water and dilute ammonia solution.	Complies
Quinidine solution	Gives a white precipitate with silver nitrate solution, which is soluble in nitric acid.	Complies

Uses (Kar, A. 2013)

Antimalarial and antipyretic, in the treatment of arrhythmia, influenza, Cancer, fever, leg cramps, hemorrhoids, loss of appetite, etc.

Substitutes of Cinchona (Evans, WC. 2008) Cuprea bark and false cuprea bark

Conclusion

It is concluded that cinchona is widely used in the treatment of malaria. Now a day's Hydroxychloroquine which is obtained from cinchona is administered to cure the life threatening disease i.e. Covid-19. Hence in this scenario cinchona is widely used drug.

Acknowledgement

Authors are thankful to management of S.M.B.T. Sevabhavi Trust, Dhamangaon (Nashik; India) for encouraging for preparation of this review.

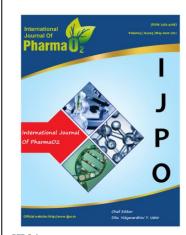
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