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A COMPREHENZIVE REVIEW OF CINCHONA ALKALOIDS --MEDICINAL PROPERTIES AND ITS VARIOUS APPLICATIONS.

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ABSTRACT

Medicinal plants which also known as medicinal herbs, chemical compounds from plant species which contain many medicinal values and so it is widely used against many diseases not only internal and external diseases also. Since ancient times plants and plant products used as medicine and are used till now. Nowadays many medicinal plants are extinct because of the unawareness of their medicinal values or medicinal properties. Cinchona is one of the most important medicinal plants widely distributed in South America and this plant was introduced in India in 1859. In India cinchona plant is distributed throughout the Western Ghats (Nilgiris and Anamali) and it is also grown in Darjeeling (west Bengal).cinchona plant collectively known as koina plant, Peruvian bark, Jesuits bark etc., coming under the family Rubiacea. This plant is rich sources of alkaloids, more than 30 types of alkaloids present. Out of these Quinine is most valuable and is used as anti-malarial agent from ancient days and are used still today. Literature study revealed that along ant malarial activity, the cinchona plant has many other medicinal properties like, Anti-bacterial, Anti-fungal, Anti-oxidant, Anti-cancerous,and Anti-inflammatory and some Nano particles are synthesized from this plant extract.

Keywords: Cinchona, Alkaloids,Microscopic properties,Propagation techniques,anti-malarial,ant-microbial, anti-obesity, anti-cancer, anti-oxidant, antiinflammatory, applications.

INTRODUCTION

Cinchona is a large medicinal plant. Cinchona plant lives in the tropical rain forest region. Cinchona is believed to originate from the Andes Mountains in South America.It is believed that the name of cinchona was taken from the name of a Royal princess in Peru in 1638 the princess affected Malaria. After cinchona treatment the princess was recovered from malaria**[1]**. In India cinchona is widely distributed throughout the Western Ghats (Nilgiris hills in Nilgiri district) and Annamali hills (in

Coimbatore district) in tamilnadu) and it is also grown in west Bengal. Cinchona is commonly known as Jesuits bark, Peruvian bark, koina plant etc. Among all other countries Indonesia is largest producer of cinchona **[2]**. cinchona is an evergreen plant ,growing 5m to 15m in height. The plant is simple and oppositely arranged (simple panicle) leaves. Cinchona flowers are small and are rose or creamy white in colour. Flowers are in terminal clusters, the fruit capsule contain numerous seeds **[3]**

From ancient times this medicinal plant used for curing many diseases. During Second World War cinchona were the only effective drug against Malarial infection **[4]**. But today the growth of this plantations decreased. Cinchona Bark have been used as traditional medicine for thousands of years **[5]**. Cinchona plant is mainly cultivated for its Bark and it is considered as the most useful bark medicine **[6]**. Cinchona Bark rich in alkaloids, Phytochemicals and other acids etc. Different types of alkaloids present in cinchona bark **[7].** Alkaloids present in the cinchona are collectively referred to as quinoline **[8**

BOTANICAL CLASSIFICATION [9]

Kingdom – Plantae

Subkingdom – Tracheobionta

Division- Magnoliophyta

Super division- Spermatophyta

Class- Mangnoliopsida

Genus- Cinchona.L

Order- Rubiales

CULTIVATION

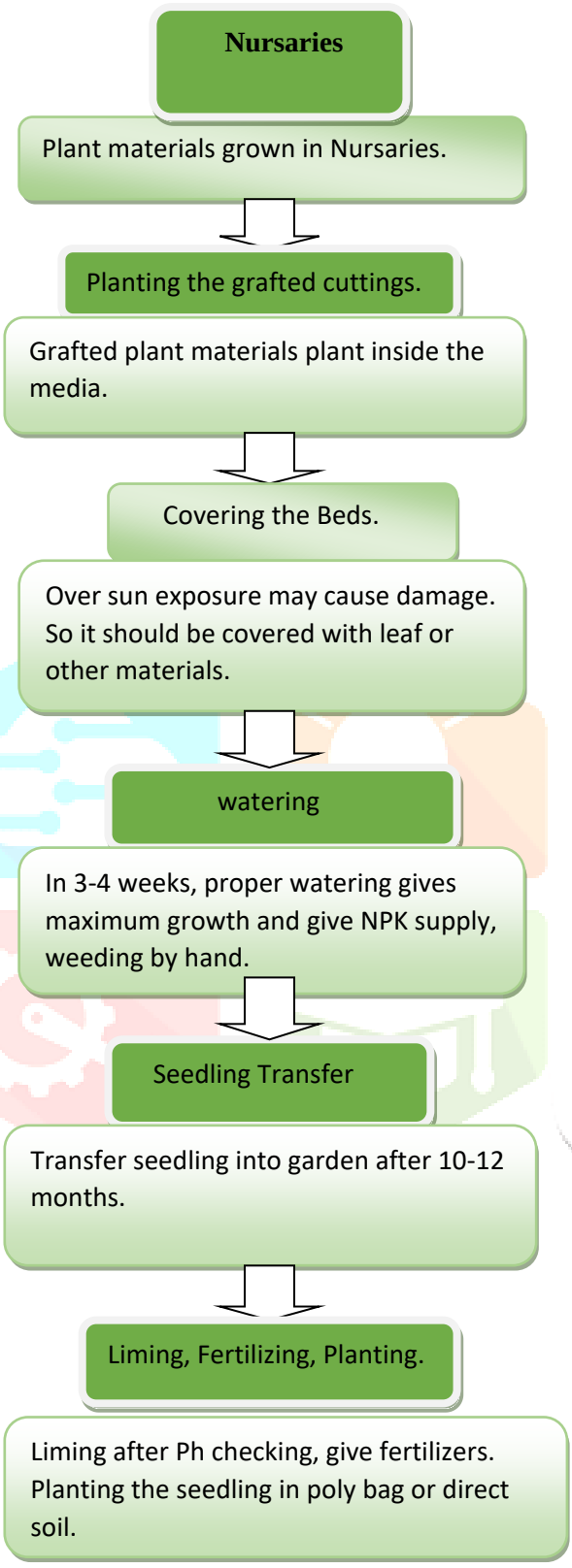
Cinchona species mainly frown in tropical rainforest areas. Cinchona plant grows upto1500-200m. Average rainfall 200-400cm.cinchona plant grown in fertile and porous soil. In India first cinchona plantation created by British.Many studies revealed that Cinchona plant cultivated by different methods. Seed sowing method is the most common and widely accepted method. In 2020 visahal prajapti, Piyush Yadav et al studied and conformed that seed of cinchona scatter in the boxes and they are transformed to the nurseries when the seedlings gain 5cm height. This study also reported that direct sunlight may cause harmful effect to the seedlings, so the nurseries should be provided by ceiling coverings..

According to (Setyawath, 1993) **[10]** stem cutting method or vegetative propagation is the very good method to maintain parent plant. (Dinas Pertanin, et al 2018) **[11]** Reported that in Indonesia many cinchona or quinine plant propagated by stem cutting. In modern times, Tissue culture techniques also developed in cinchona plant clones.

MICROSCOPIC PROPERTIES.

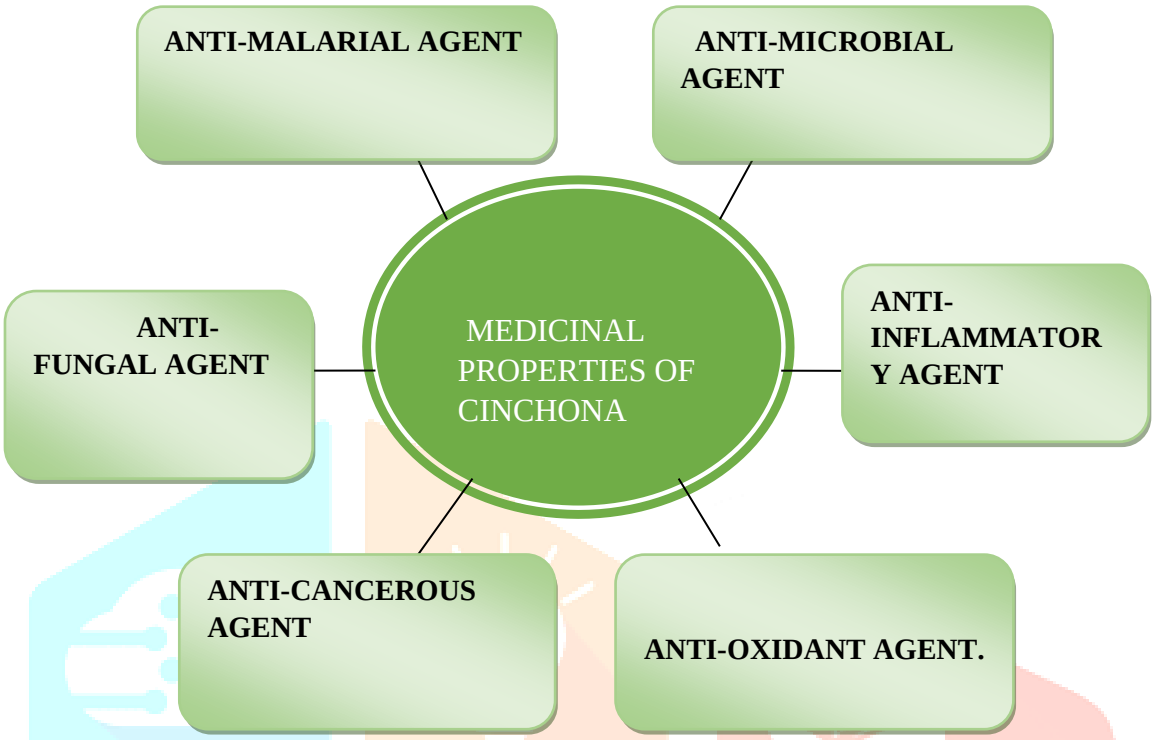
In 2020 vishal prajapathy et al mentioned the most realistic microscopic characteristics of cinchona show in the bark. Microscopic studies of cinchona plant revealed many amazing aspects about this plant. several phloem fibres and secretory channels are shown in the cortex of the cinchona transverse section. calcium oxalates are the most important microcrystal's present in the cinchona bark, mainly the idioblasts of calcium oxalates.Microcrytals are arranged randomly in the cortex cells.starch grains and parenchymatous cells also present in the cortex of the bark. The transverse section of cinchona plant contain some secretory canals also. stone cells are the cork cells arranged frequently in the structure **[12]**.

Vegetative propagation Techniques in Cinchona plant. (13)



MEDICINAL VALUES OF CINCHONA

From ancient times Cinchona plant used mainly for the production of quinine. Mainly the bark contain quinolone alkaloids, which contain quinine, cinchonine, quinidine, and cinchonine. Approximately 35 plant chemical compounds have been identified in this plant.



CINCHONA ALKALOIDS

Quinine

Quinine is an alkaloid of cinchona; It is one of the main alkaloid of cinchona. Chemical formula of Quinine is $C_2OH_24N_2O_2$**[14]**. It is always in the form of salt **[15].** It is often used as anti malarial agent [16]. A major side effect of Quinine overdose is Cinchonism **[17].**

Quinidine

Quinidine alkaloid present in the bark of cinchona ranges from 0.25% to 3.0% **[16].** Quinidine alkaloid mainly used against malaria and arrhythmia **[18].**

Cinchonine

Chemical formula of cinchonine expressed as C19H22N2O **[19]**, present in the bark of cinchona plant and also used as anti malarial agent**.[20].** As compared with Quinine cinchonine has less toxicity and has high activity than other alkaloids associated with Quinine **[21].** Cinchonine also used as anti microbial agent against fever, amoebiasis, influenza and schizonticide. Act as an irritant against gastric mucosa**[22].**

ANTI-MALARIAL AGENT

According karol michal karpracak Cinchona bark mostly used as anti malarial agent, dried bark used to treat in malarial therapy. In europe untill 1820 plasmodium falsiparum ia malarial agent which cause malaria.Malaria was one of the most dangerous disease at that time.cinchona plant considered as the best medicine to show maximum resistant capacity of malarian vector plasmodium falsiparum**[23].** The first discovered antimalarial drug is the quinine. cinchonine were most active cinchona alkaloids used in malarial therapy followed by other two alkaloids such as quinine and cinchonidine. quinidine shows maximum activity against plasmodium falsiparam **[24].**

But unfortunately it cannot be safely used as ant malarial agent due t its cardiac activity, therefore among all four alkaloids of cinchona quinine is historically continued to be an anti malarial drug**.[24-26].** However there are some reports on resistance of plasmodium falsiparam towards quinine. In south America, south east asia, africa and some other countries conformed the high resistant activity of plasmodium falsiparam towards quinine also**[27].**

ANTI-MICROBIAL AGENT

Staphhylococcus aureus is one o the most important bacteria which can cause bacterial infection against humans and animals. Pankaj et al studied that cinchona alkaloids showed antimicrobial activity against this bacteria *staphylococcus aureus.* The inhibition zone ranged from 8-18mm by disc diffusion method**. [28,29]..**Based on the concentration level of cinchona alkaloids The anti microbial activity also may varie ie,if the concentration of alkaloids present in the cinchona plant is high, which shows high anti microbial activity. Amebiasis is one of the most dangerous intestinal infection caused by entameba histolytica. many studies showed that the extraction of cinchona alkaloids effective against this intestinal infection amebiasis .

Plasmodium falsiparam and herpes are pathogens strains which causes many diseases. In 2016 Tyaghi R,et al **[30]** mentioned that dried bark of cinchona used to treat against these strains. Microorganisms are harmful to the human body indifferent ways. Rojas JJ et al confirmed that cinchona was very effective against diseases caused by microorganisms.

ANTI-CANCEROUS AGENT

As described by krishnaveni and suresh (2015), quinine influences the cell death and apoptosis in cancer cell line and inhibit the proliferation of cancer cell in a dose and time dependent manner.(krishnaveni M,suresh et al **[32].** It has been confirmed that quinine which contain anti cancer agents such as bleomycine,cisplatin, can increase ROS generation inside the cell or promote intracellular ROS generation. Kampa M,Alexia et al **[33]** described the Cinchona alkaloid quinin induces some morphological changes in the cell such as condensation of chromatid,cell adhesion and contraction,nuclear fragmentation,apoptotic signals.quinin has high apototic activity in cancer,so it is considerd as an effective anti cancer drug in future. Induction of apoptosis by indirect mitochondrial activity is one of the major anti-cancer treatement. But in some cases it altered in drug resistant cancer cells.

ANTI-INFLAMMATORY AGENT

Commonly cinchona known as anti malarial agent but rather than it is also used as a very good anti – inflammatory agent, used to treat arthritis, prion disease, and nocturnal muscle/leg cramps.During 1894 the active agents such as quinine and cinchonine were isolated and used to treat against lups **[34].** The ant-inflammatory properties act by inhibiting the endosomal and lysosomal function, inhibiting the T-Cell activation and antigen processing **[35].**

ANTI-OXIDANT AGENT

Cinchona alkaloid which contain phenolic constituents.due to the presence of this phenolic compounds,cinchona considered as effective antioxidant properties. (Ravishankar MN,Harish padh et al,2003 **[36]** .Biological properties of cinchona are inhibition of lipid peroxidation, anti-virus,Anti-HIV **[37,38].** Superoxide hydroxyl,nitric oxide are two main radicles and these radicles are responsible for the oxidative damage of cellular componentsin the human body **[39,40,41,42]**. Methanolic extract showed maximum anti-oxidant properties.

ANTI-OBESITY AGENT

Cinchoquine is one of the strong alkaloid of cinchona bark or Peruvian bark. cinchona alkaloids are mainly used as anti- malarial agents. But in the case of cinchoquine it is used as a very good medicine for peoples those who suffering obesity problems. many studies revealed that cinchoquine is more effective than any other chemicals extracted from other plants.Sae-Tan.Grove KA reported that Pentachloroquine is a good dietary phytochemical used to control fat inflammation and obesity **[43].**

APPLICATIONS OF CINCHONA PLANT AND ITS ALKALOIDS.

Many of the studies showed that cinchona plant introduced to europe by the spanish countries in 1638.Famous scientist carl linnaeus named it “cinchona”in 1742 cinchona have many broad spectrum of applications mainly in medicinal, economical, ecological etc. Mainly cinchona alkaloids used in medical and in food industry. Some of the important applications of cinchona medicinal plant are;-

- Used in the food industry
- First pure chemotherapeutic
- Used in pharmaceutic products.
- Used in the production of cosmetic items.
- Functioned as Anti-malarial agent, Ant-microbial agent, Anti-obesity agent etc.
- Serving as drugs, selectors, chiral catalysts, bitter taste agents (in Tonics).
- Widely used in beverage and confectionary industry **[44, 45, 46,47].**

CONCLUSION

From the beginning of the world medicinal values of plants was very famous in one or another way. our today’s world so many medicines have been developed from various herbal sources. Cinchona or the Peruvian bark is one of the major medicinal plant. Cinchona plant Can cure many diseases. one of the most significant medicinal property of cinchona is the presence of alkaloids. Cinchona commonly known for its anti-malarial activity. Other biological properties of cinchona are: - Anti- malarial activity, Anti-fungal, Anti-parasitic, Anti-inflammatory, Anti-bacterial, Anti-cancer, Anti- oxidant activities etc. Toxicity of cinchona is dose dependant manner. Over dose of cinchona may cause some diseases also. However cinchona considered as the Good medicine for many diseases.

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