



THE MEDICINAL AND AROMATIC ACTIVITIES OF CINCHONA: A REVIEW

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AUTHORS' CONTRIBUTIONS

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ABSTRACT

Cinchona belongs to the Rubiaceae family. Due to its antimalarial activity, it is very popular and becoming more and more important for hundreds of years. There are many alkaloids present in the extracts of this tree, including chichonine, quinidine, quinine and cinchonidine, that are main alkaloids, but the quantitative share varies among species to species. Compared with one of them, the combined action of more than two dozen alkaloids is more effective in terms of drug properties. Since the beginning of the 17th century, bark of Cinchona has been used to treat and cure various health problems related to malaria. Cinchona can also be used to treat various other diseases because its alkaloids have antioxidant, anti-cancer, anti-obesity, anti-inflammatory, and antibacterial activities. This article introduces the medicinal and aromatic activities of cinchona.

Keywords: Cinchona; quinine; anti-inflammatory; antibacterial; anti-obesity; anti-cancer; antioxidant.

1. INTRODUCTION

Cinchona is known as Peruvian bark and is the member of Rubiaceae family. It is originated from South America, especially the Andes. It is also found in Vietnam, India, Cameroon, Java, and some other African and Asian countries. Because of planting, it is widely found in the mountains of India. Among them, Indonesia is the world's largest producer of cinchona. Cinchona is a 10 m to 20 m tall tree with a 0.3 m diameter of the right trunk. It has an irregular spherical shape, a dark green crown, an oval leaf shape, a thick central vein, and a complete edge, found to have white or pink flowers, white hair in

panicles, fruits are 2-4 cm long, dark brown, and contains 3-4 seeds. The bark is the plant part that is widely used for medicinal and other purposes. The thickness of the bark is between 2 to 6 cm and the length is between 30 cm. The tube looks like cinchona bark and mostly bends during the aging process. Immediately after harvest, the bark is usually visible on the trunk or branches, with a reddish-brown inside and a gray-brown outside. Commonly known yellow Cinchona are *Cinchona calisaya*, *Cinchona ledgeneria*, and *Cinchona succirubra*, commonly known as red Cinchona. (This sentence is not making the Complete sense) Cinchona bark contains 20 alkaloids containing 15% content, cinchonidine

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quinidine, cinchonine, quinine, and cinchonine, combined with main active compounds such as tannin (3-10%) [1]. In addition to these ingredients, the bark also contains minerals, essential oils, and acids, such as triterpenes (quinovinic acid), organic (quinic acid), phenols (caffeic acid), flavonoids (anthocyanidins), Phytosterols [2]. Cinchona bark was used as an antipyretic by South American Indians and was first introduced to Europe in 1640. In 1820, when Europe separated pure quinine and replaced natural substances in large quantities, cinchona became more important. Quinine can be called as the first pure and truly effective chemotherapy. Although the therapeutic window of quinine is small, and even today, the resistance of the malaria vector *Plasmodium falciparum* is still increasing, it can still compete with new antimalarials and is still an important drug for severe malaria cases. Considering that quinine may be the oldest known drug, it is surprising that, according to some estimates, of all the drugs introduced in the treatment, cinchona saved the most lives [3].

2. HISTORY

Cinchona has been considered an antimalarial drug since the 1600s [4] when a high fever Indian drank from a bitter stagnant pool in the Andean jungle. The pool was polluted by cinchona trees. He recovered unexpectedly, shared his experience with the folks, and then treated the fever with the extracted cinchona bark [5]. Cinchona was introduced to Europe in 1638 by the Spanish Countess Cinchon. The Chinichona botanist Carl Linnaeus named it "Cinchona" in 1742 [6].

3. CINCHONA ALKALOIDS

3.1 Quinine

The chemical formula of quinine is $C_{20}H_{24}N_2O_2$ [7]. Quinine is an alkaloid of Cinchona, which belongs to the aryl amino alcohols group of drugs. As it is highly basic compound, so it always appears in the form of a salt [8]. There are many preparations, including hydrochloride, dihydrochloride, sulfate, bisulfate, and gluconate; among them, dihydrochloride is the most widely used. Quinine has no rapid effect on *Plasmodium falciparum* [9]. It is distributed in body fluids and is highly bound to proteins, mainly α -1 acid glycoprotein. The plasma binding capacity is related to the concentration, but also related to the level of α -1 acid glycoprotein, so it is difficult to compare between different studies [10]. The most significant characteristic alkaloid of the cinchona bark is the presence of quinine with 16% [11] but the percentage will vary (6-10%) depending on type of Pranay Gurung. A representative sample of dried cinchona

bark has been found to contain 0.4-4% [11]. It is often used as an antimalarial with other purposes, such as a flavoring agent in carbonated drinks [12], a skeletal muscle relaxant, treatment of hemorrhoids, various veins, and also used as an oxytocic agent [11]. Quinine has also a toxic effect, due to overdose. The main site of quinine toxic damage are the Nervous system, including optic nerve and auditory nerve followed by vascular and nerve damage [13] and fatal cardiac arrest [14]. A common side effect of quinine overdose is Cinchonism [15].

3.2 Cinchonine

Cinchonine is chemically expressed as $C_{19}H_{22}N_2O$ [7]. The quinine present in the bark of cinchona, is also used as an antimalarial drug [16]. Compared with quinine, it has less toxicity and high activity than other quinine-associated compounds [17]. It is used as an antimicrobial agent and is widely used to fight influenza, fever, dysentery, amoebiasis, and schizonticide. It acts as a mild irritant to the gastric mucosa [11].

3.3 Quinidine

Quinidine is a significant alkaloid present in the bark of cinchona, and the main variation of quinidine ranges from 0.25% to 3.0% [12]. Its function is anti-malaria and anti-arrhythmia [18].

4. SOME OTHER FUNCTIONS OF CINCHONA ALKALOIDS

4.1 Anti-obesity Properties

Cinchoquine is a strong alkaloid derived from the cinchona bark. It is mainly used for anti-malaria activities, but it can solve the problem of obesity. According to demonstrations of Jung in 2012, cinchoquina is more effective than other chemical substances extracted from other plants, which can fight obesity [19]. Compared with EGCG and curcumin, chincinnovine showed greater body weight loss [20]. Pentachloroquine is a useful dietary phytochemical to prevent obesity and fat inflammation [19].

4.2 Anticancer Agents

Quinine influences the apoptosis during cancer cells and inhibits cell proliferation in a dose and time dependent manner [21]. It has been demonstrated that it has anticancer agents, comprising of bleomycin, cisplatin, anthracyclines, and radiation presently used for cancer treatment, can cause an increase in the production of intracellular ROS generation. The

action of quinine induces typical morphological changes such as apoptotic signals, loss of apoptotic bodies and adhesion, cell contraction, membrane blistering, chromatid condensation, and nuclear fragmentation [22]. Because quinine has a huge apoptotic activity in cancer, it may be an effective anticancer drug in the future.

4.3 Antioxidant Performance

Due to the presence of phenolic compounds, cinchona has effective antioxidant properties [23]. Inhibition of lipid peroxidation, anti-HIV, anti-virus, and anti-tumor are the biological properties of phenols [24,25].

4.4 Anti Microbial Activity

Plants have some beneficial microbes also [26, 27, 28, 29]. The antibacterial effect of cinchona alkaloids on *Staphylococcus aureus* using the disc diffusion method is 8 to 18 mm [30]. According to the concentration of cinchona alkaloids, its antibacterial activity increases [31]. Microorganisms that are harmful to the human body, Cinchona works against them [32]. Bark of Cinchona is used to cure diseases induced by *Plasmodium falciparum* and *herpes* [33].

4.5 Anti-inflammatory Activity

The alkaloids in cinchona are also used to treat arthritis and nocturnal leg cramps. Because of its bitter taste, it is also used as a tonic drink. Cinchona bark has been used for anti-malaria and anti-inflammatory purposes for hundreds of year [34].

5. CONCLUSION

Many drugs have been developed from herbal sources. Cinchona can cure various health problems. The most significant property of cinchona is the presence of many alkaloids, its combined action is the key source of drug properties. Cinchona bark contains 20 kinds of alkaloids among these 20 kinds of alkaloids, 4 of which are the main cause of its anti-malaria, and contain the largest proportion of alkaloids. While other alkaloids present in cinchona also have important biological properties, such as anti-parasites, anti-inflammatory, anti-obesity, anti-cancer, antioxidants, and antibacterial agents. Small amounts of alkaloids may be impactful molecules for above-mentioned characteristics of this wonderful herb. Cinchona has dose- and time-dependent side effects. Sinkson's disease, neurotoxicity, and cardiotoxicity are problems that hinder the use of the drug in medicine. However, the toxicity of cinchona is dose-dependent. The modification of alkaloids has produced a drug for the treatment of many diseases.

Therefore, it is necessary to develop a new drug with no or few side effects.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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