

## The Integration of the Development History of Artemisinin in Pharmacy Introduction Teaching

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**Keywords:** *Pharmacy Introduction*, Artemisinin, History of Development, Teaching

**Abstract: Objective:** In order to improve the learning efficiency, quality and the comprehensive ability of *Pharmacy Introduction* for non-pharmacy students in medical colleges and universities. **Methods:** In “Introduction”, “Pharmacognosy”, “Natural medical chemistry”, “Medical chemistry”, “pharmacy”, “Pharmaceutical analysis science”, “biopharmaceuticals” and “pharmacology” teaching process, introduce project 523, the Lasker-DeBaakey Clinical Medical Research Award and the Nobel Prize in physiology or medicine 2015 for Youyou Tu, the originate, harvest time and genuine producing area of Qinghao, redesigned the process for isolating at lower temperatures using ether as a solvent and the determination of artemisinin structure, the feature and synthesis of artemisinin and its derivatives, the formulation and its preparation and clinical application of artemisinin derivatives, the pharmacopeia situation and quality control methods of raw materials and preparation, the frontier exploration of biological fermentation method to produce artemisinin, the new pharmacological findings of artemisinin derivatives, respectively. **Results:** The development history of artemisinin integrated in *Pharmacy Introduction* teaching can cultivate achievement consciousness, motivate learning interests and exploration spirit and improve teaching efficiency and quality. **Conclusion:** The thawing methods can improve the learning efficiency, quality and the comprehensive ability of *Pharmacy Introduction* for non-pharmacy students.

### 1. Introduction

Artemisinin is a natural active ingredient contained in *Artemisia annua* (qinghao in Chinese), and a herb mixture to stop a fever for hundreds of years in traditional Chinese medicine (TCM). Since its initial isolation in 1972, artemisinin and its derivatives have become the leading treatments for one of the world's most deadly diseases-malaria, and have saved countless lives. It has developed into a new anti-malaria medicine from the native compound which is a systems engineering, and the cooperation among different scientists and institutes played significant roles in the following aspects: the effective crude extract of Qinghao (the sweet wormwood); the extraction process of the effective anti-malarial monomer; clinical validation of the effective monomer; the determination of artemisinin structure <sup>[1-7]</sup>. *Pharmacy Introduction* is one of the important courses for students in non-pharmacy specialty in higher medicine colleges and universities, and is the basic class to help students to understand the pharmacy discipline and the pharmacy occupation. It is of great significance and necessity to open the course of Pharmacy Introduction. The curriculum take the medicine discovery, drugs production, quality control, drugs circulation and use, the medicine matter managements, as the master line. It introduces the corresponding pharmacy occupation content and the occupation development to the correlation knowledge and the skill request. It builds the concept of the occupation outline and the characteristic for the students from the pharmacy class specialty before the professional course study, and it is the guidance following curriculum study. The students feel the curriculum covering with widespread abstract, monotonous in the study process. The history of development of artemisinin integrates in *Pharmacy Introduction* teaching introduces the knowledge below in “Introduction”, “Pharmacognosy”, “Natural medical chemistry”, “Medical chemistry”, “pharmacy”, “Pharmaceutical analysis science”, “biopharmaceuticals” and “pharmacology” teaching process respectively: the project 523, the Lasker-DeBaakey Clinical

Medical Research Award, and the Nobel Prize in physiology or medicine 2015 for Youyou Tu, the originator and harvest time and genuine producing area of Qinghao, redesigned the process for isolating at lower temperatures using ether as a solvent and the determination of artemisinin structure, the feature and synthesis of artemisinin and its derivatives, the formulation and its preparation and clinical application of artemisinin derivatives, the pharmacopeia situation and quality control methods of raw materials and preparation, the frontier exploration of biological fermentation method to produce artemisinin, the new pharmacological findings of artemisinin derivatives. Through the vivid scene reappearance, it arouses students' national sense of pride and achievement consciousness fully, and then stimulates the student enormous study interest and science exploration spirit, enhances the teaching effect and the quality of teaching effectively.

## **2. Methods**

### **2.1 “introduction” integrates project 523, the Lasker–DeBaakey and the Nobel Prize**

Malaria, caused by *Plasmodium falciparum*, has been a life-threatening disease for thousands of years. Malaria as one of the important and global widespread public health problem, is also extremely serious during initial establishment period in People's Republic of China. In the early 1960s, the malignant malarial parasite with the anti-chloroquine question has already been found in many areas, especially in Southeast Asia. During the Vietnam War (1955-1975), the Chinese government supported Vietnam, and then had a war with the United States. North Vietnamese leaders, suffering equally heavy losses of soldiers due to malaria from warfare, asked the government of China to urgently find malaria remedies. A clandestine venture named Project 523 was established on 23<sup>rd</sup> May 1967 to set out to develop antimalarial therapies<sup>[1-7]</sup>. The covert nature of the project created a milieu in which few scientific papers were published, with the earliest ones inaccessible outside of China. Many other details about the project are still cloaked in secrecy. On 12<sup>th</sup> September 2011, Youyou Tu, who has since retired as a research fellow from the China Academy of Chinese Medical Sciences (CACMS) in Beijing, won the Lasker–DeBaakey Clinical Medical Research Award and the Nobel Prize in physiology or medicine 2015 for her pioneering work on this agent. Then, the video about Lasker official interview with You you Tu professor regarding winning an award (6min) and anti-malaria records (1): the Fearful Malaria was broadcasted “the Exploration Discovery” in CCTV-10.

### **2.2 “Pharmacognosy” integrates the originate, harvest time and genuine producing area**

Qinghao originates from the dried aerial parts of compositae annual herb *Artemisia Annu* L. Artemisinin is the high-efficiency and low-toxicity anti-malaria drugs that separated and identified from China's scientific researchers for the first time. Its emergence and development with the excellent performance in the treatment of malaria have a far-reaching influence for traditional Chinese medicine. The active ingredient artemisinin is present only in the leaves, and the research has worked out the best time to harvest it. Qinghao grows in Guangxi, Yunnan, Sichuan, Chongqing mainly. Sometimes, the video about anti-malaria records (2): Chinese Special Effects Medicine was broadcasted in “the exploration discovery” in CCTV-10.

### **2.3 “Natural medical chemistry” integrates artemisinin isolation and structure determination**

More than 380 extracts obtained from 200 Chinese herbs had been tested on a mouse model of malaria. However, the progress was not smooth, and there were not significant results emerged easily. The turning point came when an *Artemisia annua* L. extract showed a promising degree of inhibition against parasite growth. However, this observation was not reproducible in subsequent experiments and appeared to be contradictory to what was recorded in the literature. The only reference relevant to the use of qinghao for alleviating malaria symptoms appeared in Ge Hong's *A Handbook of Prescriptions for Emergencies*: “A handful of qinghao immersed with 2 liters of water, wring out the juice and drink it all”. This sentence gave Youyou Tu the idea that the heating involved in the conventional extraction step might have destroyed the active components, and that

extraction at a lower temperature might be necessary to preserve antimalarial activity. Therefore, she redesigned the process for isolating at lower temperatures using ether as a solvent, and the determination of artemisinin structure <sup>[1-7]</sup>.

## **2.4 “Medical chemistry” integrates the feature and synthesis of artemisinin and its derivatives**

Artemisinin and its derivatives mainly are artemether, artesunate, dihydroartemisinin <sup>[8]</sup>. A video about anti-malaria records (3), named the Chinese Medicine is the Medicine? was broadcasted in “the Exploration Discovery” in CCTV-10. The anti-malaria effect of new medicine artemisinin excavated from the Chinese medicine is good. However, due to the theoretically difference between the Chinese and western medicine, it resulted in artemisinin cannot obtain the international medical arena approval. Nevertheless, artemisinin derivatives goes out the world finally thanks to the good curative effects.

## **2.5 “pharmacy” integrates artemisinin formulation and clinical application**

The formulations of artemisinin and its derivatives are suppository, tablets, capsules, and injections mainly. And “Pharmacy” explains various dosage-forms preparation methods and the clinical practice characteristic in detail. The video about anti-malaria records (4): Final Defense Line was broadcasted in “the Exploration Discovery” in CCTV-10. After the human being discovers the quinine for 100 years, with the anti-quinine questions, the global anti-malaria situation is extremely stern. Although the artemisinin’s chemical constitution and the function mechanism are brand-new, the malarial parasite could not have the antibiotic nature to artemisinin.

## **2.6 “Pharmaceutical analysis science” integrates the pharmacopeia situation and quality control**

In “Pharmaceutical analysis science”, it explains the pharmacopeia situation and quality control methods of raw materials and preparation of artemisinin and its derivatives. And the video about anti-malaria records (5): Elimination Malaria was broadcasts in “the Exploration Discovery” in CCTV-10. Malaria is disseminates by mosquitos, and the elimination of mosquitos is difficult, which make the global anti-malaria one extremely complex and difficult process. China was once a nation with large number of cases of malaria, but now, the steady progress in eliminating malaria is ultimate objective. Can artemisinin resist the crazy attack from parasite? If the defense line falls into enemy’s hands, how will the human being face malaria? Regarding this, how should the scientists propose the plan to stop it?

## **2.7 “biopharmaceuticals” integrates the frontier exploration of biological fermentation method**

In the world, artemisinin medicine production mainly depends upon our country to collect directly from the wild Qinghao, but the wild resources have not been able to meet the worldwide scale daily aggregate demand for the artemisinin raw material; And due to the complexion of the synthesizing artemisinin, the big poisonous side effect, high cost, it cannot begin the production. However, the biological fermentation method can provide a brand-new way to solve the problem.

## **2.8 “pharmacology” integrates the new pharmacological findings of artemisinin and derivatives**

Youyou Tu redesigned the extraction process by using solvents with a low boiling temperature, and also separated the extracts into acidic and neutral by treating them with either acidic or neutral aqueous solutions during the process. Finally obtained the extract number 191 from the neutral solvent, which was found to be 100% effective against parasitemia in both *P. berghei*-infected mice and *P. cynomolgi*-infected monkeys on 4<sup>th</sup> October 1971. This discovery symbolized the breakthrough in the discovery of qinghaosu (qinghao is the Chinese name of *Artemisia annua* L., and su means “basic element”). Qinghaosu was later called artemisinin. The modern research indicated that artemisinin and derivative can be the treatment systematic lupus erythematosus and tumor and so on. Through the biology research, expounding the action mechanism for artemisinin in

the human body as soon as possible, we can develop the second, the third generation of artemisinin.

### 3. Conclusion

The history of development of artemisinin integrates in *Pharmacy Introduction* teaching can cultivate achievement consciousness, motivate learning interests and exploration spirit and improve teaching efficiency and quality. The thawing methods can improve the learning efficiency, quality and the comprehensive ability of *Pharmacy Introduction* for nonpharmacy students.

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