

## HISTORICAL OVERVIEW OF QUININE ISOLATION AND ITS IMPORTANCE

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The use of quinine bark was first documented in 1630 by Jesuit missionaries, after which it occupied the great attention of scientists (1). In 1746 Count Claude Toussaint Marot de la Garaye was the first to crystallize a substance from quinine bark and called it "sel essentiel de quinquina", which was later found to have no clinical effects. With the development of acid-base extraction procedures, in 1820, two French scientists, pharmacists Pierre Pelletier and Joseph Caventou, isolated the active substance and called it quinine. They used the "yellow" bark of quinine, which was known to be more effective against malaria than the "gray" bark used by scientists in previous attempts at isolation. Having received numerous awards and honors, these two scientists established a factory in Paris for the extraction of quinine, an activity that is often mentioned as the beginning of the modern pharmaceutical industry. After isolation, doctors confirmed its efficacy and specificity in the treatment of malarial fever, making quinine preparations become part of the official *Materia medica*. Isolation enabled quantitative assessment of bark quality, more precise dosing and higher efficiency (1,2). Quinidine, cinchonine and cinchonidine are isolated after quinine, and the effectiveness of these four alkaloids was evaluated in one of the earliest clinical trials, conducted from 1866 to 1868 on 3,600 subjects. Quinine is included in a number of pharmacopoeias, and the *Pharmacopée universelle* describes more than 100 official quinine-based preparations for the treatment of a large number of diseases (2).

### References

1. Gachelin G, Garner P, Ferroni E, Tröhler U, Chalmers I. Evaluating Cinchona bark and quinine for treating and preventing malaria. *Journal of the Royal Society of Medicine*. 2017; 110(1), 31-40.
2. Kaufman TS, Rúveda EA. The quest for quinine: those who won the battles and those who won the war. *Angewandte Chemie International Edition*. 2005; 44(6), 854-885.

## ISTORIJSKI PREGLED IZOLOVANJA HININA I NJEGOV ZNAČAJ

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Primena kore hininovca prvi put je dokumentovana 1630. godine od strane Jezuitskih misionara, nakon čega ova biljna droga okupira veliku pažnju naučnika (1). Godine 1746. grof Claude Toussaint Marot de la Garaye prvi izoluje supstancu iz kore hininovca i nazvava je "sel essentiel de quinquina", za koju se kasnije utvrđuje da nema kliničke efekte. Sa razvojem postupaka kiselinsko-bazne ekstrakcije, 1820. godine dva francuska naučnika, farmaceuti Pierre Pelletier i Joseph Caventou konačno izoluju aktivnu supstancu i nazivaju je hinin. U ovom eksperimentu koristili su „žutu“ koru hininovca, za koju se znalo da je efikasnija protiv malarije od „sive“ kore koju su koristili naučnici u brojnim prethodnim pokušajima izolacije. Dobivši brojne nagrade i počasti, ova dva naučnika u Parizu otvaraju fabriku za ekstrakciju hinina, delatnost koja se često pominje kao početak moderne farmaceutske industrije. Ubrzo nakon izolacije lekari potvrđuju njegovu efikasnost i specifičnost u terapiji malaričnih groznica čime preparati hinina postaju deo oficinalne Matrije medike. Izolacija je omogućila kvantitativnu procenu kvaliteta kore, preciznije doziranje i veću efikasnost (1,2). Nakon hinina bivaju izolovani i hinidin, cinhonin i cinhonidin, a efikasnost ova četiri alkaloida procenjena je u jednom od najranijih kliničkih ispitivanja, sprovedenih od 1866. do 1868. godine na 3600 ispitanika. Hinin ulazi i u brojne farmakopeje, a Pharmacopée universelle opisuje više od 100 zvaničnih preparata zasnovanih na hininu za terapiju velikog broja bolesti (2).

### Literatura

1. Gachelin G, Garner P, Ferroni E, Tröhler U, Chalmers I. Evaluating Cinchona bark and quinine for treating and preventing malaria. *Journal of the Royal Society of Medicine*. 2017; 110(1), 31-40.
2. Kaufman TS, Rúveda EA. The quest for quinine: those who won the battles and those who won the war. *Angewandte Chemie International Edition*. 2005; 44(6), 854-885.