Process, Yield, and Cost of the Production of Quinine Salts from Cinchona Bark by Hoshi Pharmaceuticals in Japan during the 1920s

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1920 年代の星製薬における規那樹皮からのキニーネ塩類製造の工程と収率、経費

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Abstract

　　Quinine salts produced from cinchona bark were essential anti-malarial drugs before and during World War II. This article describes the process, yield, and cost of quinine salt production by Hoshi Pharmaceuticals Co., Ltd. in Japan during the 1920s, providing an objective understanding of industrial quinine salt production in Japan based on a report by Miyamoto Teiichi of Hoshi Pharmaceutical Co., Ltd. to the Japanese Cabinet Planning Board on 11 January 1942. The quinine salt production process involved pulverizing cinchona bark, extracting the quinine base, and converting it to quinine sulfate in the first step. This was followed by the conversion of the sulfate to hydrochloride, bisulfate, or ethyl carbonate in the second step. In the Dutch East Indies, petroleum was used as the extraction solvent, but Hoshi switched to benzene in 1923. The yield from pulverization to pure quinine sulfate production was approximately 85%, and that to produce quinine hydrochloride, quinine ethyl carbonate, and quinine bisulfate was about 80%. In 1920, the cost of producing 1 kg of purified quinine sulfate was 20.9 yen for the bark (18.56 kg), 5.4 yen for chemicals, 1.4 yen for labor, and 2.7 yen for factory costs, totaling 30.3 yen. The most significant cost was the cinchona bark. The conversion to ethyl carbonate was complex and required specialized chemicals, resulting in higher chemical and labor costs compared to other salt conversions.

（日本語要約）

　　キナの樹皮から製造されるキニーネ塩は第二次世界大戦前、中を通じて重要なマラリア薬であった。この論文では、1920 年代の星製薬におけるキニーネ塩製造の工程、収率、経費内訳を紹介する。資料は星製薬の取締役であった宮本貞一が内閣企画院の要請に応じて 1942 年 1 月に提出した報告書である。キニーネ塩の製造工程は、キナ樹皮の粉砕、キニーネ塩基の抽出、キニーネ硫酸塩への変換が第一段階で、第二段階の硫酸塩から塩酸塩、重硫酸塩、エチル炭酸塩への変換が続く。蘭印では抽出溶媒に石油を用いていたが、星製薬では 1923 年にベンゼンに切り替えた。キナ皮の粉砕から精製硫酸キニーネまでの収率は約 85％、重硫酸キニーネ、塩酸キニーネ、エチル炭酸キニーネまでの収率は約 80％であった。1920 年に 1 kg の精製硫酸キニーネを製造するコストは、樹皮（18.56 kg）20.9 円、薬品 5.4 円、労賃 1.4 円、工場費 2.7 円、合計 30.3 円で、最大のコストはキナ樹皮であった。精製硫酸キニーネから他の塩への変換工程でも最大のコストは原料の精製硫酸キニーネであった。エチル炭酸塩への変換は複雑で、ホスゲンなど特殊な薬品が必要であったので、薬品費と労賃の割合が他の塩への変換よりも多かった。

1. Introduction

　　The objective of the present study was to describe the process, cost, and yield of each step in producing quinine salts from cinchona bark, as reported by Miyamoto Teiichi of Hoshi Pharmaceutical Co., Ltd. to the Japanese Cabinet in January 1942 (Miyamoto 1942). This was to obtain an objective numerical understanding of an industrial quinine production in Japan before the Pacific War.

　　Quinine salts, derived from cinchona bark, were crucial antimalarial medications for both the Japanese military and civilians before and during World War II, even after the introduction

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Quinine [$C_{20}H_{24}N_2O_2$; MW 324.42]

Quinine sulfate dihydrate [$(C_{20}H_{24}N_2O_2)_2.H_2SO_4.2H_2O$; MW 782.94]

Quinine hydrochloride dihydrate [$C_{20}H_{24}N_2O_2. 2H_2O. HCl$; MW 396.91]

Quinine bisulfate [$(C_{20}H_{24}N_2O_2).H_2SO_4$; MW 422.50]

Quinine ethylcarbonate (Euquinine or Euchinin) [$C_{23}H_{28}N_2O_4$; MW 396.48]
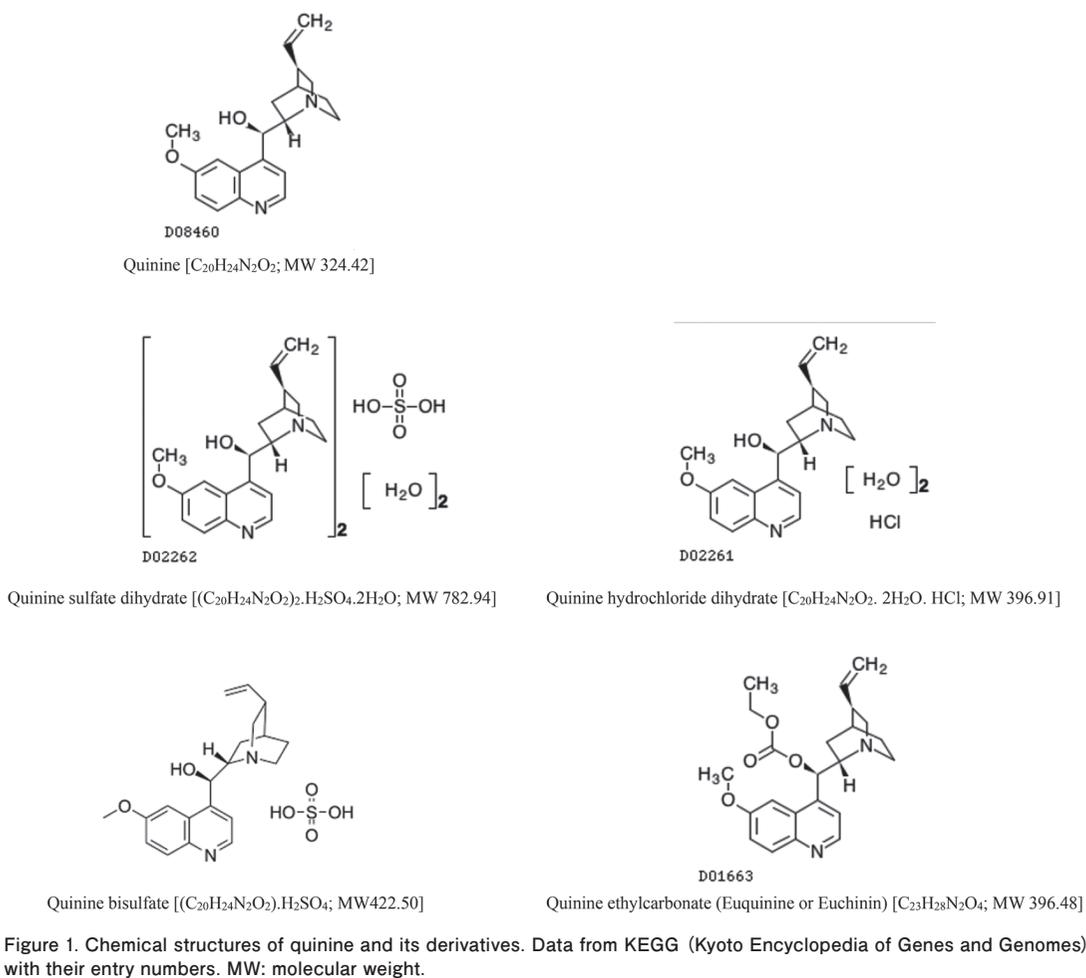
Figure 1. Chemical structures of quinine and its derivatives. Data from KEGG (Kyoto Encyclopedia of Genes and Genomes) with their entry numbers. MW: molecular weight.

of synthetic medicines such as Atebrin and Plasmochin (Sakata 2022, 2023). Since quinine [$C_{20}H_{24}N_2O_2$; MW 324.42] itself is water-insoluble, more water-soluble derivatives such as quinine sulfate (dihydrate) [$(C_{20}H_{24}N_2O_2)_2.H_2SO_4.2H_2O$; MW 782.94], quinine hydrochloride (dihydrate) [$C_{20}H_{24}N_2O_2. 2H_2O. HCl$; MW 396.91], quinine bisulfate [$C_{20}H_{24}N_2O_2 \cdot HSO_4$; MW 422.50], or quinine ethyl carbonate [$C_{23}H_{28}N_2O_4$; MW 396.48] (Figure 1) were used. Due to the low water solubility of quinine sulfate (1.2 g/liter), the other three forms were used for injection.

Japanese armed forces experienced the first severe outbreak of malaria during the expedition to Taiwan in 1874 (Sakata 2022). Thereafter, Japanese pharmaceutical companies, such as Takeda Pharmaceuticals and Hoshi Pharmaceuticals, began producing quinine salts from cinchona bark imported from the Dutch East Indies (Sakata 2022).

However, it is not easy to imagine how quinine salts were produced, how labor- or equipment-intensive the process was, and what the main cost was. Therefore, the analysis of the price and yield of the process of quinine production in Japan should give us a concrete figure of quinine production from cinchona bark at that

time, and should provide the basis to characterize the production of quinine salts in Japan.

A part of this study was orally presented at the 13th ICAS in Surabaya on 1 August 2024.

2. Data source

The data for the present study are basically based on a report entitled "Quinine Business of Hoshi Pharmaceutical Co., Ltd. (Hoshi Seiyaku Kabushikigaisha no Kina Jigyō)" (Miyamoto 1942) in the Okamoto Minoru Archive of the Diet Library of Japan. The catalogue of the Archive is electronically available (National Diet Library of Japan, 2025).

Teiichi Miyamoto of Hoshi Pharmaceutical Co., Ltd. (Hoshi in short) compiled data and submitted this report to the 4th Department of the Cabinet Planning Board[1] (Naikaku Kikakuin) on 11 January 1942. The report consisted of 473 pages of text, 12 photos, and 8 diagrams.

2.1. Author of the report

The author of the above 1942 report, Teiichi Miyamoto, was a pharmacist and a board executive of Hoshi Pharmaceuticals Co. Ltd. (Anonym 1940). He graduated from Kumamoto College of Pharmacy in 1925. He was awarded a Bachelor of Science degree from the University of California, Berkeley in 1927. He received an MSc in 1929 for his study of amino acids and a PhD in 1932 with a thesis entitled "Biochemical Study of Calcium." After working as a research assistant at UC Berkeley from July 1929 to June 1932, he became a lecturer there. Miyamoto took a position as a research assistant at the Faculty of Science, Kyoto Imperial University in April 1933. Then, Miyamoto joined Hoshi Pharmaceuticals in September 1933.

2.2. Okamoto Minoru

Okamoto Minoru (1910-2000) was a pharma-cist. After graduating from the College of Pharmacy at Chiba Medical University in March 1928 (Ministry of Finance, 1928, p. 256), he worked for Chiba Prefecture for 11 years. Then, he moved to the 4th Department of the Planning Board sometime between 1937 and 1940, where Okamoto was responsible for the supply and demand planning of pharmaceutical and hygiene-related products, including chinchona bark and quinine salts. It was Okamoto who asked several pharmaceutical companies, a trading company, and other government sectors for suggestions on setting up a supply plan for anti-malarial medicines sometime at the end of 1941.

2.2. Quinine business of Hoshi Pharmaceutical Co., Ltd.

Yang (2013) described the Hoshi Pharmaceutical Co., Ltd., stating that "The company managed plantations for growing coca and cinchona in Taiwan, at its peak in the early 1920s. In 1925, an opium trading violation raised suspicions of Hoshi. Although the company was a key supplier of medicines to Japan's military during World War II, it could not financially recover from the fallout of the opium scandal." Yang (2013) mentioned quinine sulfate production by Hoshi; however, the dissertation did not provide the numerical details of quinine production by Hoshi.

Hoshi was one of the leading companies in quinine production in Japan, besides Takeda Pharmaceuticals. According to Miyamoto, Hoshi was able to process 2,500 tons of cinchona bark per year to produce 120 tons of quinine sulfate per year. This capacity was smaller than that of the Bandoengsche Kininefabriek (BKF, Bandung Quinine Factory) in 1942, at 300 tons per year of quinine sulfate (Chief of the Staff, the Army South, 1942), but still of some significance in the world market.

Quinine sulfate, quinine hydrochloride, quinine

ethyl carbonate, and quinine bisulfate accounted for 51%, 32%, 6% and 10% of shipping weight, and 41%, 36%, 11% and 8% of sales amount of quinine salts produced by Hoshi, respectively, in fiscal year 1928. (Table 1)

The total amount of quinine salt production reached a peak of 46,965 kg in 1924. This was approximately 1/2 to 2/3 of the BKF's production from 1911 to 1914, as quoted by Miyamoto. Nevertheless, we may consider Hoshi to be one of the leading factories producing quinine salts. (Table 2)

The Opium incident in 1925 damaged Hoshi

seriously (Yang 2013), and its quinine production ceased in 1932 (Table 2). However, many buildings and facilities for quinine production remained. Accordingly, Miyamoto suggested to the Cabinet Planning Board that they repair their quinine factory to reach the following annual handling/production scale:

Pulverization	1,000,000 kg
Extraction	2,010,000 kg
Quinine sulfate	47,000 kg
Quinine hydrochloride	21,000 kg
Quinine ethyl carbonate	3,000 kg.

Miyamoto noted that the above extraction facility included an excess capacity to accommodate the extraction of other alkaloids, such as caffeine, morphine, and cocaine, which were also needed by the Japanese armed forces.

The Japanese Army conducted a survey in January 1942 to assess the condition of the once-operational quinine factory of Hoshi Pharmaceuticals (Japanese Army, 1942). This was to estimate the possibility of restoring the ability to process cinchona bark obtained in Java after the

Table 1 Sales of quinine salts by Hoshi Pharmaceuticals in fiscal year 1928.

	(kg)	(Yen)	(Yen/kg)
Quinine sulfate	11,860	311,203	26.2
Quinine hydrochloride	7,500	273,900	36.5
Quinine ethyl carbonate	1,500	86,400	57.6
Quinine bisulfate	2,500	62,400	25.0
By products	2,364	28,371	12.0

Table 2 Production of quinine (Q) salts by Hoshi Pharmaceuticals from 1917 to 1932 (kg).

Year	pure Q sulfate	Q hydrochloride	Q ethyl carbonate	Q bisulfate	Total as Q sulfate
1917	76	8			83
1918	540	110			651
1919	6,862	3,163			845
1920	11,094	10,049			10,601
1921	12,698	4,017		2,284	22,087
1922	18,438	10,056	11	2,142	19,062
1923	27,442	10,782	58	5,065	31,478
1924	27,859	11,612	147	7,347	43,728
1925	10,757	18,790	1,793	2,470	35,870
1926	16,510	11,038	1,065	2,047	31,766
1927	14,632	8,429	1,538	2,830	28,120
1928	10,330	5,143	1,534	3,498	20,647
1929	10,233	10,613	1,531	1,717	25,261
1930	3,321	1,827	243	4	5,648
1931	2,016	1,915	1		4,166
1932	71	3			74

planned seizure. The survey reported that some equipment, piping, and valves were damaged; however, they could be easily repaired with 48.9 tons of steel, the assistance of 12 engineers, and the involvement of 111 workers. The repair was expected to take approximately 60 days and cost 245,235 Yen. The predicted yearly production scale after the repair would be 1,000 tons of cinchona bark pulverization, 2,010 tons of extraction, and the production of 47 tons of quinine sulfate, 21 tons of quinine hydrochloride, and 3 tons of quinine ethyl carbonate, in agreement with Miyamoto's suggestion above. There are no records to indicate that this repair was realized.

3. Process of quinine salt production from Cinchona bark at Hoshi factory

After the pulverization of cinchona chips, natural salts of quinine, such as quinine tannate, were converted into free quinine base and extracted into an organic solvent. The quinine base was made into a sulfuric acid salt (quinine sulfate dihydrate). After purification, a portion of the quinine sulfate was used to produce other quinine salts.

3.1. Process for quinine sulfate production

Chips of cinchona bark imported from the Dutch East Indies were the starting material. The first step was the mechanical pulverization to prepare cinchona bark powder. The powder was mixed with alkaline lime milk[2] to liberate quinine base bonded with acids such as tannic acid. Quinine in the mixture was extracted with petroleum in BKF or benzene[3] in Hoshi to isolate the water-insoluble quinine base. The solution was mixed with dilute sulfuric acid to transfer the quinine base to the sulfuric acid solution. By neutralizing with soda ash[4], quinine sulfate precipitated. (Table 3)

Hoshi used petroleum extraction from 1919 to 1921, then changed to benzene extraction in 1922. Miyamoto stated that the latter was able

Table 3 Materials to produce 1 kg crude quinine sulfate by Hoshi Pharmaceuticals in 1925

Materials	(kg)	(Yen)
Cinchona bark	22.31	23.30
Benzene	1.16	0.29
Bone chrcoal	0.13	0.17
Soda ash	9.53	0.51
Sulfuric acid	1.65	0.08
Petrolium	0.06	0.01
Total		24.36

to handle more bark (2.0 vs. 3.8 t/day), used markedly less solvent (61.9% vs. 4.8% of the bark mass), and resulted in better yield of purified quinine sulfate (4.4% vs. 5.1% of the bark mass).

According to the report from the 16th Army of Japan in 1942 (JGSDF Medical School 1972, 200–203), just after the seizure of BKF, 2 liters of petroleum were necessary to extract quinine from 1 kg of cinchona bark, and the 16th Army required to send 900 kiloliters of petroleum (boiling point 180°C) from Sumatra for a half-year operation of the BKF. Hoshi used approximately 1/4 of petroleum as BKF to extract from the same amount of cinchona bark. It is possible that Hoshi saved the consumption of precious petroleum by sacrificing the yield.

The difference in the extraction solvent between BKF and Hoshi may have reflected the difference in their industrial background. BKF should have easy access to petroleum produced within the Dutch East Indies. However, Japan imported practically all of its petroleum before the Pacific War. On the other hand, Japan had many coal mines in the inland and in Manchuria. Chemical industries based on coal also developed in Japan. Thus, it should have been easier to obtain benzene than petroleum in Japan[5].

The precipitated crude quinine sulfate was purified to produce pure quinine sulfate by ab-

sorbing contaminants on bone charcoal. Pure quinine sulfate was converted to other salts such as quinine hydrochloride, quinine ethyl carbonate, or quinine bisulfate.

3.2. Process for quinine hydrochloride production

Pure quinine sulfate was dissolved in 15 times the volume of hot dilute hydrochloric acid, and then further mixed with a hot barium chloride solution. The precipitated quinine hydrochloride crystals were obtained by filtration while the mixture was still hot.

3.3. Process for quinine bisulfate production

To obtain crystallized quinine bisulfate, quinine sulfate was dissolved in warm distilled water plus diluted sulfuric acid, and then left to stand.

3.4. Process for quinine ethyl carbonate ester production

Production of quinine ethyl carbonate ester (Euchinin) was more complex than the production of other salts. Phosgene gas, made from carbon monoxide and chlorine gas, was introduced to ice-cold pure ethyl alcohol to produce diethyl carbonate ester. Quinine bisulfate and benzene were brought to a boil over a water bath, while ethyl carbonate was gradually added to obtain a quinine ethyl carbonate ester dissolved in benzene. Then, benzene was removed by distillation. After the distillation of benzene, the residue was dissolved in water with an excess of natron[6] filtrate to obtain a candy-like crude quinine ethyl carbonate ester. The crude quinine ethyl carbonate ester was dissolved in ethyl alcohol, and then water was added to obtain pure quinine ethyl carbonate ester crystals.

4. Yield of quinine salt production

4.1. Yield of quinine sulfate production from cinchona bark

The following analysis indicated that the purification of crude quinine sulfate to pure quinine sulfate was accompanied by the largest loss of quinine.

4.1.1. Pulverization

The pulverization was a simple mechanical step. The actual loss ranged from -0.15% to 2.1%. Miyamoto considered the negative loss to be due to the increase in weight caused by absorbing atmospheric water after pulverization. The loss of 2.1% was attributed to the insufficient collection of the powder left in the vessel. He considered that a 1% loss should have been an appropriate figure for the loss during pulverization, meaning the yield of 99% through this process.

4.1.2. Yield of crude quinine production

The extraction process was cumbersome and challenging. It took Hoshi a year to plan and construct the factory for extraction. Hoshi tried various methods and finally decided to employ a batch system using hot benzene as the solvent. The production of crude quinine sulfate from cinchona powder by Hoshi was accompanied by a loss of 13.6% or 7.8%, using petroleum extraction or benzene extraction, respectively. The higher loss of petroleum extraction was confirmed by the detection of a certain amount of quinine sulfate in the residues after petroleum extraction in 1924.

4.1.3. Yield for the purification of quinine sulfate

The overall mean yield of the purification of quinine sulfate from 1919 to 1932 was 90.6%. (Table 4) In other words, approximately 10% of the quinine base was lost during this process. The mean yield was improved from 83.6% be-

Table 4 Yield of crude and pure quinine sulfate (Q-SO$_4$) from cinchona bark by Hoshi Pharmaceuticals from 1919 to 1931, with means of different time frames calculated by the present author.

Year	crude Q-SO4 (% of processed bark)	pure Q-SO4 (% of processed bark)	pure Q-SO4 (% of crude Q-SO4)
1919	3.6	3.6	99.1
1920	6.2	4.8	77.9
1921	5.2	3.9	73.6
1922	5.8	5.0	86.7
1923	5.5	4.6	83.9
1924	5.8	4.7	80.5
1925	5.8	6.2	106.9
1926	6.9	6.3	91.2
1927	5.3	6.4	119.1
1928	7.1	6.2	87.4
1929	7.3	6.9	94.7
1930	6.9	6.1	88.7
1931	6.3	5.6	87.9
Overall mean	6.0	5.4	90.6
Mean 1919-1921	5.0	4.1	83.6
Mean 1922-1930	6.3	5.8	93.2

tween 1919 and 1921 (with petroleum extraction) to 93.2% between 1922 and 1930 (with benzene extraction).

Nevertheless, approximately 7% of quinine was still lost during this simple process. Takeda Pharmaceuticals improved this step by changing from the water recrystallization method, which had been used since 1924, to the acidic quinine sulfate method in 1926. They further repeated minor improvement and became able to obtain high-quality quinine sulfate crystals easily by 1929 (Sakata 2022). However, there was no mention of such an improvement in Miyamoto's report.

4.2. Yield of the conversion into other quinine salts

The yield of converting purified quinine sulfate into quinine hydrochloride, quinine ethyl carbonate, or quinine bisulfate was 94% to 95% of the theoretical value. Although the loss was smaller than during the extraction and purification of quinine sulfate, it could have caused the shift from quinine hydrochloride to quinine sulfate in the standard treatment procedure of the Japanese Army in 1940 (Takeda 200nenshi Henshū Iinkai 1983, 295; Anonym JACAR Ref. C13120606800; Sakata 2022).

4.3. Overall yield

The yield from pulverization to pure quinine sulfate production was approximately 85% (0.990 × 0.922 × 0.927=0.846). The overall yield of quinine hydrochloride, quinine ethyl carbonate, and quinine bisulfate should be about 80%.

5. Cost of quinine salt production

The largest cost for pure quinine sulfate production was the cost of cinchona bark. The largest cost for producing other quinine salts was the main material, pure quinine sulfate. Therefore, the cost of cinchona bark was the major

Table 5 Buildings for the quinine factory of Hoshi Pharmaceuticals

Factory for	Structure	Total area (m²)	Construction cost (Yen)
Pulverization	Two-story wooden building with zinc roofing	409	8,698
Extraction	Single-story building made of iron mesh and concrete	449	24,480
Crude quinine sulfate	One floor of a three-story brick and concrete building	502	45,600
Pure quinine sulfate and quinine sulfate dihydride	One floor of a three-story reinforced concrete building	634	56,900
Quinine hydrochloride	One floor of a three-story brick and concrete building	502	45,600
Quinine ethylcarbonate	One floor of a three-story reinforced concrete building	158	14,400

determinant of the cost of all quinine products by Hoshi.

5.1. Initial investments in the buildings and equipment

The following tables (Tables 5–11) indicate that the processes for pulverizing and extracting quinine required a substantial investment in both buildings and equipment.

5.1.1. Buildings

The areas of buildings for different processes were not significantly different, except for those related to quinine ethyl carbonate production. However, the cost of building varied. (Table 5) Buildings to produce final products costed more.

5.1.2. Equipment

Extraction required an expensive extraction machine. Equipment to reuse benzene (condenser and benzene tank) was also costly. On the other hand, the investment for producing quinine hydrochloride or quinine ethyl carbonate was not substantial.

5.1.2.1. Equipment for pulverization

The most significant investment for the pulverization was 14 crushers. (Table 6) This indi-

Table 6 Equipment for pulverization

Equipment	Quantity	Price
Crusher	14	9,401
Bucket elevator	1	7,185
Rolling mill	1	2,900
Conveyor	1	3,269
Packer	1	145
Dust collector	1	79
Kneading machine	2	2,431
Centrifugal pump	1	115
Automatic parallel sieve	2	2,156
Motor	7	5,869
Total		33,541

cates that Hoshi pulverized cinchona bark in parallel, a necessity to handle very bulky materials.

5.1.2.2. Equipment for extraction

The investment in equipment for the extraction process was the largest among all processes. (Table 7) Many leaching machines, condensers, and tanks for benzene indicate that the extraction was conducted in parallel to handle a large amount of cinchona powder. These are the

Table 7 Equipment for extraction

Equipment	Quantity	Price
Leaching machine	8	61,011
Washington pump	9	3,780
Condenser	10	37,817
Heater	2	6,490
Separater	12	7,792
Filter	6	3,732
Conveyer	1	17,357
Motor	2	3,882
Tanks for benzol	11	31,082
(total capacity 26,000 L)		
Total		172,941

main investments for this process.

5.1.2.3. Equipment to produce quinine salts

Equipment for the processes to obtain different quinine salts costed less than 40% of the cost of extraction. (Tables 8-11) The equipment used to conduct the reaction and recover the resultant crystals, including a pump, filter, centrifuge, and distiller, comprised the central part of the investment for these processes.

Table 8 Equipment for crude quinine sulfate production

Equipment	Quantity	Price
Compression filter	1	1,295
Turbine pump	1	328
Rotary pump	5	1,636
Washington pump	4	1,693
Squeeze pump	2	3,105
Centrifuge	3	6,942
Cooling tank	15	3,000
Motor	5	4,120
Total		67,781

Table 9 Equipment for pure quinine sulfate and quinine sulfate bisulfate production

Equipment	Quantity	Price
Washington pump	2	1,370
Vacuum pump	3	1,200
Rotary pump	10	4,376
Squeeze pump	1	875
Centrifuge	5	9,075
Filter	9	5,400
Water distiller	1	1,782
Double pot	4	850
Iron tank	30	6,260
Tank for crystal	40	4,000
Distiller	1	8,306
Motor	8	4,850
Total		48,344

Table 10 Equipment for quinine hydrochloride production

Equipment	Quantity	Price
Press filter	4	2,479
Vacuum pump	1	1,654
Centrifuge	3	3,207
Washington pump	1	395
Filter press	2	1,304
Rotary pump	1	427
Air compresser	1	390
Ether distiller	1	355
Water distiller	1	265
Vacuum evaporator	2	3,593
Mixer	2	690
Vacuum tank	2	780
Motor	2	450
Total		15,034

Table 11 Equipment for quinine ethylcarbonate production

Equipment	Quantity	Price
Cupper distiller	3	7,536
Washington pump	2	750
Centrifuge	7	1,750
Decolorization machine	2	1,560
Distiller	2	2,700
Double pot	3	888
Filter	5	542
Total		15,726

5.2. Operational cost

5.2.1. Cost of cinchona bark

The cost of the cinchona bark at the delivery to the Hoshi factory was 1.14 to 1.17 yen/kg. The cost of the bark itself was 93.2% or 97.2 % before or after joining the Quinine Convention, respectively. (Table 12) Thus, quinine bark was a highly valued and expensive commodity. Joining the Quinine Convention almost halved the miscellaneous cost. However, this difference was by far smaller than the price fluctuation of the bark itself.

Miyamoto provided a precise batch-wise detail of the cost from the port in Java to the Hoshi factory in Tokyo. The case for batch number 513 (date unknown) involved 60,972.2 kg of cinchona bark, containing 3,509.524 kg of quinine sulfate, as follows.

Cost before handling over to Hoshi in Batavia (Jakarta) port[7].

Bark	56,752.41 guilders
1/2 Sampling fee	44.55
1/2 Analysis fee	184.40
Warehouse	70.05
Insurance	26.78
Freight	305.50
Loading	72.84
Customs duty	162.95
Communication	75.00
Commission	1,287.26
Stamp fee	30.00
Shipping commission	75.34
Sub-total	58,671.79 guilders
	(56,559.70 yen)
Interest	2,064.44 yen
Total:	58,624.14 yen

Cost thereafter

Warehouse	1,236.30 yen
Freight	1,423.78
(Batavia to Yokohama)	
Insurance	510.00
Unloading and labor	513.38
Sorting	67.55
Transportation for inspection	
	12.40
Inspection laborers	19.40
Freight	526.89
(Yokohama to Tokyo)	
Handling fees	13.50
Total	4,362.70 yen

Grand total	62,968.84 yen
	(1.033 yen/kg bark)
	(17.942 yen/kg quinine sulfate)

Table 12 Cost of the cinchona bark before (from January 1923 to January 1927) and after (from January 1927 to December 1930) joining the Quinine Convention.

		Befor joining	After joining
Amount of imported bark	(kg)	2,469,525.228	1,166,640.464
Price of bark	(Yen)	2,358,233.478	1,329,815.19
	(Yen/kg)	0.955	1.140
Miscellaneous cost	(Yen)	182,929.06	38,687.105
	(Yen/kg)	0.074	0.033
Total cost	(Yen)	2,678,422.44	1,368,502.295
	(Yen/kg)	1.085	1.173

Table 13 Cost of crude quinine production.

		Bark	Chemicals	Wages	Factory operation	General cost	Total
Feb. - Mar. 1921	(Yen/kg)	23.6	6.0	1.4	2.8		33.7
	(%)	70	18	4	8		100
Mar. - Apr. 1921	(Yen/kg)	20.5	4.2	0.7	1.5		26.8
	(%)	76	16	2	5		100
Jun. 1923 - Sep. 1926	(Yen/kg)	20.5	1.2	0.8	2.0	1.2	25.7
	(%)	80	5	3	8	5	100

5.2.2. Cost of the processing for quinine salts

Material (cinchona bark for crude quinine sulfate, and purified quinine sulfate for other salts) was the main cost for all quinine salts; approximately 70–80% for crude quinine sulfate, 80% for pure quinine sulfate, 90% for quinine hydrochloride, and 65% for quinine ethyl carbonate. (Table 13)

5.2.2.1. Cost of crude quinine production

The cost of starting material, cinchona bark, accounted for 70%–80% of the cost to produce crude quinine sulfate. However, pulverization and extraction required the handling of bulky material and used a large amount of benzene. The total cost, as well as the proportion of chemicals and wages in Table 13, shows the improvement of this process.

5.2.2.2 Cost of quinine salts production

Chemicals and wages accounted for 25% and 10% of the cost of quinine ethyl carbonate production from purified quinine sulfate, respectively. (Table 14) For other products, chemicals, wages, and factory and general costs accounted for a minor portion, at most 6% of the total cost.

The production of quinine ethyl carbonate required more chemicals, factory operation, wages, and depreciation than those of other quinine salts. This reflects the complex process using various chemicals, equipment, and energy to produce quinine ethyl carbonate.

The additional cost of 4.1 yen/kg to produce quinine hydrochloride from pure quinine sulfate might have been one of the causes to shift the army standard treatment protocol from quinine hydrochloride to quinine sulfate in 1940 (Takeda 200nenshi Henshū Iinkai 1983, p. 295;

Table 14 Cost of quinine salts production in fiscal year 1928.

		Material	Chemicals	Factory operation	Wages	Depreciation	Others	Total
Pure quinine sulfate	(Yen/kg)	37.5	3.3	2.6	1.5	0.6	1.1	46.4
	(%)	81	7	6	3	1	2	100
Quinine hydrochloride	(Yen/kg)	46.4	0.5	1.5	0.9	0.3	0.8	50.5
	(%)	92	1	3	2	1	2	100
Quinine ethyl carbonate	(Yen/kg)	46.4	4.5	7.1	4.5	3.1	4.3	70.0
	(%)	66	6	10	6	4	6	100

Anonym, JACAR Ref. C13120606800; Sakata 2022).

6. Conclusion

The quinine salt production process involved pulverizing cinchona bark, extracting the quinine base, and converting it to quinine sulfate in the first step. This was followed by the conversion of the sulfate to hydrochloride, bisulfate, or ethyl carbonate in the second step. The use of benzene by Hoshi, instead of petroleum in BKF, for quinine extraction was characteristic and reflected the Japanese resource situation.

The yield from pulverization to pure quinine sulfate production or quinine bisulfate production was about 85%. The overall yield to produce quinine hydrochloride and quinine ethyl carbonate was about 80%. The loss during the extraction and purification of quinine sulfate was significant.

The most considerable cost was the cinchona bark for all products. Therefore, the price of cinchona bark, which the Kina Bureau controlled before the Japanese invasion of the Dutch East Indies, had significant implications for Hoshi's quinine business. The conversion of quinine sulfate to quinine hydrochloride and quinine bisulfate was simple and less labor-intensive. The conversion to ethyl carbonate was complex and required special chemicals, resulting in higher chemical and labor costs compared to other salt conversions.

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[1] Article 1 of the Planning Board's Official Regulations dictates that the Planning Board is under the control of the Prime Minister and is responsible for the following affairs: 1. Drafting plans for the expansion and operation of the overall national power in times of peace and war, and submitting them to the Prime Minister with explanations; 2. Reviewing the outline of important matters related to the expansion and operation of the overall national power in times of peace and war, that are submitted to the Cabinet by the Ministers of each ministry, and submitting them to the Cabinet through the Prime Minister with opinions of the Board; 3. Submitting opinions regarding budgetary control of important matters related to the expansion and operation of the overall national power in times of peace and war to the Cabinet through the Prime Minister; 4. Coordinating and unifying the affairs of each agency related to the establishment and implementation of the national mobilization plan. (Kikakuin 1941, 1)

[2] A mixture of calcium hydroxide and water.

[3] In Japan, benzene fractions were recovered as by-products of coke ovens and city gas production, and used as a raw material for dyes and chemical intermediates.

[4] Crude sodium carbonate, Na_2CO_3.

[5] The benzene production in Japan was calculated to be 1,137~2274 tons as follows. We may assume that the 0.05 ton of crude coal tar was produced by the production of 1 ton of coke, and that approximately 5% to 10% of benzene was obtained from crude coal tar (Mochida and Korai 1991). The annual coke production in Japan was 454,800 tons in 1940 (Shimono 1986), from which $454,800 \times 0.05 = 22,740$ tons of coal tar should have been produced, from which $22,740 \times 0.05 \sim 0.10 = 1,137 \sim 2274$ tons of benzene should have been produced.

[6] Natron is a naturally occurring mixture of sodium carbonate decahydrate ($Na_2CO_3 \cdot 10H_2O$) and around 17% sodium bicarbonate ($NaHCO_3$), along with small quantities of sodium chloride and sodium sulfate.

[7] The exporter and the importer shared the cost for sampling and analysis according to the rule of the Quinine Convention.