



Recent Poisoning by *Benikoji* Supplements (Choleste-Help) in Japan

Shaw Watanabe*

Tokyo University of Agriculture, Japan

*Corresponding Author: Shaw Watanabe, Tokyo University of Agriculture, Japan.

Received: October 03, 2024

Published: November 01, 2024

© All rights are reserved by Shaw Watanabe.

Fermented foods have contributed to healthy longevity in Japan, but the recent poisoning by red yeast rice supplements is a reputational hazard for koji foods [1]. Japan is a treasure trove of fermented and brewed foods such as miso, soy sauce, natto, sake, and shochu, which are made from three types of actinomycetes: black, white, and yellow yeast, collectively known as “Japanese yeast molds”. Red yeast mold (*Benikoji*) belongs to the same phylum as the Japanese yeast mold, the *Euromycota*. Still, it is divided into the *Monasciaceae* and *Aspergillaceae* families, which are entirely different types of molds.

Red yeast has been used to make Chinese rice wine and Okinawan fermented tofu. In Japanese koji, seed koji is planted on rice and becomes koji in about three days. Fermentation for another five days produces many spores on the surface. The seed koji maker selects the best spores from these spores individually. Kobayashi Pharmaceutical Co. began producing *Benikoji* about 40 years ago to obtain red dye but extended the incubation period to 50 days to extract a particular ingredient as many as possible. This facilitated the invasion of miscellaneous bacteria and the coexistence of blue-green mold, and the sloppy production control system is believed to have resulted in the shipment of defective products.

In the case of a health food containing Kobayashi Pharmaceutical's red yeast ingredient that caused kidney problems in people who consumed it, 52 companies supplied the ingredient, which was found to have been sold to other companies through several of these wholesalers. These include prestigious companies such as Kibun Shokuhin, Takara Shuzo, Mamefuku, and Takeya Miso.

Of the 225 companies to which *Benikoji* ingredients were shipped, five products from five companies exceeded the daily intake (100 mg) of *Benikoji*, which has been reported to cause health problems.

Kobayashi Pharmaceutical Co announced a voluntary recall of health supplements containing this ingredient on March 22, and several companies that had been supplied with *Benikoji* also fol-

lowed suit. The three recalled supplements are Red Yeast Rice Cholestehelp (45 capsules for 15 days, 90 capsules for 30 days, 60 capsules for 20 days), Naisi Help + Cholesterol, and Nattokinase Sarasara Granules GOLD.

Osaka Prefecture conducted interviews at health centers nationwide. On May 15, the Ministry of Health, Labor and Welfare compiled the results of their analysis of approximately 2,050 people who complained of health problems [2]. As for the 1,467 people for whom the month of onset was known, 70% of all cases occurred between November of last year and March of this year. The daily intake was as used in 1684 (82%), small amounts in 257 (13%), excessive amounts in 22 (1%), other in 12 (1%), and unknown in 75 (4%). 1015 (50%) were taking other health foods concomitantly, 944 (46%) were not, and 91 (4%) were unknown. There were five deaths, but on June 28, Kobayashi Pharmaceutical Co announced that another 76 deaths were suspected to be related to red yeast Cholesteherp [2].

The company launched “*Benikoji* colestehelp” in 2021. This was the first functional food labeled with ingredients derived from *Benikoji*, and sold more than million tablets.

Symptoms included edema, headache, fatigue, anorexia, nausea/vomiting, palpitations/shortness of breath, dizziness, lightheadedness, etc. Many patients presented with Fanconi syndrome due to tubular damage, 57% of whom received outpatient treatment only, 5% recovered after hospitalization, and 3% had kidney and other dysfunctions. The proportion of patients who did not receive medical treatment was 35%. Thirty-five percent of the patients did not visit a medical institution.

Treatment is often steroids, but sometimes hemodialysis is used temporarily to compensate for severely deteriorated kidney function. The reason for such a large number of patients is that Kobayashi Pharmaceutical Co was slow to disclose information. The company first learned of the kidney disease cases on January 15, 2024. It took two months to disclose the risk information to the public.

In addition, problems surrounding Kobayashi Pharmaceutical's red yeast rice supplements, a product containing red yeast rice ingredients that may have been contaminated with "puberulic acid," which is derived from blue mold.

Furthermore, in the issue surrounding Kobayashi Pharmaceutical's red yeast rice supplements, two companies were found to have sold products containing red yeast rice material that may have been contaminated with "puberulic acid," which is derived from contaminated blue mold.

Red yeast rice has long been used as a food coloring agent in China and Taiwan. In addition, the component called lovastatin in *Benikoji* has a cholesterol-lowering effect, and many health foods derived from *Benikoji* have been sold. On the other hand, *Benikoji* contains a toxin called citrinin, which may cause kidney disease.

The non-toxic dose is 20 ug/kg body weight, and the level of no concern for nephrotoxicity is 0.2 ug/kg body weight/day multiplied by an uncertainty factor of 100. In Europe, there have been reports of health hazards from *Benikoji*, and the standard level of citrinin in health foods has been set at 2 mg/kg of body weight. In France, the doctor must be consulted, and in Switzerland, products with red yeast rice as an ingredient are prohibited from being sold or traded [4]. The U.S. is not promoting the sale of lovastatin-containing *Benikoji* in 2021 because of the risk of severe side effects.

According to Kobayashi Pharmaceutical Co, *Benikoji* products do not contain citrinin, but instead, puberulic acid was found [5]. National Institute of Health Sciences May 28 Identified Puberulic acid and two other compounds only in lots with damage information. It was estimated that puberulic acid was produced by blue-green mold collected from both Wakayama and Osaka factories, and the other two compounds were produced by modification of monacolin K through co-cultivation with *Benikoji* and blue mold.

More than 8,000 functional foods have been registered, but there are unforeseen dangers when active ingredients are extracted and concentrated from natural foods and included. In addition, it is difficult to know how far the damage could spread when many companies supply raw materials for production. We want to ensure safety through a diet based on natural foods [6].

Bibliography

1. www3.nhk.or.jp
2. xtech.nikkei.com
3. www.kobayashi.co.jp
4. <http://eur-lex.europa.eu/LexUriServ.do?uri=OJ:L2014:067:0003:0004:EN:PDF>
5. Food Safety Committee.
6. Watanabe S. "Medical Foods: Beyond the Functional Food Claim". *Acta Scientific Nutritional Health* 8.2 (2024): 37-40.