This is provisional English translation of an excerpt from the original full report.

Risk Assessment Report

Dipotassium DL-Tartrate

(Food Additive)

Food Safety Commission of Japan (FSCJ)
September 2020

ABSTRACT

The FSCJ conducted a risk assessment of dipotassium DL-tartrate (CAS No. none), an additive used as a food manufacturing agent, based on results from various studies.

The data of the following studies were analyzed: toxicokinetics; genotoxicity; acute toxicity; repeated dose toxicity; and scientific findings in human, etc. of DL-tartaric acid, DL- tartrate, tartaric acid or tartrate.

The FSCJ examined the potassium ions and D-, L-tartrate ions which are expected to be produced *in vivo* when an additive dipotassium DL-tartrate is administered orally.

Potassium ion

The FSCJ did not conduct advanced evaluation of the toxicokinetics and toxicity of potassium ion because there had been no new findings since the previous assessments for this substance. Taking into the following all facts, the FSCJ determined that potassium derived from dipotassium DL-tartrate is of no concern for food safety as long as it is used appropriately as a food additive:

- Potassium is an ion widely distributed in human blood, urine and each organ;
- Target intake of potassium is 2,600 ~ 3,000 and more mg/person per day for men/women of 18 years and over; and
- The estimated daily intake (EDI) of potassium derived from dipotassium DL-tartrate used as an additive (1.17 mg/person per day) is very small, about 0.050 % of current daily intake of potassium (2,362 mg).

D-, L-tartrate ions

The FSCJ conducted the extensive assessment based on the data of DL-tartaric acid and DL-tartrate which are expected to produce D-, L-tartrate ions.

Toxicokinetics of dipotassium DL-tartrate

Insoluble calcium salt of DL-tartaric acid is likely to be accumulated in the kidney of rat. Meanwhile, the FSCJ noted that interspecies difference among animals are assumed and absorption rate of humans is lower than that of rats.

From the fact that dipotassium DL-tartrate was negative both *in-vitro* reverse mutation test and chromosomal aberration test, the FSCJ determined that dipotassium DL-tartrate has no genotoxicity relevant to human health.

Evaluating data of a 13-week repeated dose study of potassium DL-bitartrate in rats, Inoue et al. (2015) reported that an increasing trend in urinary WBC count and urinary protein level was observed in a group of rats dosed 0.5 % of potassium DL-bitartrate reputedly. This report together with histopathological findings suggested adverse effects on the kidney. Consequently, the FSCJ identified the NOAEL of 60 mg/kg bw per day (DL-tartaric acid) for a group of rats treated with 0.125 % potassium DL-bitartrate in this report.

Judging from the obtained human data, the FSCJ determined that a NOAEL could not be identified.

Given the above, the FSCJ established the NOAEL of DL-tartaric acid of 60 mg/kg bw per day.

On the basis of the explanation of the applicant to request the Ministry of Health, Labour and Welfare for designating “Dipotassium DL-Tartrate” as an additive and setting its standards, the FSCJ estimated daily intake of DL-tartaric acid on the assumption of the maximum calcium concentration in wine of 210 mg/L-which might be possibly overestimated. Presuming a removal process in accordance with the recommended dietary allowance relevant to this concentration, the FSCJ estimated the residue of DL-tartaric acid in wine of 46.7 mg/L. Adding the intake amount of the production statistics survey to this value, the FSCJ estimated the daily intake of DL-tartaric acid of 0.0409 mg/kg bw per day.

Research papers indicate that most of “DL-potassium tartrate” is removed by filtration because this substance aims at precipitating and removing excess calcium in wine as “calcium DL-tartrate” under the standards for use (draft). On this ground, the FSCJ assumed that the intake of DL-tartaric acid derived from additive “dipotassium DL-tartrate” would be small. Further, the FSCJ thought that the following facts need to be taken into account for the intake of additive “dipotassium DL-tartrate”:

1) While DL-tartaric acid, sodium DL-tartrate and potassium DL-bitartrate are the specified additives already used as food additives, any major food safety issues from its use has not been raised;

2) The above-mentioned estimated daily intake (EDI) of DL-tartaric acid was overestimated on the assumption of maximum calcium concentration in wine of 210 mg/L. Therefore, actual intake of DL-tartaric acid is deemed to be less than that value; and

3) Dipotassium DL-Tartrate has been already ingested due to the following reason:

- a small amount of D- tartaric is produced from L-tartaric in wine; and
- DL-tartaric acid is contained in wine prior to the addition of the assessed item.

From the above findings, intake of DL-tartaric acid derived from additive “dipotassium DL-tartrate” appears to be small. Subsequently the FSCJ decided to carry out the assessment applying the MOE (Margin of Exposure).

There is a sufficient safety margin between NOAEL of 60 mg/kg bw per day (DL-tartaric acid) and the domestic EDI of DL-tartaric acid (0.0409 mg/kg bw per day) relating to use of additive “dipotassium DL-tartrate”. For that reason, the FSCJ determined that DL-tartaric acid derived from additive “dipotassium DL-tartrate” is of no concern relevant to human health as long as used appropriately as an additive.

The FSCJ concluded that additive “dipotassium DL-tartrate” has no concern relevant to human health as long as used appropriately as an additive, subject to the above-mentioned assessment of potassium ion and D-, L-tartrate ions.