

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

Risk Assessment Report

Zinc gluconate (Food Additives)

Food Safety Commission of Japan (FSCJ)
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ABSTRACT

FSCJ conducted a risk assessment of zinc gluconate (CAS No. 4468-02-4, as zinc gluconate anhydride), an additive used as a nutritional enrichment, based on results from various studies.

The data used in the assessment include genotoxicity, acute toxicity, repeated dose toxicity, carcinogenicity, reproductive and developmental toxicities, and human data on zinc gluconate as the test substance.

FSCJ considered it appropriate to evaluate as the intake of zinc on the assessment of zinc gluconate. Zinc as an essential nutrient for living organisms is also considered in the assessment. According to the report from Study Group for Development of Dietary Reference Intakes for Japanese (2015), the recommended intake of zinc for an adult was 7~10 mg/person which is equivalent to 0.13~0.18 mg/kg bw/day assuming that the average body weight is 55.1 kg.

Ministry of Health, Labour and Welfare (MHLW) requested FSCJ to revise the standards for use of zinc gluconate for a supplementation of zinc to comprehensive nutritional foods which are used as a substitute for a hospital diet. An addition of zinc gluconate is currently approved as Food with Health Claims up to the recommended daily intake of 15 mg as zinc. FSCJ therefore decided to assess food safety risk of zinc considering for ordinary people who intake zinc only from meals or from both meals and Food with Health Claims, as well as for the people who intake zinc solely from zinc-supplemented nutritional foods for patients.

Data on pharmacokinetics of zinc gluconate suggest that zinc is absorbed after dissociation with gluconate at high pH conditions, in spite of the presence as zinc gluconate in gastric pH environment.

Mean bioavailabilities of zinc compounds have been reported to be from 49.9% to 61.3%. After intakes of zinc gluconate or zinc citrate, their bioavailabilities were estimated to increase to about 60% due to inhibition of complex formation between zinc and food ingredients. These values are higher than that of zinc oxide, 49.9%.

The intake of zinc is thus assessed based on the data of zinc gluconate among zinc compounds.

FSCJ concluded that zinc gluconate as an additive has no genotoxicity relevant to human health.

At human intervention researches on zinc gluconate, superoxide dismutase (SOD) activity of red blood cells is reported to decrease at the dose equivalent to zinc of 65.92 mg/person/day (0.94 mg/kg bw/day). Although the effect is unlikely to cause directly the clinical symptoms, FSCJ considered it as a toxicologically suggestive event induced from the intake of zinc gluconate. Hence, FSCJ specified a low-observed-adverse-effect level (LOAEL) for toxicity of zinc gluconate to be 65.92 mg/person/day (0.94 mg/kg bw/day) as zinc. No reliable data was available for evaluation of the carcinogenicity.

On the additive use of zinc gluconate, FSCJ has recognized the necessity to specify an upper limit for intake of zinc for both the people who eat comprehensive nutritional foods for patients and ordinary people who eat ordinary meal, in considering with the observed toxicity and the daily intake of 30 mg/person/day as zinc estimated for the use as comprehensive nutritional foods in Japan. On the specification of the upper limit, FSCJ considered the following facts. FSCJ specified LOAEL for toxicity of zinc gluconate to be 65.92 mg/person/day (0.94 mg/kg bw/day) as zinc based on the decrease in SOD activity in red blood cells, although the decrease was only a slight. It is considered the fact that zinc is an essential nutrient for living organisms. Consequently, FSCJ specified an upper limit for intake of zinc gluconate for both patients, who eat as the comprehensive nutritional foods, and non-patients who eat ordinary meal, to be 0.63 mg/kg bw/day as zinc dividing 0.94 mg/kg bw/day by an uncertainty factor of 1.5. It is to note that an uncertainty factor of 1.5 was also used for calculating tolerable upper intake level in the report from Study Group for Development of Dietary Reference Intakes for Japanese (2015), and in Institute of Medicine (IOM).

In addition, relevant organizations should call appropriately people's attention to prevent from excess intakes of zinc in considering the amount of zinc from ordinary meal.

The above mentioned upper limit for intake of zinc gluconate, for both the patients ingesting comprehensive nutritional foods and non-patients eating ordinary meal, was the value for adults of above 18 years old. Although zinc is an essential nutrient for living organisms, excess intake of zinc by children, infants, pregnant and lactating women shall be prevented through the appropriate calling for attention.