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# Risk Assessment of "Other Substances" – L-Tyrosine

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***Authors' contributions***

*This work was carried out in collaboration among all authors. The opinion has been assessed and approved by the Panel on Nutrition, Dietetic Products, Novel Food and Allergy of VKM. All authors read and approved the final manuscript.*

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## ABSTRACT

The Norwegian Scientific Committee for Food Safety (Vitenskapskomiteen for mattrygghet, VKM) has, at the request of the Norwegian Food Safety Authority (Mattilsynet; NFSA), assessed the risk of "other substances" in food supplements and energy drinks sold in Norway. VKM has assessed the risk of doses given by NFSA. These risk assessments will provide NFSA with the scientific basis for regulating the addition of "other substances" to food supplements and other foods.

"Other substances" are described in the food supplement directive 2002/46/EC as *substances other than vitamins or minerals that have a nutritional or physiological effect*. It is added mainly to food supplements, but also to energy drinks and other foods. VKM has not in this series of risk

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assessments of "other substances" evaluated any claimed beneficial effects from these substances, only possible adverse effects.

The present report is limited to the use of L-tyrosine in food supplements. Risks related to tyrosine added to food and drinks, protein hydrolysates or high dietary protein intake are outside the scope of the opinion. The report is based on previous risk assessments of tyrosine and scientific papers retrieved from a comprehensive literature search.

L-tyrosine, an aromatic amino acid, is considered a conditionally indispensable amino acid because it can be synthesised from L-phenylalanine in the liver. The magnitude of endogenous synthesis of L-tyrosine is not known, but is related to the intake of phenylalanine.

L-tyrosine is a precursor of several biologically active substances, including catecholamine neurotransmitters, thyroid hormones and melanin skin pigments. L-tyrosine is available from all protein-containing foods such as meat, eggs, fish, dairy products, grains and pulses. According to information from the NFSA, L-tyrosine is an ingredient in food supplements sold in Norway. The NFSA has requested a risk assessment of the following doses of L-tyrosine food supplements: 1250 mg/day, 1500 mg/day, 1750 mg/day, and 2000 mg/day. Dietary intake of tyrosine in Norway is not known, but data from NHANES III (USA) suggest a mean dietary intake of about 2.8 g per day.

In phase 1 seven previous reports that assessed the safety of L-tyrosine supplementation in humans were identified. For the present report, a literature search was performed to retrieve relevant human or animal studies on the safety of L-tyrosine. One relevant animal study assessing the toxicity of tyrosine by feeding rats different doses of tyrosine daily by oral gavage for 13 weeks was identified. No human studies have been identified.

No major specific issues related to adverse effects from L-tyrosine used as food supplements were identified in previous reports. However, a lack of studies in healthy adult individuals as well as in children was pointed out, and in particular the absence of long-term studies in healthy individuals.

A lowest observed adverse effect level (LOAEL) and a no observed adverse effect level (NOAEL) of 2000 and 600 mg/kg bw per day, respectively, for tyrosine have been identified in a 90-day toxicological study in rats. At 2000 mg/kg bw per day, significant increases, were found in weights of livers and kidneys in addition to increased plasma lipids and hypertrophy of centrilobular hepatocytes in both sexes.

The NOAEL at 600 mg/kg per day was used to calculate the margin of exposure (MOE), the ratio of the NOAEL to the specified doses of 1250, 1500, 1750 and 2000 mg/day of Ltyrosine in food supplements. The MOE-values range from 13 for the highest supplement dose in children to 34 for the lowest supplement dose in adults.

Given the low MOE-values (range 13-34), and the severity of the adverse effects at the LOAEL (3.3 times the NOAEL), VKM concludes that all the specified doses may represent a risk of adverse effects. No evidence was found to assume specific tolerance levels for L-tyrosine for children or adolescents. Therefore, a similar tolerance as for adults relative to body weight was assumed for these age groups.

Based on these data, the Norwegian Scientific Committee for Food Safety (VKM) concludes that:

- In adults (≥18 years), the specified doses of 1250, 1500, 1750, and 2000 mg/day Ltyrosine in food supplements may represent a risk of adverse health effects.
- In adolescents (14 to <18 years), the specified doses of 1250, 1500, 1750, and 2000 mg/day L-tyrosine in food supplements may represent a risk of adverse health effects.
- In children (10 to <14 years), the specified doses of 1250, 1500, 1750, and 2000 mg/day L-tyrosine in food supplements may represent a risk of adverse health effects.

Children below 10 years were not included in the terms of reference.

*Keywords: Adverse health effect; L-tyrosine; food supplement; negative health effect; Norwegian Scientific Committee for Food Safety; other substances; risk assessment; VKM.*

Available:https://vkm.no/download/18.645b840415d03a2fe8f25cb4/1502802270055/Risk%20assessment%20of%20%22other%20substances%22%20%E2%80%93%20L-tyrosine.pdf

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**NOTE:**

This work was carried out in collaboration between all authors. The opinion has been assessed and approved by the Panel on Food Additives, Flavourings, Processing Aids, Materials in Contact with Food and Cosmetics of VKM. All authors read and approved the final manuscript.

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## COMPETING INTERESTS

Authors have declared that no competing interests exist.