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. The risk assessments are the scientific basis for NFSA in its efforts to regulate the use of "other substances" to food supplements.

"Other substances" are described in the food supplement directive 2002/46/EC as substances other than vitamins or minerals that have a nutritional and/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
assessments of "other substances" evaluated any claimed beneficial effects from these substances, only possible adverse effects.

The present report is a risk assessment of L-leucine, L-isoleucine and L-valine and it is based on previous risk assessments and articles retrieved from a literature search. In this report L-leucine, L-isoleucine and L-valine may occasionally be termed merely leucine, isoleucine or valine.

L-leucine, L-isoleucine and L-valine are essential amino acids. L-leucine, L-isoleucine and L-valine are commonly known as Branched Chain Amino Acids (BCAAs), and are found in food items containing proteins and in particular, in protein-rich foods such as dairy products, meats, eggs, nuts, whole grains, seeds, avocados and edible seaweed.

According to information from NFSA, L-leucine, L-isoleucine and L-valine are ingredients in food supplements sold in Norway. NFSA has requested a risk assessment of the following doses of L-leucine, L-isoleucine and L-valine in food supplements for adults, adolescents and children 10 years and above: L-leucine: 2500, 3000, 4000, 5000 and 5250 mg/day, L-isoleucine: 1500, 1750, 2000 and 2500 mg/day and L-valine: 1500, 1750, 2000, 2250 and 2500 mg/day. Usual dietary intakes of these amino acids in Norway are not known. Based on data from the 1988–1994 NHANES III, mean daily intakes in adults of leucine, isoleucine and valine from food and supplements are 6.1, 3.6 and 4.0 g/day, respectively (IOM, 2005).

Most studies on BCAAs have focused on the three amino acids taken as single amino acids or together combined in food supplements. It has been shown that BCAAs are not metabolized in the liver as is common for most other amino acids but taken up by most peripheral tissues (in particular muscle) where they are either used in protein synthesis or as precursors for nitrogen and/or a number of carbon containing molecules.

There is a lack of relevant well-designed supplementation studies with L-leucine, L-isoleucine and L-valine in humans designed to address adverse effects and dose-response relationships as primary outcome.

However, daily doses of as much as 30 g BCAA per day given to athletes have been investigated and reported to improve performance. In these reports adverse effects were not addressed and not reported. L-leucine has been administered orally in single doses for one day of up to 50 g without showing any adverse effects. There are no published studies on the effects of longitudinal supplementation with either L-isoleucine or L-valine.

Thus, there are no published studies that can be used for suggesting a "value for comparison", and there is no scientific data in the literature suitable for assessing the specific doses in the terms of reference.

WHO (2007) recommendations for BCAAs are: Leucine 2730 mg/day, isoleucine 1400 mg/day and valine 1820 mg/day. For a 70 kg person, this corresponds to 39 mg leucine/kg body weight (bw) per day, 20 mg isoleucine/kg bw per day and 26 mg valine/kg bw per day.

The acute upper tolerable metabolic limit of L-leucine for men between 20 and 35 years was determined by administration of single doses of 550-700 mg/kg bw over one day. This corresponded to 39 to 50 g/day for a person of 70 kg. Furthermore, based on several studies investigating L-leucine, L-isoleucine and L-valine supplemented as single doses ranging from 10 to 30 g/day without any reported adverse effects. The uncertainties for this consideration are described in chapter 5.

VKM concludes that:

Due to lack of studies addressing adverse effects for the specified doses 2500, 3000, 4000, 5000 and 5250 mg/day L-leucine, 1500, 1750, 2000 and 2500 mg/day L-isoleucine and 1500, 1750, 2000, 2250 and 2500 mg/day L-valine in food supplements, no conclusions can be made for adults (≥ 18 years), adolescents (≥ 10 and < 18 years) or children (< 10 years).
Keywords: Adverse health effect; BCAA; branched chain amino acids; food supplement; Lisoleucine; L-leucine; negative health effect; Norwegian Scientific Committee for Food Safety; other substances; risk assessment; L-valine; VKM.

Available: https://vkm.no/download/18.645b840415d03a2fe8f2600d/1502800765788/Risk%20assessment%20%22other%22%20substances%22%20%E2%80%93%20L-leucine,%20L-isoleucine,and%20Valine,%20the%20branched%20chain%20amino%20acids%20(BCAA).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 Nutrition, dietetic products, Novel Food and Allergy of VKM. All authors read and approved the final manuscript.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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