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## **Risk Assessment of "Other Substances" – L-Histidine**

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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.*

### **Article Information**

DOI: 10.9734/EJNFS/2020/v12i830266

**Grey Literature**

**Received 16 May 2020**  
**Accepted 22 July 2020**  
**Published 05 August 2020**

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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 "other substances" in 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. In this series of risk assessments of "other substances" VKM has not evaluated any claimed beneficial effects from these substances, only possible adverse effects.

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The present report is a risk assessment of specified doses of L-histidine in food supplements, and it is based on previous risk assessments and articles retrieved from a literature search.

According to information from NFSA, L-histidine is an ingredient in food supplements and energy drinks sold in Norway. NSFA has requested a risk assessment of 550 and 600 mg/day of L-histidine from food supplements. The recommended dietary allowance (RDA) for adults of L-histidine is 14 mg/kg body weight/day (IOM, 2005), which corresponds to 980 mg/day for a 70 kg person. Oral doses has a bioavailability of 80% or higher. Foods rich in histidine are generally protein rich foods such as meat, dairy products, legumes, fish, nuts, seeds, eggs and whole grains. Based on NHANES III (1988-1994), the overall mean intake of L-histidine from food and food supplements in the United States was 2.2 g/day.

L-histidine is a conditionally essential amino acid which is a normal constituent of most body proteins. L-histidine is also a part of many plasma proteins. It has anti-oxidant and anti-inflammatory properties. Moreover, L-histidine is also a precursor of histamine and is necessary for the regulation and metabolism of trace elements such as metal ions. The human body has a large pool of L-histidine in plasma proteins, but also as carnosine in skeletal muscles and in haemoglobin.

Due to the lack of adequate scientific information, a no observed adverse effect level (NOAEL) or lowest observed adverse effect level (LOAEL) have not been identified, and a tolerable upper intake level for histidine has not been established. Effects of histidine supplementation have been studied in trials with duration of up to 3-4 months. Previous risk assessments concluded that supplementation with 4.0 to 4.5 g/day of L-histidine above the dietary content does not have adverse effects in human beings, and new data retrieved in the present literature search were in accordance with these conclusions. No particular population groups have been identified as particularly susceptible to adverse effects of consuming histidine supplements. We have not identified any studies in children or adolescents.

VKM concludes that:

- In adults ( $\geq 18$  years), the specified doses 550 and 600 mg/day L-histidine in food supplements are unlikely to cause adverse health effects.
- In adolescents (14 to  $< 18$  years), the specified doses 550 and 600 mg/day L-histidine in food supplements are unlikely to cause adverse health effects.
- In children (10 to  $< 14$  years), the specified doses 550 and 600 mg/day L-histidine in food supplements are unlikely to cause adverse health effects.

Children younger than 10 years were not within the scope of the present risk assessment.

**Keywords:** *Histidine; food supplement; adverse health effect; negative health effect; Norwegian Food Safety Authority; Norwegian Scientific Committee for Food Safety; other substances; risk assessment; VKM.*

Available: <https://vkm.no/download/18.645b840415d03a2fe8f26029/1502799994850/Risk%20assessment%20of%20%22other%20substances%22%20%E2%80%93L-glutamine%20and%20L-glutamic%20acid.pdf>

**ISBN:** 978-82-8259-214-7

**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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**Suggested citation:** VKM. (2016). Risk assessment of "other substances" – L-histidine. Opinion of the Panel on Nutrition, dietetic products, Novel Food an Allergy of the Norwegian Scientific Committee for Food Safety, ISBN: 978-82-8259-214-7, Oslo, Norway.

## **COMPETING INTERESTS**

Authors have declared that no competing interests exist.

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