Risk Assessment of "Other Substances" – Inositol

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Authors’ contributions

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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ABSTRACT

The Norwegian Scientific Committee for Food Safety (Vitenskapskomiteen for mattrygghhet, 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 while 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 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 potential beneficial effects from these substances, only possible adverse effects.

The present risk assessment is based on previous risk assessments of inositol and articles retrieved from a literature search.

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According to information from NFSA, inositol is an ingredient in energy drinks sold in Norway. NFSA has requested a risk assessment of 10 mg/100 ml inositol in energy drinks. Drinking patterns reflecting a high acute intake, a mean chronic intake and a high chronic intake were assessed.

Inositol (CAS no. 6917-35-7) is a sugar alcohol. Among the nine possible stereoisomers, myo-inositol (CAS no. 87-89-8) is the most abundant. The name inositol is frequently used as a synonym for myo-inositol. Inositol occurs naturally in all organisms including humans, and is an important component in all human cells. Inositol-containing lipids and phosphates are required for various structural and functional processes, including membrane formation, signalling, membrane trafficking and osmoregulation. Endogenous production of inositol in humans amounts to about 4 g/day (about 57 mg/kg bw per day in a 70 kg adult) (EFSA, 2014). The total dietary intake of inositol in adults is estimated to range between 500 to 1000 mg/day (about 7-14 mg/kg bw per day).

Inositol added to energy drinks in Norway denotes the compound myo-inositol, according to information from NFSA.

Myo-inositol is a water-soluble compound naturally occurring in the cells of all living organisms including humans, animals, plants and microorganisms.

Certain plant (fruits and vegetables) and foods from animals contain inositol, and seeds of cereals and legumes show high levels of the inositol storage form, phytic acid (inositol hexaphosphate).

With regard to hazard identification and characterisation of inositol, most of the adverse effects observed in several human studies were related to gastrointestinal symptoms such as nausea, flatulence, loose stools and diarrhoea.

Drinking patterns reflecting a high acute intake, a mean chronic intake and a high chronic intake were assessed for energy drinks containing 10 mg inositol per 100 ml, for the age groups children (3 to <10 years and 10 to <14 years), adolescents (14 to <18 years) and adults (≥18 years).

For the high acute drinking pattern, the intake was estimated to be 1000, 1500, 2000 and 2000 ml/day for children (3 to <10 years), children (10 to <14 years), adolescents (14 to <18 years) and adults (≥18 years), respectively. For the mean chronic drinking pattern, the intake was estimated to be 58, 65, 64 and 71 ml/day for children (3 to <10 years), children (10 to <14 years), adolescents (14 to <18 years) and adults (≥18 years), respectively. For the high chronic drinking pattern, the intake was estimated to be 163, 180, 210 and 320 ml/day for children (3 to <10 years), children (10 to <14 years), adolescents (14 to <18 years) and adults (≥18 years), respectively.

The data on toxicity of inositol was very limited. The human study with the longest exposure at highest doses (3 months treatment at maximum tolerated dose) that was available for risk assessment was a clinical study of 40-74 year old smokers with bronchial dysplasia, from which a NOAEL of 18 g/day of myo-inositol was established (Lam et al. 2006). VKM estimated the margins of exposure (MOE) based on the NOAEL established in this study.

The MOE is the ratio of the NOAEL value to the exposure. An acceptable MOE value for a NOAEL-based assessment of inositol based on a human study is ≥10, taking into account a factor 10 for the interindividual variation between humans in toxicokinetics and toxicodynamics. Due to the uncertainty regarding the relevance of the study by Lam et al. (2006) for the general healthy population, an additional safety factor of 3 was used. Therefore, an acceptable MOE value was 30. For all age groups, the MOE values were in the range of 857 to 2570 for mean chronic intake and in the range of 367 to 857 for high chronic intake of energy drinks, respectively, i.e. far above the acceptable MOE value of 30.
Since neither the sub-optimal human study by Lam et al. (2006) or the animal studies in rodent models of chronic diseases available were on healthy subjects, as a supplement to the MOE values calculated from the human study, comparisons with endogenous production and amounts in food of inositol were also performed.

No studies specifically on children (3 to <10 years and 10 to <14 years) and adolescents (14 to <18 years) were identified. Based on the included literature there was no evidence indicating that age affects tolerance or endogenous production of inositol. Therefore, in this risk characterisation a tolerance and an endogenous production of inositol as for adults, based on body weight, was assumed for these age groups.

For the high acute drinking pattern, and for the mean chronic and the high chronic drinking patterns all estimated intakes of inositol from energy drinks containing 10 mg/100 ml were far below the endogenous production (57 mg/kg bw per day), and also below the dietary intake (7-14 mg/kg bw per day).

VKM concludes that it is unlikely that the exposure to inositol from the high acute, the mean chronic or the high chronic drinking patterns causes adverse health effects in children (3 to <10 years and 10 to <14 years), adolescents (14 to <18 years) and adults (≥18 years).

Keywords: Adverse health effect; energy drink; inositol, myo–inositol; negative health effects; Norwegian Food Safety Authority; Norwegian Scientific Committee for Food Safety; other substances; phytic acid; risk assessment; VKM.

Available: https://vkm.no/download/18.645b840415d03a2fe8f260ae/1502803918452/Risk%20assessment%20of%20%20other%20substances%22%20%E2%80%93%20Inositol.pdf


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.