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Risk Assessment of Coumarin Intake in the Norwegian Population

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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 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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Grey Literature

ABSTRACT

The Norwegian Scientific Committee for Food Safety (Vitenskapskomiteen for mattrygghet, VKM) has at the request of the Norwegian Food Safety Authority (Mattilsynet) conducted a risk assessment of the coumarin intake in the Norwegian population. VKM was asked to assess if any part of the population has a total intake of coumarin that will exceed the tolerable daily intake (TDI). It should further be considered whether an intake of coumarin exceeding TDI 1-2 times a week for several years would represent a risk to the health of the consumer.

The assessment has been performed by the VKM Panel on Food Additives, Flavourings, Processing Aids, Materials in Contact with Food and Cosmetics (Panel 4).

Coumarin is a naturally flavouring substance in cinnamon and occurs in many plants. The substance can be found in different types of cinnamon to a varying degree. The two main types are Ceylon (*Cinnamomum zeylandicum*) and Cassia cinnamon (*Cinnamomum aromaticum*). Cassia

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cinnamon, which currently is most frequently used in food products on the Norwegian market, contains more coumarin than the lesser used Ceylon cinnamon.

Oral intake of coumarin is mostly related to consumption of cinnamon-containing foods or cinnamon as a spice. This includes both direct addition of cinnamon to foods as well as the use of cinnamon oils and other cinnamon extracts by the food industry. Other important sources of exposure could be food supplements based on cinnamon or the use of cosmetic products through dermal exposure, as synthetic coumarin is added as a fragrance ingredient to perfumes, skin gels, lotions and deodorants.

It is known from animal experiments that coumarin can cause liver toxicity. It is considered as a non-genotoxic carcinogen in mice and rats. In 2004, the European Food Safety Authority (EFSA) established a TDI of 0.1 mg coumarin/kg body weight (bw), based on a no observed adverse effect level (NOAEL) for liver toxicity in a 2-year dog study. This TDI was maintained when the substance was re-evaluated in 2008. EFSA further concluded that exposure to coumarin resulting in an intake 3 times higher than the TDI for 1-2 weeks was not of safety concern.

In order to answer the second question as stated in the terms of reference, the VKM Panel on Food Additives, Flavourings, Processing Aids, Materials in Contact with Food and Cosmetics found it necessary to further examine the data on toxicity of coumarin, which were the basis for the TDI established by EFSA. The most significant hazards of coumarin appears to be liver toxicity, which is well documented, and demonstrated in mice, rats, dogs, baboons and humans, and kidney adenomas in male rats. In a review of human case reports, a small subgroup of the human population appears for unknown reasons to be more susceptible to medical treatment with coumarin. The lowest reported dose of coumarin associated with liver toxicity in humans is around 0.4 mg/kg bw/day. It should be noted that the liver toxicity of coumarin in humans usually is reversible. Since there were no dose-response data for humans, animal data were used in the hazard characterisation.

The VKM Panel decided to use the benchmark dose (BMD) approach to determine a point of departure for adverse effects of coumarin. The 2-year chronic toxicity/carcinogenicity study in rats by the US National Toxicology Program (NTP) was chosen for model simulation and BMD/BMDL (benchmark dose lower confidence limit) calculations. The best model fit of the dose-response data combined with the lowest BMDL05 (dose where the response is likely to be smaller than 5%) was seen for increased relative liver weight in female rats, which gave a BMDL05 of 7 mg/kg bw/day (converted from 10 mg/kg bw, 5 times per week).

The VKM Panel used the BMDL05 for relative increase in liver weight in female rats to establish a TDI of 0.07 mg/kg bw/day using an uncertainty factor of 100 to account for interand intraspecies variation.

The intake calculations for coumarin from food and drinks in this opinion are based on both data from the nationally representative food consumption surveys Norkost, Ungkost, Småbarnskost and Spedkost, as well as on assumed worst intake scenarios of different cinnamon-containing food products. The average coumarin levels found in cinnamoncontaining food categories such as ginger bread, cinnamon buns and similar bakery products, cinnamon-containing cakes, thin pastry with cinnamon and cinnamon-based tea sold on the Norwegian market, were used to calculate the total coumarin intake in different age groups in the population. For the calculation of the coumarin intake from cinnamon powder sprinkled on oatmeal porridge and rice porridge, a coumarin level of 3000 mg/kg in cinnamon powder was used. The frequency of consumption and the amount of cinnamon powder (from ¼ - 1 teaspoon) sprinkled on the porridge were taken into account in the calculations.

To assess if any part of the Norwegian population has an intake of coumarin that will exceed the TDI, the different intake scenarios presented in the opinion have been compared with the TDI of 0.07 mg/kg bw/day established by VKM. The main conclusions from the VKM Panel were:

The total estimated intake of coumarin for mean and high consumers of cinnamon-containing foods are below the TDI for all age groups when consumption of cinnamon-based tea and porridge with cinnamon was excluded.

Children and adults who regularly consume oatmeal porridge sprinkled with cinnamon may exceed the TDI by several folds depending on the frequency of consumption and the amount of cinnamon used.

Small children (1- and 2-years old) who have a mean or high consumption of oatmeal porridge may exceed the TDI even if they use moderate amounts of cinnamon powder on the porridge. In a worst case scenario with high consumption of porridge and use of high amounts of cinnamon powder, the estimated coumarin intake could exceed the TDI by about 20-fold.

This intake is similar to dose levels of coumarin used in medical treatment of adults and where cases of liver toxicity have been reported.

Drinking of cinnamon-based tea, which may have a high content of coumarin, can also result in a total intake of coumarin that exceeds the TDI both for children and adults.

Other relevant sources of coumarin are cosmetics and food supplements with cinnamon. The recommended dose of two cinnamon supplements sold on the Norwegian market can lead to an exceedance of TDI in adults. It is not anticipated that children will consume supplements with cinnamon. Cosmetic products (shower gels, body lotions, deodorants and oils) are important sources of coumarin exposure both for children and adults, but quantification of the coumarin exposure from cosmetics was not possible due to lack of data.

The VKM Panel concludes that based on the available data, the possibility of an adverse health effect by exceeding the TDI 3-fold for 1-2 times per week for several years cannot be assessed. Generally, a minor or an occasional exceedance of TDI is not considered to increase the risk of adverse health effects.

The coumarin intake could exceed the TDI by 7-20 fold in some instances. Liver toxicity may occur shortly after the start of coumarin exposure. Such large daily exceedances of TDI, even for a limited time period of 1-2 weeks, cause concern of adverse health effects.

Keywords: Coumarin; cinnamon; liver toxicity; kidney adenomas; benchmark dose (BMD); benchmark dose lower confidence limit (BMDL); tolerable daily intake (TDI); cinnamon-containing foods; oatmeal porridge; rice porridge; cinnamon-based tea; food supplements; cosmetics.

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NOTE:

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COMPETING INTERESTS

Authors have declared that no competing interests exist.