

Does the consumption of liquorice by pregnant women impair the mental and physical development of children?

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In a Finnish observational study, children of mothers who had consumed more than 250 g of liquorice (approx. 500 mg glycyrrhizic acid) per week during pregnancy were compared with children of mothers who had consumed no or only about 125 g of liquorice per week. The results showed that the children in the first group differed in some parameters of their physical and mental development from the children whose mothers had not consumed any liquorice or had consumed much less liquorice per week. The authors of the study interpreted the observed differences as adverse effects of the exposure of the unborn child (fetus) to glycyrrhizic acid - an ingredient of liquorice. Based on the study results, they recommended that pregnant women should be warned against eating liquorice.

The Federal Institute for Risk Assessment (BfR) evaluated the study performed by Rääkkönen et al. (2009; 2010; 2017a) and, like the Norwegian Scientific Committee for Food and Environment (VKM, 2018), came to the conclusion that the data collected in the study are not suitable for making reliable statements about a possible causal relationship between the consumption of liquorice during pregnancy and the physical and mental development of the offspring.

It is known that glycyrrhizic acid can lead to a change in the mineral metabolism with sodium accumulation and potassium loss when consumed in large quantities. The consequences are increased blood pressure, water retention in the tissue (oedema) and muscle weakness. Since the consumer information on liquorice packaging does not indicate the glycyrrhizic acid content of the individual product, consumers suffering from high blood pressure, cardiovascular diseases and diabetes, as well as pregnant women, should refrain from continuously consuming large quantities of liquorice.

One of the main criticisms of the study by Rääkkönen et al. (2009; 2010; 2017a) is that there is uncertainty about the actual amounts of liquorice consumed or the intake of glycyrrhizic acid during pregnancy, as liquorice consumption was not recorded prospectively but retrospectively when the pregnant women were admitted to the maternity ward. Furthermore, this is a long-term observational study that was initiated in 1998 with more than 1000 pregnant women, of whom, however, only about one third of the mothers with their children were still available for the study in 2009-2011. The observations of Rääkkönen et al. (2017a) on the physical and mental development of the children thus refer to a relatively small group of participants, of which it is not known how they differed from the original cohort. It is also questionable whether the calculated statistically significant differences between children of high and low consumers of liquorice have clinical relevance. Observational studies are usually not suitable on their own to derive causal relationships, so that it is unclear to what extent the observed differences can actually be causally attributed to liquorice consumption. The question of the health risk of high liquorice consumption during pregnancy can therefore not be answered on the basis of the studies by Rääkkönen et al. (2009; 2010; 2017a). In response to a comment by Keyes and Susser (2017), the authors themselves confirm that the data from their observational study do not allow any reliable conclusions to be drawn about a causal relationship and that further data - including mechanistic data - from well-designed studies would be necessary to investigate whether and at what doses prenatal exposure to liquorice or its ingredients could negatively affect child development (Rääkkönen et al., 2017b).

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For glycyrrhizic acid, which enters foods such as liquorice through the use of liquorice or liquorice root extract in the production of these foods, there are no legal maximum levels in the EU so far. However, the use of glycyrrhizic acid and its ammonium salt as a flavouring substance in food is restricted to certain food categories with maximum levels according to Regulation (EC) No. 1334/2008. According to the Food Information Regulation (Regulation (EU) No 1169/2011), confectionery containing glycyrrhizic acid or its ammonium salt due to the addition of the substance(s) itself or the liquorice plant *Glycyrrhiza glabra* at a concentration of 100 mg/kg or above must bear the statement "contains liquorice" and from concentrations of 4 g/kg the statement "contains liquorice - people suffering from hypertension should avoid excessive consumption".

In 2003, the former Scientific Committee on Food (SCF) of the European Commission was unable to derive an acceptable daily intake (ADI) for glycyrrhizic acid on the basis of the data available at that time, but assessed a maximum intake of 100 mg/day for most population groups as being of no health concern (SCF, 2003). However, the SCF pointed out that the known high use levels indicate that the actual intake of glycyrrhizic acid has been underestimated - and requested more detailed data on the use of glycyrrhizic acid (e.g. data on the market share of certain products in the relevant food categories) for a final assessment. Within the framework of the programme for the evaluation of the use of flavouring substances in foods according to Regulation (EC) No 1565/2000, the European Food Safety Authority (EFSA) re-evaluated the use of glycyrrhizic acid (FL-No. 16.012) as a flavouring substance in 2008 and also emphasised the need for further information on use and intake levels of glycyrrhizic acid. As far as the BfR is aware, however, such data are still lacking.

The Federal Institute for Consumer Health Protection and Veterinary Medicine (BgVV), a predecessor institution of the BfR, had already recommended in 1999 to refrain from regular consumption of larger amounts of liquorice as a precautionary measure. The BgVV had especially consumers suffering from high blood pressure, cardiovascular diseases and diabetes mellitus as well as pregnant women in mind. Taking into account the data and knowledge gaps described above, the BfR still considers this recommendation valid.

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Further Information on the BfR website on the subject of glycyrrhizic acid

Liquorice: https://www.bfr.bund.de/de/a-z_index/lakritze-5079.html

https://www.bfr.bund.de/de/presseinformation/1999/02/bgvv_raet_zur_vorsicht_beim_verzehr_von_lakritze_-861.html

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