Exposure

In this guide

115. TOX/2021/26 discussed exposure to ginger via the diet and in supplement form. TOX/2020/51 examined in more detail exposure to ginger in the form of highly concentrated juices (‘shots’). This statement reviews ginger from all sources described previously.

116. A number of ginger supplements (Tables 1 and 2, Annex C) are purported to support digestive and joint health, alleviate nausea, upset stomach, and travel sickness. Currently, a number of commercially available pregnancy supplements, including ‘Seven Seas Pregnancy’ and ‘Seven Seas Pregnancy Plus Follow On’, contain ginger extracts in their formulations.

117. The availability of supplements in different forms, along with a lack of information with regards to extraction processes involved and therefore composition of the extracts, meant it was not possible to consider aggregate exposures. As such, ginger exposure from the diet and from supplements were

separately considered.

118. In addition to supplements, pregnant women may also consume ginger as part of their general diet to various degrees. There are anecdotal reports of women consuming ginger products (Tables 3, Annex C) such as ginger biscuits and ginger ale, to alleviate morning sickness and nausea. Some may use these in combination with juice shots or tinctures (Table 4, Annex C).

119. Table 1 shows calculated exposures from the diet, supplements and drinks (including teas and shots). Mean acute ginger exposure from the diet of women aged 16-49 years old was 0.026 g/kg bw/day, and 97.5th percentile exposure was 0.16 g/kg bw/day. The corresponding mean and 97.5th percentile chronic exposures were 0.0083 and 0.058 g/kg bw/day, respectively. The upper value of the range of exposure from drinks and supplements was more than double (%) that of those estimated from 97.5th percentile acute exposure from the diet.

Table 1: Estimated mean and 97.5th percentile acute and chronic ginger exposures from a variety of sources in women aged 16 – 49 years old.

Commodity	**Range of daily exposures (g/day)**	**Range of daily exposures (g/kg bw/day)**	**Mean acute exposure* (g/day)**	**Mean acute exposure* (g/kg bw/day)**	**97.5th percentile acute exposure* (g/day)**	**97.5th percentile acute exposure* (g/kg bw/day)**	**Mean chro expo (g/da**
Food[a]	NA	NA	1.7	0.026	11	0.16	0.55
Drinks (Including tea and shots) [b1,b]	0.5 - 32.5	0.0071 - 0.46	NA	NA	NA	NA	NA
Supplements [c]	0.010 - 24	0.00014 - 0.34	NA	NA	NA	NA	NA

1This assumes only one serving is consumed per day.

a Data obtained from the National Diet and Nutrition surveys years 1-8 calculated from women of a childbearing age (16-49 years) (Bates *et al*., 2014; 2016; Roberts *et al*., 2018).

b Data obtained online from retailers, see Appendix 1 for further details.

c Data obtained online from retailers, see Appendix 1 for further details.

*Rounded to 2 significant figures.

120. As previously mentioned, 1 - 1.5 g per day of ginger may be advised during pregnancy (NHS, 2022, Healthline, 2020; Mother and baby, 2022). Some highly concentrated ginger shots commercially available contain up to 30 g of fresh ginger per serving, over 30 times that recommended by healthcare professionals.

121. As the NDNS does not provide data for pregnant women, there was uncertainty as to whether the data presented an accurate reflection of consumption during pregnancy. This uncertainty also extended to data presented for drinks and supplements, as the pattern of consumption during pregnancy to alleviate symptoms of sickness is unknown.

Toxicology conclusions

Reproductive and developmental toxicity

122. The COT considered a number of epidemiological studies investigating the use of ginger during pregnancy (TOX/2021/26). For the most part, few studies explicitly addressed the safety of ginger consumption during pregnancy. Most were focused on the use of ginger as a treatment for nausea (Fischer-Rasmussen *et al*., 1990; Smith *et al*., 2004; Ensiyeh *et al.*, 2009), age-related neurological disorders or pregnancy-induced sickness and therefore focused on efficacy (Willetts *et al.*, 2003; Stanisiere *et al.*, 2018). However, safety was considered in a few studies. The studies considered by the Committee included observational and randomised clinical studies, lasting from 4 days to 20 weeks in duration (Vutyavanich *et al.*, 2001; Portnoi *et al*., 2003). Ginger in various forms was investigated in doses ranging from 750 mg/day to the equivalent of 7 g/day.

123. The animal studies on reproductive toxicity considered in TOX/2021/26 reported a number of findings, including reduced maternal weight

gain, increased foetus weight, increased serum testosterone level in F1 generation males and an increase in embryonic loss.

124. The study results in pregnant women were also varied and the overall findings inconclusive. Findings reported included abdominal discomfort, vomiting and diarrhoea. There were reports of incidences of spontaneous abortion (Portnoi *et al*., 2003, Ensiyeh *et al.*, 2009), however, this effect was observed in both the treated and control groups and therefore, cannot directly be attributed to the consumption of ginger. Portnoi *et al*., reported 8 spontaneous abortions in the comparator group, compared to 3 occurring in the group taking ginger and Ensiyeh *et al.*, reported 2 spontaneous abortions in the ginger group compared to 1 in the group taking vitamin B6. This study reported no congenital abnormalitiespost-partum following exposure to ginger.

125. In their 2003 review of interventions for nausea and vomiting in early pregnancy (first trimester), Mathews concluded high-quality consistent evidence is lacking to support advice regarding the safety of ginger during pregnancy (Mathews et al., 2015). However, it was noted that a review by Bryer et al. (2005) concluded that maternal consumption of ginger shows no evidence of teratogenicity in infants. More recently, Stanisiere et al. (2018) conducted a review of the safety and efficacy of ginger rhizome for decreasing nausea and vomiting in women during early pregnancy, based on systematic literature searches until the end of December 2017. The group concluded that the in vivo results do not suggest any major concerns with respect to reproductive and developmental safety of ginger root, as no associations were found between the use of ginger and malformations in humans. However, in vitro results could not be extrapolated to humans and safety could be dependent on ginger quality. The majority of the studies included in this review have already been included in this draft statement. Some recent studies have been conducted evaluating the effectiveness and safety of ginger in pregnancy, and these will be discussed in detail. Overall, most studies reported gastrointestinal effects such as abdominal discomfort, vomiting and diarrhoea. Other effects included dizziness, headaches and drowsiness with some more serious effects such as spontaneous abortion also being reported in 5 out of the 14 randomized clinical studies. The review by Jewell and Young focuses on the reported effects rather than statistical significance, therefore more details on the studies reporting more serious effects are given below.

Anti-platelet aggregation activity

126. Several reports have been published on the pharmacological properties of ginger, with varying results. The potential effect of ginger extract and components thereof on the reduction of platelet aggregation and their potential antithrombotic activity has been noted as a concern in both literature and by health professionals.

127. Ginger was reported to have antiplatelet activity (Srivastava, 1986,1989; Young *et al.*, 2006), with some studies reporting effects in animals at doses of 500 mg/kg bw (Thomson *et al.*, 2002). Ginger was found to inhibit platelet thromboxane and prostaglandin endoperoxcides (PGF2α, PGE2 and PGD2) in human platelets, in a dose-dependent manner (Srivas, 1984).

128. With regards to the relevance of such effects in pregnancy, literature reports note that pregnancy is associated with an increased incidence of thrombotic events; mainly related to a pro-thrombotic state, physiologically useful to reduce bleeding at delivery. These changes are more pronounced in the third trimester (Patti *et al.,* 2014). It has also been hypothesised that antiplatelet agents might prevent or delay the development of pre-eclampsia (Duley *et al.*, 2019). The implications and clinical significance of the anti-platelet activity of ginger exposure during different stages of pregnancy remain undetermined.

129. This further highlighted the need to differentiate exposure from the normal diet to that from supplements. Members noted that associations with haemorrhagic effects were reported following supplemental exposure to ginger, (Kruth *et al.*, 2003; Rubin *et al.*, 2019; Al Askar *et al.*, 2020) though these were inconclusive.