TOX/2023/06

Committee on Toxicity of Chemicals in Food, Consumer products and the Environment

Discussion paper on the effects of pica during pregnancy

Introduction and background

1. In 2019, The Scientific Advisory Committee on Nutrition (SACN) agreed to conduct a risk assessment on nutrition and maternal health focusing on maternal outcomes during pregnancy, childbirth and up to 24 months after delivery; this would include the effects of chemical contaminants and excess nutrients in the diet.

2. SACN agreed that, where appropriate, other expert Committees would be consulted and asked to complete relevant risk assessments e.g., in the area of food safety advice. Following a discussion at the Committee on Toxicity of Chemicals in Food, Consumer products and the Environment (COT) meeting of September 2020, a list of components were decided upon, including heavy metals, that would be presented to the Committee. At the COT meeting in May 2022, as part of the discussions regarding the contribution of soil and dust to lead exposure in the maternal diet, the Committee requested further information on pica practices. This information was incorporated into the second draft statement of the effects of lead on maternal health; at the September 2022 COT meeting members discussed the additions and determined that there was justification to expand upon the theme of pica and that the effects of pica during pregnancy should be considered as a stand-alone paper.

3. The International Classification of Diseases (ICD-10) is a diagnostic tool listing clinical classifications standards that are used across the NHS. The ICD-10 defines pica as ‘the regular consumption of non-nutritive substances, such as non-food objects and materials (e.g., clay, soil, chalk, plaster, plastic, metal and paper) or raw food ingredients (e.g., large quantities of salt or corn flour) that is persistent or severe enough to require clinical attention in an individual who has reached a

developmental age at which they would be expected to distinguish between edible and non-edible substances (which is approximately 2 years). That is, the behaviour causes damage to health, impairment in functioning, or significant risk due to the frequency, amount or nature of the substances or objects ingested.'(WHO 2022).

4. The most frequently reported pica behaviours globally are: geophagia- that is the consumption of earth, soil or clay, amylophagia- the consumption of starch, and pagophagia- the consumption of ice (Miao et al., 2015). As the COT is currently reviewing exposure to contaminants in the maternal diet, substances that would be found in the normal diet such as starch and ice will not be further considered in isolation in this paper.

5. The literature provides numerous case studies describing individual occurrences of pica behaviour relating to consumption of non-food substances such as moth balls (naphthalene), soap and talcum powder (Moore, 2017; Pennycuff et al., 2018; Shafer et al., 2020). However, none of these case-studies relate to UK women and are unlikely to pose a quantifiable risk to pregnant women in the UK, thus these substances will not be considered further in this paper.

6. It is likely that the majority of the pica in pregnant women in the UK is as a result of the consumption of soils and clays as part of the practice of geophagia and therefore the risks posed to women of maternal age is likely to be from contaminants present within these substances.

Prevalence of Pica in Pregnancy

Global Prevalence

7. Pica has long been associated with pregnancy, however, the exact prevalence in this population remains uncertain. This is, in part, because the advice to women who practise pica remains to simply stop the behaviour and this has resulted in limited descriptions of pica behaviour and its subsequent health effects (Horner et al., 1991). Additionally, comparisons between studies can be difficult when the definition or diagnostic criteria of pica varies between studies. Additionally, confounding factors such as ethnicity and socioeconomic status may skew the data.

Therefore, the current estimates of the prevalence of pica behaviour vary greatly depending on the population being studied. For example, when specifically looking at the consumption of soil and clay (geophagia), prevalence ranges from 0.004% in Demark to 92.5% of pregnant and lactating women in Nigeria (Izugbara, C. O, 2003; Mikkelsen et al., 2006).

8. Horner et al. (1991) were the first to systematically review the practice of pica during pregnancy. The authors identified 16 studies published during the period between 1950 and 1990 across the United States. Pica prevalence in pregnant women was measured as prevalence odds (that is the odds of practicing pica relative to the odds of not practicing pica). Prevalence odds for a particular demographic were obtained by multiplying the sum of the population from a study with the weighted odds for a characteristic (i.e. pica). The results of the analysis found that race was the biggest risk factor for pica during pregnancy with there being a four-fold increase in the prevalence of pica recorded in individuals who were African American and pregnant compared to women who were white and pregnant. This observation was supported by an updated meta-analysis by (Fawcett et al., 2016). The authors analysed 70 studies from across the world and found an aggregate prevalence rate of pica during pregnancy and the post-partum period of 27.8% with the behaviour most prevalent in Africa. Prevalence estimates were calculated as the percentage of pica reported within each individual study assessed. Pica prevalence referred to geophagia, amylophagia, pagophagia, other substances or any combination of the above. Geophagia was studied separately, however, it’s relation to any of the moderating variables did not cause a difference in prevalence figures when compared to overall pica prevalence. The aggregate estimate was calculated using a random-effects model, scrutiny of which revealed substantial variability between studies. The authors suggested that this value is a poor indicator of pica prevalence and, to demonstrate this, calculated a prediction interval to determine a plausible range of pica prevalence which was found to be 4.2%- 77.3%, further indicating a high degree of variability of global prevalence. When the sources of the observed heterogeneity were isolated, it was found that pica was most prevalent in Africa and participants of African American ethnicity were 2.2 times more likely to have pica when compared to other ethnic groups. While Fawcett et al., (2016) did not look for associations between Pica and cultural practice, the

authors did acknowledge that cultural traditions can strongly influence the practice and acceptance of pica. Additionally, Fawcett et al., (2016) found that women with anaemia were over 1.5 times more likely to report pica compared to women without pica.

9. Only 4.2% of the studies included in the meta-analysis were based on data produced in European populations. The prevalence of pica in Europe is the least well defined. In a study by Mikklesen et al. (2006) of 70,132 women from the Danish National Birth Cohort found that only 0.02% of pregnant women had consumed a substance that was not food. The women, who were all in gestation week 25, were mailed a questionnaire in which they were asked about pica in a food frequency survey. The study authors concluded that there were too few women with pica in the cohort to make a meaningful analysis on the risk factors for pica in the Danish population of pregnant women (Fawcett et al., 2016).

10. Both Horner et al (1991) and Fawcett et al (2016) agreed that the size of this difference between ethnic groups appeared to decrease over time with Horner adding that there was a consistent decline in the prevalence odds over time, stating that women in the 1970’s and 1980’s were about half as likely to report pica behaviour than women in the 1950’s. However, Horner et al. (1991) also state that this decline has not continued since the 1970’s.

11. Fawcett et al. (2016) also found that higher education attainment was associated with a lower pica prevalence although the authors indicated that this finding may reflect a reporting bias whereby as education levels increase, individuals become less likely to disclose their pica practices due to the behaviour being perceived as bad or abnormal.

Pica Prevalence in the UK

12. In the UK there are no specific data for the prevalence of pica and the available literature describing the practice of pica is very limited and dated. In a study from 1958, one of the only papers describing pica behaviours with the UK population, Harries and Hughes (1958) summarised the pica behaviours of women following a discussion on the BBC radio programme ‘Is there a Doctor in the

House?'. During the discussions, listeners were invited to write in about their experiences of pica. 509 letters were received to the BBC, of which, 187 women reported strong desires for food substances such as coal, soap, disinfectant, toothpaste, mothballs, petrol, metal polish, tar, paraffin, wood, soil chalk, charcoal, cinders. However, it is not stated whether these women consumed any of these commodities or just experienced cravings for them. Additionally, the authors do state that the study design is not robust and cannot be assumed to be either random or representative of the whole population. Furthermore, there is a likely bias towards individuals with something of interest to say whereas unremarkable experiences would likely remain unreported (Harries and Hughes, 1958).

13. Dickens and Trethowan (1971) provided 100 white British women with a questionnaire regarding dietary habits with the aim to better understand the prevalence of cravings and aversions during pregnancy. No instances of pica were identified (Dickens and Trethowan, 1971).

14. As a result of the lack of recent peer-reviewed literature describing pica in British women, a search of the parent forum, Mumsnet, was undertaken using the search term 'Pica and pregnancy'. The anecdotal evidence available suggests that cravings for non-food items are not unusual. Substances such as talcum powder, household cleaning products, furniture polish, paint, petrol and shower gel are all discussed. However, these cravings are often described as being satisfied by smelling rather than consumption. Notable exceptions are in 3 women who discuss consumption of toilet paper, a stick of chalk and bath sponges respectively. This highlights that pica behaviour may be more prevalent in the UK than the literature suggests and women may be under-reporting their symptoms (Mumsnet, 2023).

Aetiology of Pica Behaviour

15. The aetiology of pica during pregnancy is complex and obscure. Hooda et al., (2004) , suggests that in addition to being a potential response to physiological reasons such as nutrient deficiency, pica behaviour can be a result of psychological reasons and cultural expectations, traditions or religious beliefs (Hooda et al., 2004).

Micronutrient Deficiencies

16. Pica has long been associated with micronutrient deficiencies and in particular, iron deficient anaemia. However, the strength and direction of the causal relationship is often unclear. A meta-analysis by Miao et al., (2015) of 43 studies including 6,407 individuals with pica behaviours and 10,277 control subjects found that individuals who reported pica were 2.35 times more likely to also be anaemic (95% CI: 1.94–2.85, $p<0.001$). Similarly, plasma zinc levels were also found to be significantly lower in the pica group compared to the non-pica group (−34.3 μg/dL, 95% CI: −59.58–−9.02 μg/dL, $p=0.008$). Furthermore, statistical significance persisted in sub-populations of the data, including pregnant women. This suggests that there is a relationship between pica and micronutrient deficiencies and that pica is a risk factor.

17. Some pica substances such as earth, clay, raw starch and ash may contribute to iron deficient anaemia by interfering with micronutrient absorption; soil components may bind to the mucosal layer of the gut and thus prevent absorption of micronutrients. These materials may also, themselves, absorb micronutrients from ingested food thus preventing them from being available to metabolism by the body. (Fawcett et al., 2016).

18. Hooda et al (2004) aimed to elucidate the direction of the relationship between geophagic pica and nutrient deficiency by creating an in vitro soil ingestion simulation test that is broadly similar to the GI tract. Five bulk samples of geophagic materials were collected from geophagia prevalent countries: Uganda, Tanzania, Turkey and 2 from India. These soil samples were used to produce geophagia simulation solutions. Alongside these, nutrient solutions were produced to simulate the in vivo conditions of nutrients already available for uptake in the GI tract, these were formulated on the basis of recommended daily allowances of selected essential nutrients. Dilutions were also prepared to represent a cross section of dietary intakes. Geophagic simulations were produced on the assumption of 300 g equivalent of dry mass/ day soil being consumed and the assumption of 6 L of fluids (liquid intake and gastric juices) passing through the GI tract every day. Solutions were then filtered through Whatman paper No. 542. The filtrate was then analysed by inductively coupled plasma optical emission spectrometry (ICP-OES) to

determine total concentrations of a range of mineral elements including iron . Results showed that in all soil samples there were significant losses of iron from the solutions. The averages ranged from 41% to 75% across the five different soils when compared to iron present in the nutrient solutions. The study, although a rudimentary in vitro simulation of a complex biological process, highlighted that geophagia may potentially reduce absorption of already bioavailable nutrients such as iron which may lead to conditions such as anaemia (Hooda et al., 2004).

19. A study by Beyan et al., (2009) suggests that pica is a frequent symptom in iron deficient anaemia, thus proposing that the anaemia is pre-existing before pica behaviour is initiated. In a study of 119 patients with iron deficient anaemia, 41 (34.4%) were found to also exhibit pica. The rate was 33.3% in pregnant patients, although it must be noted that only 6 of the 119 participants were pregnant. Interestingly, however, the most commonly reported pica behaviour was pagophagia and thus adding weight to the suggestion that micronutrient deficiency may drive pica rather than pica driving anaemia as ice would not have the same absorptive effects on Fe as soil might (Beyan et al., 2009).

20. Furthermore, Fawcett et al (2016) added that individuals who practice pica do not often experience iron specific cravings and many pica substances often provide little to no bioavailable iron. And finally, it should be noted that more individuals with anaemia do not engage in pica more than those that do.

21. A case control study by Kettaneh et al. (2010) of iron deficient adults living in the suburbs of Paris which aimed to describe the epidemiology of pica in France found that among patients with iron deficiency the prevalence of pica was significantly lower in European patients than Non-European patients (6% vs 55%). The authors found that pica was associated with iron deficiency even after adjusting for pregnancy and geographic origin of the patient. The most commonly reported non-food ingested was clay which was reported by 44% of the 79 subjects. The authors determined that cultural factors are likely to affect the dietary practises of these women (thus the pica could be contributing to the anaemia) and suggested that this was the reason for variability in results between population demographics (Kettaneh et al., 2005 abstract only). Mikklesen et al. (2006) hypothesised that in privileged populations, pica during pregnancy is more a myth than a reality due to

the high levels of nutrition already present within these demographics. This could partly explain why there are so few studies analysing the practice in pregnant women within Europe as the behaviour is not prevalent enough to produce meaningful data.

As a Cultural Practice

22. Two reports have been identified that aim to evaluate the cultural practice of geophagia in the South Asian population of the UK and the associated hazards (Abrahams et al., 2006; Al-Rmalli et al., 2010). These are discussed in more detail in paragraphs 28 and 29.

23. An audit conducted in a north London borough among black African women aimed to understand the reasons for the behaviour in a UK context. The study specifically sought to understand the barriers and facilitators to booking appointments with health care providers among Black African women who are over represented in the proportion of 'late bookers'. The study used qualitative approaches, including interviews, during which ingesting clay emerged as an important aspect of pregnancy. The authors found that clay ingestion during pregnancy is a culturally embedded common practice amount black African women and in countries of origin. The reasons for clay ingestion included curbing morning sickness, satisfying cravings, perceived mineral deficiencies and other life sustaining beliefs. The women acknowledged that they were unlikely to disclose engaging in pica behaviours to health care providers due to the stigma associated with eating 'dirt' in a context where this is deemed dangerous. Thus suggesting that pica in the context of geophagia may be more prevalent in the UK than studies suggest (Madziva and Chinouya, 2020).

Chemical Hazards Associated with Geophagia

24. The hazards from pica behaviour in the UK largely come from the practice of geophagia. Geophagia primarily occurs in migrant populations from Africa and South Asia where the practice is common place. As such, the soils, chalks and clays that are consumed are not of UK origin. The soils are frequently imported from regions where the practice is prevalent following rudimentary processing such as being oven baked into blocks (Dean et al., 2004).

Kaolin Clays and Sikor

25. Kaolin is the term used to describe a broad range of clay-compounds including those that are consumed as part of geophagia. Kaolin clays are predominantly made up of kaolinite which is a silicate mineral (Bonglaisin et al., 2022). It is known to be stable within its natural environment and in its pure state is primarily composed of silicon dioxide (45-47 %) although the mineral composition may vary and the additional minerals may be present (Bonglaisin et al., 2022).

26. The Expert Group on Vitamins and Minerals (EVM) evaluated silicon in 2003. Based upon the results of a chronic dietary study in rats where no relevant adverse effects were observed at doses up to 2,500 mg/kg bw/ day silica (silicon dioxide) it derived a Safe Upper Level of 700 mg/ day for supplemental intake of elemental silicon. Uncertainty factors of 10 for inter-species variation and 10 for inter-individual variation were applied. It was further concluded that there were no groups that were considered particularly vulnerable to silicon toxicity (EVM 2003).

27. EFSA evaluated silicon dioxide as a food additive in 2018, it concluded that there was no indication for toxicity or adverse effects. However, it was noted that the results from the available chronic toxicity studies do not cover the full size range of nanoparticles which could be present in silicon dioxide. Silicon dioxide is a material comprised of aggregated nanosized particles, the agglomerates can further aggregate to form even larger structures, the size of which is normally in excess of 100 nm, however, it cannot be totally excluded that some aggregates could contain particles smaller than 100 nm. Due to the limitations of the dataset no acceptable daily intake (ADI) for silicon dioxide was set (EFSA, 2018).

28. Calabash chalk is a kaolin clay that is traditionally eaten by some pregnant women in Nigeria and West Africa. It is available in a variety of forms including powders, moulded forms and blocks. An analysis of trace elements in calabash chalk using energy dispersive X-ray fluorescence spectroscopy (EDXRF) was able to quantify 18 different elements present alongside its mineral constituents. These included: aluminium, potassium, titanium, chromium, manganese, iron, nickel, copper, zinc, rubidium, strontium, yttrium, zirconium, niobium, tin, barium, cerium and lead. The levels at which these were detected ranged from 1.8 mg/ kg for copper to 14,770 mg/ kg for iron. (Dean et al., 2004). It was also observed that other

toxic elements including arsenic, cadmium and mercury were not detected in any of the samples analysed. Therefore it is important to consider that as these clays are taken from their natural environment with little processing before being sold, these results are only indicative of the samples studied at the time and have the potential to vary both in quantities of contaminants present and which contaminants are present. For example, Bonglaisin et al., (2022) noted that lead is water soluble and can therefore leech into calabash following rainfall and increase the concentration present. Bonglaisin et al 2015 studied local kaolin varieties available in Cameroon and similarly found contamination with lead but also cadmium and mercury which is in contrast to the Dean et al 2004 study (Bonglaisin et al., 2015; Dean et al., 2004). However, it was noted that the differences in lead and cadmium mean values once at market compared to the values from the mining site were higher suggesting that there is an additional risk of contamination post mining, standard deviations also showed that there was a large variation in the contamination observed at the market level.

29. Dean et al. (2004) also highlighted the presence of persistent organic pollutants (POPs) in some samples of calabash chalk (alpha lindane, endrin, endosulphan II and p,p'-DDD, concentrations range between 0.05 and 0.94mg/ kg). However, it was noted that they were only observed in 1 of 5 samples and could also be contamination post mining. Dietary intake of POPs at any level is not recommended. POPs are a contaminant then enters the food chain from the environment, they can have widely differing chemical structures and properties although they share 3 common properties: persistence and stability in the environment, toxicity at certain levels and the ability to bioaccumulate in organisms. Where there is sufficient evidence POPs are listed in the Stockholm Convention, an international agreement which aims to control or eliminate the use of these chemicals. (FSA 2021).

30. A type of soil known as sikor is often imported into the UK from the Bengal area of South Asia and is sold for consumption as a 'tonic' during pregnancy. Abrahams et al (2006) conducted an appraisal of geophagy undertaken by pregnant women in UK Asian communities. As part of the study, samples of sikor were purchased from two ethnic shops, one in Birmingham and one in London. The

samples were subsequently characterised to understand their similarities. It was found that the sikor purchased from Birmingham was moderately acidic (pH 4.4) and very low in organic carbon (0.8%). The sikor purchased from London was similarly acidic (pH4.2) however it had a very high organic carbon content (27.6%). The concentrations of 11 elements were determined by atomic absorption spectrometry (AAS) and flame emission spectrometry (FES) following an acid digestion. This procedure will only determine 'pseudo total' concentrations as it is possible that there is not 100% recovery of the element if the soil is not completely digested. However, with this taken into consideration, the sikor obtained from London contained high amounts of calcium compared to the Birmingham sample, both samples contained traces of potassium and sodium but the London sample was also found to contain low amounts of lead, iron and manganese. This highlights the large degree of variability in elemental content even between samples of the same geographical location (Abrahams et al., 2006).

31. Al-Rmalli et al., (2010) expanded on the Abrahams study by performing a trace element analysis of baked sikor samples from Bangladesh using inductively coupled plasma mass spectrometry (ICP-MS). Results showed arsenic (3.8-13.1 mg kg-1), cadmium (0.09-0.4 mg kg-1) and lead (21-26.7 mg kg-1) present in the sikor samples. Further speciation analysis revealed that sikor samples contained mainly inorganic arsenic. The authors concluded that modest consumption of 50 g of sikor is equivalent to ingesting 370 μg of arsenic and 1235 μg of lead per day, based on median concentration values (Al-Rmalli et al., 2010).

32. The UK Food Standards Agency (FSA) issued repeated warnings in 2002 and 2012 over the consumption of calabash chalk. The statement was released following local sampling conducted by the London Borough of Greenwich which found high levels of lead in calabash chalk. A Food Hazard Warning was issued by the Agency asking Environmental Health officers to check whether chalk was being sold in their areas and if so to remove it from sale. The warning was reissued in 2012 after high levels of lead and arsenic were discovered in products being distributed by online retailers (FSA 2002, FSA 2012).

33. The analyses presented above highlight that the major concerns from pica behaviour is the practice of geophagia and as such the hazards are mainly from the

presence of heavy metals in the soils and clays that are consumed, predominantly but not exclusively lead, arsenic and cadmium. However, it is important to consider that this is not an exclusive list as at least 18 elements have previously been found in some samples of calabash chalk. Furthermore, there are numerous environmental reasons for large variations in the concentrations of the contamination both between geographical regions (arsenic, for example, is naturally found in high levels in ground water in the Bengal region) and within geographical regions (heavy rainfall may cause an increase in lead leaching into calabash clay) (Al-Rmalli et al., 2010; Bonglaisin et al., 2022). For these reasons assessing the risk to pregnant women is highly challenging.

Consumption Levels of Kaolin Clays and Sikor

34. Determining how much of the clay is consumed by an individual is not a straightforward task owing to the nature of cultural consumption pertaining to numerous different reasons ranging from specific motives, such as to ease feelings of sickness, to more general motives, such as soil representing new life. Additionally, there are a wide variety of migrant populations within the UK each with their own practices. These soil and clay products are frequently purchased online or in ethnic shops having been imported from the source country with vague accompanying instructions. Abrahams (1997) reported that '*Usually the purchased samples are broken up before being mixed with water to make a paste or a more dilute suspension. Typically for the preparation of the latter, soil is added to about 0.25 l to produce a 'discoloured solution'. Adults may then consume between a tablespoon to a 'half a glass' of the medicine, three times a day*.' However, the author later added that some samples observed were consumed directly by breaking pieces off from the purchased sample (Abrahams, 1997).

35. In the appraisal of geophagy undertaken by pregnant women of UK Asian communities by Abrahams et al (2006), sikor was purchased in tablets of 16.2g, however, the authors were informed by Asian geophagists that it is likely that 3-4 tablets would be consumed per day by the pregnant women of the Bengali community, resulting in a daily consumption of approximately 48.6 – 64.8 g. This average value is supported by Vermeer and Frate (1979) who suggested that the

population practicing geophagia in rural Mississippi would have an average daily consumption of clay of 50 g (Vermeer and Frate, 1979). Geissler et al (1999) recorded a median daily intake of 41.5g similar to that of Abrahams and Vermeer, however, Geissler further added that the range was 2.5- 219.0 g. As a result, reports of average daily consumption are often misleading due to the large degree of variation in consumption levels (Geissler et al., 1999).

Health Risks from Geophagia

Animal Studies

36. Aprioku (2018) investigated the gestational toxicity of calabash chalk in Wistar rats. Twenty-four pregnant Wistar rats were orally administered calabash chalk daily by gavage at doses of 0, 400 or 800 mg/kg from gestational day 0 to day 20. The calabash chalk was excavated from a local mining site in Ohia, Nigeria, it was subsequently oven dried at 110°C before being powdered and dissolved in distilled water. The authors found that following calabash exposure, uterine implantations were absent in 85% of calabash chalk exposed rats and the number of implantation sites were significantly decreased when compared with the control (P= 0.0262). Additionally, 58% of pregnancies were aborted in calabash chalk exposed rats and 5% of foetuses were still birth (Aprioku, 2018). The results were described as dose dependent and indicate that calabash chalk consumption may result in negative effects during pregnancy, however, this is only based upon two dose concentrations It is not established what the cause of the observed toxicity is as the calabash chalk was not characterised prior to the study and thus it is not clear whether a particular contaminant was involved in the results seen or whether there was another mechanism behind the observations.

37. Ekong et al., (2014) studied the effect of calabash chalk from Calabar, Nigera in gestating rats' behaviour. Female rats were exposed to 0, 200, 400 or 600 mg/kg of calabash chalk suspension daily from gestation day 7. On pregnancy day 21, behavioural tests using the open field and the light/dark mazes were carried out. Following the behaviour tests the animals were euthanized and their brains were

processed for histological studies using haematoxylin and Eosin. The authors reported that animals exposed to 600 mg/kg had more transition frequency and were more averse to the dark ($p < 0.05$) which the authors suggested indicated an anxiolytic effect. Treatment group rats also showed higher hypertrophied pyramidal cells and vacuolations in the cerebral cortex ($p < 0.05$) which the authors suggested indicated access and damage to the brain, possibly from heavy metal contamination of the calabash although this was not confirmed (Ekong,et al., 2014).

38. Owhorji et al (2019) studied forty-five Cd-1 mice of mixed sex which were randomly assigned into 3 groups of 15 mice each: control, 10% calabash diet and 20% calabash diet. Mice were granted ad libitum access to feed. Calabash was obtained from a local market in Calabar, Nigeria. Feeding lasted for 30 days and thereafter their locomotor and social behaviours were assessed using an open field maze. Their social behaviour was studied using a nesting behaviour test. Results showed that the calabash chalk diet-fed mice (both dose concentrations) had significantly reduced locomotion ability (various locomotion tests) compared to control ($p < 0.05$) and a significantly lower nesting score compared to the control ($p < 0.05$) suggesting that consumption of calabash chalk impairs locomotion and social behaviour in mice (Owhorji et al., 2019).

Health Risks from Geophagy During Pregnancy

39. Exposure to heavy metals in calbash chalk and sikor is highly variable depending on the geographic origin of the substance being consumed. For example, in a study investigating the heavy metal levels in the residential soils of Lagos and Ibadan (Nigeria) lead levels in samples was found to range from 1.56 – 419 mg/ kg (Adeyi and Babalola, 2017). Another study from the urban region, Doula, in Cameroon showed soil lead concentrations in excess of 1,000 mg/kg (Asaah et al., 2006). Chaney et al., (1989) reported lead values as high as 45,000 mg/kg within a US city. Sikor is less well studied, however, in the analyses discussed earlier in this paper (Abrahams et al., 2006; Al-Rmalli et al., 2010) lead was found in samples with a range of 18- 30 mg/ kg, arsenic with a range of 3.8- 13.1 mg/ kg and cadmium with a range of 0.09- 0.4 mg/ kg.

40. The toxicity profiles of lead, cadmium and arsenic are well characterised and have been discussed previously by the COT (COT 2013, COT 2016, COT 2022). Most recently as part of a review of the risks of toxicity for chemicals in the diet of infants aged 0 – 12 months and children aged 1-5 and currently as part of an on-going review of toxicity for chemicals in the maternal diet. Conclusions on these heavy metals are discussed briefly below.

41. The central nervous system is the main target organ for lead toxicity. Lead can cause developmental neurotoxicity in young children but can also cause cardiovascular effects and nephrotoxicity in adults. In 2013, EFSA conducted a review of the risks of exposure to lead. EFSA used the benchmark dose (BMD) approach to establish guidance levels. The BMD corresponds to the level at which a specified adverse response is seen. For lead, a BMDL was determined for the reduced development of intellectual function in offspring. Specifically, a dietary exposure of 0.5 µg/kg bw/day was associated with a 1% change in full scale IQ score (EFSA, 2013). This BMDL is particularly relevant to pregnant women. The COT advised that efforts should continue to reduce exposure to lead from all sources since it is not possible to identify a threshold for the toxic effects of lead COT (2016).

42. In typical surface soils, the most significant inorganic forms of arsenic are arsenite and arsenate, with the latter dominating under aerobic/oxidising conditions (EFSA, 2009). Organic arsenicals are not expected to be present in soil at high concentrations. The main adverse effects associated with long-term ingestion of inorganic arsenic in humans are skin lesions, cancer, developmental toxicity, neurotoxicity, cardiovascular diseases , abnormal glucose metabolism, and diabetes (EFSA, 2009). The COT advised that dietary exposure to inorganic arsenic should be as low as reasonably practicable (ALARP), because it is genotoxic and a known human carcinogen (COT 2016).

43. The liver and kidneys are the major organs of cadmium accumulation. The liver MT-Cd complex in the blood is filtered through the glomerulus and is then reabsorbed by the cells of the proximal tubule where it is degraded by lysosomes and the cadmium is sequestered by renal MT. As this process continues, the proximal tubule cells' capacity to produce MT is exceeded and free cadmium causes damage at multiple sites. dietary exposure to cadmium should stay below 0.36 µg/kg

bw/day or 2.52 µg/kg bw/week. Since cadmium has a long biological half- life, the Panel on Contaminants in the Food Chain (CONTAM) established a tolerable weekly intake (TWI) of 2.5 µg/kg bw, the COT agreed with this value (EFSA 2009, COT 2022.

Conclusions and Uncertainties

44. The information presented in this discussion paper suggests that the toxicological risks to pregnant women from pica are primarily found in those women who practice geophagia, predominantly as a cultural practice. There is little evidence to suggest that consumption of other non- food substances is common place in the UK and there is some evidence to suggest that pica in pregnant women of well-nourished populations is more likely to be a myth than a reality.

45. Numerous studies have found that the hazards present in the clays and soils consumed as part of geophagia are likely to be from heavy metal contamination with lead, arsenic and cadmium all commonly reported and have well defined toxicity profiles.

46. Considering geophagia as the primary source of pica behaviour in the UK, multiple uncertainties exist regarding the toxicological risk to pregnant women. The nature of the soil and clays that are eaten is highly variable both in mineralogical profile but also contaminant profile. The heterogenous nature of the products is because they are often imported into the UK from a variety of countries. Even those soils and clays that are imported from the same country will display geographical variations, with factors such as industrialisation of the areas contributing to contamination.

47. Furthermore, it is difficult to establish how much of these substances are reasonably consumed as they are often consumed as and when the individual deems it appropriate. Literature has suggested consumption of up to 219 g a day but values could be even higher than this.

48. A lot of studies rely upon self-reporting of pica behaviours through questionnaires. This could lead to bias in the data and under-reporting due to the stigma associated with consuming non-food substances. Therefore, the information

presented in this discussion paper could be a gross underestimation of the real prevalence of pica behaviour in pregnant women of the UK.

Questions for the Committee

49. Members are asked to consider:

a) Taking into consideration the high uncertainty and potential variability on consumption of pica substances within the UK, would the Committee like to see a full exposure assessment for any individual contaminants?

i) If so which contaminants?

b) Based on these limited data sets and discussion do the Committee want to see any follow up action to this discussion paper?

c) If no further action is required, would Members wish to see a stand-alone statement on pica, or have it incorporated into an overarching statement on the maternal diet?

Secretariat

February 2023

Abbreviations

AAS	Atomic absorption spectrometry
ADI	Acceptable daily intake
ALARP	As low as reasonably practicable
BMDL	Benchmark dose level
CONTAM	The Panel on Food Contaminants in the Food Chain
COT	Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment
EDXRF	Energy dispersive X-ray fluorescence spectroscopy
EFSA	European Food Safety Authority
EVM	Expert Group on Vitamins and Minerals
FES	Flame emission spectrometry
FSA	Food Standards Agency
ICD-10	International Classification of Diseases
ICP-MS	Inductively coupled plasma mass spectrometry
ICP-OES	Inductively coupled plasma optical emission spectrometry
MT	Metallothionein
PMTDI	Permitted maximum tolerable daily intake
POPs	Persistent organic pollutants
SACN	Scientific Advisory Committee on Nutrition
TWI	Tolerable weekly intake
UK	United Kingdom

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