Exposure assessment

In this guide

Dietary exposure

74. Curcumin powder is authorised for use as a colouring agent in food (E 100), where its purity is specified as “not less than 90% total colouring matters” (i.e. curcumin, DMC, and BDMC) (EC, 2008). Assimilated additives legislation 1333/2008 sets out the maximum permitted levels (MPLs) for E 100 in foodstuffs as 500 mg/kg (total limit in combination with other group III additives; see Annex 2 and 3 of assimilated additives legislation 1333/2008) depending on the food item and beverages (which range from 100 to 200 mg/L) (EC, 1994).

75. EFSA have assessed the exposure to curcumin through the diet in 2010 and again in 2014. In their 2010 assessment, EFSA used the UK NDNS data to estimate dietary curcumin exposure in the adult population in the UK, and the NDNS (UK) and EXPOCHI (other EU countries) data to estimate the exposure in children (1.5 – 4.5 and 1 – 10-year-olds, respectively). Based on maximum permitted levels, for adults, mean estimated exposure was 0.8 mg/kg bw/day,

which is within the JECFA 2004 ADI of 0 - 3 mg/kg bw (FAO/WHO, 2004a). For children, mean estimated exposures ranged from within to slightly above the upper bound of the ADI (0.5 – 3.8 mg/kg bw/day). There were some slight exceedances of the ADI in children regardless of whether MPLs or maximum reported use levels were used to estimate exposure.

76. Considering the estimated exceedances of the dietary ADI by 1 – 10-year-old children at the mean and high level, EFSA (2014) conducted a refined exposure assessment for curcumin. This refined exposure assessment considered additional information on the consumption of curcumin-containing foods gathered from the EFSA Comprehensive European Food Consumption Database. Each age category was contributed to by a range of countries, and consumption by the UK population was represented only in the “adult” category (18 – 60-years-old). Additional information on use levels was also obtained from Member States.

77. Using the additional information, the refined assessment (EFSA, 2014) estimated lower intakes of curcumin for both adults and the elderly (no UK estimate) than the 2010 assessment. Exposures for adolescents (no UK estimate), adults, and the elderly (no UK estimate) were below the ADI at the mean and high level (97.5th percentile). Estimated exposures were also lower for children (no UK estimate) and toddlers (no UK estimate) at the mean and high levels, although some high-level estimates were close to the upper bound of the ADI and slight exceedances were observed in one (non-UK) survey for each age group. More details of EFSA ANS Panel’s (2010; 2014) curcumin exposure assessments are presented in Annex B.

78. The above information is indicative of the current exposures to curcumin and/or turmeric as part of the diet (food colour and as a spice). However, consumption of raw and powdered turmeric in large quantities to promote wellbeing is becoming increasingly popular. Based on information readily available on the internet it has been proposed that to benefit from turmeric’s antioxidant effects, one should consume between 500 to 1000 mg of curcuminoids per day. It is suggested that one teaspoon of fresh or powdered turmeric contains 200 mg of curcumin. Consumptions at the proposed levels could lead to exposures to curcumin above the recommended ADI.

Exposure through turmeric supplements

79. In addition to exposure to curcumin through a normal diet, turmeric supplements can also be taken. These can be bought as ‘over the counter’

supplements or by ‘self-dosing’, through consumption of spices in large quantities. The exposures for curcumin and heavy metals from supplements have been calculated using data from a recent survey by Fera (Fera Science Ltd, 2022) and are described in paragraphs 83 – 89.

80. Curcuminoids can be extracted from ground turmeric powder using organic solvents to create a turmeric oleoresin extract. JECFA lists several solvents permitted for extraction: acetone, methanol, ethanol, and isopropanol (FAO/WHO, 2004b). Assimilated regulation 231/2012 sets out a different list of permitted solvents: ethyl acetate, acetone, n-butanol, methanol, ethanol, hexane, propan-2-ol, and dichloromethane. Residual solvent concentrations must not exceed more than 50 mg/kg, singly or in combination, except for dichloromethane which has a residual concentration maximum level of 10 mg/kg. The legislation also states that CO2 may also be used as an extraction solvent and for which no maximum residual level is specified (EC, 2012). The extraction methodology used affects the curcuminoid content (37-55 %) (Li, et al., 2011), and the essential oil content (< 25%) (Braga et al., 2003) of the turmeric oleoresin.

81. Turmeric oil extract can be prepared in various ways, for example through the treatment of turmeric powder with steam distillation, supercritical CO2 extraction (Li et al., 2011), or by evaporating the organic solvent of a crude turmeric oleoresin extract (Funk et al., 2010).

82. Curcumin powder can be obtained through the purification of turmeric oleoresin by crystallisation (Li et al., 2011). However, there is limited commercial availability of authentic samples of pure curcumin, since its separation from DMC and BDMC can be difficult and time consuming. Thus, commercial “pure” curcumin is, in many cases, a mixture of at least these three curcuminoids (Li et al., 2011). For example, a sample of commercial “pure” curcumin (labelled as 94% purity) was, after HPLC analysis, found to have approximately 70% purity of curcumin (Li et al., 2011). In addition, the composition of a sample of commercial “curcumin” was found to be approximately 71.5% curcumin, 19.4% DMC, and 9.1% BDMC (Pfeiffer et al., 2003).

83. As mentioned earlier in this statement and described in paragraphs 23 - 31, in supplements it is common practice to alter the curcumin product in an effort to change its metabolism and enhance its bioavailability, by addressing the metabolism, membrane transfer or both. Methods used for this include the use of liposomal curcumin, nanoparticle dispersion, the use of curcumin phospholipid complex and the use of structural analogues of curcumin that are water soluble.

Assessment after 2021 sample survey - Curcuminoids

84. Previously, in discussion paper TOX/2019/52, a range of supplement information was used to estimate exposure to curcuminoids. Since this paper was written a sample survey has been commissioned by the FSA and undertaken by Fera Science Ltd in Summer 2021. The final report for this survey can be found on the FSA website (Fera Science Ltd, 2022).

85. Thirty samples were purchased from a variety of sources (online suppliers, large supermarkets and small retailers) and analysed by Fera Science Ltd using mass spectrometry. The samples consisted of supplements (n=15), ground/powdered turmeric (n=10) and fresh turmeric root (n=5). One of the fresh samples arrived dried.

86. All samples were analysed in duplicate for the curcuminoids: curcumin, BDMC and DMC as well as the black pepper derived alkaloid, piperine.

87. Of the supplements sampled, 5 had total curcuminoids over 10%, with one at almost 30%, and one at almost 50% absolute concentration. Of the 5 supplements providing concentrations of total curcuminoids on the label, all results were within ± 20% of the stated concentration.

88. From the survey, taking the recommended doses daily according to the supplement's label, would result in exposure levels for a 70 kg adult ranging from 0.1 to 7 mg/kg bw/day (mean of 1.7 mg/kg bw/day). Two of the 15 supplement samples would lead to exposures above the dietary ADI of 0 - 3 mg/kg bw. Taking the supplement that provides 7 mg/kg bw/day for a 70 kg adult, would contribute a further approximate 3-fold exposure to curcuminoids than would be expected from a high dietary exposure (2.6 mg/kg bw/day, see Table 2 in Annex B).

89. Ten of the 15 supplements contained detectable concentrations of piperine with 6 of those >1%, which could potentially alter the TK of the curcumin compounds consumed within the same supplement. One of the samples containing piperine did not state this on the label. Three of the supplements contained piperine at approximately 10% or higher.

90. From the powder samples analysed, i.e., where turmeric is sold as a spice ingredient, if these samples were to be taken as a supplement rather than a food ingredient, e.g., at a teaspoon (4 g) a day, exposures would all be within the ADI

of 0 - 3 mg/kg bw.

Assessment after 2021 sample survey - Heavy Metals and other trace elements

91. From the recent survey undertaken by Fera Science Ltd (Fera Science Ltd, 2022) described above, all samples were analysed for 69 trace elements, which included the heavy metals Pb, Hg, As, and Cd.

92. Twenty-nine of the 30 samples tested had heavy metal concentrations of low concern, i.e., below the maximum level (ML) set for supplements by assimilated EU legislation EC No. 1881/2006 or below the EU ML set for root spices by the amendment EU 2021/1317 (due to the recent date, this amendment to the EU regulation is not in UK legislation). For supplements, the MLs are 3 mg/kg for Pb, 1 mg/kg for Cd and 0.1 mg/kg for Hg. For root spice powders the EU ML is 1.5 mg/kg for Pb. Arsenic does not have a ML set for supplements, but all concentrations, bar two samples at 0.45 and 0.29 mg/kg, were below the 0.2 mg/kg ML set for white rice by EU 2015/1006.

93. One sample, a turmeric spice powder, contained a Pb concentration approximately 10 times higher than the majority of other samples analysed, at 2.25 mg/kg. This would be over the amended recent EU ML of 1.5 mg/kg for root spice powders. This sample also had the second highest concentration of chromium (Cr) at 2.11 mg/kg, which may indicate adulteration with lead chromate. If this sample were taken as a supplement at, for example, a teaspoon per day (4g) the total exposure to lead from this source alone would be 0.13 µg/kg bw/day for a 70 kg adult. This is approximately 25% of the estimated dietary exposure of 0.5 µg/kg bw day, equivalent to the BMDL01 of 12 µg/L blood Pb concentration, for effects of Pb on developmental neurotoxicity (EFSA Panel on Contaminants in the Food Chain (CONTAM), 2010), i.e. MOE of 3.8. As this is greater than 1, it would suggest that in itself any risk from such exposure to Pb is likely to be small. but may be of significance when added to other sources of Pb exposure.

94. When the heavy metal results for supplement samples were compared against spice powders and fresh turmeric there were no clear trends or significant differences between the groups (supplements against powder & fresh samples).

95. On evaluation of the other trace elements from the 30 samples, results that differed by greater than the mean plus 2 x the standard deviation and 5 x the

mean of that sample type (i.e., fresh, powder or supplement) are summarised in Tables 4 and 5 in Annex B. If the supplements are taken as described on their labels, no estimated exposures for any trace elements would exceed any health-based guidance values (HBGVs), where HBGVs exist.

96. Overall, the trace element profile of each sample was variable. This is explained by:

a) the different geographical sources of the products and therefore the differing background trace element concentrations in the environments from which the products were derived

b) the varying chemical nature of the different supplement formulations

97. Since the recent 2021 Fera survey, the FSA in 2022 have commissioned a further 70 turmeric spice powder sample analyses for Pb. All results were < 0.5 mg/kg and of hence of no health concern.

Exposure to other potential adulterants

C.zedoaria

98. The occurrence data within the literature of adulteration of C. longa with C. zedoaria is extremely limited. Sasikumar et al., (2004) describe 3 samples of turmeric powder bought from an Indian market that were found to contain more of the contaminant C. zedoaria than the expected C. longa. Due to the much lower price and easier availability of the potential adulterant C. zedoaria (Dhanya et al., 2011), adulteration of products appears to be assumed rather than any direct evidence in the available literature from chemical analysis. Sasikumar (2019) describes wild curcuma species as common adulterants of turmeric products.

Azo dyes

99. The occurrence data of Sudan red and Metanil yellow dyes in turmeric powders is primarily from surveys undertaken from Indian and Pakistan spice markets. Dixit, Khanna and Das, (2008) with a sample size of 15 turmeric powders from an Indian market, report concentrations of adulteration with Sudan dyes between 0.09% and 1.2% and Metanil yellow between 0.15% and 0.46%.

100. Dixit et al., (2009) report results for a much larger survey across Indian markets, analysing for Metanil yellow only. This included 100 branded turmeric powders and 612 non-branded products. None of the branded products contained the dye, 17% (105 samples) of the non-branded powders contained Metanil yellow ranging in concentration between 0.1% to 0.85%.

101. In other surveys from the literature, from a survey of 9 non-branded products Rao et al., (2021) found two products contained Metanil yellow at approximately 0.1%. Ullah et al., (2022) from a survey of branded and non-branded turmeric powders from Pakistan markets (total sample numbers unknown) found Sudan dyes between 1.5 mg/kg (0.00015 %) and 8,460 mg/kg (0.84 %) in the non-branded samples only.

102. From a recent FSA survey of 30 turmeric spice products (this included 6 non-branded products) in 2022, no illegal dyes were detected, although this did not include analysis for the Sudan red dyes or Metanil yellow. In 2023, the FSA commissioned a further 21 turmeric spice powder sample analyses for illegal dyes (method included Sudan red dyes but did not include Metanil yellow), with all samples negative.