Cases of adverse liver effects due to turmeric or curcumin in food supplements

Numerous food supplements containing turmeric or its active substance curcumin are available on the French market. In ten years, the French and Italian vigilance systems have recorded over 40 cases of hepatitis that occurred following consumption of this type of food supplement. Consumers, healthcare professionals and the companies marketing these products need to be made aware of the risk, so that in the event of a liver disorder, a link can be sought between its occurrence and the turmeric, and consumption of the food supplement containing it can rapidly be stopped. Moreover, when they occur, these adverse effects should be reported to the nutrivigilance scheme in order to improve knowledge on this topic.

Turmeric rhizomes have historically been used in powder form as a spice (curry, ras-el-hanout, etc.) in various cuisines, but also in traditional Indian and Chinese medicine, mainly for their digestive (stimulation of bile secretion), antioxidant and anti-inflammatory properties. There are also many food supplements on the French market containing turmeric, or its active compound curcumin. In the past five years, more than 1600 products containing turmeric or curcumin have been notified to the Directorate General for Competition, Consumer Affairs and Fraud Control (DGCCRF) with a view to placing them on the French market.

Since the nutrivigilance scheme was established in 2009, 15 cases of adverse liver effects potentially associated with the consumption of food supplements containing turmeric or curcumin have been reported to and analysed by ANSES. In one of these cases, the consumer's symptoms were life-threatening. Italy, meanwhile, also reported around 20 cases of hepatitis involving turmeric in food supplements between November 2018 and June 2019 [1,2].

ANSES therefore decided to conduct a review of knowledge on this plant, estimate the exposure of the French population to curcumin present in food and, if necessary, take action to protect the most exposed and vulnerable populations [3].

The various adverse effects reported

From January 2009 to August 2021, ANSES was made aware of 120 cases of adverse effects of all types potentially associated with the consumption of food supplements containing turmeric or curcumin. Of these 120 cases, 67 were sufficiently well documented to be analysed for their causality[1]. The most commonly reported adverse events were hepatitis, headache, dizziness and digestive disorders such as diarrhoea or nausea.

The food supplement's causality in the occurrence of these effects was considered "very likely" for one case, "likely" for 31 cases, "possible" for 24 cases and "unlikely" for 10 cases. The severity[2] of the adverse events was low (Level 1) in 28 cases and moderate (Level 2) in 25 cases. Fifteen cases were of high severity (Level 3), four of which were life-threatening (Level 3 with life-threatening prognosis). These involved acute lung oedema, a recurrence of myocardial infarction and mixed hepatitis[3] (in these three cases causality was considered "likely"), as well as cardiorespiratory arrest in which causality was "possible". No deaths were reported.

This article reviews the adverse liver effects of greatest concern, which led to an in-depth expert appraisal by ANSES.

Focus on adverse liver effects

- **Data from the nutrivigilance system**

Among the 120 cases reported to the nutrivigilance scheme, 15 cases of hepatitis were identified. The food supplement's causality was "very likely" for two cases, "likely" for seven, "possible" for four and "unlikely" for two cases. Three cases were of high severity (Level 3), one of which was life-threatening (Level 3 with LTP). The distribution of these cases according to causality and severity is shown in Figure 1.

The consumers' ages ranged from 22 to 74 years old, with a median age of 56. Almost 75% of the cases involved women. The adverse liver effects occurred within three days to one year of the start of consumption, with a median time to onset of two months. The consumers all had a history of liver or biliary disease.

1.Causality enables a causal relationship to be defined. It has five levels: excluded, unlikely, possible, likely and very likely.
2.The scale of severity in nutrivigilance goes from Level 1 (low severity) to Level 4 (death).
3.Hepatitis in which transaminases (ASTs and ALTs), alkaline phosphatases and GGTs are increased.

Twelve cases involved concomitant consumption of at least one other food supplement or medicine. In 14 other cases, the food supplements involved were multi-ingredient, i.e. turmeric or curcumin was combined with other ingredients. Some of these ingredients, such as green tea, *Garcinia cambogia* and Chinese cinnamon, are described as hepatotoxic. In eight cases the dose of curcumin consumed was known. It ranged from 10 mg per day to 1.2 g per day with a median dose of 186 mg per day.

- **Data from the literature**

In addition to these vigilance data, eight cases of hepatitis involving the consumption of food supplements containing turmeric have been published in the literature. All of these patients recovered upon cessation of use. Only one patient had a history of liver disease and all of them were taking one or more medicines in parallel. In four cases the dose of curcumin consumed was known: it ranged from 50 mg to 1 g per day [3].

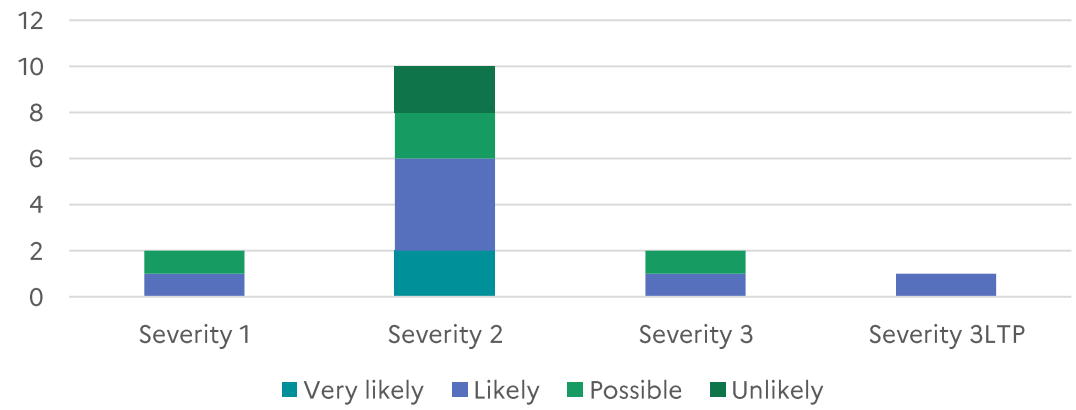

Figure 1: Distribution of cases of hepatotoxicity from food supplements containing turmeric according to their causality and severity (N=15)

Conclusions and recommendations

Hepatotoxicity associated with the consumption of food supplements containing turmeric or curcumin was therefore identified by the nutrivigilance scheme, by the reports received, and from the analysis of the literature. No risk factors specific to the consumers were found; in particular the majority of these turmeric consumers had no history of liver disease. At present, therefore, there are no special warnings for people with prior liver damage. This finding will nevertheless need to be confirmed through increased vigilance. Consumers of food supplements, healthcare professionals and the companies marketing these products are invited to pay closer attention to any possible link between turmeric consumption and the occurrence of this hepatitis, in order to take prompt action to cease consumption. These adverse effects should also be reported to the nutrivigilance scheme.

In addition, anyone being treated with medication is advised to seek the opinion of their doctor or pharmacist before taking food supplements in general, and in particular if they contain turmeric or curcumin.

Lastly, because turmeric promotes bile secretion, consumption of turmeric is not recommended for anyone with biliary tract disease.

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To report an adverse effect following the consumption of a food supplement: https://www.nutrivigilance-anses.fr/nutri#

FIND OUT MORE:

ANSES opinion on the assessment of risks associated with the consumption of food supplements containing turmeric.

References

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