

Fatal fulminant hepatitis associated with consumption of a food supplement

ANSES received a report of fatal fulminant hepatitis likely to be associated with consumption of the food supplement Slim Metabol® marketed by Zuccari. The Agency felt it necessary to bring this case to the attention of the general public and health professionals, and strongly advises against consumption of this food supplement.



As part of its nutrivigilance scheme set up in 2009, ANSES received a report of fatal fulminant hepatitis likely to be associated with consumption of the food supplement Slim Metabol® marketed by the Italian company Zuccari [1].

Case description

This involved a 71-year-old woman with high blood pressure, treated with antihypertensive drugs. She had no other known medical conditions. She started taking the food supplement Slim Metabol® in January 2019. Three months later, she "felt unwell" and consulted her general practitioner. The biological examinations carried out then revealed major abnormalities in liver biology, requiring the patient to be hospitalised. The biological abnormalities indicated acute hepatitis with predominant cytolysis (i.e. corresponding to liver cell destruction), while the liver biopsy performed suggested autoimmune hepatitis, a diagnosis that was initially accepted. Despite appropriate treatment, the situation deteriorated and the patient died of fulminant hepatitis three weeks later.

Doctors concluded as to fulminant hepatitis of autoimmune and toxic origin, complicated by sepsis and multiple organ failure.

The product Slim Metabol® was also analysed. This analysis found lovastatin and hydroxycitric acid, confirming the presence in the product of red yeast rice and *Garcinia cambogia*. No adulteration¹ with any active medicinal substance was found.

1. Adulteration is a fraudulent practice that involves adding a product of inferior quality to another product, which is then sold or given away as something that it is not.

Nutrivigilance causality score

The method for determining causality in nutrivigilance [2] was applied to establish the plausibility of a causal link between consumption of the food supplement and fulminant hepatitis. In this case, the time to onset of the adverse effect was deemed "compatible" and the progression was described as "suggestive". Given the clinical findings, the hypothesis of an autoimmune type hepatitis induced or facilitated by the toxin was a possibility. The responsibility of the food supplement in the occurrence of fatal fulminant hepatitis was therefore considered likely, especially since the patient had no history of immune disease.

Literature data

The literature search focused on the potential hepatotoxicity in humans of each ingredient in the food supplement Slim Metabol®.

According to the package leaflet, the product contains red yeast rice, olive (*Olea europea*), rhubarb (*Rheum palmatum*), hibiscus (*Hibiscus sabdariffa*), cola (*Cola acuminata*), *Garcinia cambogia*, moringa (*Moringa oleifera*), nopal (*Opuntia ficus-indica*), guggul (*Commiphora mukul*), *Coleus forskohlii*, green coffee (*Coffea arabica*), shiitake (*Lentinula edodes*), hawthorn (*Crataegus oxyacantha*), rhodiola (*Rhodiola rosea*), Siberian ginseng (*Eleutherococcus senticosus*), cassia nomame (Cassia mimosides), *Orthosiphon stamineus*, caigua (*Cyclanthera pedata*), maqui (*Aristotelia chilensis*), blackcurrant (*Ribes nigrum*), magnesium, zinc, chromium, marine collagen and water.

"Red yeast rice" is a red mould grown on white rice. It contains monacolin K, also called lovastatin, which has the chemical characteristics and pharmacological activity of statins. In February 2014, ANSES published an opinion on the risks associated with the presence of red yeast rice in food supplements [3]. In order to supplement the data in this opinion and identify new clinical cases, a literature search was conducted. Two articles of interest were identified, including one from the Italian natural health product surveillance scheme, which between 2002 and 2015 recorded ten reports of adverse liver effects following consumption of food supplements containing red yeast rice [4-5].

Garcinia cambogia (GC) extracts or products containing this plant are among the most popular food supplements on the weight-loss market. Its supposed properties are attributed to the hydroxycitric acid found in the pericarp of the fruit. According to the French National Agency for Medicines and Health Products Safety (ANSM), GC meets the definition of a medicinal product by function, because of its glucose-lowering and lipid-lowering properties. This plant is also monitored under the pharmacovigilance scheme. This led to a ban on the importation, preparation, prescription and dispensing of magistral, officinal and hospital preparations consisting of GC, as well as the prescription, dispensing and administration to humans of the GC plant as of 12 April 2012, following a decision by the Director General of the ANSM.

Four cases of severe acute hepatitis in women who used this plant for weight loss purposes were identified by the Italian natural health product surveillance scheme [6]. Seventeen articles also reported acute liver damage observed in 50 patients who had consumed food supplements containing GC or pure GC extracts. It is important to stress the major role of GC in the occurrence of fulminant hepatitis, similar to the clinical case reported above (see first paragraph), with eleven cases collected. Only two involved another factor potentially responsible for hepatitis (hepatitis B for one, and use of montelukast – a drug known for its hepatotoxicity – for the other). In the remaining cases, no differential diagnosis other than that of GC-induced hepatitis could be suggested, even though most of them involved a histological study of the liver. Eight cases had a context of autoimmune hepatitis but very atypical for this disease. It is therefore possible that the GC hepatotoxicity may involve an autoimmune mechanism, at least in some cases.

A systematic review of the literature on plants causing liver damage was published in 2019. The authors pinpointed 334 cases of liver damage where a plant was identified. Rhubarb (*Rheum officinale*) was responsible for 24 of these [7]. Experimental studies in rats have also shown the hepatotoxic potential of rhubarb [8-9].

A few clinical cases of hepatitis involving the consumption of

products containing rhodiola, guggul, green coffee, *Orthosiphon stamineus* and cassia nomame have been published [6, 10, 11, 12, 13, 14]. Some of these products also contained GC [6, 10, 13].

The literature search did not identify any cases of liver damage for olive, hibiscus, cola, moringa, nopal, coleus, shiitake, hawthorn, Siberian ginseng, caigua, maqui, blackcurrant, zinc gluconate or chromium picolinate.

Search for similar cases in the nutrivigilance database

To date, no other reports concerning the food supplement Slim Metabol® have been recorded by the nutrivigilance scheme. However, cases of liver damage likely to be associated with the consumption of other food supplements containing at least one of the components of Slim Metabol® – Siberian ginseng, cassia nomame, caigua, maqui, blackcurrant and marine collagen – have been recorded in the nutrivigilance database [1] since its creation in 2009.

Conclusion and recommendations

Given all this evidence, the causality of consumption of this product in the occurrence of the serious adverse event – in this case death – was considered likely (I3, on a scale from I0 = excluded to I4 = very likely). This food supplement contains numerous ingredients: mainly plants including *Garcinia cambogia*, and red yeast rice. Other reports of liver damage associated with the consumption of *Garcinia cambogia*, some of them severe, have been identified in the literature and observed in other countries. This led the experts to consider the link between this consumption and the liver effects as well documented. In addition, red yeast rice, which is another ingredient in this supplement, has a similar literature score for liver damage. Moreover, ANSES noted that *Garcinia cambogia* is the subject of an ANSM decision prohibiting the importation, preparation, prescription and dispensing of magistral, officinal and hospital preparations, as well as the prescription, dispensing or administration to humans of this same plant.

Lastly, from a regulatory point of view, ANSES notes on the one hand that the product Slim Metabol® is not among the food supplements declared in France, and on the other hand that the plant *Garcinia cambogia* is not listed in the Order of 24 June 2014 establishing the list of plants other than fungi authorised in food supplements, as well as the conditions of their use. However, it does appear under the name *Garcinia gummi-gutta* (L.) Roxb in the January 2019 version of the list of plants that can be used in food supplements, published by the DGCCRF on its website (commonly known as the "Plant List"), without any health recommendation or restriction.

In view of all these points, and although this is the first report to the nutrivigilance scheme of a case associated with this food supplement, ANSES strongly advises against consumption of the food supplement Slim Metabol® marketed outside France.

Since *Garcinia cambogia* appears to be a common ingredient in food supplements on the weight-loss market, ANSES also reiterates that according to its expert appraisal published in 2010, seeking to lose weight without a formal medical indication involves risks and requires support from a health professional (ANSES 2010).

Lastly, ANSES has issued an internal request to determine whether safe conditions for the use of food supplements containing *Garcinia cambogia* can be identified.

ANSES reiterates its usual recommendations concerning food supplements:

- Consumers should:
 - * notify a healthcare professional of any adverse effect occurring after consumption of a food supplement;
 - * comply with the conditions of use specified by the manufacturer;
 - * avoid taking food supplements on a multiple, prolonged or repeated basis throughout the year without having sought the advice of a healthcare professional (doctor, dietician, etc.);
 - * exercise great vigilance with regard to improper claims;
 - * exercise great vigilance regarding the purchase of products sold through alternative channels (internet, gyms, etc.) and without personalised advice from a health professional.
- Healthcare professionals should report to its nutrivigilance scheme any cases of adverse effects they suspect are associated with the consumption of food supplements.

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Where should reports be sent?

Adverse effects can be reported on the [Adverse Health Event Reporting Portal](#) of the Ministry of Social Affairs and Health or directly by completing [the online reporting form](#).

POUR EN SAVOIR PLUS, VOUS POUVEZ CONSULTER:

[Opinion of the French Agency for Food, Environmental and Occupational Health & Safety on a case of fatal fulminant hepatitis associated with consumption of the food supplement Slim Metabol®](#)

References

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