

# Hallucinations and mental confusion associated with consumption of a sleep-promoting food supplement containing melatonin and California poppy



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ANSES received a report of a severe adverse effect – hallucinations and mental confusion – potentially associated with consumption of the product Novanuit® Triple Action, marketed in France. Given the severity of the adverse effect described, ANSES wished to bring this case to the attention of the general public and healthcare professionals. It alerted consumers to the risk of interaction between medicines and products containing melatonin and California poppy. It also invited them and healthcare professionals to report adverse effects to the national nutrivigilance scheme.

Through its nutrivigilance scheme, ANSES received a report of a severe adverse effect (Level 3 severity)<sup>1</sup> potentially associated with consumption of the food supplement Novanuit® Triple Action marketed in France. ANSES published an opinion detailing this case (ANSES, 2024). The product contains passion flower (*Passiflora incarnata*), lemon balm (*Melissa officinalis*), California poppy (*Eschscholzia californica*), melatonin and vitamin B6.

## THE ALERT

The report concerned a 93-year-old woman with a medical history of diabetes and heart disease. She was being treated with magnesium, potassium, Lantus®<sup>2</sup> and four other unspecified medicinal products.

In June 2022, she began taking Novanuit® Triple Action, one tablet a day, in the evening at bedtime. Nocturnal and diurnal hallucinations and mental confusion occurred from the very beginning. Following admission to hospital and a period of convalescence for heart problems, she stopped taking Novanuit® Triple Action and no longer reported any hallucinations or mental confusion. When she returned home, she began taking Novanuit® Triple Action once again and reported new hallucinations. The following day, she stopped taking Novanuit® Triple Action for good and noted that the adverse effects ceased.

## LINK WITH USE OF THE FOOD SUPPLEMENT

The causality of the food supplement in the occurrence of the hallucinations and mental confusion was assessed (ANSES, 2019). This takes four components into account, namely the onset time, the outcome after discontinuing the product, whether or not the effect reappears upon reintroduction of the product and the absence of any other possible explanation for the observed adverse effect.

<sup>1</sup> The scale of severity in nutrivigilance varies from Level 1 (low severity) to Level 4 (death).

<sup>2</sup> Lantus® contains insulin glargine, a long-acting analogue of human insulin, used to regulate glucose metabolism.

For the food supplement Novanuit® Triple Action, the time to onset of the effect was considered «compatible». Indeed, the reported effects were observed from the night after the medicine was taken for the first time. The outcome was described as «suggestive» because the effects ceased when the patient stopped taking the product. Reintroduction was described as «positive», since the patient, who began taking the food supplement again on the first night of her return from convalescence, reported that the adverse effects had reappeared. Regarding the aetiological investigation, despite some missing information (biological data, imaging results), in application of the method used for determining causality in the nutriviigilance scheme, the involvement of the Novanuit® Triple Action product in the occurrence of the hallucinations and mental confusion was deemed very likely, i.e. 14 on a scale ranging from 10 (causality excluded) to 14 (causality very likely).

## NO IDENTICAL CASES IN THE SCIENTIFIC LITERATURE

In the current case, the literature search focused on examples of clinical studies or other cases of hallucinations and mental confusion in humans associated with consumption of the active ingredients of the food supplement Novanuit® Triple Action, namely California poppy (*Eschscholzia californica*), lemon balm (*Melissa officinalis*), passion flower (*Passiflora incarnata*), vitamin B6 and melatonin.

This literature search did not identify any studies or clinical cases reporting the occurrence of hallucinations or mental confusion related to the active ingredients in the food supplement Novanuit® Triple Action. In the ANSES opinion published on 11 April 2018 (Request 2016-SA-0209), the risks of neurological and psychological disorders – including hallucinations and confusion – associated with the consumption of food supplements containing melatonin were assessed: only nightmares, agitation and mood disorders were reported (ANSES 2018).

In view of the «very likely» level of causality and the absence of evidence in the literature, ANSES studied other explanatory hypotheses that could account for a possible direct cause-and-effect relationship between consumption of an ingredient in the Novanuit® Triple Action product and the onset of hallucinations or confusion.

## DRUG INTERACTIONS?

In its 2018 report, ANSES identified that melatonin could interact with certain medicines, especially substances acting on the central nervous system and hyp-

notics in particular (ANSES, 2018), potentiating the neuropsychiatric adverse effects. A study has also shown that an extract of California poppy and its main active substances can inhibit certain enzymes involved in drug metabolism. A list of medicinal products, comprising 127 active ingredients able to interact with melatonin or Californian poppy, was therefore appended to the Agency's opinion published in 2024.

Furthermore, the patient leading to the alert presented here was diabetic and being treated with Lantus®. Neuropsychiatric symptoms such as hallucinations and confusion could be explained by a blood sugar imbalance, due to either hypo- or hyperglycaemia.

## CONCLUSIONS AND RECOMMENDATIONS

For the case reported here, the causality of the Novanuit® Triple Action food supplement in the occurrence of the hallucinations and mental confusion was deemed very likely. The literature search did not identify any ingredient that seemed directly responsible for these adverse effects. They might be explained by a possible interaction of melatonin or California poppy with certain medicinal products that can induce mind-altering effects.

As a general rule, therefore, ANSES urges caution regarding the concomitant consumption of food supplements and medicinal products for which interactions cannot be ruled out. It therefore recommends that the risk of drug interaction be systematically considered when taking any food supplement.

Lastly, ANSES reiterates its general recommendations for 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.);
- be wary of any «miracle» properties claimed by some manufacturers;

very vigilant when purchasing products sold on certain websites or social media, which are subject to less stringent monitoring.

ANSES also reminds healthcare professionals of the im-

portance of reporting to its nutrivigilance scheme any cases of adverse effects they suspect are associated with the consumption of food supplements.

**Sandrine Wetzler (ANSES)**

### FIND OUT MORE

[1] ANSES, 2024. <https://www.anses.fr/fr/system/files/NUT2023VIG0188.pdf>

[2] ANSES, 2018. <https://www.anses.fr/fr/system/files/NUT2016SA0209.pdf>

[3] ANSES, 2019. <https://www.anses.fr/fr/system/files/NUT2018SA0026.pdf>

### REFERENCES

[1] Anses. 2018. Opinion of the French Agency for Food, Environmental and Occupational Health & Safety on the risks associated with the consumption of food supplements containing melatonin (Internal Request 2016-SA-0209). Maisons-Alfort: ANSES.

[2] Anses. 2019. Revised Opinion of the French Agency for Food, Environmental and Occupational Health & Safety on the updating of the method for determining causality in reports of adverse effects in nutrivigilance (Request 2018-SA-0026). Maisons-Alfort: ANSES.

[3] Anses. 2024. Opinion of the French Agency for Food, Environmental and Occupational Health & Safety on a case of hallucinations due to consumption of the food supplement Novanuit® Triple Action (Request 2024-VIG-0188). Maisons-Alfort: ANSES.