Positive opioid tests due to consumption of poppy-seed bread sandwiches

In early 2019, consumption of sandwiches made from poppy-seed bread was linked to positive results from urine opioid screening tests. Although the offending foods were promptly removed from the market, the fact remains that depending on the type of poppy seeds used, the cleaning process applied to those seeds and the bakery product recipes and manufacturing processes, the alkaloid content of the poppy may remain high enough to yield a positive test result or, more rarely, to cause clinical signs. Discussions are under way at EU level to amend the regulations.

The alert

In late February 2019, the poison control centres (CAPs) alerted ANSES because commercial drivers had tested positive for alkaloids (morphine and codeine) even though they denied taking any illegal products, or pain or cough medication containing opioids. The toxicology laboratory at the Garches University Hospital, whose expertise had been sought by the company employing the drivers, linked these results to the fact that they had consumed sandwiches made from poppy-seed bread. It alerted the CAPs to the abnormally high alkaloid content (morphine, codeine and thebaine) in 50 g of poppy seeds scraped off these sandwiches. Analyses showed that a baguette sandwich containing about 15 g of seeds yielded about 4 mg of morphine (a dose higher than 1.9 mg for a 60-70 kg subject is considered as potentially having a clinical effect).

To confirm the veracity of the positive test results leading to the alert, ten people from the Garches laboratory consumed poppy-seed bread sandwiches from the incriminated brand, purchased in two *départements* of the Ile-de-France region. For all of them, morphine was detectable in their urine[1] for up to 18 hours after consumption, and for 50% of them it was detectable for up to 48 hours.

The saliva test was positive until 10 hours after ingestion. One subject agreed to give blood samples 1, 2 and 3 hours after consumption: all were significantly positive for morphine. Poppy-seed bread sandwiches from other brands were studied, and the people who consumed them also tested positive in urine tests [1].

ANSES promptly alerted the health authorities and the Directorate General for Competition, Consumer Affairs and Fraud Control (DGCCRF). The foods concerned were immediately recalled and withdrawn from the market. A press release of 1 March 2019 called on consumers to avoid consumption of bakery products containing significant quantities of poppy seeds, especially before engaging in any activity requiring special attention (e.g. driving) or for populations most at risk (pregnant or breastfeeding women, children, and people with urinary retention or respiratory risk factors[2]).

The DGCCRF issued a European alert under the "Rapid Alert System for Food and Feed" (RASFF) on 21 March 2019, enabling the withdrawal of all products from the incriminated brand that may have been placed on the market in other EU Member States or other countries.

1. Determination by liquid chromatography coupled with mass spectrometry (LC-MS/MS)

2. https://www.economie.gouv.fr/files/files/directions_services/dgccrf/presse/communique/2019/CP-DGCCRF-DGS-Signalement-aux-autorites-sanitaires-de-teneurs-anormalement-elevees-en-alcaloides-dans-des-graines-de-pavot.pdf

Another case of poppy seed poisoning was reported by the Paris CAP on 6 May 2019. A woman in her fifties had eaten a 300 g poppy seed loaf purchased from a bakery in the Paris region every day for the previous three years. She had been experiencing clinical signs of opioid contamination such as a dry mouth, tachycardia, dizziness, drowsiness and nausea for several months. Informed of the alert issued by the health authorities, she contacted the Paris CAP. Blood and urine tests showed the presence of thebaine, characteristic of opioid contamination associated with the consumption of poppy seeds. After stopping consumption, she experienced sweating and tremor, symptoms consistent with a withdrawal syndrome. In addition, the other signs, mainly the dizziness she had complained about and for which she had undergone a number of additional tests – all negative – disappeared. The urine test was then negative. Although it was not possible to analyse the bread consumed, the chronology of events and the dosages involved very much supported a causal link.

Changing European regulations

Poppy seeds are oil seeds derived from the plant *Papaver somniferum L.* These plants can be grown for food or pharmaceutical purposes. In the latter case, the varieties are selected for their high opium alkaloid content, concentrated in the plant capsule.

In the natural state, poppy seeds contain few or no opium alkaloids. However, they can become contaminated as a result of insect damage or during harvesting, when dust from the capsule adheres to the seeds. Food processing steps such as washing, soaking, grinding and cooking can reduce the alkaloid content of poppy seeds by 25-100%.

In a report published in November 2011 [2], the European Food Safety Authority (EFSA) assessed the health risks associated with exposure to opium alkaloids in poppy seeds. In this first report, it acknowledged that consumption of poppy products could lead to the pharmacological effects of morphine. However, EFSA only considered morphine in this assessment. Based on this substance's pharmacological properties, the acute reference dose (ARfD) was estimated at 10 µg of morphine per kg of body weight.

In 2014, the European Commission published Recommendation 2014/662/EU on good practices to prevent and to reduce the presence of opium alkaloids in poppy seeds and poppy seed products [3]. These recommendations relate to harvesting, post-harvest cleaning, and specific labelling for seeds that need to undergo further physical treatment to reduce the opium alkaloid content before human consumption or use as an ingredient in foodstuffs. Treatments such as washing, soaking, grinding and cooking at a temperature of at least 135°C but preferably above 200°C can potentially reduce the alkaloid content of poppy seeds by 25-100%.

A target level of 10 mg of morphine per kg of poppy seeds was accepted by Member States on 25 November 2016. This applies to seeds intended to be sold to the final consumer or to food sector operators, without any indication of the need to subject these poppy seeds to further physical treatment. If this target value is exceeded, producers are encouraged by the competent authorities in each Member State to comply with guides to good practice, in order to reduce the opium alkaloid content. Discussions are under way to establish restrictive regulations, i.e. with maximum authorised values in morphine equivalent for seeds sold to the consumer.

The European Commission asked EFSA to update its scientific opinion in the light of new data on the alkaloid content of poppy seeds. A new opinion [4] published in May 2018 confirmed "the safe level of 10 µg of morphine equivalent per kg of body weight, i.e. a "group ARfD" that, in addition to morphine, takes codeine content into account when calculating dietary exposure. This is because the new data show that in some samples of poppy seeds on the European market, the codeine concentration may be higher than that of morphine". A full assessment of the risks of other poppy alkaloids (thebaine, oripavine, noscapine and papaverine) could not be carried out due to a lack of available data, but according to EFSA's experts, dietary exposure to thebaine might pose a health risk. Additional data, in particular on the toxicity of thebaine, are needed to clarify this issue".

There is currently no European or French legislation setting a maximum alkaloid content for poppy seeds used for food purposes. Such a value would enable foods placed on the market to be withdrawn if testing found that the limit had been exceeded.

3. The acute reference dose (ARfD) is an estimate of the amount of a substance in food – normally expressed in terms of body weight (mg per kg or µg per kg of body weight) – that can be ingested in a period of 24 hours or less without appreciable health risk to the consumer.

DGCCRF surveys of French products

The DGCCRF obtained full traceability of the seeds used for the sandwiches incriminated in the first alert: they had a high morphine content (80 mg/kg). Two factors combined to lead to a high alkaloid content in the bakery products: (i) the large quantity of seeds used and (ii) insufficient cleaning of the seeds along with a manufacturing process that led to a fairly small reduction in the amount of morphine compared to that usually found in the literature.

In March 2019, the DGCCRF launched a national survey. Thirty-one samples were taken from eight regions (15 *départements*) and were analysed by the SCL (Joint Laboratories Service) laboratory in Strasbourg (six samples of seeds, two of biscuits, one of brioche, three of crackers, five of bagels and 14 of bread loaves or baguettes).

- Seven samples of foodstuffs containing poppy seeds (one brioche, two bagels and four bread samples) were declared "unfit for consumption", as eating them could lead to EFSA's ARfD being exceeded, at least for certain categories of the population. The operators concerned were asked to put in place the necessary corrective measures, in conjunction with their poppy seed suppliers. These exceedances were moderate for all samples except the brioche, whose consumption could lead to the ARfD being exceeded for all consumer categories considered.
- One poppy seed sample was declared "unsatisfactory" because it exceeded the target value for morphine.

The survey also found that manufacturers of foodstuffs containing poppy seeds and their poppy seed suppliers had little or no awareness of this health risk.

A new survey was undertaken in early 2020 to verify the effectiveness of the measures taken.

In Luxembourg, in 2016 and 2017, the Food Safety Unit tested about 20 samples of raw poppy seeds from different origins for opium alkaloids [5], with results similar to those of the DGCCRF survey.

Prospects

To ensure that consumers are not wrongly accused of consuming illicit substances in the event of a positive opioid screening test, prosecutors will be informed that screening tests may be declared positive after consumption of bakery products containing poppy seeds and that, by using more complex toxicological tests, it is possible to differentiate between a food origin and a medicinal or illicit origin by identifying the presence of thebaine, which is specifically associated with the consumption of poppy seeds.

What can be done in the meantime?

Pending the entry into force of the new European regulations and full awareness in the profession of the manufacturing processes leading to a reduction in the alkaloid content of poppy seeds and products containing them, ANSES recommends limiting their consumption and avoiding them completely when driving a vehicle or when an activity requires full alertness. These measures especially concern children, pregnant women and people at risk of urinary retention or interrupted breathing.

In the event of a positive test leading to legal proceedings, it is possible, with analyses carried out in toxicology laboratories such as that of the Garches University Hospital, to prove the food origin of the alkaloids by the presence of thebaine among the alkaloids assayed. Even when the urine or blood tests have not been carried out within 48 hours, thebaine can still be found in hair.

It is important for consumers, police officers, lawyers and magistrates to be informed.

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4. Full results in the DGCCRF's 2020 annual report (publication pending).

Références bibliographiques

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[3] Commission Recommendation of 10 September 2014 on good practices to prevent and to reduce the presence of opium alkaloids in poppy seeds and poppy seed products. https://op.europa.eu/en/publication-detail/-/publication/747ae0f2-3a42-11e4-8c3c-01aa75ed71a1/language-en

[4] Opium alkaloids in poppy seeds: assessment updated https://www.efsa.europa.eu/en/press/news/180516

[5] Alcaloïdes opioïdes dans les graines de pavot [Opium alkaloids in poppy seeds] https://securite-alimentaire.public.lu/dam-assets/fr/professionnel/Denrees-alimentaires/Contaminants/opioides/F-167-Alcaloides-opioides.pdf