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Is wild asparagus really edible?

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Photo 1 : Wild asparagus (*Loncomelos pyrenaicum, Ornithogalum pyrenaicum*)

Wild asparagus is a commonly eaten wild plant. However, for a number of years now, poison control centres have been receiving reports of clinical manifestations, such as swelling of the throat and difficulty swallowing, following consumption of this asparagus. These symptoms are not immediate, generally occurring three to four hours after the meal. Based on its analyses of wild asparagus to search for toxic compounds, ANSES has developed some theories on the possible causes and mechanisms of its toxicity.

AN INCREASINGLY POPULAR DELICACY

Wild asparagus (*Loncomelos pyrenaicum, Ornithogalum pyrenaicum*) is a wild, almond-green plant belonging to the Asparagaceae family (formerly Liliaceae), whose spiky flower buds (*photo 1*) are eaten with vinaigrette or as an accompaniment to a meal. It has a flavour somewhere between asparagus, pea and artichoke.

It is a seasonal plant, growing between late April and early June in meadows, embankments and woods throughout most of mainland France and Corsica. Picking is sometimes restricted by prefectoral decree in order to protect the species[1].

The plant can also be grown by individuals in their vegetable gardens from commercially available seeds. It has been sold at markets and in some supermarkets for a number of years now.

FIRST ALERT IN 2019

Wild asparagus is considered to be edible. Nevertheless, although no studies so far have reported any toxicity in humans, poison control centres (PCCs) have received several calls over the years from people experiencing symptoms after eating it.

In May 2019, the Nancy PCC alerted ANSES following a case of serious poisoning with life-threatening symptoms. Two hours after a meal of wild asparagus purchased at a market, a man experienced a tightening of the throat with difficulty swallowing, followed by angioedema[2] combined with generalised urticaria. This case required hospitalisation, and had a favourable outcome following treatment. The patient's wife had shared the same meal and experienced the same symptoms, but to a lesser degree, supporting the assumption of food poisoning.

In 2020, an analysis of calls recorded by PCCs between January 2010 and June 2020 identified cases of poisoning following 37 meals of wild asparagus. Out of 66 diners (the same meal was sometimes shared by several diners),

[1] Order of 13 October 1989 on the list of wild plant species that may be subject to permanent or temporary prefectoral regulation https://www.legifrance.gouv.fr/loda/id/LEGITEXT000006059328/

[2] Rapid swelling of the skin and mucous membranes, mainly in the head and neck.

48 people, i.e. 73% of diners, were symptomatic. The main symptoms were intense oropharyngeal pain (42%), swelling in the mouth or throat (29%) and difficulty swallowing (29%). One notable point was that the first signs did not occur immediately after eating the wild asparagus, as can happen with an allergic reaction or immediate irritation, but were delayed by an average of three hours.

These observations led to questions being asked about the possible causes and mechanisms of this poisoning. Was another plant mistaken for wild asparagus? Might the origin of the plant, the way it was cooked or the amount ingested have influenced the onset of symptoms? Does the plant contain toxic substances?

A SPECIFIC STUDY

To better document the poisoning cases and search for any toxic compounds in wild asparagus, a study was carried out from 2022 to 2023 by the Nancy PCC and the pharmacognosy[3] laboratory at the Paris Faculty of Pharmacy, with financial support from ANSES. Its aim was to gather detailed information on poisoning cases due to wild asparagus reported to PCCs over two consecutive years, while at the same time developing methods for analysing the plant in order to identify its constituent substances.

Samples of wild asparagus were collected from poisoning victims who had called a PCC during the study period. Other asparagus purchased from markets was used, without being consumed, to develop analysis techniques. These uneaten samples were then compared with the ones responsible for poisoning.

A DOZEN WELL-DOCUMENTED CASES OF POISONING DUE TO WILD ASPARAGUS

Between 2022 and 2023, eight collective cases of food poisoning due to wild asparagus were reported to the PCCs: five in 2022 and three in 2023. These meals were shared by a total of 20 people – with two to five people per meal – 12 of whom reported symptoms.

The majority of the poisonings (seven meals) occurred in May, with one meal in April. For six meals, the consumed asparagus had been picked in the north-east of France, while for one meal it had come from the Nouvelle-Aquitaine region. For the last meal, the origin was unknown. For six meals, the asparagus had been picked for personal consumption. For the other two, it had been purchased at a market. A photograph of the plant was available for four meals, enabling the identification of wild asparagus to be confirmed by specialist botanists.

Once picked, all of the asparagus had been eaten fresh, after being boiled, steamed or pan-fried. The amounts consumed varied and were sometimes difficult to assess, ranging from a half to 30 asparagus spears.

The poisonings concerned eight men and four women aged between 36 and 72 years. None had any history of food allergies. The onset of symptoms was delayed, averaging four hours after the start of the meal. Otorhinolaryngological signs were reported by 10 of the 12 symptomatic patients. These included difficulty swallowing, which was severe in eight cases and less so in a ninth, and swelling in the throat (six cases) or mouth (three cases). A doctor who examined one patient confirmed the occurrence of angioedema. Digestive (two cases), dermal (two cases) and respiratory (one case) symptoms were also reported. In total, four patients had consulted a doctor, four went to the hospital emergency department and four were monitored at home.

AN INITIAL LABORATORY ANALYSIS OF WILD ASPARAGUS

A review of the scientific literature showed that the phytochemical[4] characteristics of wild asparagus had never previously been studied.

In order to develop methods for analysing wild asparagus, three batches of plants not associated with any poisoning cases were purchased from a greengrocer or at a market. After being reduced to a powder and dissolved in water, the plant had a viscous texture. Microscopic examination revealed the presence of large quantities of mucilage, a plant substance made up of chains of polysaccharides[5] that swell on contact with water, taking on a viscous, sometimes sticky, gelatinous consistency. Microscopic analysis also discovered abundant calcium oxalate raphides (photo 2).

© Pharmacognosy laboratory, Paris Faculty of Pharmacy.

Photo 2 : Calcium oxalate crystals (raphides) found in a sample of wild asparagus.

[3] Study and teaching of living substances of therapeutic interest.
[4] Organic chemical compounds found naturally in plants.
[5] Complex carbohydrates made up of a large number of simple sugars.

These microscopic crystals in the form of fine needles are found in many plant families, including Araceae, houseplants that are known to irritate the skin and mucous membranes upon contact.

Lastly, extracts of wild asparagus were analysed using chromatographic[6] techniques to characterise the main organic substances contained in the plant. These analyses revealed the presence of sugars, fatty acids and sitosterol, a non-toxic sterol found widely in plants.

Analysis of a sample of wild asparagus associated with one of the poisoning cases showed high concentrations of mucilage and calcium oxalate raphides, as well as an organic substance profile similar to that of the samples of asparagus not responsible for poisoning.

WHAT CAUSED THE OBSERVED SYMPTOMS? THEORIES BUT NO CERTAINTY

The most likely hypothesis is that the raphides, which consist of minute needles, become embedded in the oropharyngeal mucosa and mechanically cause irritation, facilitating the entry of inflammatory or toxic substances. The higher the raphide concentration, the more the mucosa is damaged and the less it can act as a local protective barrier. These substances could then have caused the inflammation responsible for the swelling of the skin and mucous membranes, and the discomfort when swallowing.

They do not seem to be destroyed by heat, as all the asparagus eaten by the poisoning victims had been cooked. However, at this stage of the research, the active substances in the plant responsible for this inflammation have not been identified. Further research is therefore needed.

The mucilage found in asparagus might initially play a protective role, acting as a gel that traps the raphides, then gradually releasing them during digestion. The calcium oxalate raphides would therefore not immediately come into contact with the mucous membranes of the mouth and throat, which could explain the delayed onset of symptoms after ingestion.

Moreover, only some of the people who had eaten the meal of wild asparagus had symptoms. There could therefore be an individual susceptibility, which is by definition specific to each person. Furthermore, certain patients had eaten wild asparagus in previous years without experiencing any particular discomfort, which may suggest sensitisation to certain substances or a higher concentration of irritants in the plant.

Lastly, the amount of asparagus consumed, although difficult to assess, did not appear to play any part in the occurrence of poisoning.

Further work could supplement this study by quantifying the calcium oxalate raphides in wild asparagus, in order to compare them with plants known to be toxic and also rich in these raphides (Arum, Dieffenbachia, etc.), and seek a relationship between the calcium oxalate concentration and the triggering of clinical manifestations.

It would also be interesting to continue analysing the wild asparagus samples in the study, using biological tests to precisely identify the substances responsible for the inflammation.

IS IT SAFE TO CONTINUE EATING WILD ASPARAGUS?

The wider availability of wild asparagus at markets and in supermarkets could lead to an increase in the number of people affected by poisoning. ANSES therefore urges the public authorities to consider specific recommendations and management measures, which could go as far as prohibiting the sale of these plants. In the immediate future, the general public and healthcare professionals should be informed about the risks associated with consumption of wild asparagus, in order to improve the reporting and documenting of new cases of poisoning.

If symptoms develop following consumption of wild asparagus, ANSES recommends calling a poison control centre or consulting a doctor, and dialling 15 (in France) or 112 in the event of a life-threatening condition, mentioning this consumption.

Taking photographs of the plants you pick before cooking can help identify them in the event of poisoning. If any meal leftovers are available, they can be analysed for toxic substances.

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[6] Chromatography is a physico-chemical method used to separate the constituents of a sample.

Essential oils should be used with caution !

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Essential oils are used for a variety of purposes. Their chemical composition combines multiple substances and can vary depending on the species of plant. In 2022, in response to an interministerial request, ANSES examined cases of exposure to essential oils reported to poison control centres. The increase in the number of calls received between 2011 and 2021 mainly concerned children, with accidental ingestion of essential oils left within their reach or inadvertent administration instead of vitamin D. Because they contain toxic substances, essential oils should be used with caution. The advice of a healthcare professional should be sought before use, and a poison control centre should be called without delay in the event of accidental exposure or overdose.

Essential oils can be used for a wide range of purposes, such as flavouring foods, relieving different ailments or adding fragrance to cleaning products. Depending on the oils and their uses, they can be applied to the skin, inhaled or ingested. They come in a wide range of formats, from small vials containing just one oil to mixtures with other ingredients, such as biocidal sprays or cosmetic creams.

With their use on the rise, in October 2022, ANSES was asked by its five supervisory ministries to carry out work based on vigilance data to obtain information on their adverse effects, for all the different uses. ANSES therefore analysed the calls to poison control centres.

WHAT IS AN ESSENTIAL OIL?

Essential oils are used for a variety of purposes. Their chemical composition combines multiple substances and can vary depending on the species of plant. In 2022, in response to an interministerial request, ANSES examined cases of exposure to essential oils reported to poison control centres. The increase in the number of calls received between 2011 and 2021 mainly concerned children, with accidental ingestion of essential oils left within their reach or inadvertent administration instead of vitamin D. Because they contain toxic substances, essential oils should be used with caution. The advice of a healthcare professional should be sought before use, and a poison control centre should be called without delay in the event of accidental exposure or overdose.

Certain chemicals can be the sole component of an essential oil: this is the case with methyl salicylate found in wintergreen essential oil (*Gaultheria procumbens*; *Gaultheria fragrantissima*). Others are found in several different essential oils in highly variable concentrations: this is true of limonene, found at over 90% in sweet orange essential oil (*Citrus aurantium ssp dulcis*) and at less than 1% in palmarosa essential oil (*Cymbopogon martini*).

It is difficult to know the exact chemotype of an essential oil sold in a shop. The vials sold commercially sometimes contain mixtures of essential oils from different geographical origins, extraction periods or botanical subspecies.

Data from the PCCs' national database on products and compositions (BNPC) have shown that some vials of essential oils sold actually contained a mixture of several essential oils from the same family but from different species and subspecies. For example, under the name «lemongrass essential oil», one product actually contained a blend of four essential oils of lemongrass from different species and subspecies, all with different chemotypes.

In addition, many products labelled as «essential oil» actually contain other ingredients, sometimes in concentrations of more than 50%: this includes certain essential oil sprays containing more than 70% ethanol, or topical oils containing more than 50% vegetable oil or emollients.

For all these reasons, it is difficult to know exactly which essential oils and chemicals a person is exposed to when using them.

Table 1 – Examples of chemicals found in three essential oils defined by plant genus, species and subspecies (source: ANSES, 2024)

HUILE ESSENTIELLE	FAMILLE	GENRE	ESPÈCE	NOM VERNACULAIRE	CHIMIOTYPE (PAR CONCENTRATION DÉCROISSANTE DANS L'HUILE ESSENTIELLE)
Cedar	*Pinaceae*	*Cedrus*	*atlantica (Endl) Carrière ou G.Manetti*	Atlas cedar	b-Himachalene a-Pinene a-Himachalene g-Himachalene Deodarone Himachalol (Z)-a-Atlantone (E)-a-Atlantone
Mint	*Lamiaceae*	Mentha	*piperita - Mentha x piperita L.*	Peppermint	Menthol Menthone 1,8-Cineole Isomenthone Menthyl acetate Neomenthol b-Caryophyllene Limonene Menthofurane Pulegone
Mint	*Lamiaceae*	Mentha	*spicata L.*	Spearmint, garden mint	Carvone Limonene cis-Dihydrocarvone trans-Dihydrocarvyl acetate b-Bourbonene Menthone trans-Sabinene (Z)-Jasmone cis-Carvyl acetate Viridiflorol 3-Octanol

HOW ARE THEY REGULATED?

An essential oil may not be sold without a specific purpose: as a cosmetic, food flavouring, food supplement, etc. The company placing the product on the market must inform consumers of the directions and precautions for use (Article L. 111-1 of the French Consumer Code). The intended use stated by the manufacturer determines the applicable regulations and therefore the requirements that the product must meet.

Some essential oils have claimed uses as biocides and are therefore governed by Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products. *Eucalyptus citriodora* and lavandin essential oils are currently being assessed as insect repellents. Geraniol, a substance found in many essential oils, is also awaiting approval as a repellent and insecticide. At present, no essential oils or any of their constituent chemicals have been approved for biocidal use.

Few essential oils have been classified according to Regulation (EC) No 1272/2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures (known as the CLP Regulation). The European Chemicals Agency (ECHA) has proposed classifying tea tree essential oil (*Melaleuca alternifolia*) as a category 1B reprotoxic substance «may damage fertility» (hazard phrase H360F) and a category 2 reprotoxic substance «suspected of damaging the unborn child» (hazard phrase H361d). This classification is currently under discussion at European level. Other essential oils are also being assessed with a view to harmonised classification, such as those of sweet orange and lavandin. In addition to the harmonised classification, the CLP Regulation lists certain hazards of chemicals found in essential oils. This is the case with substances self-classified (i.e. classified by the manufacturers themselves) as «skin irritants» or «skin sensitisers» (hazard phrases H315 or H317, respectively), for which consumers must be warned of the risk of dermatitis in the event of dermal application.

In accordance with Decree no. 2007-1198 of 3 August 2007, 15 essential oils may only be dispensed in pharmacies because of their neurotoxic, irritant, phototoxic or carcinogenic properties[1]. They must comply with the pharmaceutical quality described in the European or French Pharmacopoeia, i.e. regarding their exact scientific name, chemotype and chemical composition.

Essential oils that are not covered by the pharmaceutical monopoly are sold over the counter and must not make any therapeutic claims, because their composition is not guaranteed with regard to their potential therapeutic effect [2].

WHAT CONCLUSIONS CAN BE DRAWN FROM THE CALLS RECEIVED BY POISON CONTROL CENTRES?

In response to the interministerial request made to ANSES in 2022, the analysis of exposures to products containing only essential oils (with no other ingredients) reported to poison control centres between 1 January 2011 and 31 December 2021 found an increase in the number of calls received: 1926 in 2011, 3715 in 2017, then more than 4000 cases from 2018 to 2020 before falling to 3752 cases in 2021 (essential oils were used extensively during the COVID-19 epidemic). This increase may reflect greater use of essential oils by the public.

These cases essentially related to acute exposure (calls to poison control centres are less likely to be about medium- and long-term exposure).
Exposure mainly concerned young children: median age 3 years with 14% under 1 year of age. In more than a third of accidents (38%), the cause was a lack of risk perception on the part of the child, who had handled a vial of essential oil left within their reach (see Figure 1). It is important to remind parents and carers never to leave bottles of essential oils within the reach of young children.

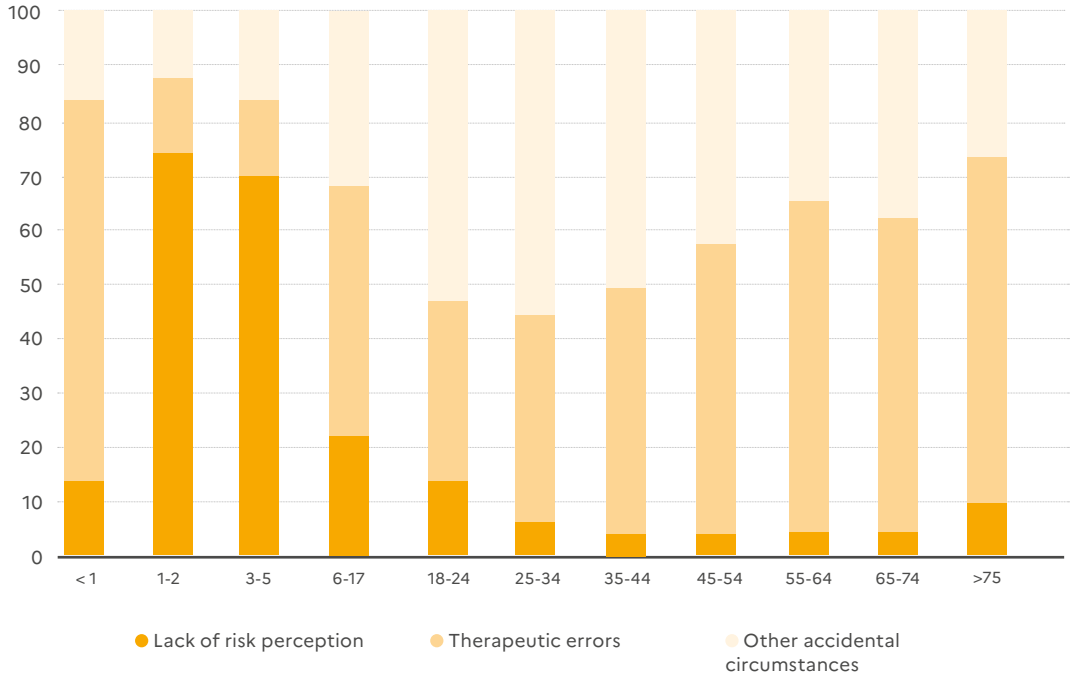
More than a third of cases (36%) were due to the essential oil being confused with another product because of similar packaging. This was the leading cause of accidents in children under 1 year of age. In the majority of these cases, a parent or relative of the child had mistakenly administered an essential oil instead of vitamin D (79%). There were also cases of confusion with bottles of vitamin K or sodium fluoride. This confusion was not helped by the similarity between the bottles, and could have been avoided if the packaging had been more distinctive. However, some poisonings involved the accidental administration of essential oils instead of anti-allergy medicines or probiotics intended for children, despite the lack of similarity in the respective packaging. In general, parents and carers of young children should never place vials of essential oils near products used to care for newborns and infants.

The study reported a serious case of poisoning in an adolescent girl who, after ingesting a bottle of an unidentified essential oil, developed coughing and recurrent vomiting that progressed to aspiration pneumonia.

She recovered after being treated in hospital. According to the CLP Regulation, certain chemicals contained in essential oils have been self-classified as an «aspiration hazard» (hazard phrase H304).

[1] Common wormwood (*Artemisia absinthium L.*), Roman wormwood (*Artemisia pontica L.*), common mugwort (*Artemisia vulgaris L.*), white mugwort (*Artemisia herba-alba Asso L.*), tree wormwood (*Artemisia arborescens L.*), white cedar (*Thuja occidentalis L.*), Korean arborvitae (*Thuja koraiensis Nakai*), hyssop (*Hyssopus officinalis L.*), sage (*Salvia officinalis L.*), tansy (*Tanacetum vulgare L.*), western red cedar (*Thuja plicata* Donn ex D. Don.), sassafras (*Sassafras albidum* [Nutt.] Nees), savin juniper (*Juniperus sabina L.*), rue (*Ruta graveolens L.*), epazote (*Chenopodium ambrosioides* and *C. anthelminticum L.*), mustard greens (*Brassica juncea* [L.] Czernj. and Cosson).

Figure 1: Percentages, by age group, of circumstances of accidental exposure to essential oils reported to PCCs from 01/01/2011 to 31/12/2021 (source: ANSES, 2024)



This class corresponds to the hazard from a substance entering the respiratory tract directly through the mouth or nose, or indirectly during regurgitation, causing airway obstruction or aspiration pneumonia due to its physico-chemical properties.

SPECIFIC CHARACTERISTICS OF CERTAIN ESSENTIAL OILS

Some essential oils contain chemicals that are pharmacologically active and potentially toxic.

Wintergreen essential oil contains almost 100% aspirin-like derivatives, and one millilitre of this essential oil provides 1.4 times more salicylate ions than one gram of aspirin.

Regardless of its genus, species or subspecies, wintergreen essential oil contains salicylate derivatives that may be toxic, particularly if taken concomitantly with medicines containing aspirin. Its use is contraindicated in people who are allergic to aspirin or salicylates, and in people on anticoagulant therapy. Furthermore, it should not be ingested. Consumers need to be warned of this characteristic, which could cause serious poisoning, particularly if ingested accidentally.

***Melaleuca* essential oils (tea tree, niaouli, cajeput)** should be kept cool and in the dark to prevent the formation of ascaridole, a toxic chemical. For this reason, it should not be administered to children, or pregnant or breastfeeding women.

Oral consumption of ***Melaleuca* essential oils (niaouli and cajeput)**, which are rich in 1,8-cineole, is not recommended for children under 30 months of age, children with a history of epilepsy or febrile convulsions, or pregnant or breastfeeding women.

Lastly, the same chemical may be found in several essential oils of different genera and species – such as the camphor found in **lavender and lavandin essential oils** – at varying concentrations depending on the genus and species. The concomitant use of several essential oils containing the same toxic chemical is not recommended, especially for children, to avoid overdose.

CONCLUSION

Given the wide range of uses for essential oils, consumers need to be warned of the risks associated with the substances they may contain. The DGCCRF recently issued recommendations to prevent a number of these risks, including not applying pure essential oils to mucous membranes and washing hands thoroughly after applying them to the skin or using them for massage [3]. The advice of a healthcare professional should be sought before using an essential oil and in the event of any doubts about them.

In the event of accidental exposure or overdose, it is recommended to call a poison control centre, with the product label at hand, in order to determine the best course of treatment.

Jérôme Langrand (Paris poison control centre), Cécilia Solal (ANSES)

FIND OUT MORE

[1] ANSES. 2024.Essential oils. Summary of cases reported to poison control centres between 2011 and 2021 and cases recorded by the RNV3PE between 2001 and 2021. 58 pp. https://www.anses.fr/fr/Content/rapport-2022-SA-0190

[2] National Agency for Medicines and Health Products Safety (ANSM). Herbal medicines and essential oils. https://ansm.sante.fr/qui-sommes-nous/notre-perimetre/les-medicaments/p/medicaments-a-base-de-plantes-et-huiles-essentielles#title

[3] Directorate General for Competition, Consumer Affairs and Fraud Control (DGCCRF). 2023. Essential oils. https://www.economie.gouv.fr/dgccrf/Publications/Vie-pratique/Fiches-pratiques/Huiles-essentielles

Beware of the risk of burns from using microwave hair removal wax!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Despite a warning issued in 2017 and the corrective measures taken, there have been new reports of burns after using hair removal wax that can be heated in the microwave. These cases are most often due to a failure to follow the instructions. To avoid these accidents, ANSES reiterates that it is essential to follow the instructions concerning heating and resting times and, in the event of a burn, to seek the advice of a healthcare professional. ANSES also invites consumers and healthcare professionals to report these burns to the national cosmetovigilance scheme.

Hair removal has been a way of life for decades, for legs, arms, armpits, «bikini lines» and other parts of the body. A technique commonly used at home is hot wax hair removal. It involves pulling out the entire hair including the root using wax that has been heated before being applied to the skin. The instructions for use generally call for the product to be heated in a microwave oven, but this creates a risk of burns if the user fails to comply with the preparation conditions.

In 2017, due to an increased number of reports of serious second- and third-degree burns caused by poor preparation and handling of tubs of «Nair Cire Divine Monoï des Îles» heated wax, the French Health Products Safety Agency (ANSM), which was then responsible for monitoring adverse effects of cosmetic products, contacted the manufacturer and asked for corrective measures to be taken. This company amended the wording on the packaging to mention the risk of burns, and changed the product formulation to reduce the risk of a crust forming on the surface of the liquid wax, as this promotes splashing when the spatula is inserted into the tub.

The ANSM had issued a warning to consumers in 2018[1]. The manufacturer's amendment to the instructions and the reformulation of all its wax products took effect in 2019. As a result of these measures, the annual number of cases of burns due to these products fell, while not disappearing completely (see Figure 1). Since 2020, 21 new cases of burns linked to the preparation of hot wax have been reported (to the ANSM until December 2023, then to ANSES following the transfer of the national cosmetovigilance scheme on 1 January 2024, as well as to poison control centres).

A RECENT CASE

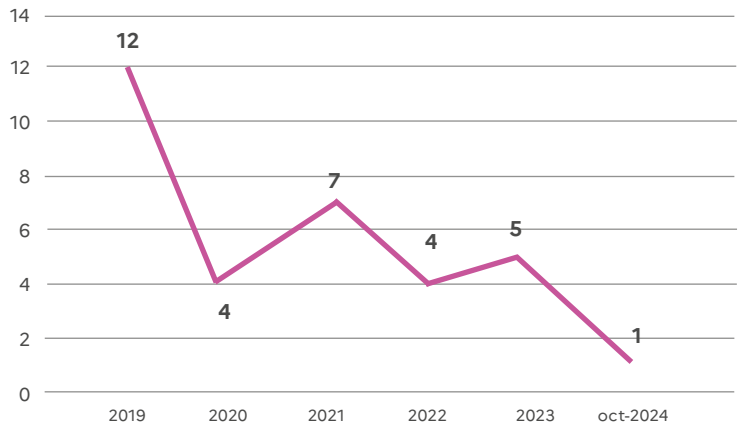
In 2024, ANSES was notified of the case of a young woman with burns to her thumb, neck and part of her thighs. After heating the wax in the microwave, the tub had become soft, and when she took it out, the pressure of her hands on the tub caused the wax to spatter over her body. This resulted in a second-degree burn that required medical monitoring for more than three weeks.

[1] https://ansm.sante.fr/informations-de-securite/nair-cire-divine-rappel-des-precautions-demploi-a-lattention-des-utilisateurs-information-de-securite#:~:text=Nair%20cire%20divine%20%2D%20Rappel%20des%20pr%C3%A9cautions%20d'emploi%20%C3%A0%20l,des%20utilisateurs%20%2D%20Information%20de%20s%C3%A9curit%C3%A9&text=En%20accord%20avec%20l'Ansm,pr%C3%A9venir%20le%20risque%20de%20br%C3%BBlure

The packaging stated that the product's appearance should be checked before it was taken out of the microwave. In the event of overheating (very liquid wax, deformed tub, presence of smoke), it was recommended to wait 25 minutes before removing the tub from the microwave.

This report prompted ANSES to analyse the circumstances surrounding the 21 cases of burns reported since 2020 and to warn users of the risk of burns associated with this hair removal technique.

Figure 1 : Évolution annuelle des cas de brûlures à la cire dépilatoire chauffée au micro-onde recueillis dans le cadre du dispositif de cosmétovigilance



BURNS CAUSED BY HANDLING ERRORS

In 43% of the reported cases (n=9), the users did not follow the precautions specified in the instructions for use. This included:
• heating time exceeded (n=1/9);
• failure to comply with resting times (n=6/9);
• incorrect positioning of the tub in the microwave with respect to the manufacturer's instructions (n=2/9).

The circumstances of the accident were not specified for the remaining 57% of cases (n=12), but the hypothesis of misuse remains strong.

Despite users reporting that they had followed the precautions for use, the circumstances mentioned included perforation of the tub, splashing of hot wax, spillage after letting go of the tub due to it being hot, poor handling, or deformation of the protective lid under the effect of heat.

HOW CAN THESE BURNS BE PREVENTED?

Hair removal wax intended to be heated in a microwave oven requires particular care to be taken. Users are recommended to read the labels and leaflets carefully and to follow the manufacturer's instructions for each type of wax.

When manufacturers suggest using microwaves, they provide detailed instructions: indication of the microwave power and the recommended heating time, details of the position of the tub in the microwave (in the centre of the turntable for some, in an offset position for others), indication of the resting time before taking the tub of wax out of the microwave, precautions when inserting the spatula into the wax and when mixing to avoid any wax splashes.

WHAT SHOULD BE DONE IF A PERSON IS BURNED WHILE PREPARING WAX?

Despite all the precautions, if a burn occurs, the French health insurance website ameli.fr recommends:

• running lukewarm water (15-25°C) over the burn for at least 15 minutes or as long as the burn is painful;
• covering the burned area with a clean, dry cotton cloth;

• not applying anything to the burn (e.g. greasy substances, creams, ointments, butter or oil), and not applying ice or ice water, which can damage the skin further;

• consulting a healthcare professional if the skin burn meets the severity criteria, i.e. if blisters appear or if pain persists, in order to receive suitable care.

In addition to treating the burn, the incident should be reported on the Ministry of Health's adverse health event reporting portal https://signalement.social-sante.gouv.fr/.

CONCLUSION

The use of hair removal wax that can be heated in the microwave can lead to burns if the preparation instructions are not strictly followed. Accidents continue to be reported, often due to handling errors after heating the wax in the microwave. It is therefore essential that consumers take the time to read the instructions carefully and follow them scrupulously to avoid serious incidents.

Although some cases of burns are due to misuse, they should still be notified via the adverse health events reporting portal. These reports lead to a better understanding of the circumstances of incidents with a view to holding manufacturers accountable. Thanks to this feedback, adjustments to the wording of instructions or precautions for use can be requested, to make them clearer and more visible. This helps to improve product safety and limit accidents.

Elodie Lontsi (ANSES)

FIND OUT MORE

https://vigilanses.anses.fr/sites/default/files/VigilAnsesN23_.Juillet2024_Cosmetovigilance.pdf

Poisoning in humans from administering medicines to horses

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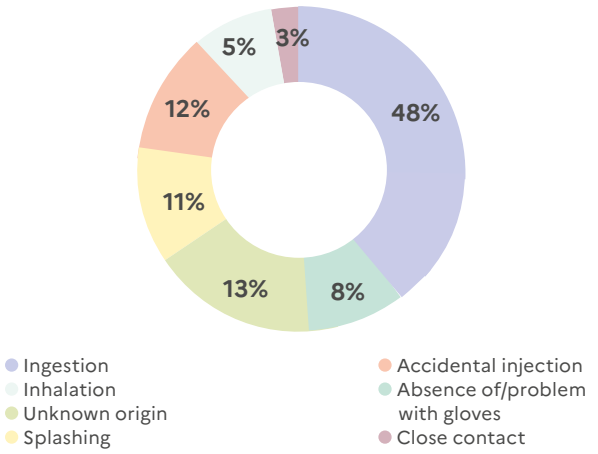
When a horse is treated with a veterinary medicinal product, humans can also be exposed. The most common scenario is accidental ingestion, accounting for more than half of all reported cases, followed by accidental injections and splashes onto the face or unprotected skin.
Two very different circumstances are behind these accidents:
confusion between a veterinary medicine and one intended for humans, or difficult administration due to an inability to control an agitated horse. Horse owners therefore need to be properly informed about the risks involved and the ways of preventing such accidents.

BACKGROUND

France has more than a million horses, and like all pets, they are increasingly being treated with medicines, sometimes over the long term. As a result, the risk of owners and professionals being exposed to medicinal products intended for this species should not be overlooked. While this risk is well managed by professionals (veterinarians and veterinary assistants), horse owners are less aware of it, even though they are often responsible for continuing treatments dispensed initially during the veterinary consultation. However, any therapeutic procedure exposes the owner and other people nearby to products about which they do not always have prior knowledge, and which may have health consequences in the event of accidental exposure.

As part of its veterinary pharmacovigilance scheme, the French Agency for Veterinary Medicinal Products (ANMV), which is part of ANSES, records all human adverse effects reported spontaneously by field workers (veterinarians, owners, breeders, etc.) following exposure to a veterinary medicine. A retrospective study of the reports recorded in the national pharmacovigilance database from 2008 to June 2024 identified the main exposure circumstances for users, whether professionals or owners, during the treatment of horses. The term «horse» in the study includes both horses and ponies. Of the 3000 symptomatic human cases recorded over this period, only those involving a veterinary medicinal product authorised exclusively for horses or explicitly indicated as having been administered to this species were selected. A total of 130 cases were selected and their exposure circumstances analysed.

Figure 1: Nature of the 130 accidental exposures



THE DIFFERENT ACCIDENTAL EXPOSURES (FIGURE 1)

• Accidental ingestion

Ingestion accounted for the majority of accidental exposures to veterinary medicines in the equine sector: 63 cases out of 130 exposures reported. Confusion between equine and human medicines was common, especially if the product was in tablet form. The main medicines concerned by this exposure circumstance were Prascend® and its generics (pergolide), intended for the treatment of Cushing's disease in horses. This is due to the fact that since horses are often kept a long way from their owners, the tablets may be kept at the owner's home and then mistaken for the owner's own tablets. Moreover, the treatment is sometimes prepared in advance, and if the tablet (or part of it) is hidden in fruit or bread, or dissolved in a liquid, and then put aside without being clearly identified, it could be inadvertently ingested by a third party.

Other reported confusions concerned solutions of external antiparasitic products (e.g. Butox® 50 ‰ or Sébacyl® 50%) which, once diluted, were stored in bottles with unclear or no labelling. There were also reports of accidental ingestion of deworming pastes after owners used their mouth to remove the cap.

• Splashes on the face or any other exposed part of the body

The administration of liquid preparations carries a higher risk of splashing. A sudden movement of the animal or pressing too quickly on the syringe plunger were the main causes of accidents with this type of medicine, especially since users rarely wear gloves or protective clothing. Splashes from dewormers, injection products and external medicines such as antiparasitic ointments or solutions were regularly the subject of reports.

• Skin contact due to not wearing gloves

Only certain medicines known to pose a risk to humans, such as those containing altrenogest (Regumate Equine®), have a leaflet that explicitly mentions the need to wear gloves when using them. However, it should be borne in mind that any active substance, regardless of its dosage form (ointment, tablet or solution), can pass through the skin barrier to varying degrees and cause a potentially severe localised reaction. Gloves are not normally used when handling horses, and even when they are worn, they are sometimes removed without taking care (touched with the other hand, torn during removal), which can also lead to accidental exposure.

• Inhalation

Most treatments are administered outdoors, making the risk of accidental inhalation of a medicament higher in windy conditions. Inhalation of oral powders, but also

of medicines in liquid form, was reported in 5% of the cases analysed.

• Accidental injections

The presence of two operators during an injection is specific to horses. The risk of accidental injection therefore concerns both the person injecting the medicine and the one holding the horse. A sudden movement of the animal is often the cause of accidental needlesticks, mainly to the fingers and hands.

Accidental injections of equine medicines into humans have also been reported, in particular equine vaccines kept in the refrigerator next to an injection product intended for humans.

• Close contact with the animal

Although less commonly reported than with pets, there have also been a few reports of adverse effects occurring after close contact with an animal that was just treated.

NOT FORGETTING THE RISK TO CHILDREN

Although children are more likely to be exposed to medicines intended for pets, the study identified 18 cases of exposure involving children aged between 2 and 13 years (average 4.4 years) over the period examined. As in the general population, accidental ingestions were mainly due to a tablet or oral syringe being left within the child's reach, or to confusion between a medicine intended for humans and one for horses, the latter being inadvertently administered to the child. A child's close contact with their treated pony can also be a source of adverse effects.

PREVENTIVE MEASURES TO BE ADOPTED

Preventive measures should address both the risk of inadvertent ingestion and the risk of accidents, whether caused by confusion with other medicines or handling of the animal.

With regard to the risk of ingestion or confusion, the precautions to be taken are those that apply to all medicines:

- medicines for horses must be stored in their original packaging and grouped together in the same place;

- they must be stored separately from human medicines, particularly those that need to be kept in the refrigerator (in a separate, reserved part of the refrigerator), and properly identified.
This is particularly true of equine vaccines kept in a refrigerator that also contains an injection product intended for humans.
- they must be stored out of the reach of children and in locked cupboards, particularly in riding schools;

- if the product is prepared in advance because this cannot be done in situ, it must be clearly identified and prepared in only limited quantities;

- liquids to be diluted must be stored in a labelled non-food container to avoid confusion; avoid decanting into plastic bottles.

Furthermore, horses are animals that can react quickly and sometimes violently. Although they are used to regular handling, some still remain fearful of medical procedures. In addition, the close contact with the animal during treatment increases the risk of bodily injury if the horse should bite, push, kick, etc. To limit the risk of accidents, veterinarians should be told about any difficulties encountered with a horse during handling, in order for them to prescribe the most appropriate medication for the situation – oral rather than injection, for example.

Administering medication to a horse requires a good knowledge of the animal's behaviour and, above all, experience. Veterinarians are increasingly providing training directly in stables, in order to teach users about prevention and getting horses used to veterinary care and procedures. Online resources are also available, such as the series of short videos by the British Equine Veterinary Association («Don't break your vet»[1]) on YouTube.

Lastly, personal protective equipment such as gloves, protective clothing and goggles should be worn to limit exposure of the eyes or skin. Users should always remember to remove gloves carefully and wash their hands after a procedure, even when gloves have been worn.

CONCLUSION

The risks of exposure associated with administering medicines to horses are often underestimated, particularly by their owners. Appropriate prevention depends above all on a good understanding of these risks. Horse owners should be informed and aware of all the risks that can arise when treating their horse.
It is also important to remember that while accidental exposure concerns humans, it can also affect an animal

[1] Don't Break Your Vet! - YouTube

other than the one being treated (horse or other species). Hygiene measures – such as one bucket per horse, isolation of the horse at the time of administration and hand washing after each treatment – remain essential to limit this risk.

To report an adverse effect in a human following the use of a veterinary medicinal product:
https://signalement.social-sante.gouv.fr/

Sandrine Rougier et Sylviane Laurentie
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FIND OUT MORE

[1] Vigil'Anses no. 9 • The ANSES bulletin of vigilance • November 2019: Altrenogest: veterinary medicinal products to be used with caution
https://vigilanses.anses.fr/sites/default/files/VigilAnsesN9_Novembre2019_Pharmacoveterinaire_Altrenogest.pdf

[2] Vigil'Anses no. 15 • The ANSES bulletin of vigilance • November 2021 : PRASCEND® tablets for horses: be aware of the risk of accidental ingestion and the steps to take in the event of an accident
https://vigilanses.anses.fr/sites/default/files/VigilAnsesN15_November2021_Prascend.pdf

[3] News update on veterinary medicinal products • 28 July 2022: Good practices in the use of veterinary medicines for pets
https://www.anses.fr/fr/content/m%C3%A9dicaments-pour-animaux-de-compagnie-quelles-bonnes-pratiques

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)[1] 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®[2] 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.

[1] The scale of severity in nutrivigilance varies from Level 1 (low severity) to Level 4 (death).
[2] 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 nutrivigilance scheme, the involvement of the Novanuit® Triple Action product in the occurrence of the hallucinations and mental confusion was deemed very likely, i.e. I4 on a scale ranging from I0 (causality excluded) to I4 (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 hypnotics 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

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[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.

Editorial board

ANSES, which is responsible for several health vigilance schemes (pharmacovigilance of veterinary medicinal products, nutrivigilance, phytopharmacovigilance, toxicovigilance and vigilance for occupational and environmental diseases), reports on its vigilance activities through a dedicated newsletter: Vigil'Anses.

Reflecting the latest news from each of the vigilance schemes, this four-monthly newsletter presents the main results of the Agency's work as part of its vigilance missions, in conjunction with its partners, professional networks and expert groups, along with the actions undertaken. The articles, which are deliberately short, are aimed at all environmental and occupational health players: public authorities, health agencies, ANSES's expert appraisal partner organisations and institutes, managers of prevention policies, the scientific community, professionals, associations and users.
They encourage the interested reader to read the publications, opinions or reports available on the Internet for further information.

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