Penicillium expansum
and other patulin-producing moulds

Phylum: *Ascomycota*
Class: *Eurotiomycetidae*
Order: *Eurotiales*
Family: *Trichocomaceae*

Moulds

anses
French agency for food, environmental and occupational health & safety

The main patulin-producing species are *Penicillium expansum* (the most predominant in economic and health terms) and other microscopic fungi (moulds) such as *Penicillium griseofulvum*, *Aspergillus clavatus* and *Byssochlamys nivea*, as well as its asexual form (*Paecilomyces niveus*). Patulin is known to cause gastrointestinal disorders with ulceration, distension and haemorrhage, and even disruption of renal function at higher doses.

Pure patulin, whose molecular formula is $C_7H_6O_4$, is an unsaturated lactone of low molecular weight (154 g/mol).

Characteristics and sources of *Penicillium expansum*

Main microbial characteristics

The conidiophores are formed of smooth stipes 200 to 500 µm long and ending in typically triverticillate penicilli (presence of one or more branches on the stipe, see Figure 1). The length of the metulae ranges from 12 to 15 µm, that of the tightly packed phialides is 8 to 11 µm, while the conidia are smooth walled and ellipsoidal and are from 3 to 3.5 µm long.

Ascomycetes responsible for contamination multiply according to a growth cycle that takes place in the environment, then spread through conidia (asexual forms) produced within conidiophores (for example, *P. expansum*), or through ascospores (sexual forms) (for example, *B. nivea*) produced within asci, which give them a form of resistance.

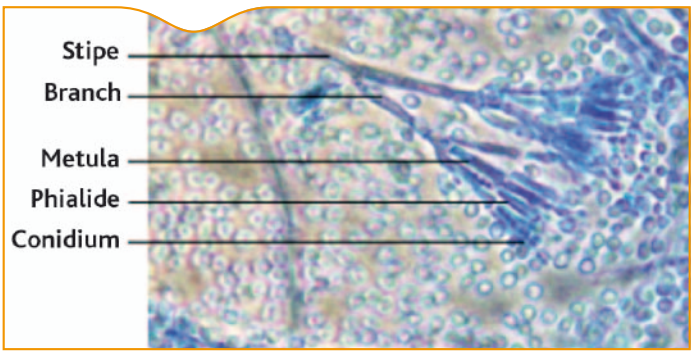

Figure 1. **Microscopic appearance of *P. expansum***

Table 1. **Growth and toxicogenesis characteristics of *Penicillium expansum***

Growth	Min.	Opt.	Max.
Temperature (°C)	-6 - (-2)	23 - 27	30 - 35
pH	2	5,6	10
a_w	0.82-0.83	0,98	/
Toxicogenesis	**Min.**	**Opt.**	**Max.**
Temperature (°C)	0	16 -17	24
a_w	0.96	/	/

Hazard sources

Penicillia are ubiquitous (vegetation, water, soil, etc.). Conidia are dispersed in the environment mainly through the air, but also by water, animals and humans.

P. expansum occurs in healthy fruit but it only produces significant amounts of patulin when developing in the form of a necrotic disc on the fruit (see Figure 2).

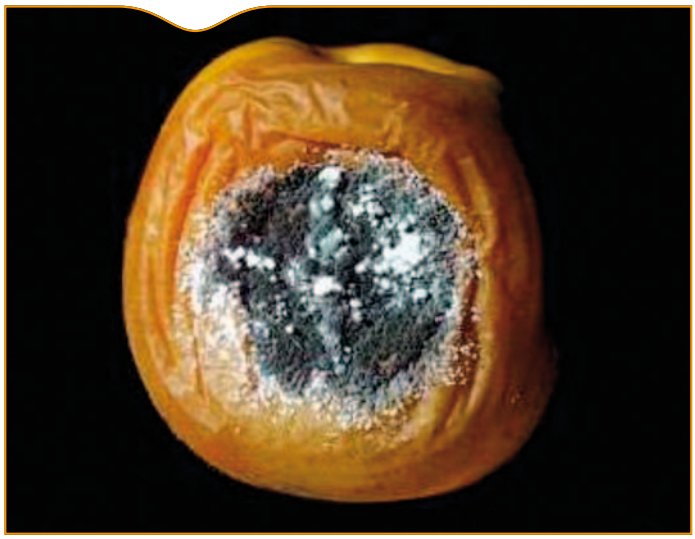

Figure 2. **Macroscopic appearance of *P. expansum* on an apple**

Data sheet on foodborne biological hazards
November 2011

This saprophytic fungus of apples is the primary cause of patulin contamination in juices, compotes and other processed apple products. Patulin production is favoured by fruit injury (bruises, insect damage, etc.). In addition to *Pomaceae* (apples, pears, quinces), *P. expansum* is a saprophyte of other crops. Patulin has thus been found in bananas, peaches, apricots, grapes, grape juice and wine, although in general, the patulin level remains much lower than in products from the "apple" sector.

Other natural substrates allow toxicogenesis, including cereals (wheat, rice), beet pulp and straw. Maize silage and grass silage are the two main sources of patulin in animal husbandry. Some species of *Paecilomyces* are responsible for patulin production in grass silage, while *Byssochlamys nivea* is the organism producing patulin in maize silage. This fungus may appear on recently exposed silage.

Transmission routes

Humans are exposed by consuming food contaminated with patulin.

Recommandations pour la production primaire

- **Preventing the hazard at the source is the only measure possible because there is no effective way of fully detoxifying food contaminated with patulin:**
  - **apples should ideally be used within 24 hours of picking, or placed in cold storage (< 2°C) within 3 or 4 days of harvest;**
  - **the use of a controlled atmosphere (< 1.8% O_2) is recommended when storing apples for longer than three months;**
  - **fruit with lesions greater than 10 cm^2 should be discarded (cutting out the rotten parts is insufficient for completely eliminating the risk of ingestion of patulin). A monthly examination of fruit is recommended.**

Human foodborne illness

Nature of the toxic effects

After its absorption by the gastrointestinal tract, patulin is rapidly degraded. However consumption of food contaminated with patulin is suspected of having adverse effects on health.

At a high dose, oral intake of patulin leads to weight loss, intestinal disorders and renal function disturbances. A repeated dose leads to signs of neurotoxicity and enzyme inhibition in the intestine and brain in particular.

Many *in vitro* studies have demonstrated the immunotoxic effects of patulin.

Animal experiments have been unable to confirm the carcinogenicity of patulin. Patulin is classified in Group 3 (the agent is not classifiable as to its carcinogenicity to humans) by the IARC(1).

Dose-effect(2) and dose-response(3) relationships

The dose-effect and dose-response relationships for patulin have not been established in humans.

The JECFA(4) (1995), the CSHPF(5) (1999) and the SCF(6) (2000) have established a provisional maximum tolerable daily intake (PMTDI) for patulin of 0.4 µg/kg body weight calculated from the observed effects on weight reduction and mortality from lung and laryngotracheal inflammation in rats (NOEL(7), at 43 µg/kg body weight per day).

Epidemiology

There are no epidemiological data.

Role of foods

Main foods to consider

Patulin production has mainly been demonstrated in products from the "apple" sector (from *P. expansum*), which includes fruit juices (especially non-clarified products), compotes and other processed apple products. Fermented products such as cider are not affected because alcoholic fermentation destroys patulin. However, patulin can occur in fermented products to which apple juice was added after fermentation.

The results of the second Total Diet Study (TDS 2, ANSES 2011) on exposure of the French population show that patulin was only detected in samples containing apple. Accordingly, the food groups with the highest levels are compotes and cooked fruits (1 µg/kg), non-alcoholic beverages (0.12 µg/kg) and fruit (0.04 µg/kg).

There is no published information on dietary exposure *via* food from animals that consumed food contaminated with patulin.

In adults, fruit appears to be the majority contributor to patulin exposure (45-50%), followed by compotes and cooked fruit (38%). In children, the main contributors to exposure are compotes and cooked fruit (47%) and non-alcoholic beverages (40%).

The TDS 2 results show a decrease in exposure to patulin compared to the estimates made in the previous exposure monitoring programme (TDS 1, AFSSA 2004) and no instances of the PMTDI being exceeded in adults or children.

The decrease in exposure to patulin can be partly explained by the introduction of regulations on maximum levels of certain mycotoxins in food in 2006. Patulin levels are also dependent on changing climate conditions over the seasons and years.

Inactivation treatments for fungal spores and patulin

Spores of patulin-producing mould are sensitive to the chemical disinfectants (for antifungal purposes) authorised in the food-processing industry, on condition that the recommended procedures for use are followed.

Ascospores are resistant to pasteurisation: 90°C for 10 seconds.

Patulin is water-soluble and stable in acid, but loses its activity in alkaline medium. Its melting point is 110°C and it is very heat stable. It is adsorbed on plant cell walls. Physical separation treatments are the only ones capable of eliminating a significant fraction.

Monitoring in foods

Regulation (EC) No 1881/2006(8) sets the maximum legal levels of patulin in foodstuffs intended for human consumption. These maximum levels are as follows:

- 50 µg/kg for fruit juices (including those reconstituted from concentrate), fruit nectars, spirits and ciders and other drinks made from apple juice and apples;
- 25 µg/kg for solid products made from apples (compotes, purees) intended for direct consumption;
- 10 µg/kg for juices and products made from pieces of apple;
- 10 µg/kg for foods (other than those prepared from cereals) intended for infants and young children, and labelled and sold as such.

(1) International Agency for Research on Cancer.

(2) Relationship between the dose and the effect on an individual.

(3) For a given effect, the relationship between the dose and the response, i.e., the probability of this effect appearing in the population.

(4) Joint FAO/WHO Expert Committee on Food Additives.

(5) Conseil supérieur d'hygiène publique de France (French High Council for Public Health).

(6) European Union's Scientific Committee on Food.

(7) No Observed Effect Level.

(8) Commission Regulation (EC) No 1881/2006 of 19 December 2006 setting maximum levels for certain contaminants in foodstuffs.

Regulation (EC) No 178/2010[9] for the collection and analysis of samples in foods, supplements the previous Regulation (EC) No 401/2006[10].

Recommendations to operators

- Observe good practice with regard to storage (see the recommendations for primary production).
- Observe good hygiene practice for food production and preservation.
- Sorting food to remove mouldy products is the most critical step for reducing the amount of patulin present in the finished product.
- Clarification of fruit juices can significantly reduce the patulin content, depending on the process used.

Domestic hygiene

Recommendations for consumers

- Store food in dry areas.
- Fruit with visible mould should not be consumed or used for making compotes or other products. For small-scale production of cider and apple juice, the use of rotten apples is strongly discouraged.

(9) Commission Regulation (EU) No 178/2010 of 2 March 2010 amending Regulation (EC) 401/2006 as regards groundnuts (peanuts), other oilseeds, tree nuts, apricot kernels, liquorice and vegetable oil.

(10) Commission Regulation (EC) No 401/2006 of 23 February 2006 laying down the methods of sampling and analysis for the official control of the levels of mycotoxins in foodstuffs.

References and links

General references

- AFSSA, 2009. Risk assessment for mycotoxins in human and animal food chains: final report.
- ANSES, 2011. National survey of dietary exposures to chemicals – Second French Total Diet Study 2006-2010 (TDS 2). Report 1: Inorganic contaminants, minerals, persistent organic pollutants, mycotoxins and phytoestrogens.
- Bissessur J., Permaul K., and Odhav B., 2001. Reduction of patulin during apple juice clarification. Journal of Food Protection. Vol. 64 No. 8. Pages 1216-1219.
- Commission Recommendation of 11 August 2003 on the prevention and reduction of patulin contamination in apple juice and apple juice ingredients in other beverages. Official Journal of the European Union L203, 54-59.
- INRA, 2004. Étude de l'alimentation totale française. Mycotoxines, minéraux et éléments traces [French Total Diet Study. Mycotoxins, minerals and trace elements]. 68 pages.

Useful links

- European Union Reference Laboratory for Mycotoxins: The Joint Research Centre of the European Commission - Geel, Belgium.
- National Reference Laboratory (NRL) for Mycotoxins (Group B3d according to Annex I of Council Directive 96/23/EC): ANSES Maisons-Alfort Laboratory for Food Safety.
- National Reference Centre (NRC) for Mycology and Antifungals: Molecular Mycology Unit - Institut Pasteur, Paris.