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Current Opinion in Food Science

Patulin in food

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Patulin is produced by species of *Penicillium*, *Aspergillus* and *Byssochlamys*. It is a mycotoxin that primarily contaminates pome fruit products, but is being reported from other fruit and foods, for example shellfish and cheese. New findings reveal that patulin binds to the bases of DNA, in addition to its well-established ability to conjugate sulfhydryl groups. Novel cellular targets are also being uncovered. In the EU, patulin levels in apple products are now mostly below specified limits. Biocontrol agents either prevent infection by mycotoxigenic fungi or lower patulin levels. More knowledge about critical control points, the role of patulin in plant disease, and the environmental cues that stimulate patulin production will enable the tailoring of effective, future control measures.

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Introduction

Patulin is an α,β-unsaturated γ-lactone (Figure 1), a secondary metabolite and mycotoxin. The presence of patulin in many different foods is a reflection of the ubiquitous nature of its producers, which comprise at least 60 different species of fungi. Several species of *Penicillium*, *Aspergillus* and *Byssochlamys* (anamorph *Paecilomyces*) are patulin producers [1,2]. *Penicillium expansum* is regarded as the prime fungal species responsible for patulin contamination of pome fruit, and this is where most advances have been made. *P. expansum* causes blue mould, a soft, brown fruit rot, which with time develops greenish to blue conidiophores and conidia (Figure 2). Patulin accumulates in the infected fruit as a consequence of the fungal attack. An individual strain of *P. expansum* usually produces several secondary metabolites, in addition to patulin [3]. Patulin contamination is best avoided at the outset, by selecting healthy fruit and vegetables when making juices and purees. However, if patulin reaches the processed products, there are decontamination measures — chemical, biological or physical treatments [1]. Controls in every single step in the processing of apples into apple puree — homogenization, pulping, pasteurization and aseptic packaging — contribute to reducing the final levels of patulin [4].

The content of patulin in some foods is subject to regulation set by authorities. In the EU, the limit is set to 50 μg/kg for apple juice and cider, to 25 μg/kg in solid apple products and 10 μg/kg in infant and baby food [5]. Analytical methods for patulin in food and feed have been extensively reviewed [e.g. [1,6]]. The most recent advances in analytical methods for patulin are summarized on an annual basis; the latest report being compiled by Berthiller *et al.* [7]. Several new and improved methods for patulin detection are emerging continuously, for example, a NIR (near-infrared) method, using fluorescently conjugated anti-patulin antibodies can detect patulin quantities as low as 0.06 μg/L in diluted apple juice [8].

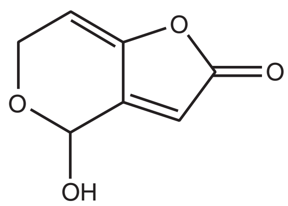
This review presents an update of recent reports of patulin in different foods, with an emphasis on findings in apples and apple products. It summarizes the latest developments in understanding its chemical and cellular modes of action and the role of patulin in plant disease.

Presence of patulin in foods

Patulin is a contaminant of a number of berries and fruit, where pome fruit, that is apples and pears, and their processed products have by far received most attention [6]. Patulin can be present in figs, some vegetables [9], cereals, cheeses [10] and also in seafood [11]. Two strains of *Penicillium antarcticum* isolated from shellfish were confirmed to produce patulin in potato dextrose and malt extract agars [11]. This finding implies that edible shellfish should be checked for the presence of patulin [12•].

Marín *et al.* [13] lists records of patulin reported in apple products in several countries between 2000 and 2011. During that period of time, a few surveys (from Iran, Turkey and Argentina) documented that patulin contamination of apple juice and purees exceeded the limits established by the EU [14,15]. Since 2012, samples taken from apple products on the European market have not proven to exceed the established limit [9,16], with the exception of a study from Romania, in which the EC limit of 50 μg/L was exceeded in 6% of the samples of commercial apple juice [17]. Outside of the EU, for example, two surveys from Iran in 2013 and 2015, in which 11% and 37.5% of apple juices were sampled from supermarkets, reported contents of more than 50 μg patulin/L [18,19],

Figure 1



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The structure of patulin.

respectively. In a Tunisian study from 2013, 18% of apple juices and mixed juices sampled from the market exceeded the limit of 50 μg patulin/L, and 28% of the sampled apple products designated as baby foods exceeded the EU limit for baby food, and ranged from 0 to 165 μg/L [20]. In another from 2015, similar results were found [21], clearly indicating the need for rigorous controls.

Sources and control of patulin contamination

Patulin contamination of apple fruit is best avoided by pre-harvest and post-harvest practices that limit infections by *P. expansum*, such as application of fungicides, biocontrol agents, the use of induced resistance, good harvesting practices, irradiation, hot water, cooling, etc. [22]. After apple harvest and during processing to puree, levels of patulin can be lowered by as much as 29–80% through the processing [4]. The most important measures to reduce accumulation of patulin in apple juice during harvest to processing were identified to be the complete avoidance of using controlled atmosphere (CA)-stored apples, or sorting and discarding fruit from CA storage with rot lesions larger than 10 cm^2 [23]. Patulin in decaying apple fruit is mostly concentrated in the infected tissue, since rot removal significantly reduces patulin contamination in the processed product [24]. Although effective, this so-called trimming practice is considered too expensive to implement in industrial processing [23]. A recent survey in Ontario, Canada, using fresh and stored apples of five cultivars, revealed that apple cores were inhabited by patulin-producing fungi, 22–24% were *Penicillium* species, including *P. expansum* [25•]. *P. expansum* produced patulin in situ when introduced into apple cores [26] and patulin is also known to diffuse into apple tissue adjacent to a rot [27]. Therefore, the apple juice and puree industry cannot avoid patulin from entering the processing chain if it resides in this hidden location, thus possibly posing a novel threat. This port of entry is not regarded as a major source of patulin, but it should be taken into account in the current author's opinion.

Figure 2

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An apple infected with blue mould. On the brown fruit rot, the fungal conidiophores emerge, seen as blue and white coremia.Courtesy of W. Janisiewicz.

Toxicity of patulin

The toxicity of patulin is evidenced in many different assays. The mycotoxin also targets different organs [28]. Patulin has anti-cancer activity [12•,29] as shown in tests on human epidermoid carcinoma cells [29]. On the other hand, patulin has well-documented tumour-inducing activity in mouse skin cells, through the activation of a ROS-induced MAPK signalling pathway [30]. The International Agency for Research on Cancer, however, has since 1986 maintained that patulin is not a carcinogen, because of the lack of studies demonstrating its carcinogenicity, but this classification may change in the future, as more reports emerge on the toxicity of patulin. A recent breakthrough in understanding the mode of action was presented by Pfenning *et al.*, demonstrating on the chemical level that patulin forms adducts to individual bases of DNA, thus causing strand breaks, even in the presence of glutathione [31••]. This DNA-binding activity works in parallel with the well-established activity of patulin, which is to form adducts with thiol-containing compounds, for example to glutathione (GSH), a cysteine-containing tripeptide (γ-Glu-Cys-Gly) [32], and to enzymes that contain thiol groups. The lowering of the GSH pool in living cells, including human cells, leads to a disturbance in the redox equilibrium, resulting in oxidative stress.

Patulin production is influenced by the environment

Patulin production depends on environmental factors, and varies among strains and species of *Penicillium* and other fungi. In non-alcoholic cider, room temperature, low pH and the cultivar used for production were important factors [33]. In stored apples, temperature and % O_2 are important [23]. The single nutrient components that