Advanced International Journal for Research (AIJFR)
E-ISSN: 3048-7641 ● Website: www.aijfr.com ● Email: editor@aijfr.com

A Brief Review of Patulin and Its Biological Significance

Kalaiselvi Vaithi[1], Elavarasi Rajavel[2], Vasanthabharathi Venkataraman[3]

[1,2] Bharathi Women's arts and Science College, Thatchur, Tamil Nadu
[3] Atham Organics & Naturals, Chidambaram, Tamil Nadu.

Abstract

Patulin is a secondary metabolite primarily produced by several fungal species, particularly *Penicillium expansum*, which commonly contaminates apples and other fruits during post-harvest storage. Traditionally, patulin has been regarded as a terrestrial mycotoxin associated with food spoilage and toxicological risks to human health. However, recent developments in marine mycology and natural product research have demonstrated that marine-derived fungi, including species of Penicillium, Aspergillus, and Byssochlamys isolated from marine sediments, seawater, and sponges, are also capable of producing patulin and structurally related analogs. These findings expand the ecological significance of patulin biosynthesis and suggest that marine ecosystems may serve as alternative reservoirs of bioactive mycotoxins. This review summarizes current knowledge on the occurrence, biosynthesis, and biological activities of patulin, with particular emphasis on its antimicrobial potential and its implications as a food contaminant and public health hazard.

Key words: Patulin, Mycotoxin, Antimicrobial activity, Food safety, Toxicity

1. Introduction

Mycotoxins are toxic secondary metabolites produced by various fungal species that across diverse ecosystems. Among these, patulin (4-hydroxy-4H-furo[3,2-c]pyran-2(6H)-one) has gained considerable attention due to its biological activity and public health significance. Traditionally, patulin is associated with terrestrial fungi—especially *Penicillium expansum* and *Aspergillus clavatus* commonly found in decaying fruits and stored agricultural commodities (Puel et al., 2010; Pitt & Hocking, 2009). Other names for patulin include Clavacin, Claviformin, Expansin, Mycoin, Penicidin, and Terinin. It also has other less common synonyms like Gigantin, and Leucopin.

Marine fungi are relatively unexplored microorganisms for biotechnological applications compared with terrestrial fungi (Vasanthabharathi and Jayalakshmi 2012, Xie et al., 2018). Marine fungi are important sources of natural compounds with various bioactivities. Several marine fungi have been reported to produce bioactive compounds with antimicrobial, antiviral, anticancer, anti-inflammatory, and antioxidant activities (Ameen et al., 2021).

The marine environment has emerged as an unexplored source of fungal secondary metabolites, including patulin. Marine-derived strains of Penicillium and Aspergillus species has been isolated from marine sediments, algae, mangroves, and invertebrates such as sponges and corals. These isolates have demonstrated patulin production under laboratory fermentation, suggesting that marine conditions can induce or enhance the biosynthetic potential of these fungi (Ebel, 2011, Blunt et al., 2018, Vasanthabharathi et al.,2022).

Beyond its toxicity, patulin also serves as a valuable research tool for understanding oxidative stress, enzyme inhibition, and fungal metabolism. Ongoing studies focus on biosynthesis, detection, and detoxification methods, including biological degradation by yeast and bacterial strains. Thus, patulin represents a double-faced compound one side revealing its antimicrobial potential, and the other exposing its role as a silent contaminant threatening food safety.

Recent fungal metabolism researches have been focused on understanding the biosynthetic pathways, regulatory genes, and environmental factors influencing patulin production. The biosynthesis of patulin is associated with polyketide metabolic pathways, where enzymes such as polyketide synthases (PKS) play a significant role in toxin formation. Studies have shown that factors including pH, temperature, humidity, and nutrient availability strongly affect fungal metabolism and patulin accumulation in fruits and fruit-derived products. Also, recent investigations highlighted the involvement of specific genes such as *patK*, *patG*, and *patL* in the regulation of patulin biosynthesis in *Penicillium expansum* (Bacha et al ,.2023, Yu et al .,2023, Jiang et al 2024, Bao et al .,2025).

Characterization of Patulin and Its Properties

The capacity of various fungi to produce toxic metabolites is well established, but the potential role that many of these toxic compounds play in disease processes is not as well understood. Hence, for obvious reasons, it would appear desirable to develop a data bank on these compounds. One of the metabolites that falls into this uncertain category with respect to involvement in mycotoxicoses is patulin, which has formula as C 7 H 6 0 4 and molecular weight as154. It showed colourless to white crystal in appearance, melting at 110.5 °C and optically inactive with a single peak in the ultraviolet range at 276nm. It is a neutral substance which is soluble in water and organic solvents except pentane-hexane (Pal et al .,2017).

Some of the studies have been performed to identify anti-phytopathogenic compounds in marine fungi. For example, Stemphyperylenol and Alterperylenol, identified from marine Alternaria spp., exhibit antifungal and antibacterial activities against phytopathogens such as *Alternaria brassicicola* and *Clavibacter michiganensi*s, respectively (Zhao et al., 2018). Pleosporalone B, isolated from marine Pleosporales sp. CF09-1, displays antifungal activity against *A. brassicicola* and *F.oxysporum* (Cao et al., 2019). In addition, 3-decalinoyltetramic acid derivatives from marine *F.equiseti* D39 inhibit the growth of the phytopathogenic bacterium *Pseudomonas syringae* (Zhao et al., 2019). However, antibacterial compounds from marine fungi against phytopathogenic bacteria remain largely unknown.

Ellis and Mccalla (1973) observed the effect of patulin on growth stages of wheat plant and showed a single exposure to patulin on produce yield reduction considerably. Wilson and Nuovo (1973) investigated on *P. expansum* isolated from decayed apples which produced 10 µg /ml of patulin. This amount was found to be sufficiently cytotoxic to apple cells and patulin was determined by thin-layer chromatography.

Yamamoto et al., 1995 reported nucleotide sequence of a large rRNA gene and its flanking regions in cloned fragments of mitochondrial DNA of a patulin producer, *Penicillium urticae* NRRL2159A, which was done by dideoxy sequencing and intron-exonborder of the 1-rRNA gene, was determined by primer extension analysis and RNA sequencing.

Sewram et al., (2000) estimated patulin in apple juice samples using liquidchromatography–mass spectrometry (LC-MS) and HPLC and quantified it as 10 and 135 µg/l. Tabata et al., 2012 reported 5 mg/kg patulin quantified by GC/MS method. Dombrink (2008) reported the presence of idh gene in *P.griseofulvum* and found to be responsible for the patulin production. Lugauskas et al., 2005 worked on the diversity of micromycete species which are potential mycotoxin producers spread on vegetables stored under various conditions during winter, and selected strains of high yield synthesizing toxic secondary metabolites.Tournas and Memon (2009) isolated Penicillium sp from decayed apple.

Patulin production was optimized using different media such as potato dextrose, malt extract, and glucose, yeast extract and peptone both with and without manganese supplementation. At 96 hrs potato dextrose broth supplemented with manganese resulted in maximum production of patulin (Dombrink , 2008) .

Champdore et al., 2007 described the synthesis of two new derivatives of patulin along with their conjugation to the bovine serum albumin for the production of polyclonal antibodies. Finally a fluorescence competitive immuno assay was developed for the on-line detection of patulin.

Ricelli et al., 2007 isolated a bacterium from patulin-contaminated apples which was capable of degrading patulin to a lesser-toxic compound. Human exposure to patulin can lead to serious health problems, and according to a long-term investigation in rats, the World Health Organization has set a tolerable weekly intake of 7 ppb body weight. The content of patulin in foods had been restricted to 50 ppb in many countries. Analytical detection methods involve chromatographic analyses, such as HPLC, GC, and, more recently, techniques such as LC/MS and GC/MS are also been engaged.

Larous et al., 2007 optimized *P. expansum* strain from moulded apple fruits and maximum patulin production was shown at 25 o C. Patulin showed inhibitory activity against *Escherichia coli* and *Bacillus subtilis*. Collin et al., (2008) observed the degradation related issue in the process of chemical detoxication of patulin. The influence of pH and sulfites was also observed. Arbizu et al., (2009) determined the level and dietary intake of patulin (PAT) from apple juices consumed. PAT was extracted by a liquid–liquid extraction technique and analyzed with a micellar electro kinetic chromatography. Average Intakes were calculated for consumers among adults, children and babies and then compared with the provisional maximum tolerable daily intake.

Reddy et al., (2010) investigated the pathogenicity and patulin production by ten strains of *Penicillium expansum* on various fruits such as apples, apricots, kiwis, plums and peaches. Janotova et al., 2011 reported patulin and its potential health hazard especially in apple based baby foods. The apple samples were spiked with patulin at four levels of concentration 539 µg/kg, 140 µg/kg, 23 µg/kg and 2 µg/kg. The patulin content changed during the various processing stages such as the homogenization, pulping, pasteurization and aseptic packaging. All operations of apple juice purification resulted in patulin reduction. The patulin levels were reduced from 29% to 80% of the original content.

Vansteelandt et al., (2012) reported thirty-two secondary metabolites in crude extracts of *Penicillium antarcticum* in which patulin was found to be the major metabolite and it induced acute neurotoxicity on dipteran larvae. Bevardi et al., (2013) isolated *Gluconobacter oxydans* from apple surface and determined its effectiveness in controlling the growth and patulin production of *Penicillium expansum.*

Although patulin is mainly regarded as a contaminant and health hazard, it has also been studied for several potential applications in biotechnology and pharmacology:

Spectrum of antimicrobial activity Patulin exhibits broad-spectrum antibacterial properties, particularly against Gram-positive bacteria (Béahdy et al., 1974). Early research explored its potential as a natural antibiotic, though its toxicity limited practical use.

Antimicrobial potential: Early and subsequent in vitro studies show patulin inhibits both Gram-positive and Gram-negative bacteria, often with stronger activity reported against Gram-positive species. However, activity varies with test organism, medium, and patulin concentration. These antibacterial effects led to early interest in patulin as an antibiotic. Patulin also shows antifungal/antagonistic activity against certain fungi and phytopathogens in laboratory assays; this contributes to its proposed role as a fungal virulence factor or competitor molecule in fruit microbiomes. Recent screenings show patulin can inhibit a range of plant-associated bacteria and fungi in vitro (Chung et al.,2023).

Due to its ability to interfere with cellular thiol groups and inhibit enzyme systems, patulin is used as a biochemical probe to study oxidative stress and enzyme regulation in cells (Pillay et al., 2015).

Patulin serves as a model compound in studies investigating mycotoxin biosynthesis pathways and fungal secondary metabolism, contributing to our understanding of toxin regulation and production (Tannous et al., 2018).

Conclusion

Patulin is an important mycotoxin commonly associated with fungal contamination in fruits and fruit-derived products, posing significant risks to human and animal health. Although primarily recognized as a toxic contaminant, patulin has also demonstrated notable antimicrobial properties against a wide range of Gram-positive and Gram-negative bacteria, as well as certain pathogenic fungi These antimicrobial activities have attracted scientific interest in understanding its possible applications in biotechnology, agriculture, and pharmaceutical research. It has also been widely used as a biochemical probe for studying oxidative stress, enzyme inhibition, and fungal secondary metabolism, contributing to a deeper understanding of mycotoxin biosynthesis and cellular regulation mechanisms.

Despite these promising findings, the toxic nature of patulin limits its direct practical application. Therefore, further studies are needed to investigate its antimicrobial mechanisms, spectrum of activity, safe concentration limits, and possible structural modifications to reduce toxicity while retaining beneficial biological activity. Additional research on patulin-derived compounds and their potential therapeutic or agricultural applications may provide new opportunities for the development of novel antimicrobial agents.

Moreover, fungal infections and mycotoxin contamination continue to pose major threats to food safety and public health worldwide. Although traditional detection and detoxification methods have improved, challenges still remain in the rapid detection and simultaneous removal of multiple mycotoxins. Biodegradation has emerged as a promising eco-friendly strategy due to its efficiency, specificity, and reduced environmental impact. However, more research is required to better understand detoxification pathways, improve enzyme purification methods, and develop advanced technologies for mycotoxin control. Overall, continued scientific investigation is essential to ensure food safety while also exploring the potential beneficial applications of patulin in future biomedical and biotechnological fields.

References

1. Ameen F., AlNadhari S., Al-Homaidan A. (2021). Marine microorganisms as an untapped source of bioactive compounds. Saudi J. Biol. Sci. 28, 224–231. 10.1016/j.sjbs.2020.09.052
2. Arbizu, M., Amézqueta, S., González-Peñas, E., & de Cerain, A. L. (2009). Occurrence of patulin and its dietary intake through apple juice consumption by the Spanish population. *Food Chemistry*, *113*(2), 420-423.
3. Bacha SAS, Li Y, Nie J, Xu G, Han L and Farooq S (2023) Comprehensive review on patulin and Alternaria toxins in fruit and derived products. Front. Plant Sci. 14:1139757. doi: 10.3389/fpls.2023.1139757.
4. Bao, M., Shi, Y., Gong, X., Guo, Y., Wang, J., Chen, X., & Liu, L. (2025). New bioactive secondary metabolites from fungi: 2024. Mycology, 16(3), 961-987.
5. Béahdy, J. (1974). Recent developments of antibiotic research and classification of antibiotics according to chemical structure. Advances in applied microbiology, 18, 309-406.
6. Bevardi, M., Frece, J., Mesarek, D., Bošnir, J., Mrvčić, J., Delaš, F., & Markov, K. (2013). Antifungal and antipatulin activity of *Gluconobacter oxydans* isolated from apple surface. Arhiv za higijenu rada i toksikologiju, 64(2), 279-283.
7. Blunt, J. W., Carroll, A. R., Copp, B. R., Davis, R. A., Keyzers, R. A., & Prinsep, M. R. (2018). Marine natural products. Natural Product Reports, 35(1), 8–53.
8. Cao F., Meng Z., Mu X., Ye Y., Zhu H. (2019). Absolute configuration of bioactive azaphilones from the marine-derived fungus *Pleosporales sp*. CF09-1. J. Nat. Prod. 82, 386–392. 10.1021/acs.jnatprod.8b01030
9. Chakraborty, K., Thilakan, B., Raola, V. K., & Joy, M. (2019). Antimicrobial secondary metabolites from marine fungi: chemistry and bioactivity. Marine Drugs, 17(6), 340.
10. Champdore, M., Bazzicalupo, P., De Napoli, L., Montesarchio, D., Di Fabio, G., Cocozza, I.,& D'Auria, S. (2007). A new competitive fluorescence assay for the detection of patulin toxin. Analytical chemistry, 79(2), 751-757.
11. Chung D, Nguyen HT, Yu NH, Yu WJ, Kwon YM, Bae SS, Choi G, Kim JC. 2023. In vitro and in vivo antimicrobial activity of the fungal metabolite toluquinol against phytopathogenic bacteria. Front Microbiol. 31;14:1221865. doi: 10.3389/fmicb.2023.1221865. PMID: 37583517; PMCID: PMC10424571.

12. Collin, S., Bodart, E., Badot, C., Bouseta, A., & Nizet, S. (2008). Identification of the main degradation products of patulin generated through heat detoxication treatments. Journal of the Institute of Brewing, 114(2), 167-171.
13. Dombrink Kurtzman, M. A. (2008). A gene having sequence homology to isoamyl alcohol oxidase is transcribed during patulin production in *Penicillium griseofulvum.* Current microbiology, 56(3), 224-228.
14. Duncan H, Agulló C, Mercader JV, Abad-Somovilla A, Abad-Fuentes A(2024). Harnessing the Intrinsic Chemical Reactivity of the Mycotoxin Patulin for Immuno sensing. Nal Chem. 15;96(30):12370–7. doi: 10.1021/acs.analchem.4c01631. PMID: 39007758; PMCID: PMC11295118.
15. Ellis JR, McCalla TM. (1973).Effects of patulin and method of application on growth stages of wheat. Appl Microbiol. 25(4):562-6. doi: 10.1128/am.25.4.562-566.1973. PMID: 4699215; PMCID: PMC380862.
16. Janotová, L., Čížková, H., Pivoňka, J., & Voldřich, M. (2011). Effect of processing of apple puree on patulin content. Food Control, 22(6), 977-981.
17. Jiang, Y., Wu, Y., Zheng, X., Yu, T., & Yan, F. (2024). Current insights into yeast application for reduction of patulin contamination in foods: A comprehensive review. Comprehensive Reviews in Food Science and Food Safety, 23(6), e70044.
18. Larous, L., Hendel, N., Abood, J. K., & Ghoul, M.(2007). Research Paper (Physiology: Fungi).Arab J. Pl. Prot. 25,1 .
19. Lugauskas, A., Repeckiene, J., Novosinskas, H. (2005). Micromycetes, producers of toxins, detected on stored vegetables. Annals of Agricultural and Environmental Medicine, 12(2), 253-260.
20. Pal S, Singh N, Ansari KM. (2017).Toxicological effects of patulin mycotoxin on the mammalian system: an overview. Toxicol Res (Camb). 9;6(6):764-771. doi: 10.1039/c7tx00138j. PMID: 30090541; PMCID: PMC6062217.
21. Pillay, Y., Phulukdaree, A., Nagiah, S., & Chuturgoon, A. A. (2015). Patulin triggers NRF2-mediated survival mechanisms in kidney cells. Toxicon, 99, 1-5.
22. Pitt, J. I., & Hocking, A. D. (2009). Fungi and food spoilage. Springer.3rd Edition, Springer Dordrecht Heidelberg London New York Cambridge, 519 https://doi.org/10.1007/978-0-387-92207-2
23. Puel, O., Galtier, P., & Oswald, I. P. (2010). Biosynthesis and toxicological effects of patulin. Toxins, 2(4), 613–631.
24. Rateb, M. E., & Ebel, R. (2011). Secondary metabolites of fungi from marine habitats. Natural Product Reports, 28(2), 290–344.
25. Reddy, K. R. N., Spadaro, D., Lore, A., Gullino, M. L., & Garibaldi, A. (2010). Potential of patulin production by *Penicillium expansum* strains on various fruits. Mycotoxin Research, 26(4), 257-265.
26. Ricelli, A., Baruzzi, F., Solfrizzo, M., Morea, M., & Fanizzi, F. P. (2007). Biotransformation of patulin by Gl*uconobacter oxydans*. Applied and environmental microbiology, 73(3), 785-792.
27. Sewram, V., Nair, J. J., Nieuwoudt, T. W., Leggott, N. L., & Shephard, G. S. (2000). Determination of patulin in apple juice by high-performance liquid chromatography–atmospheric

pressure chemical ionization mass spectrometry. Journal of Chromatography A, 897(1-2), 365-374.
28. Tabata, S. (2012). Development of analytical methods for mycotoxins, and research for food safety. JSM Mycotoxins, 62(2), 63-75.
29. Tannous, J., Keller, N. P., Atoui, A., El Khoury, A., Lteif, R., Oswald, I. P., & Puel, O. (2018). Secondary metabolism in *Penicillium expansum:* Emphasis on recent advances in patulin research. Critical reviews in food science and nutrition, 58(12), 2082-2098.
30. Tournas, V. H., & Memon, S. U. (2009). Internal contamination and spoilage of harvested apples by patulin-producing and other toxigenic fungi. International Journal of Food Microbiology, 133(1-2), 206-209.
31. Vansteelandt, M., Kerzaon, I., Blanchet, E., Tankoua, O. F., Du Pont, T. R., Joubert, Y. Grovel, O. (2012). Patulin and secondary metabolite production by marine-derived Penicillium strains. *Fungal biology*, *116*(9), 954-961.
32. Vasanthabharathi V., Vaithi, K., & Singaram, J. (2022). Bioactive Novel Natural Products from Marine Sponge: Associated Fungi. In Fungal Reproduction and Growth. IntechOpen. https://doi.org/10.5772/intechopen.101403
33. Vasanthabharathi, V., Jayalakshmi, S. (2012). Bioactive potential of symbiotic bacteria and fungi from marine sponges. African Journal of Biotechnology, *11*(29).
34. Wilson DM, Nuovo GJ. (1973). Patulin production in apples decayed by *Penicillium expansum.* Appl Microbiol. 26(1):124-5. doi: 10.1128/am.26.1.124-125.1973. PMID: 4726831; PMCID: PMC379731.
35. Xie C., Xia J., Wang J., Lin D., Yang X. (2018). Metabolomic investigations on *Nestrenkonia flava* revealed significant differences between marine and terrestrial actinomycetes. Mar. Drug. 16, 356. 10.3390/md16100356
36. Yamamoto H, Naruse A, Ohsaki T, Sekiguchi J. (1995).Nucleotide sequence and characterization of the large mitochondrial rRNA gene of *Penicillium urticae*, and its comparison with those of other filamentous fungi. J Biochem. 117(4):888-96. doi: 10.1093/oxfordjournals.jbchem.a124792. PMID: 7592555.
37. Yu, W., Pei, R., Zhang, Y., Tu, Y., & He, B. (2023). Light regulation of secondary metabolism in fungi. Journal of Biological Engineering, 17(1), 57.
38. Zain, M. E. (2011). Impact of mycotoxins on humans and animals. Journal of Saudi Chemical Society, 15(2), 129–144.
39. Zhao D., Wang D., Tian X., Cao F., Li Y., Zhang C. (2018). Anti-phytopathogenic and cytotoxic activities of crude extracts and secondary metabolites of marine-derived fungi. Mar. Drugs 16, 36. 10.3390/md16010036
40. Zhao D., Han X., Wang D., Liu M., Gou J., Peng Y., et al. (2019). Bioactive 3-decalinoyltetramic acids derivatives from a marine-derived strain of the fungus Fusarium equiseti D39. Front. Microbiol. 19, 1285. 10.3389/fmicb.2019.01285.
41. Zhao, W., Hong, S. Y., Kim, J. Y., & Om, A. S. (2024). Effects of temperature, pH, and relative humidity on the growth of *Penicillium paneum* OM1 isolated from pears and its patulin production. *Fungal Biology*, *128*(4), 1885-1897.