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Review on (Yelow Pigment) Citrinin

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Abstract

Many of the fungal species producing mycotoxin. Citrinin is produced by *Penicillium, Aspergillus* and *Monascus* species. It is a yellow pigmented mycotoxin and having antimicrobial, antioxidant activity. It is used in the production of rice wine preparation which is used as fish and meat preservative. Thus, the present review focused on Citrinin.

Introduction

The genus *Penicillium* contains approximately 100 toxigenic species, and the range of mycotoxin classes produced is much broader than that of any other genus [1]. listed 27 mycotoxins produced by 32 species which possessed varying range of toxicity. *Penicillium* toxins can be placed in two broad groups based on effect as renal and neurotoxins [2]. Mycotoxins are secondary metabolites produced by certain filamentous fungi. The toxic response due to fungal growth in food is called as mycotoxicosis. Aflatoxins are produced mainly by *A. flavus, A. parasiticus* and *A. nominus*. *Aspergillus, Fusarium* and *Penicillium* [3] and when ingested through food they intoxicate higher vertebrates including human. Monascus pigments, which are produced by various species of *Monascus*, often have been used as a natural colourant and as traditional natural food additives, especially in Southern China, Japan and Southeastern Asia. The limitation of wide using *Monascus* pigment is attributed to one of its secondary metabolites named citrinin.

Citrinin is a fungal metabolite was isolated from *Penicillium citrinum* in 1931. It was characterized as an antibiotic. Active against bacteria and also activity against bacteriophages, sarcomas, protozoa and animal cells. It is a quinine methide with two intra molecular hydrogen bonds. It is well established renal toxin affecting monogastric domestic animals such as pigs and dogs. Citrinin ($C_{13}H_{14}O_5$) is sparingly soluble in water but soluble in diluted sodium hydroxide, sodium carbonate, sodium acetate, methanol, acetonitrile, ethanol and most of other polar organic solvents [4]. It is a lemon-yellow crystalline substance, Melting point is 172 °C at room temperature. It possesses antibiotic, bacteriostatic, antifungal and antiprotozoal properties [5-8] reported occurrence of aflatoxin B1, citrinin and ochratoxin A in rice variety raised in five provinces of the central region of Vietnam. [9] explain about the Safety Evaluation of Citrinin in Foods. Anthraquinone-citrinin isolated from sea fan-derived *P. citrinum* PSU-F514 displayed moderate antibacterial activity against both *S. aureus* and methicillin-resistant *S. aureus* [10].

Application of citrinin

There have been several reports on the isolation of bioactive metabolites, and the investigation of the ethyl acetate extracts from the broth and mycelia of *P. citrinum* has led to the extraction of nearly eighteen metabolites [11]. Bioactivity of citrinin possesses antibiotic, bacteriostatic, antifungal and antiprotozoal properties [12]. Citrinin was isolated from a *Penicillium janczewskii* strain found to inhibit the root-rot pathogen *Heterobasidion annosum.* Tarlov IM [13] carried out antimicrobial activity by using partially purified and purified citrinin. When partially purified citrinin was used it showed 8mm zone of clearance against *P. mirabilus*, whereas 12mm zone of clearance was observed against the same pathogen when purified citrinin was used. In the same research and Partially purified citrinin showed 4mm zone of clearance against fungi *P. thae.* Purified citrinin showed 6mm against *P. thae.* Another researcher [14] extracted citrinin from sponge associated *Penicillium sp*. and studied for its strong antibacterial activity against multi-drug resistant human pathogens like methicillin resistant *S. aureus,* rifampicin-resistant *S. aureus*, wild type *S. aureus*, vancomycin-resistant *E. faecium* and also *C. neoformans.* Further, its having cytotoxicity against brine shrimp larvae.

Mazumde et al. [15] observed Minimum Inhibitory Concentration (MIC) against some gram positive strains viz. *Staphylococcus aureus, Bacillus pumilus, Bacillus subtillis, Bacillus cereus, Klebsiella pneumoniae, Streptococcus pneumoniae, Lactobacillus arabinosus* and gram negative strains *E. Coli, Shigella dysenteriae, shigella sonnei, shigella boydii, Salmonella typhimurium, Proteus mirabilis* and *Vibrio cholerae* by using citrinin. Antioxidant JBIR-124 [16], Cytotoxic penicitrinols C and E, topo IIαinhibitory tricitrinol B and the cytotoxic dicitrinone B [17]. The isolation of five polyketides including two benzopyranones, one isochroman and two anthraquinone-citrinin derivatives were reported from the sea fan-derived fungus *P. citrinum* [18]. Citrinin used in the production of cheese and Sake. It plays a role in inducing motility of *Paenibacillus polymyxa* [17] Ciegler et al. [19] studied the biological activity of citrinin from *Penicillium expansum.* Pengnoi et al. [20] evaluate the effects of various purple rice varieties on the production of citrinin, and monacolin K, red pigments by *Monascus purpureus* CMU002U (UV-mutant strain) and their antioxidant properties.

Characterization of citrinin

Citrinin contaminated many food items has been widely reported. However, research on the citrinin biosynthesis pathway and its regulation mechanism in *P. citrinum is* rarely reported. Iwahashi et al. [21] monitored the citrinin induced mRNA expression profiles in yeast using the ORF DNA microarray and Oligo DNA microarray. HPLC, TLC, enzyme linked immunosorbent assay, and bacteriostatic circle methods were used in the detection of citrinin [22]. A total of 19,967 uni genes were annotated by BLAST in Nr, Nt, Swiss-Prot and Kyoto Encyclopedia of Genes and Genomes (KEGG) databases. Transcriptome comparison between *P. citrinum* cultured with sucrose and glucose revealed 1085 differentially expressed unigenes. Among them, 610 were upregulated while 475 were downregulated under glucose as compared to sucrose [23]. Xu et al. [24] used TLC and HPLC to detect 40 strains of *Monascus* strains in yeast extract medium, and all the strains produced citrinin.

Production of citrinin

The fungi *Penicillium citrinum* was isolated from the sponge *Callyspongia diffusa* which was collected from Mandapam coast, Tamil Nadu, India. Optimization of citrinin was done by one factor at a time method. The optimum conditions for citrinin production were temperature 35 °C, pH 7.0 salinty20ppt, carbon source-3% glucose, Nitrogen source-0.5% sodium nitrite, 3% rice bran Compared to commercially available carbon source (glucose), rice bran gave higher production of citrinin. About 1.50μg/ml of citrinin was produced at optimized condition [12]. Likewise, another researcher Kaur et al. [25] carried out solid state fermentation for the production of pigments by using broken wheat (0.996 OD). The maximum pigment yield (137.8U/g) was seen at 12th day. Lai et al. [26] observed that Potato glucose medium is not conducive to citrinin production, however, yeast extract may promote the activity of citrinin synthase because of its rich nutrition and stimulate citrinin production. Li et al. [23] investigated the effect of different carbon sources on citrinin production by *P. citrinum* and used transcriptome analysis to study the underlying molecular mechanism. Results were indicated that glucose, used as the sole carbon source, could significantly promote citrinin production by *P. citrinum* in Czapek's broth medium compared with sucrose. Hasan [27] studied the citrinin accumulation under stress of camphor and blue-gum extract. Santos et al (2002) reported the effect of culture preservation techniques on patulin and citrinin production by *Penicillium expansum*. Wang et al. [28] observed the variability of citrinin production in *Monascus* type cultures. Prabhadevi et al. [29] isolated and characterized citrinin from *P. chrysogenum* [30].

Conclusion

Citrinin is a important mycotoxin, which is used in fermentation industry. It has antimicrobial activity against many pathogens hence it will be used as antibiotic in future.

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