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Antifungal peptides with novel specific inhibitors of glucosamine 6-phosphate synthase.

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Abstract

N3-4-Methoxyfumaroyl-L-2,3-diaminopropanoic acid (FMDP) has been found to be a strong and selective inhibitor of glucosamine 6-phosphate synthase from Candida albicans. Incorporation of FMDP into a dipeptide structure has produced effective antifungal agents (portage transport). A number of dipeptides containing FMDP have been synthesized, with Nva-FMDP showing the highest in vitro activity against different fungi, including Candida albicans (MIC90 = 2.2 micrograms/ml for 50 clinical strains), Cryptococcus neoformans and Aspergillus spp. This compound, when tested in a general candidiosis model infection in mice, gave PD50/10 and CD50/10 values of 5.0 and 1.63 mg/kg, respectively. Meanwhile, the LD50 value after i.v. administration was higher than 300 mg/kg.

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