Potent antimicrobial agents against azole-resistant fungi based on pyridinohydrazide and hydrazomethylpyridine structural motifs

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Abstract

Schiff-based derivatives have recently been shown to possess antimicrobial activity and these derivatives include a limited number of salicylaldehyde hydrazones. To further explore the structure-activity relation between salicylaldehyde hydrazones and their antifungal activity, a large series of salicylaldehyde and formylpyridinetrione hydrazones were synthesized in order to evaluate their ability to inhibit fungal growth of both azole-susceptible and azole-resistant species of Candida. While many of these analogs showed excellent growth inhibition with low mammalian cell toxicity, their activity did not extend to azole-resistant species of Candida. To further dissect the structural features necessary to inhibit azole-resistant fungal species, a new class of salicylaldehyde derivatives with modified pyridine-based hydrazones were investigated. In this seminar, synthetic procedures as well as the results from fungal growth inhibition assays, mammalian cell toxicity assays, time-kill assays and synergy studies of these novel pyridine-based hydrazones on both azole-susceptible and azole-resistant fungal species will be discussed.

Biography of Speaker

Branko S. Jursic is a Professor of Organic and Medicinal Chemistry at the University of New Orleans with primary research interests in developing new antimicrobial and anticancer drugs. He received his B.S. in Synthetic Organic Chemistry on the preparation of new amino acid derivatives, M.S. in Heterocyclic Chemistry on the preparation of oxazolone derivatives, and Ph.D. in Natural Product Chemistry on the isolation and preparation of new steroid derivatives from the University of Zagreb, Croatia. He held a Postdoctoral Fellowship at Columbia University in New York under the guidance of Professor Ronald Breslow. During this time, he devolved and synthesized several anticancer compounds from which one is commercialized under name Zolinza (Varinostat). He is the coauthor of more than 300 research papers and more than 20 patents.