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THE ARYLCYANOMETHYLENEQUINONE INHIBITION OF GROWTH AND FORMATION OF HYPHAE IN CANDIDA ALBICANS

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In humans, ten genera of fungi, i.e. Aspergillus, Candida, Cryptococcus, Blastomyces, Coccidioides, Histoplasma, Paracoccidioides, Penicillium, Pneumocystis, and Rhizopus have a high prevalence in infections, with more than 40% associated with Candida. Antifungal resistance is an increasing threat for the effective treatment of invasive mycoses, making their therapy difficult, expensive, or even impossible. Therefore, there is an urgent need for new compounds targeting different cellular processes, including phosphorylation, to deal with Candida infections. In this study, we applied various assays to find new activities of phenylcyanomethylenequinone oxime (4-AN) for potential anti-microbial applications. These assays determined (a) the antimicrobial effect on growth/cell multiplication in bacterial and fungal cultures; (b) the effect on *in vitro* activity of CK2, i.e. one of the most pleiotropic kinases, and the Rio1 kinase, which is crucial for ribosome maturation; (c) hemolytic activity towards human erythrocytes; and (d) toxicity against the Caco-2 cancer cell line. We demonstrated, for the first time, the activity of 4-AN against selected bacteria and against Candida. At 125-250 µg/ml of the minimum inhibitory concentration (MIC), the chemical significantly affected the bacterial strains. Interestingly, the MIC ranging from 3.9 µg/ml to 7.8 µg/ml showed effectiveness in inhibition of formation of hyphae and cell aggregation in Candida, which was demonstrated at the cytological level. Notably, 4-AN was found to inhibit the CK2 and Rio1 kinases with different potency. However, at low concentrations, it did not exert any evident toxic effects on human cells. The details of our studies, which describe the synthesis, activity, and proposition for the mechanism of an action of studied compounds will be presented.

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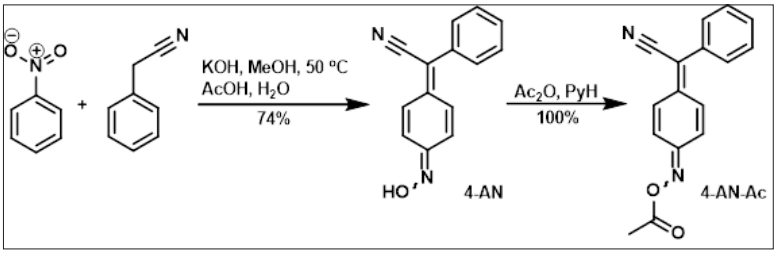

Figure 1 Synthesis of 4-AN and 4-AN-Ac