High *in vitro* activity of synthetic 5-aminoimidazole-4-carboxamidrazones against *Candida* biofilms formation on nanohydroxyapatite

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Infection is currently regarded as the most severe complication associated to the use of biomaterials. A wide range of biomaterials used in clinical practice have been shown to support colonization and biofilm formation by Candida species, with important clinical repercussions [1]. The cells within biofilms exhibit significant tolerance to antifungal therapy and have the ability to withstand host immune defenses. In addition, it represents a reservoir for persistent sources of infections [2]. In a previous work, Ribeiro et al prepared and tested a series of 5aminoimidazole-4-carboxamidrazones and three of them displayed strong antifungal activity on yeast [3]. Therefore, in the present study, the activity of these three novel imidazole derivatives was evaluated against C. albicans and C. krusei biofilm formation on nanohydroxypatite (nanoHA), a well-known biocompatible ceramic [4]. Additionally, the cytotoxicity against human osteoblastic cells (MG63) was also assessed. Two approaches were applied: (1) to investigate anti-biofilm effect the components were simultaneously incubated with yeast suspension and the number of adherent cells on nanoHA surface was assessed after 24 h incubation and (2) to access the mature biofilm eradication ability, 24 h biofilms of Candida spp established on nanoHA were exposed to 5-aminoimidazole-4-carboxamidrazones for 24 h and the number of remaining viable microorganisms was determined. Using both approaches, the metabolic activity of MG63 was assessed after 24h and 48h incubation with 5-aminoimidazole-4-carboxamidrazones. Concerning the results obtained, the presence of imidazole derivatives had a remarkable inhibitory effect on subsequent biofilm development by C. albicans and C.

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krusei on nanoHA surface. Moreover, the three tested 5-aminoimidazole-4-carboxamidrazones displayed potent in vitro activity against sessile yeast cells within biofilms, in a concentration-dependent way. Roughly, C. albicans was more sensitive to the components. The metabolic activity of MG63 cells had shown a time and concentration-dependent cytotoxicity. Together these preliminary findings indicate that these imidazole derivatives display potent activity against C. albicans and C. krusei biofilms in vitro. Future studies should be conducted to employ the potential of these components for the treatment or, even better, for the prevention of Candida biofilm biomaterial-associated infections.

References:

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