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 5-aminoimidazole-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.*

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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