NOVEL XANTHENONES WITH HIGH ANTIFUNGAL ACTIVITY AND POSITIVE MYCOSTATIC SELECTIVITY INDEX VALUES

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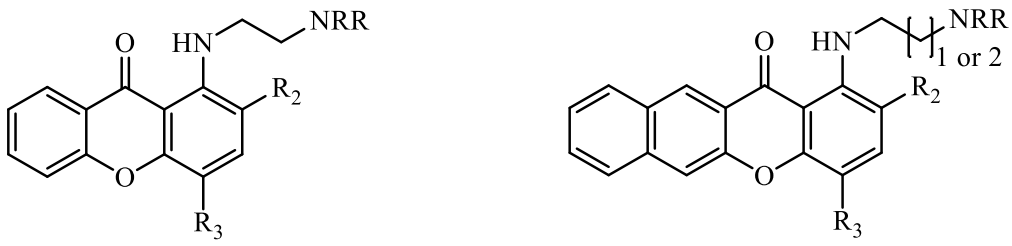
The discovery of new substances with antifungal activity has become increasingly crucial in recent years as we witness a substantial wave of drug-resistant infections. Both natural and synthetic xanthenones have exhibited encouraging results, even though such compounds still need to be thoroughly investigated for their antifungal activity. Herein we describe the design and synthesis of novel xanthenone derivatives with strong antifungal activity with MICs values in the range of 2 - 4 μg/mL against reference and fluconazole resistant C. albicans strains. Our results indicate that the most active compounds are not substrates for ABC and MFS transporters, pumps that efflux drugs from resistant cells. Moreover, yeast topoisomerase II was pinpointed as a potential molecular target. Novel synthesized compounds exhibited moderate cytotoxicity against human cell lines, although the selectivity index value for human pathogenic strains remained favourable. Furthermore, their fungicidal mode of action reduces the probability of persistent or recurrent infections and resistance development.



R_2, R_3= H, NO_2