Study of a Selected Series of 3- and 4-Arylcoumarins as Antifungal Agents against Dermatophytic Fungi: T. rubrum and T. mentagrophytes

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Abstract

The main etiological agents in dermatophytosis of human skin and nails are Trichophyton, in particular Trichophyton rubrum (T. rubrum) and Trichophyton mentagrophytes (T. mentagrophytes). A new series of twenty-three 3- and 4-arylcoumarins was synthesized and the antifungal activities against clinical isolates of T. rubrum and T. mentagrophytes were evaluated. Sixteen out of twenty-three molecules exhibited antifungal activity against one or both fungi strains. In some cases, the activity against T. rubrum has been comparable to fluconazole, one of the standards, being 8-methoxy-3-(4'-nitrophenyl)coumarin (16) the best compound within this series (minimum inhibitory concentration, MIC=6.25 μg/mL). The preliminary structure-activity relationship study showed that the antifungal activity depends on the position and nature of the substitution patterns. The cytotoxicity of eleven compounds on D-384 (astrocytoma), A-549 (lung cancer) and RKO (colorectal cancer) cell lines was also performed. With the aim of deeply understand the potential of these molecules as hits to develop new drugs, the theoretical absorption, distribution, metabolism and excretion (ADME) properties of the active compounds were calculated.

Author keywords

Antifungal agents; Arylcoumarins; Heterocycles; Synthesis.