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Cytotoxicity And Androgenic Potential Of Antifungal Drug Substances On Mda-kb2 Cells

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Abstract : The objective of this study is to evaluate in vitro the cytotoxic and androgenic potential of several antifungal molecules (amphotericin B, econazole, ketoconazole and miconazole) on MDA-Kb2 cell lines. This biological model is an effective tool for the detection of endocrine disruptors because it responds well to the main agonist of the androgen receptor (testosterone) and also to an antagonist: flutamide. The cytotoxicity of each chemical compound tested was measured using an MTT assay (tetrazolium salt, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) which measures the activity of the reductase function of mitochondrial succinate dehydrogenase enzymes of cultured cells. This complementary cytotoxicity test is essential to ensure that the effects of reduction in luminescence intensity observed during androgenic tests are only attributable to the anti-androgenic action of the compounds tested and not to their possible cytotoxic properties. Tests of the androgenic activity of antifungals show that these compounds do not have the capacity to induce transcription of the luciferase gene. These compounds do not exert an androgenic effect on MDA-Kb2 cells in culture for the environmental concentrations tested. The addition of flutamide for the same tested concentrations of antifungal molecules reduces the luminescence induced by amphotericin B, econazole and miconazole, which is explained by a strong interaction of these molecules with flutamide which may have a greater toxic effect than when tested alone. The cytotoxicity test shows that econazole and ketoconazole can cause cell death at certain concentrations tested. This cell mortality is perhaps induced by a direct or indirect action on deoxyribonucleic acid (DNA), ribonucleic acid (RNA) or proteins necessary for cell division.

Keywords : cytotoxicity, androgenic potential, antifungals, MDA-Kb2
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