

A COMPARATIVE STUDY OF THE ANTIMYCOTIC ACTIVITY OF A MICONAZOLE HP- β CYCLODEXTRIN SOLUTION AND A SURFACTANT SOLUTION.

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Miconazole (Mi) is a drug substance well known for its antimycotic activity. Unfortunately, Mi is practically insoluble in water ($< 1.03 \mu\text{g/ml}$) and was consequently formulated with a non-ionic surfactant, polyoxyl 35 castor oil (Cremophor EL[®]), for parenteral administration. The marketed solution (Daktarin[®] IV solution) has been withdrawn from the Belgian market since 1997 probably because of the side effects associated to polyoxyl 35 castor oil. It has been shown that a combination of lactic acid and cyclodextrins (CD) (more particularly hydroxypropyl- β CD (HP- β CD)) allows to solubilize more than 10 mg of Mi per ml, which is the concentration of the marketed solution^{1,2}. HP- β CD in combination with lactic acid was proposed as safe solubilizing agents alternatively to the use of surfactants for the parenteral administration of Mi.

The aim of this work was to compare the *in vitro* antimycotic activity of the surfactant solution (Daktarin[®] IV) and the new proposed formulation containing HP- β CD and lactic acid.

In this report, we compared the two solutions by determining their minimal inhibitory concentration (MIC) against 15 yeasts and 16 filamentous fungi isolates. The MIC were determined by using a broth microdilution method based upon the proposed National Committee for Clinical Laboratory Standards (NCCLS) guidelines for broth microdilution technique (NCCLS M27A).

The comparison of the MIC for the two solutions has been performed with an analysis of variance (ANOVA). All results were considered to be significant at the 5% critical level.

Results have shown that the experimental values are in good accordance with the literature values for both yeasts and filamentous fungi which means that the broth microdilution method used is an appropriate method for MIC determination of Mi against both yeasts and filamentous fungi.

An ANOVA test was applied to determine if there are significant differences between the two solutions. It appears that MIC values of the CD solution and of the Daktarin[®] IV solution are not significantly different.

It can be concluded that, *in vitro*, the CD solution has the same antimycotic activity as the surfactant solution. HP- β CD does not interfere with the activity of Mi. The new proposed formulation is a good alternative to the Daktarin[®] IV solution.

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