

DEVELOPMENT OF A CUTANEOUS HYDROGEL CONTAINING MICONAZOLE, HYDROXYPROPYL- β -CYCLODEXTRIN AND LACTIC ACID: STUDY OF ITS TOLERABILITY AND EFFICACY.

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This work was dedicated to the development of a cutaneous gel formulation containing miconazole. We chose to develop this formulation because there is no drug product available as a cutaneous hydrogel containing an antifungal drug substance, dissolved in a pure aqueous vehicle. We compared the activity of this hydrogel containing dissolved miconazole with that of Daktarin[®] cream containing miconazole nitrate. Miconazole is well known for its antimycotic activity and is practically insoluble in water (< 1.03 μ g/ml)

The combining effect of 200 mM lactic acid and 75 mM HP- β CD allowed to solubilize 17.4 mg/g miconazole. This amount is equivalent to 20 mg/g of miconazole nitrate in the Daktarin[®] cream. Hydroxyethylcellulose at a 3% concentration was used as gelling agent. The gel is transparent and has a pH value close to 3.5.

A study carried out on 15 volunteers showed that the gel containing cyclodextrins is well tolerated when applied on an unbroken skin.

With the aid of corneofungimetry, we compared the *ex vivo* activity of the gel to that of the Daktarin[®] cream. The results were difficult to interpret. Differences were observed depending on whether the mycelium growth is expressed in terms of surface or density. The study requires to be continued because it is difficult to draw a conclusion owing to the restricted number of both volunteers and strains.

On the other hand, a comparative *in vivo* study carried out on 18 volunteers suffering from tinea corporis showed that there was no significant difference between the gel and the cream in terms of clinical activity, cosmetic acceptance and side effects.

In conclusion, with the combining aid of lactic acid and HP- β CD, it was possible to develop an aqueous gel containing miconazole. Unfortunately, we were not able to show an increased activity of this hydrogel containing soluble miconazole. This gel has the potential advantage to permit an administration by several routes which would be a simplification on an industrial point of view.