

MICONAZOLE LOADED MICROPARTICLES FORMULATED AS CHEWING GUMS FOR LOCAL TREATMENT OF ORAL CANDIDIASIS IN PAEDIATRIC PATIENTS

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Purpose

The aim of this work is to incorporate Miconazole (MCN) loaded mucoadhesive microparticles into chewing gums in order i) to increase the release rate of MCN from gum matrix and ii) to prolong the effect of MCN over 4 hours.

Methods

Different microparticle batches were prepared in order to exploit MCN best release profile and to realize microparticles with suitable mucoadhesive features: a) alginate microparticles; b) chitosan coated alginate microparticles; c) chitosan microparticles with a gelatine core and d) chitosan microparticles. All batches were prepared with a mechanical instrument based on the nozzle vibration technique (Encapsulator Buchi 350 pro), using both standard and concentric nozzles. The suitable process parameters like polymer concentration, nozzle diameter and nozzle vibration frequency were selected thanks to a design of experiment (Statgraphics Centurion) with the aim of obtaining microparticles with 200 μm diameter. MCN loaded microparticles were evaluated in terms of dimensions (dynamic light scattering) and MCN encapsulation efficiency (HPLC). *In vitro* release test was performed in artificial saliva, pH 5.4, at 37°C.

Microparticles loaded chewing-gums were prepared by softening the gum base and incorporating freeze dried microparticles before cooling. All formulations were submitted to an *in vitro* release test using chewing machine in artificial saliva as release medium

Results

Alginate microparticles were discarded because of the poor MCN release after 4 hours ($20.81 \pm 3.4\%$). Chitosan coating of alginate microparticles significantly reduced MCN loading (6.21%); consequently, *in vitro* release tests were not performed on these microparticle batches. Chitosan demonstrated to be the best polymer to obtain microparticles with a good MCN encapsulation efficiency (46-51%) and fast release: after 4 hours, the percentage released was $71.78 \pm 5.2\%$ from chitosan microparticles and $65.38 \pm 4.0\%$ from chitosan microparticles with gelatin core. *In vitro* release study of final chewing-gum formulations demonstrated: i) the rapid release of undamaged microparticles from gum matrix (5' chewing) and ii) an improved (release of MCN when chitosan microparticles were incorporated into gums with respect to the release of MCN incorporated as such.

Conclusions

Chitosan microparticles demonstrated to be suitable in increasing the release rate of hydrophobic drugs like MCN from chewing gums.