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Mucoadhesive assessment of different antifungal nanoformulations

Introduction:

Oral candidiasis is an important opportunistic fungal infection, and polyenes and azoles are still the most used antifungal agents. However, most of those treatments present a poor oral absorption. Therefore, the major challenge is the improvement of the absorption of the antifungal agents in oral mucosa, and the encapsulation technology may be considered as a possible strategy to achieve this objective. Three types of mucoadhesive nanoparticles (NPs) will be prepared using nystatin (Nys) as model antifungal drug, and then drug-loaded NPs will be included in toothpaste (TP), oral gel (OG) and film patches or oral films (OF).

Materials and Methods:

For the development of NPs, alginate from brown algae, acquired from Sigma-Aldrich (St. Louis, USA), PLGA and PLA both obtained from Purac (Gorinchem, Netherlands), were applied as encapsulant material. The mean particle size, polydispersity index (PI) and zeta potential of the NPs were measured. The interaction between mucin and NPs was determined using a TA-XT2i Texture Analyser [1]. The in vitro muchoadhesion was assessed using mucus producing HT29-MTX cells as mucosal surface in a biorelevant oral cavity model [2].

Results and Discussion:

The nanoparticles had a size of about 300-400 nm and a surface charge between -26.03 and -43.52 mV. Regarding the association efficiency, it showed that these NPs systems are very successful drug carriers since they present values of 95 ± 0.41%, 71 ± 9.60% and 72 ± 15.65% for PLA, PLGA and alginate NPs, respectively. The interaction between mucin and the formulation was more evident in the mucoadhesive formulations loaded with NPs, where the peak force was around 4.90, 3.43 and 2.94 Newtons for OF, OG and TP, respectively, in comparison to the values of the formulations without NPs (Figure 1). The mucin interaction with Nys-loaded NPs was supported by *in vitro* tests using HT29-MTX cells. Nys solution showed an interaction with the mucosal surface around 3.94 ± 2.96% after 2 hours under HBSS buffer flow (1.6 mL/min). For drug-loaded formulations, this percentage increased up by a ten-fold factor.

Conclusions:

Based on analysis of all samples, we observed that the best formulation in terms of mucoadhesion was the oral film loaded with PLGA NPs. This fact was also confirmed by *in vitro* tests using HT29-MTX cell as an oral cavity cell model. Further studies will focus on *in vivo* experiments.

References

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Figures

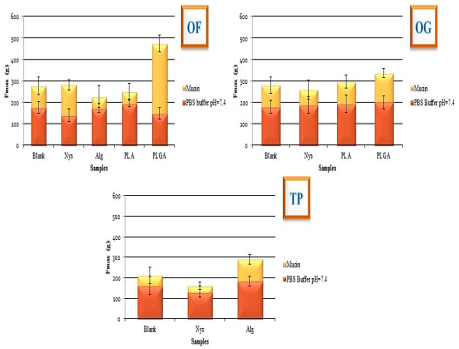

Figure 1: ***In vitro*** **detachment test of the formulations** ***versus*** **buffer (unspecific adhesion-the orange columns) and mucin dispersion (the estimated mucin interaction-yellow columns (n= 10).**