Development of an oral mucosa model useful to characterize drug delivery systems for the oral lichen planus treatment

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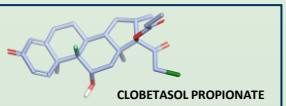
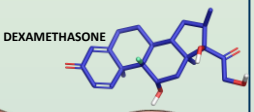
BACKGROUND

Oral Lichen Planus (OLP), a chronic mucocutaneous inflammatory disease, is a well-recognized potentially malignant disorder of the oral cavity, with a 1.5% transformation rate per year.
Current therapeutic strategies involve the administration of immunosuppressant drugs, among which topical steroids (Clobetasol propionate; Dexamethasone) are considered the gold standard, but these drugs are administered through formulations that do not guarantee a sufficient time-lapse of action necessary for inducing their function in the oral cavity, since are borrowed from dermatology.



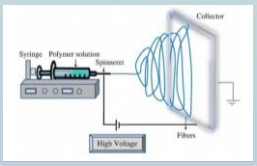


OBJECTIVE

The aims of the project are:
1. The development of specific drug delivery systems for the treatment of OLP;
2. The realization of an in vitro 3D model of the oral mucosa using a bioreactor, in order to mimic the salivary flow and oral mucus to determine the effects of oral behaviour on drug delivery systems.

METHODS AND RESULTS

1. Synthesis of Polylactic Acid Nanofibers loaded with Dexamethasone and Clobetasol (University Nicolò Cusano) by electrospinning techinque (Fig 1)



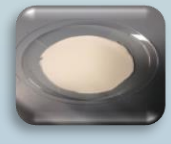


Fig.1

1.1 Drug release evaluation in EtOH and DMEM with Spectrophotometer

During the first hour, nanofibers loaded with 5% w/w of Clobetasol, release about 83% of the drug in EtOH, while those loaded with Dexamethasone release 95% (Fig. 2)

After 24 hours, nanofibers loaded with 5% w/w of Clobetasol, release about 25% of the drug in DMEM, while those loaded with Dexamethasone release 63% (Fig. 3)

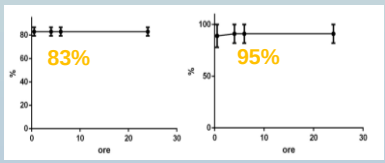


Fig. 2

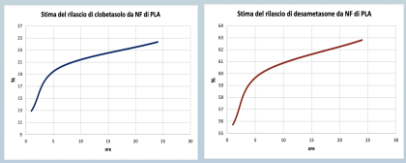


Fig. 3

1.2 Analysis with Scanning Electron Microscope (Fig. 4)

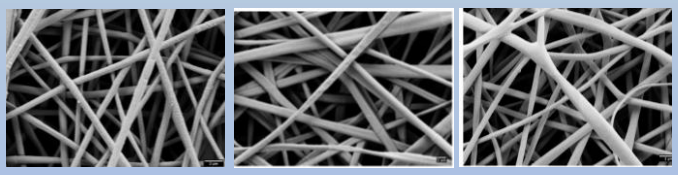


Fig. 4

1.3 MTT assay

MTT was performed on fibers loaded with 5% w/w of dexamethasone, on those loaded with 5% w/w of clobetasol and also on fibers coated with chitosan.
Results showed cells mortality ranging from 0 to 30%, which means the material is cytocimpatible (Fig. 5)

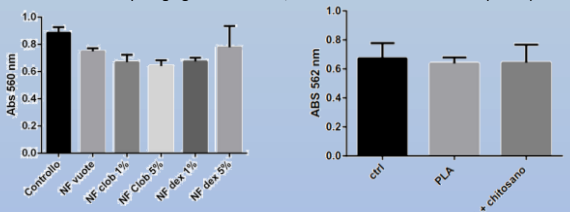


Fig.5

2. Realization of a 3D cell culture through the use of a Bioreactor (Fig 6) and PLA scaffolds (Fig 7) synthesized with a 3D printer by University Nicolò Cusano.
It was set up a down-top flow with an initial flow rate of 100µl/min to permit cells adhesion which was increased to 250µl/min to mimic the active salivary flow.

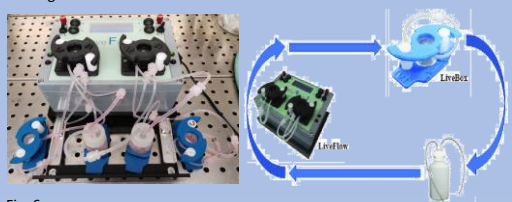


Fig. 6

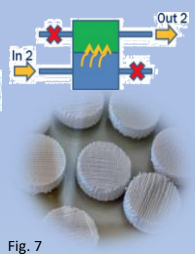


Fig. 7

CONCLUSIONS AND FUTURE PERSPECTIVES

The study now continues with the development of the Oral Mucosa Model for studying the properties of the Drug Delivery Systems, in particular:

- Optimization of the mucoadhesive carrier
- 3D cell culture with cells derived from OLP patient's biopsies