# DIRECT POWDER EXTRUSION 3D PRINTING OF MUCOADHESIVE ORODISPERSIBLE FILMS FOR PERSONALIZED CLOBETASOL PROPIONATE BASED PAEDIATRIC THERAPIES

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## DIRECT POWDER EXTRUSION (DPE) 3D PRINTING

The DPE technique can obtain the final pharmaceutical form starting directly from medicated powder pellets or blends, bypassing the intermediate step of thermoplastic filament formation provided by other printing techniques currently in use and thus preserving the active from the possibility of degradation. An additional advantage of this technique is the possibility of using different dosages of drug, even with higher concentrations of active ingredient, allowing complete customization of the final pharmaceutical form, making it adherent to the individual patient's needs[1]. With DPE, finished pharmaceuticals dosage forms, as amorphous solid dispersions, can be obtained in a single step from the direct extrusion of powder blends.

In recent years, the work of our research group has focused on the study and the development of a single-screw extruder specific for DPE technique, leading to the realization of the 3DForMe® pharmaceutical printer (Farmalabor Srl., Canosa di Puglia, ITALY), currently in commercial phase.

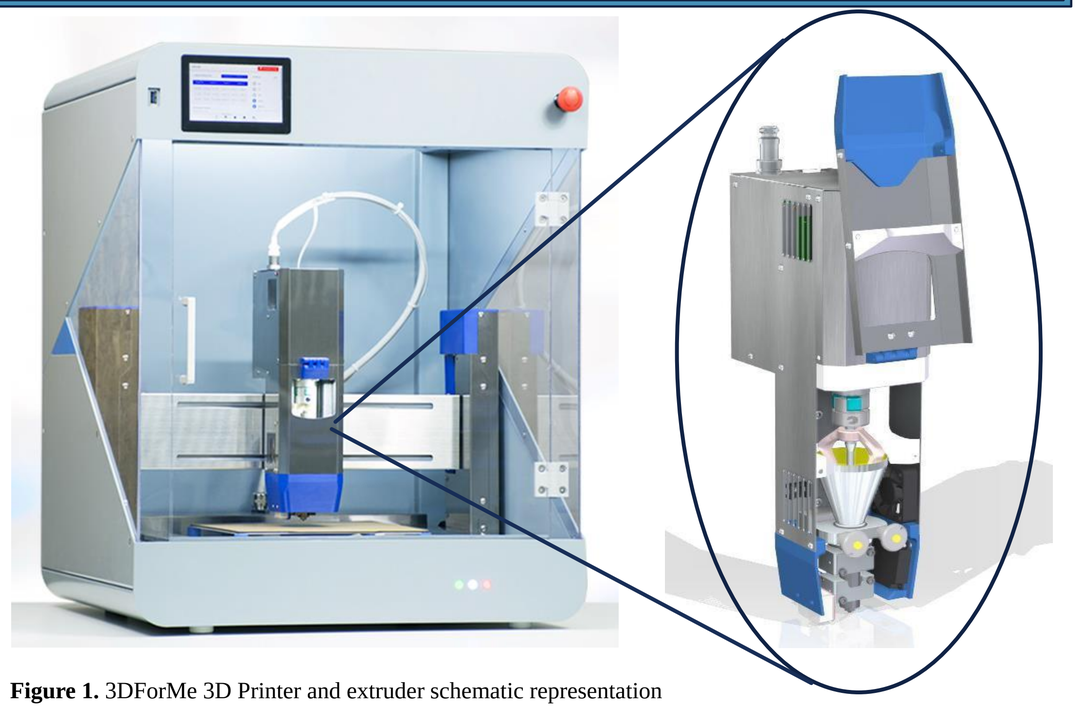

**Figure 1.** 3DForMe 3D Printer and extruder schematic representation

## PRODUCTION OF MUCOADHESIVE ORODISPERSABLE FILMS

**INTRODUCTION:** Oral Lichen Planus (OLP) is a chronic mucocutaneous disorder of the stratified squamous epithelium affecting the oral mucous membranes that shows an important occurrence in the paediatric population[2]. The use of corticosteroids, as Clobetasol Propionate (CBS), is to date the most indicated therapy for reducing the symptoms and local effects of autoimmune diseases of the oral mucosae[3]. The aim of this study was to provide 3D printed mucoadhesive oral films containing approximately 125 µg/dose of CBS, a dose deemed therapeutically appropriate and functional to ensure the OLP treatment, in order to enhance paediatric patients' compliance toward therapy[3]. In fact, the DPE 3D printing of these dosage forms can allow the reduction of frequency regimen, the therapy personalization, and reduction of oral cavity administration discomfort.

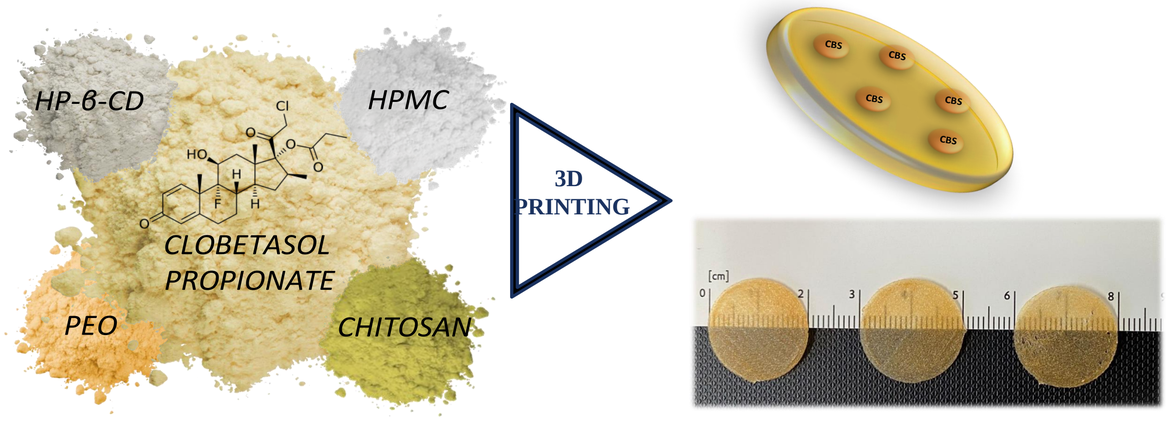


**Figure 2.** Powder blend composition and obtained mucoadhesive films.

**METHODS:** Different polymeric materials, namely hydroxypropylmethylcellulose (HPMC) or polyethylene oxide (PEO) blended with chitosan (CS), were tested in order to obtain suitable mucoadhesive films. Hydroxypropyl-β-cyclodextrin (HP-β-CD) was added to obtained powder blend to increase the CBS solubility. The films were printed using the 3DForMe® 3D printer with a cylindrical geometry and setting the printer parameters: infill 40% with infill pattern Concentric, high resolution with brim, without raft, travel speed 5 mm/s, print speed 5 mm/s, number of shells 2, layer height 0.125 mm, floor temperature 40 °C and extrusion temperature of 170 °C.

## MUCOADHESIVE ORODISPERSABLE FILMS CHARACTERIZATION

The formulations were tested in terms of mechanical, physico-chemical, and in vitro biopharmaceutical properties. The film showed a tenacious structure, with drug chemical-physical characteristics enhancement due to its partial amorphization during the printing stage and owing to cyclodextrins multicomponent complex formation. The presence of CS enhanced the mucoadhesive properties leading to a significant increase of drug exposure time on the mucosa. Finally, the printed films permeation and retention studies through porcine mucosae showed a marked retention of the drug inside the epithelium, avoiding drug systemic absorption.

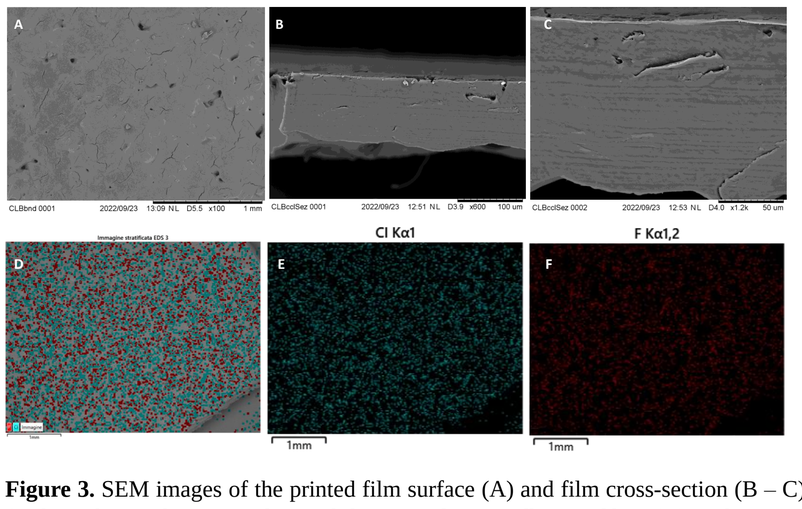


**Figure 3.** SEM images of the printed film surface (A) and film cross-section (B – C). Surface chemical microanalysis of the printed mucoadhesive films (D) with images related to the presence of the element Cl (E) and F (F).

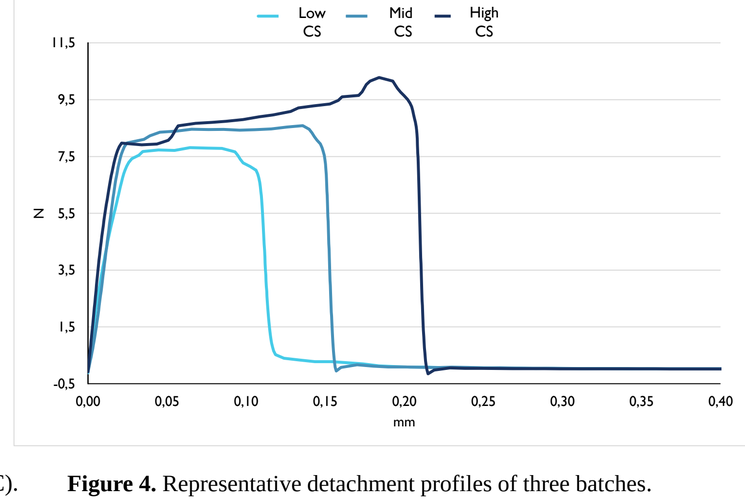


**Figure 4.** Representative detachment profiles of three batches.

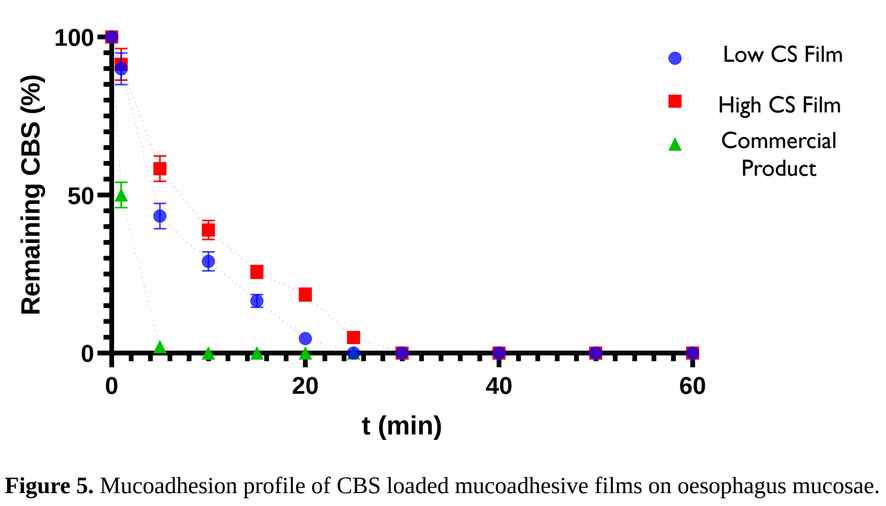


**Figure 5.** Mucoadhesion profile of CBS loaded mucoadhesive films on oesophagus mucosae.

## CONCLUSIONS

The main objective of this work was to develop a novel mucoadhesive film obtained by 3D printing DPE technique capable of giving sustained release of CBS within paediatric OLP therapy. In the obtained formulations, the chemical-physical characteristics of the drug were effectively improved due to the partial amorphization of the drug during the printing stage and owing to the formation of a cyclodextrins multicomponent complex. From the tests performed, the obtained mucoadhesive films exhibited high mucoadhesive properties, improving with increasing CS percentage inside them, an elastic and tenacious structure, and marked retention of the drug inside the epithelium, thus avoiding systemic absorption of the drug. Therefore, mucoadhesive films could represent a suitable candidate in the paediatric therapy of OLP.

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2. Laeijendecker, R. et al., 2005. Oral Lichen Planus in Childhood. Pediatr Dermatol 22, 299–304.

3. Cilurzo, F. et al., 2010. A new mucoadhesive dosage form for the management of oral lichen planus: Formulation study and clinical study. European Journal of Pharmaceutics and Biopharmaceutics 76, 437–442.