Title

Stress relieving: printing custom-made cortisol for patients with Addison's Disease.

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Background

The treatment goal for patients with Addison's Disease (AD) is to mimic physiological cortisol plasma concentrations. The current cortisol replacement therapies are suboptimal due to their drug release profile, fixed-dose character and the inability to cover nocturnal cortisol plasma concentrations. There is a high inter-individual variability in the cortisol need within this patient group, which comes with the unmet need for personalized cortisol formulations. 3D printing is a suitable technology for manufacturing oral dosage forms which allows us to easily adjust the drug dose and release profile based on patient needs. The aim of this research is to develop novel tailor-made 3D printed hydrocortisone formulations covering the daily as well as nocturnal physiological cortisol plasma concentrations.

Methods

Two sustained release (SR) formulations were printed using hydroxypropylcellulose based polymeric matrix filaments prepared by hot-melt extrusion. Formulation 1 (F1) and 2 (F2) were loaded with 20% and 30% hydrocortisone respectively. Tablets were printed with a height of 1 mm, 2 mm and 3 mm in order to assess the relationship between tablet height and drug dose. A dissolution study was performed to compare drug release profiles of the printlets with the release profile of the commercially available Plenadren©.

Results

Dissolution study data demonstrates that 3D printed SR formulations have a similar drug release profile compared to the Plenadren© 5 mg tablets (Fig. 1). Tablet height was correlated to tablet dose (R^2 0.996).

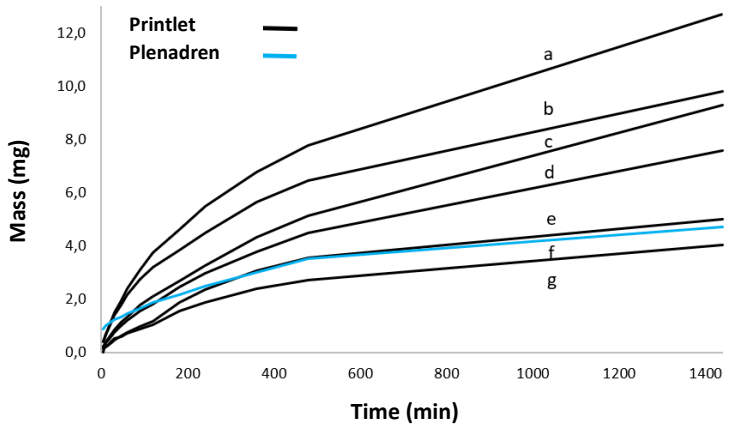

Figure 1. Dissolution study results for 3D printed tablets (black) and Plenadren (blue). Key (tablet height-formulation): 1 mm-F1 (a) 2 mm-F2 (b), 3 mm-F1 (c), 2 mm-F1 (d), 1 mm-F2 (e), Plenadren (f) and 3 mm-F2 (g).

Conclusion

In this work we have demonstrated that hydrocortisone formulations can be printed in any desired dose by adjusting the tablet height. Furthermore, the novel 3D printed formulations have a similar sustained drug release profile compared to the commercial Plenadren© formulation. 3D printed SR formulations provide more dose flexibility compared to fixed-dose commercial formulations while maintaining the same drug release profile. The high inter individual difference in the cortisol need can be addressed by printing the desired dose for the unique patient which is essential in the treatment of patients with AD.