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INJECTABLE SODIUM ALGINATE BASED HYDROGEL WITH METRONIDAZOLE IN 3D PRINTED RESERVOIR FOR PROLONGED RELEASE

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Abstract

In this work a complex reservoir-like vaginal ring was considered as a drug delivery system (DDS) which locally releases an active ingredient in a prolonged manner. Fused deposition modeling (FDM) 3D printing was used to create the porous reservoir wall with precisely controlled dimensions and microscopic pores. Metronidazole (MTZ), a first-line therapy against bacterial vaginosis[1], had to be easily transferred into the reservoir by injection. Furthermore, once inside the reservoir, this substance should not leak out through the pores and allow for a gradual and prolonged release of the drug. To this aim an alginate-based hydrogel was developed which act as the drug carrier. Alginate was selected due to its low toxicity. Calcium carbonate ($CaCO_3$) and glucono-delta-lactone were used as crosslinking agents to control the gel formation process[2]. The goal was to fill the reservoir with a flowable precursor solution that reached the solid-like consistency of the hydrogel in the cavity. Given that the required amount of MTZ for treatment was greater than its solubility limit in the alginate solution, a MTZ dispersion had to be adopted, and the effect of the drug-loaded precursor mixture composition on its flow properties was investigated. In steady state rotational tests, the precursor dispersions exhibited a yield stress, followed by a shear-thinning behavior. Out of this information the dispersion injectability was predicted, and the predictions validated in a 3D bioprinter, here used as a capillary rheometer. The ability of the suspension to crosslink despite the very high MTZ solid content was confirmed performing dynamical mechanical tests, which also showed the major effect of dispersed drug content of the complex modulus of the filled hydrogel. In particular, loss factor increased with higher amounts of dispersed drug, likely due to friction between the solid particles. The amount of alginate controlled instead of the hydrogel stability. As for drug release, the hydrogel structure had little effect. Instead, the porosity and exposed area of the 3D printed reservoir wall was found to be the main factor controlling the drug release rate.

References

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