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Formulation of a 3D printable hydrogel for the development of solid rectal drug delivery system

Muñoz Pérez Elena[1], Igartua Manoli[1,2,3], Santos Vizcaino Edorta[1,2,3], Hernández Rosa Maria[1,2,3]

[1] NanoBioCel Group, University of the Basque Country (UPV/EHU), Vitoria-Gasteiz, Spain.
[2] Bioaraba, NanoBioCel Research Group, Vitoria-Gasteiz, Spain.
[3] Biomedical Research Networking Centre in Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN).
*Correspondencia: rosa.hernandez@ehu.es

1. Introduction

Since the FDA approved the use of the first formulation manufactured by 3D printing in 2015, the application of this technology to obtain new and improved pharmaceutical formulations is on the rise [1].

Nowadays, 3D printing is considered a reproducible, reliable, fast and easily manageable technique that allows a precise design of formulations. Thus, the high precision in manufacturing allows greater control over the characteristics and behaviour of each printed design [2].

3D printing of solid rectal formulations is particularly interesting as it offers an alternative for their production, obtaining results of greater morphological complexity and modified release profiles [3]. Thus, the design of new printable materials suitable for their application in this field has become necessary [4].

The aim of this project was to design and to evaluate a hydrogel composed by alginate and Laponite XLG as a bioink suitable for the obtainment of 3D-printed rectal formulations.

2. Materials and methods

Hydrogels employed for this study were formulated by mixing ultrapure sodium alginate and different concentrations of Laponite XLG nanoclay in water. For the study, nanoclay concentration was varied from 1.5 % to 10 % (wt) in order to compare and evaluate the behaviour of various hydrogel compositions.

Rheological characteristics of the hydrogels were tested and compared in a steady state flow test. Increasing shear rates from 1 to 1000 s-1 were employed.

Frequency sweep test was performed in each of the hydrogel compositions in order to analyse their storage /loss modulus and structure stability. A strain of 1 % within linear viscoelasticity range (LVR) of the hydrogels was employed. This test was used to select the most well-structured hydrogels and discard the less promising ones.

Selected hydrogel compositions were tested in a syringeability assay in order to check their feasibility on the extrusion based 3D-printing process. Using a texturometer the forces required to extrude the hydrogels trough a syringe was determined. Three different printing nozzles were tested for each hydrogel composition (22G, 25G and 27G) to predict clogging and resolution changes during the printing process.

The most suitable hydrogel composition and printing nozzle were employed to print solid rectal formulations using a 3D bio-printer.

3. Results and discussion

In a steady-state flow test shear thinning behaviour of all tested hydrogel compositions was observed. Viscosity under small shear rates was higher when nanoclay concentration was

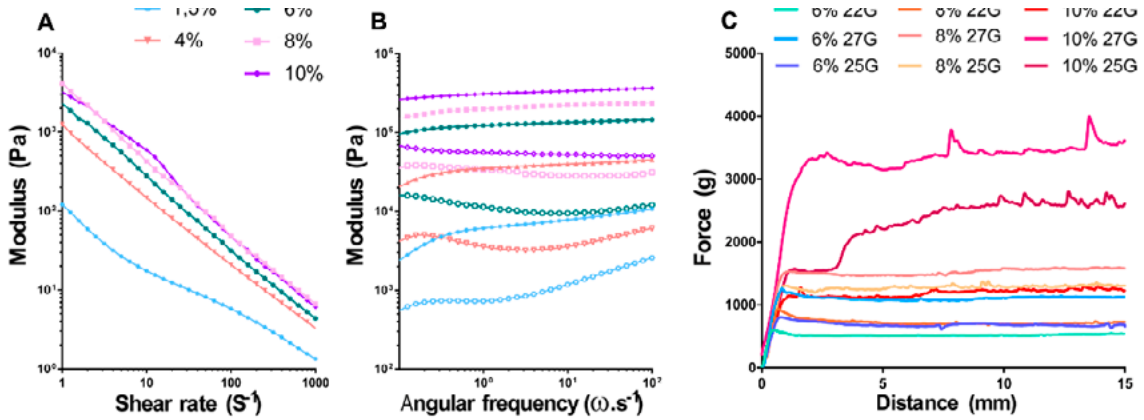

Figure 1. Rheological evaluation and syringeability assay of hydrogels (A) Viscosity curves of hydrogels. (B) Dependence of G´(Solid symbols) and G´´(open symbols) on the angular frequency for the different hydrogel compositions. (C) Syringeability assay of the selected compositions tested with different printing nozzles.

increased. All of the hydrogels presented a progressive decrease in viscosity when increasing shear rate (Fig. 1A).

Frequency sweep test showed solid-like structure of the formulated hydrogels. This structure was more stable in hydrogels containing 6 %, 8 % and 10 % (wt) of nanoclay, being their storage (G´) and loss (G´´) modulus higher without varying all over the frequency range tested (Fig. 1B). According to these results, hydrogels with 6 % to 10 % of nanoclay were selected for the syringeability assay.

As shown in Fig. 1C extrusion force required for the stable syringeability of the hydrogels with 6 % of nanoclay was notably smaller to forces required for the rest of the compositions tested. Moreover, 22 gauge printing nozzle demonstrated to be the most suitable one for the extrusion, allowing the correct flow of the hydrogels without clogging.

Fig. 2 illustrates the appearance of the solid rectal formulations printed using the hydrogel compound of a 6 % of Laponite XLG. The high resolution in the printing process allowed printing designs of different sizes.

4. Conclusions

The present study details the development and evaluation process of a new 3D-printable hydrogel for its use as a suitable bioink for the obtainment of solid rectal formulations trough an extrusion based 3D-printing process. The selected material presented suitable rheological characteristics, promising behaviour against extrusion forces and could be 3D printed in solid rectal formulations of different sizes.

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