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Investigation of Physicochemical Properties of PVA-GANT Mucoadhesive Hydrogels

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SUMMARY

The aim of this work was the manufacture and characterisation of novel chemically cross-linked mucoadhesive PVA-GANT hydrogels prepared by using autoclaving. Particularly, the study was focused on the physicochemical and pharmaceutical properties of these hydrogels with regards to potential applications for drug delivery and wound dressing. PVA-GANT hydrogels with different molar ratios and total concentrations of polymers in solution were prepared using a standard sterilisation autoclave. The physico-chemical properties were characterised by various techniques including IR spectroscopy, Texture Analysis and SEM and thermo-analytical techniques (DSC and TGA). Pharmaceutical characteristics were obtained in drug loading/release tests and microbiological assays. The results have shown that the properties of hydrogels (swelling degree, mechanical properties, internal structure, drug loading/release and antimicrobial properties) are very dependent on the polymer composition.

INTRODUCTION

Hydrogels are three dimensional, hydrophilic, polymeric networks capable of imbibing large amounts of water or biological fluids (Peppas et al., 2000). In this study two polymers, polyvinyl alcohol (PVA) and Gantrez AN® (GANT), were cross-linked at high temperature in an autoclave to produce mucoadhesive hydrogels with anti-microbial properties. The cross- linkage was achieved via esterification between carboxylic acid of Gantrez AN® and the hydroxyl group of PVA. PVA is a biodegradable, biocompatible, synthetic polymer with excellent film forming properties. Gantrez AN® [Poly (methyl vinyl ether-alt-maleic anhydride)] is a synthetic polyanhydride, which is employed as an ideal co-polymer due to its bio- adhesiveness and mucoadhesive properties.

MATERIALS AND METHODS

Polyvinyl alcohol (PVA) (98-99% hydrolysed and medium MW of 57-66 kDA) was purchased from Alfa Aesar, UK. Gantrez AN® (high MW of 216 kDA) was purchased from Sigma Aldrich, UK. The hydrogels were prepared via an autoclave method [Calo, 2016], with three molar PVA: GANT ratios (1:2, 1:1, 2:1) and different total concentrations of polymers in solution with three molar PVA: GANT ratios (1:2, 1:1, 2:1) and different total concentrations of polymers in solution (11-27%).

Physicochemical Characterisation: The chemical structure of dried hydrogels samples and polymer powders was scanned using IR spectroscopy, to identify molecular bonds and validate the cross-linkage in the hydrogels. Mechanical properties, such as strength, springiness and adhesive/cohesive

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characteristics), were investigated by Texture Analyser (penetration mode) and morphology (pore size and wall thickness) was assessed by SEM. The degree of swelling was measured gravimetrically or using TGA.

Pharmaceutical Characterisation: Antimicrobial activity was evaluated by a disk diffusion method. Drug loading and release was measured by UV-visual spectrophotometer.

RESULTS AND DISCUSSION

The SEM images of swollen hydrogels display the porous structure (Fig. 1, top). Both pores size and wall thickness are directly affected with PVA: GANT proportion. Sample (1:2) exhibits larger pores, in contrast to sample (2:1).

Data obtained by IR confirm a formation of cross-link bonds between the two polymers. The peak at 1172-1177 cm-1 could support the esterification reaction between the COOH group of Gant (formed after the ring opening) and the OH groups of PVA.

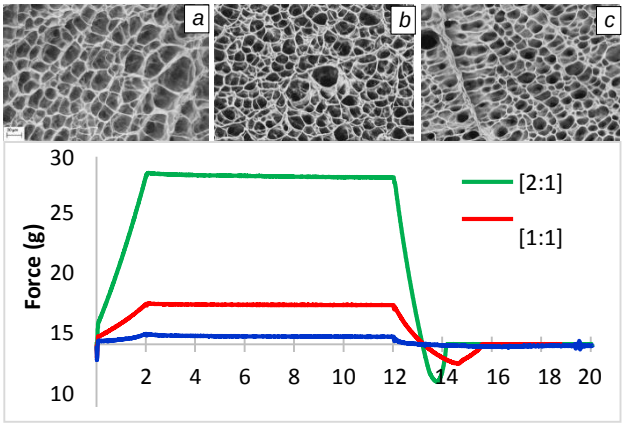

Fig. 1. *(top) SEM images (x1000) of (a) 1:2, (b) 1:1, (c) 2:1 PVA: GANT hydrogels swollen in pure water for 1 hour; (bottom) TA force profiles for hydrogels with different molar PVA:GANT ratios.*

Using the texture analyser, the mechanical strength and adhesion properties were measured using hold–on-distance mode. In the TA experiment the cylindrical probe (P/6, of 6 mm diameter) penetrated hydrogel to a depth of 1 mm, then was held for 10 sec and then withdrawn from the hydrogel. Results (Fig. 1, bottom) clearly show the effect of the composition on the mechanical properties of the hydrogels. Samples with a low PVA content (1:2) demonstrated the greater adhesiveness and still displayed low mechanical strength, whereas samples with a high PVA content (2:1) had a rigid texture and low adhesive properties.

The GANT polymer (and hydrogel with higher GANT concentration, i.e. sample 1:2), possesses a carboxylic acid (-COOH) that is primarily the key source of interaction and effectively encourages adhesion. This can result in a hydrogen bonding mechanism, anchoring the bioadhesive polymer with glycoproteins (located in mucosal linings), hence, these hydrophilic groups will also cause polymers to swell in water, exposing the maximum number of adhesive sites.

As the PVA content increases, this encourages further cross-links, yet develops rigid structure, hindering expansion of polymer network. Overall, the cross-link density is a primary factor that affects degree of swelling of hydrogel in liquid.

The swelling degree of hydrogel significantly increases during 2-3 weeks (Fig 2.). The swelling profile is strongly dependent on the polymer-water interaction and molecular flexibility allowing the polymer network to expand and maintain integral structure upon absorption, yet encompass porous features that affects penetration of water. The [2:1] sample implied a slow swelling, since cross-links are tight, restricting polymer chain mobility and expansion.

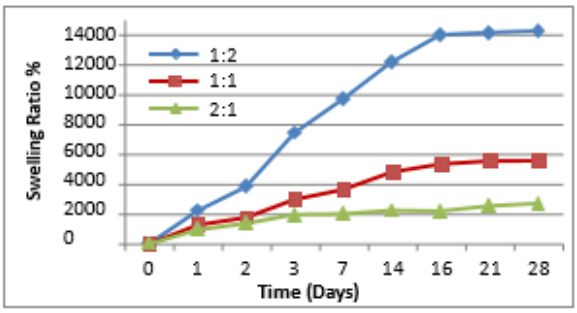

Fig. 2. *Swelling Ratio vs Time (in days) of three hydrogel ratio profiles: 1:2 (blue), 1:1 (red) and 2:1 (green)*

CONCLUSIONS

A quick and simple preparation via autoclave allowed producing an adhesive, chemically cross-linked and sterilised PVA-Gant hydrogel with no additional ingredients. The optimal characteristics of hydrogel suitable for particular pharmaceutical application can be achieved by variation in experimental conditions and composition of polymers.

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