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Sodium alginate and gelatin hydrogels: Viscosity effect on hydrophobic drug release

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ABSTRACT

Blend of biodegradable hydrogels like sodium alginate/gelatin (SA/G) usually requires use of chemical cross-linkers to remain stable in aqueous media for drug delivery applications. This study targets the feasibility of having an entire spectrum of a model hydrophobic drug (piperine) release i.e. from burst to controlled release, by varying polymer viscosity and molecular weight of plasticizer with minimal use of cross-linkers. Swelling study, drug-polymer interactions and morphology analysis reveal the impact of viscosity variation on polymer matrix.

1. Introduction

Biopolymers like starch [1], gelatin [2], alginate [3], chitosan [4] and many others have been exploited in the field of drug delivery. Systems like thin-films [5], micelles [6] etc. prepared using these polymers have been used in the controlled delivery of drugs. Hydrogel is also one of these systems that has been the choice of many researchers in recent times. Their porosity and property to swell make them excellent systems to be utilized in the field of drug delivery [7]. SA and gelatin are biodegradable polymers used in this work. Piperine was used as hydrophobic drug.

In this work, the effect of viscosity on swelling and dissolution of SA/G hydrogels was investigated. The idea here was to impart dissolution stability and achieve a controlled swelling with minimal use of toxic cross-linkers like glutaraldehyde (GTA). It was also observed that viscosity plays a very crucial role in loading and release of piperine. We have also tried to investigate the role of plasticizer like poly ethylene glycol (PEG) to improve the drug encapsulation. The overall aim was to achieve a wide spectrum of drug release, i.e. from controlled to burst release by varying polymer viscosity.

2. Material and methods

All chemicals were obtained from Alfa Aesar. SA/G hydrogels were prepared with few modification to the available method [8] i.e. use of HV (high viscosity) SA (1000–1500 cps, 1% in water) and the preparation of hybrid hydrogels (HV and LV-low viscosity SA in 1:1 ratio i.e. a 60/40 hybrid hydrogel has 30% of each HV and LV SA along-with 40% gelatin w/w). Apart from PEG 2000; 4000 and 6000 were also used. GTA was used as a cross-linker (0.2 v/v for 10 min) and 25 mg of piperine was also added to selected samples as a drug during the preparation of hydrogels. Swelling degree (SD) studies were carried out in PBS (Phosphate buffer saline pH 7.4) and 0.1 N HCl (pH 1.2). The SD was calculated by the equation: $SD\ (\%) = \frac{Ws - Wd}{Wd} \times 100$, where W_s is weight of swollen sample, while W_d is weight of dry samples. The FTIR–ATR analysis was done over a range of 500 cm^{-1}–4000 cm^{-1} using Bruker Tensor 37. Morphology of hydrogels was analyzed using a table top SEM (Phenom world ProX). Drug release was studied both in PBS and 0.1 N HCl solution at a temperature of 37 °C to mimic the intestinal and gastric pH i.e. 7.4 and 1.2. Samples were analyzed at regular time intervals using UV–vis spectroscopy (Lambda 35 Perkin Elmer) at 342 nm i.e. the λ_{max} for piperine.

3. Results and discussion

3.1. Swelling degree

60/40 and 70/30 (SA/G) cases were chosen as they are stable upto 360 min. 80/20 combination could not be chosen as high concentration (thus high viscosity) of HV SA did not allow proper stirring/ mixing of the solution. Dissolution of LV hydrogels began within 30 min making them difficult candidates for swelling analysis.

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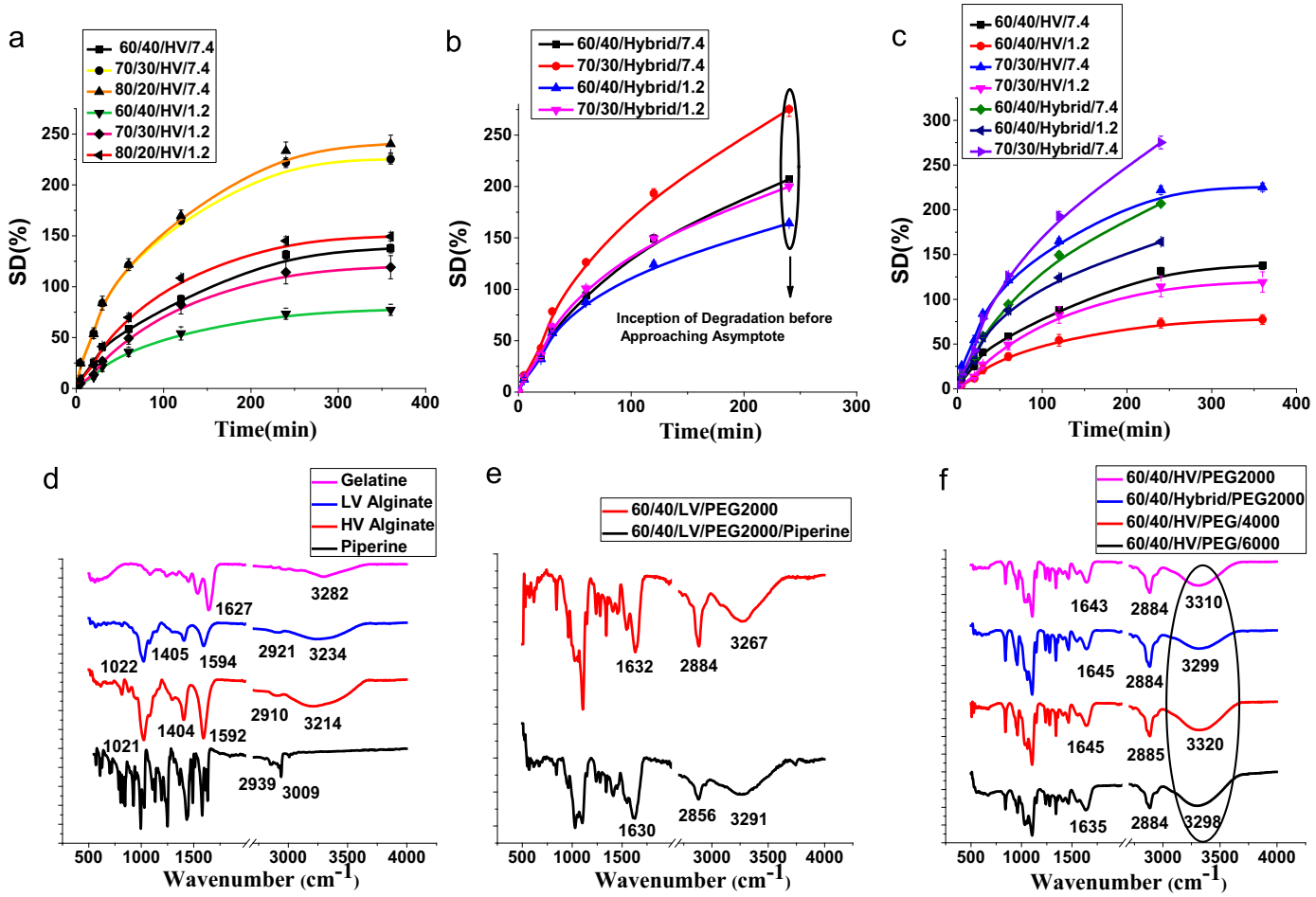

Fig. 1. Swelling Degree (a) 60/40, 70/30 and 80/20 HV hydrogels in pH 7.4/1.2 (b) 60/40 and 70/30 Hybrid hydrogel in pH 7.4/1.2 (c) SD comparison between HV and Hybrid hydrogels. FT-IR/ATR analysis (d) Gelatin, LV SA, HV SA and Piperine (e) 60/40 LV/PEG 2000 and 60/40 LV/PEG2000/Piperine (f) 60/40 HV/PEG2000, 60/40 Hybrid/PEG2000, 60/40 HV/PEG4000 and 60/40 HV PEG 6000.

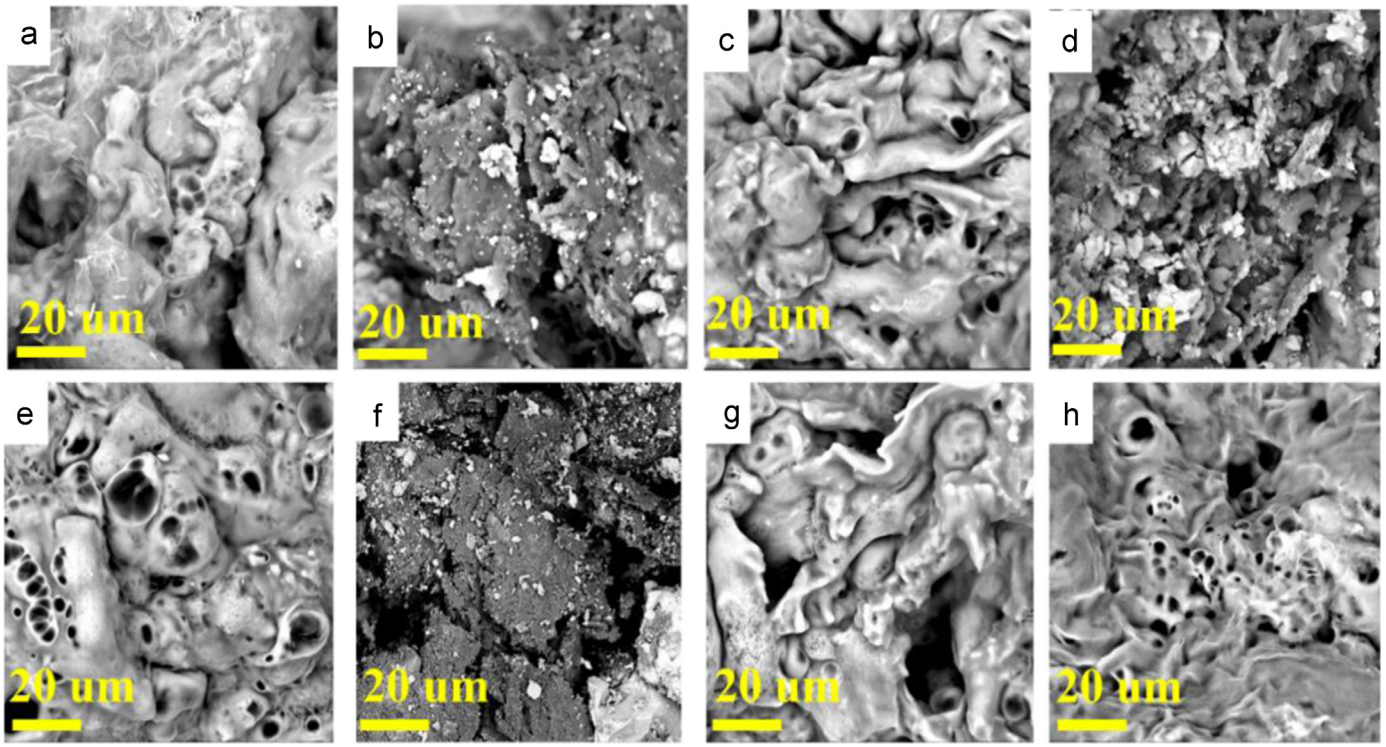

Fig. 2. SEM Analysis: (a) 60/40 LV (b) 60/40 LV 0.2% GTA (c) 60/40 HV (d) 60/40 HV – 0.2% GTA (e) 70/30 HV (f) 70/30 HV 0.2% GTA (g) 70/30 hybrid (h) 60/40 hybrid.