Formulation of Alginate–Gelatin Hydrogels within a Circular Economy Framework: Controlled Release of Grape Skin Extract via Gelatin Content Modulation

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Abstract: Hydrogels, as cross-linked polymer networks, are increasingly utilized in biomedical applications due to their high water absorption, biocompatibility, and capability to deliver bioactive substances. Compared to synthetic hydrogels, natural polymers such as alginate and gelatin provide advantages including biodegradability, low toxicity, and the formation of stable matrices suitable for biomedical use. Grape skins from the Šumadija region in Serbia, a byproduct of winemaking, are abundant in polyphenolic compounds with potent antioxidant and anti-inflammatory effects, making them suitable for incorporation into bioactive hydrogel systems. In this study, alginate–gelatin hydrogels were prepared and loaded with grape skin extract (GSE) to evaluate their physicochemical characteristics and *in vitro* release behavior. Three formulations with different alginate-to-gelatin ratios (3:1, 3:2, and 1:1) were produced, mixed with GSE (8 mg/mL), frozen, and cross-linked with $CaCl_2$. Organoleptic assessment confirmed uniform, coherent gels, with color imparted by the extract. *In vitro* release studies in PBS (pH 7.4, 37 °C) demonstrated a biphasic release, with an initial rapid phase during the first 5–10 h followed by sustained release up to 24 h. Gelatin content influenced release kinetics by altering network density and hydrogel porosity. These findings underscore the importance of optimizing alginate-to-gelatin ratios and indicate that GSE-loaded hydrogels are promising candidates for controlled delivery of natural antioxidants in biomedical applications.

Keywords: grape skins, hydrogels, drug delivery systems, release kinetics.

1. Introduction

Hydrogels are cross-linked polymer networks capable of absorbing substantial amounts of water. Due to their structural adaptability, biocompatibility, and efficiency in delivering bioactive agents, they are increasingly recognized as essential materials in biomedical and pharmaceutical applications [1]. Despite their widespread use, synthetic polymer hydrogels are limited by issues of skin compatibility, potential toxicity, and poor biodegradability, which has driven growing interest in natural polymers such as alginate and gelatin that combine biocompatibility, biodegradability, and the ability to form stable matrices suitable for biomedical hydrogel formulations [2].

Grape skins, a byproduct of winemaking, particularly those from the Šumadija region of Serbia, are rich in polyphenols that effectively neutralize reactive oxygen species and exhibit significant antioxidant and anti-inflammatory activities [3,4]. These properties position grape skins as a valuable natural resource for the development of bioactive hydrogels, nutraceuticals, and cosmetic formulations, offering a sustainable source of biologically active compounds with potential protective effects against oxidative stress [5].

Therefore, we aimed to develop gelatin–alginate hydrogels incorporating grape skin extract (GSE) from the Šumadija region and to assess their physicochemical properties as well *in vitro* extract release profile.

2. Material and methods

2.1 Preparation of GSE-loaded hydrogels (HG+GSE)

Grape skin extract (GSE) was obtained by ultrasound-assisted extraction using ethyl acetate and stored at 4 °C. Hydrogel formulations were prepared by varying the ratio of alginate and gelatin as follows: Alg/Gel-1 (3:1), Alg/Gel-2 (3:2), and Alg/Gel-3 (1:1). GSE (8 mg/mL) was mixed with alginate and gelatin, homogenized, cast into molds, frozen and cross-linked with $CaCl_2$. Hydrogels without GSE (HG) were prepared similarly using water instead of the extract [6].

2.2 Organoleptic properties of HG+GSE

The organoleptic properties of the HG+GSE, including appearance, color, and homogeneity, were assessed visually and by tactile evaluation.

2.2. In vitro extract release from HG+GSE

HG+GSE hydrogels were prepared as circular discs (8 mm diameter, 5 mm thickness) and incubated in PBS (pH 7.4) at 37 °C. At set intervals, samples of the release medium were collected and analyzed by UV–Vis spectrophotometry at 280 nm to quantify GSE release using a calibration curve [6].

3. Results and Discussion

The developed alginate–gelatin hydrogel base (HG) was solid and transparent, whereas HG+GSE appeared colored due to the incorporated grape skin extract, displaying a coherent and uniform gel structure.

The release profile of the GSE from the three hydrogel formulations (1, 2, and 3) shows a characteristic biphasic pattern (Figure 1). All formulations exhibit an initial rapid release phase within the first 5–10 h, followed by a slower, sustained release over the remaining period up to 24 h. Formulation 2 displays the highest cumulative release, reaching ~12 mg by 24 h, while formulations 1 and 3 show slightly lower total release. The initial burst is likely due to extract molecules near the hydrogel surface or loosely bound within the matrix, whereas the sustained phase reflects diffusion from the interior and gradual hydrogel matrix relaxation or degradation. Differences among the formulations can be attributed to variations in crosslinking density and gelatin content [6,7]. Overall, these results indicate that the hydrogels can provide controlled, sustained release of GSE over 24 h, which is favorable for potential biomedical applications requiring both immediate and prolonged antioxidant delivery.

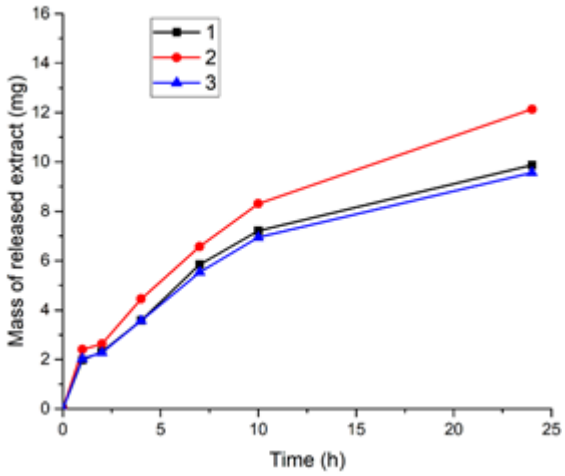

Figure 1. Mass of released extracts (mg) as a function of time for GSE.

4. Conclusions

Based on our findings we may conclude that variations in gelatin content significantly influenced hydrogel properties by modulating extract release kinetics through changes in network density and degradation-induced porosity. These results highlight the necessity of selecting specific alginate-to-gelatin ratios to achieve desired release profiles and hydrogel performance. Gelatin acted as a key structural modifier, enabling precise tuning of hydrogel behavior. Collectively, these findings demonstrate the potential of

alginate–gelatin hydrogels enriched with GSE as sutiable systems for controlled delivery of bioactive compounds from grape skins for varios biomedical applications.

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