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Exploration of Improving the Tensile Strength of a Doubly Crosslinked Polyvinyl Alcohol-Cationic Guar Gum Hydrogel for Potential Application in Tissue Engineering

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Abstract. In recent years, there has been a significant increase in the development of biomaterials for tissue engineering applications, leading to the exploration of a wide range of polymers and polymer blends. In this study, a hydrogel composed of polyvinyl alcohol and cationic guar gum was developed using a dual crosslinking strategy based on freeze-thaw cycles and borate-diol bonds. The resulting hydrogel exhibited improved mechanical performance, achieving an optimized tensile strength of 34.16 ± 5.68 kPa, higher than that of non-crosslinked and chemically crosslinked systems. This enhancement is attributed to the combined effect of physical crosslinking and chemical interactions, which generate a more cohesive polymeric network. These results suggest that dual crosslinking is a promising strategy for the development of hydrogels with improved mechanical stability, suitable for tissue engineering applications requiring soft yet mechanically resilient materials.

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Resumen. En los últimos años, se ha observado un aumento significativo en el desarrollo de biomateriales para aplicaciones en ingeniería de tejidos, lo que ha impulsado la exploración de una amplia variedad de polímeros y mezclas poliméricas. En este estudio, se desarrolló un hidrogel compuesto de alcohol polivinílico y goma guar catiónica mediante una estrategia de doble reticulación basada en ciclos de congelación–descongelación y formación de enlaces borato–diol. El hidrogel resultante mostró un mejor desempeño mecánico, alcanzando una resistencia a la tracción optimizada de 34.16 ± 5.68 kPa, superior a la de los sistemas no reticulados y reticulados únicamente por vía química. Esta mejora se atribuye al efecto combinado de la reticulación física y las interacciones químicas, que generan una red polimérica más cohesiva. Estos resultados sugieren que la doble reticulación es una estrategia prometedora para el desarrollo de hidrogeles con mayor estabilidad mecánica, adecuados para aplicaciones en ingeniería de tejidos que requieren materiales suaves, pero mecánicamente resistentes.

Introduction

Polymeric hydrogels (HGs) have gained attention in the biomedical field due to their biocompatibility, biodegradability, and ability to mimic the natural extracellular matrix [1]. HGs have three-dimensional structures that allow for high water retention, nutrient diffusion, and cellular proliferation, which makes them ideal for applications such as wound dressings, drug delivery systems, biosensors, and scaffolds for tissue regeneration [2,3]. Besides, the flexibility of synthetic methods and the opportunity to combine polymers with diverse chemical and physical properties have enabled the development of hybrid hydrogels with adaptable mechanical and biological characteristics [4].

Tissue engineering is one of the most promising fields of application for HGs due to their similarity with soft tissues and biocompatibility. However, HGs require sufficient mechanical integrity to maintain cellular behavior and physiological function under in vivo conditions [5, 6]. However, this remains a major limitation for most HG systems, particularly those based on natural polymers, since they usually lack the mechanical strength and long-term stability under physiological conditions required in many medical applications [7]. To overcome this disadvantage, they emerged strategies such as dual crosslinking, incorporation of reinforcing nanomaterials, or blending of polymers that bring support at the structure and improve mechanical properties [8,9].

Polyvinyl alcohol (PVA), a polymer widely used in the pharmaceutical industry, whose hydrogels present mechanical properties that depend on the degree of physical crosslinking[10]. Crosslinking generally arises by the method of freeze-thaw (F-T) cycles, when freezing the polymer solution, crystalline domains are generated, producing sites with high polymer concentration encouraging the formation of physical bonds and giving structure to the polymer network [11,12]. However, the structure can become mechanically weak and prone to disintegration by swelling, limiting its applicability. Wu, et al. studied the mechanical properties of PVA hydrogels by F-T cycles, obtaining lesser tensile strengths than PVA hydrogels by chemical crosslinked for different concentrations and F-T cycles [13].

On the other hand, cationic guar gum (CGG), a cationic polymer derived from the natural polymer guar gum (CG), has attracted attention for biomedical use due to its biodegradability, non-toxicity, and presence of cationic functional groups that enhance bioadhesion and interaction with negatively charged biomolecules. CGG can be crosslinked by dynamic chemical crosslinking processes [14–16]. There are several reports in which the use of borax as a crosslinker of CGG and guar gum (GG) has shown the formation of biocompatible, self-healing, mucoadhesive, and pH sensitive hydrogels with application for drug release and sensitive stimuli coatings [17,18].

In this work, we present the development of a doubly crosslinked PVA and CGG hydrogel (DCL CGG-PVA) obtained by sequential freeze-thaw cycles and borax addition. This study reports the first exploration of a dual crosslinking strategy combining CGG and PVA, which is relevant for the development of new materials. Here, we design and characterize an HG that combines the benefits of PVA and CGG and improves mechanical strength and physicochemical properties. Due to its dual crosslinked network, this system has potential

applications not only in tissue engineering but also in developing hydrogels for technologies that require soft yet mechanically resilient materials.

Materials and methods

Materials

PVA with a hydrolysis degree of 98% was purchased from Selvol™, CGG was obtained from Chemico, Mexico, and Borax was acquired from Chemical Products Mardupol (Morelos, Mexico). The solutions were prepared using water from a Milli-Q® (MQ) filtration system (Millipore, Billerica, MA, USA).

Fabrication of the PVA-CGG hydrogel

A 2⁴ experimental design including 2 center points (18 experiments in total) was conducted using Minitab® XVII software; Table 1 outlines the proposed factors and levels experimented. The procedure involved 10% PVA solubilized in deionized water. Subsequently, a CGG solution was dispersed into the system until homogenization. The resulting blends were poured onto Petri dishes and left to degas for 2 h under atmospheric conditions. For the samples that contained borax, the borax was added later to the mixture of the polymer solutions. The concentrations of polymers, number of freeze-thaw (F-T) cycles and freezing time, were varied to find the highest tensile strength. The samples were frozen at -20 ± 1 °C for the designated duration specified in the experimental design matrix. The frozen solutions were thawed at room temperature for 2 h, and this F-T procedure was repeated as needed for the experiment.

Mechanical properties

The tensile strength test was conducted to determine the levels that provide the HG with greater mechanical resistance after developing the 18 HGs generated in the experimental matrix. The tensile strength was measured using a dual-range force sensor (ZP-500N, Baoshishan, China). The probe was brought into contact with the hydrogel surface and vertically pulled at a controlled speed until detachment occurred. The maximum force required to break the interaction was recorded as TS. This TS test was performed directly on the HG obtained after the F-T cycles. Although this test is not a standardized traction test, it provides a comparative measurement of the material's structural resistance, utilizing an accessible sensor [19,20].

Characterization of hydrogel

The characterization of HGs with the best mechanical properties was performed using lyophilized powder obtained at -84 °C for collector temperature and 0.003 mBar (LABCONCO, Freezone® 6L). The HG (DCL CGG-PVA) was compared with two control HGs, a HG of CGG and PVA (CGG+PVA), which was not subjected to either physical or chemical crosslinking, and a HG of CGG and PVA subjected only to chemical crosslinking (CL CGG-PVA). The concentrations of all reagents were identical in all controls and lyophilized under the same conditions.

The swelling test involved placing 0.5 g of HG into a meshed diffuser capsule and immersing it in water at 25 °C. Samples were collected at 0.25 to 72 h intervals, dried superficially using filter paper, and weighed after each collection. The swelling percentage was determined using equation 1 [21].

$$\text{Swelling (\%)} = \frac{(W_s - W_i) * 100}{W_i} \quad \text{Eq.1}$$

Where: W_s is the weight of the swollen hydrogel, and W_i is the weight of the dry hydrogel. All measurements were performed in triplicate.

The HGs morphology was examined employing Scanning Electron Microscopy (SEM) through an MAIA3 microscope provided by Tescan®. The composition of the HGs was studied using Fourier Transform Infrared Spectroscopy (FTIR, Agilent Cary 630), performed with 150 accumulations in the spectrum of 600 to 4000 cm⁻¹, and Raman spectroscopy, executed using a Horiba® XploRA analyzer, encompassing a spectral

range from 250 to 3250 cm^{-1} . Additionally, thermal characterization was displayed by Differential Scanning Calorimetry (DSC), the experiments (range: 20 to 350 $^{\circ}\text{C}$) were carried out utilizing a TA Instrument Q20 differential scanning calorimeter, and Differential Thermal Analysis (DTA) (range: 20 to 550 $^{\circ}\text{C}$) by using a NETZSCH model STA 2500 Regulus apparatus. All thermal techniques were performed under a nitrogen atmosphere, with a heating rate of 10 $^{\circ}\text{C}/\text{min}$. The crystallization percentage was determined as the ratio between the measured enthalpy of fusion (ΔH_m) and the theoretical enthalpy of pure crystalline PVA [22]. Then, the decrease percentage was calculated relative to pure PVA to provide a comparative value.

Results and discussion

Fabrication of the PVA-CGG hydrogel

A factorial experimental design was conducted to evaluate the effect of double crosslinking, using freeze–thaw (F–T) cycles and borax, on the tensile strength of PVA–CGG hydrogels. The objective was to determine the conditions that maximize tensile strength. Table 1 presents the factors and levels considered in this study, where tensile strength was defined as the response variable. Eighteen experiments were conducted, sixteen corresponding to the design and two intermediate points; the results are shown in Fig. 1(a). The tensile strength measurement provided a practical approach for comparing the mechanical performance of soft hydrogel systems.

The Lenth method was used to estimate the experimental pseudostandard error (PSE) in the factorial design without replicates [23,24]. The results of the influence of each factor were expressed in standardized effect form and represented in a Pareto chart (Fig. 1(b)). The reference line corresponds to the critical value of the Student's *t* distribution with 7 degrees of freedom ($t=2.36$, 95 % confidence level), which allows for the identification of statistically significant factors. Under this criterion, the factors and factor interactions that presented a greater influence on tensile strength are positively the number of F–T cycles, CGG%, and the addition of borax, and negatively, the ratio of the number of F–T cycles to CGG%, which is related to the decrease in the amount of PVA that can form physical interactions with F–T. The number of F–T cycles is the most influential factor, at least in these tests where the percentage of PVA predominates. The factor that showed the least difference was the F–T time, indicating that the variation in freezing time is not relevant to the tensile strength of the hydrogel at the values used. In addition, it is important to note that the contribution of borax is primarily interpreted through the statistical analysis, where it is identified as a significant factor; the overall analysis indicates that borax contributes to network reinforcement when combined with other variables.

Table 1 summarizes the optimized conditions obtained from the factorial design, along with the predicted and experimental tensile strength values. The optimized formulation (0.1 % borax, 2.0 % CGG, and three F–T cycles of 3 h) reflects the combined contribution of chemical and physical crosslinking mechanisms. Freeze–thaw cycles promote the formation of PVA crystallites acting as physical crosslinking points, while borax induces reversible borate–diol interactions. The coexistence of these interactions leads to a more cohesive and interconnected network capable of distributing applied stress more effectively, which explains the increase in tensile strength. The predicted value (38.96 kPa) corresponds to the response estimated by the statistical model, while the experimental value (34.16 ± 5.68 kPa) represents the measured tensile strength. Although a slight difference is observed, no statistically significant difference was found between them ($p = 0.068$), indicating good agreement and validating the predictive capability of the model.

The double-crosslinked system enhanced the tensile strength of the hydrogel, yielding soft yet structurally stable material suitable for applications such as intracutaneous drug delivery, wound dressings, or cell growth scaffolds [25,26]. This exploratory study aims to lay the groundwork for future development. It is possible that increasing borax or CGG concentrations or the number of cycles produces stronger materials. Although flexibility was not quantitatively measured, the dual-crosslinked hydrogels maintained their integrity during handling and tensile testing, suggesting that the incorporation of chemical crosslinking contributes to the improved tensile strength of the hydrogels.

Table 1. Optimization of the factors studied on the response variable.

Factors (F) [Levels tested]		Optimized level by Minitab® V.17		
Borax (%) [0, 0.1]		0.1		
CGG (%) [0.5, 2.0]		2.0		
Number of F/T cycles [1,3]		3		
Time of freezing (h) [3,10]		3		
Outcome variables (OV)	Desirability	Estimated OV value	Observed OV interval**	p-value
Tensile strength	0.9323	38.96 kPa	34.16 ± 5.68 kPa	0.068
Composite desirability	0.9323			

**Mean ± Confidence interval at 95 %, n = 3.

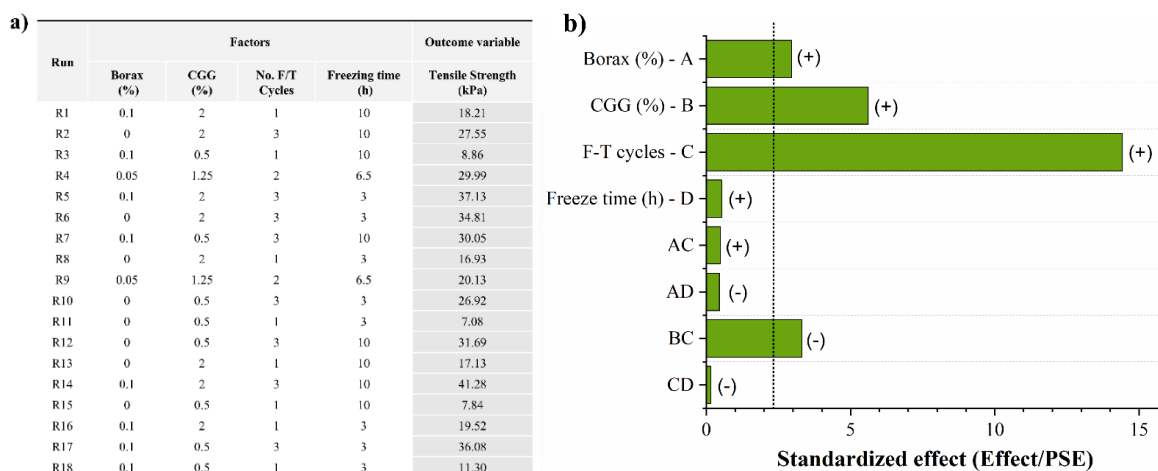


Fig. 1. Results of the factorial experimental design: **(a)** tensile strength values obtained for each experimental condition evaluated in the design; **(b)** Pareto chart showing the standardized effects of the studied factors and their interactions on tensile strength. The reference line indicates the statistical significance threshold at a 95% confidence level.

Characterization of DCL CGG-PVA hydrogel

The hydrogel that exhibited the highest tensile strength in the experimental design was the doubly crosslinked R5 (DCL CGG-PVA) formulation. This material was characterized to assess its swelling capacity, morphology, composition, and thermal behavior. The properties of the DCL CGG-PVA hydrogel were compared with those of a simple physical mixture of CGG and PVA (CGG+PVA) and with a chemically crosslinked hydrogel prepared under the same conditions but without F-T cycles (CL CGG-PVA).

Fig. 2(b) presents the swelling behavior of hydrogels. The DCL CGG-PVA hydrogel achieved a swelling of approximately 330 % after 15 h, while the CGG+PVA and CL CGG-PVA controls reached values of approximately 590 % and 480 %, respectively. These results indicate that the doubly crosslinked hydrogel

exhibits a lower equilibrium swelling capacity compared to the control systems. Additionally, differences in swelling kinetics were observed. The CGG+PVA and CL CGG-PVA hydrogels reached equilibrium within approximately 16 h, whereas the DCL CGG-PVA hydrogel showed a slower swelling process and continued to absorb water even after 72 h (527 %), indicating a delayed approach to equilibrium. This behavior is attributed to the higher crosslinking density in the DCL CGG-PVA hydrogel, resulting from the combined effect of physical (freeze–thaw-induced crystallites) and chemical (borate–diol interactions) crosslinking. The denser network restricts polymer chain mobility and reduces the diffusion rate of water molecules into the matrix, leading to both lower swelling capacity and slower swelling kinetics [21].

The SEM images (Fig. 2(c)) presented clear differences in morphology and porosity among the analyzed hydrogels. The non-crosslinked hydrogel (CGG+PVA) exhibited a highly porous and irregular structure, characterized by loosely interconnected domains. This open network facilitates water diffusion and explains its high swelling capacity. In contrast, the chemically crosslinked hydrogel (CL CGG-PVA) showed a noticeable reduction in porosity, with smaller and more uniformly distributed pores, as well as a more compact and homogeneous structure. This change is attributed to the formation of borate–diol interactions, which restrict polymer chain mobility and promote a more organized network. The doubly crosslinked hydrogel (DCL CGG-PVA) exhibited the most compact and dense morphology, with a further reduction of pores and a more continuous structure. This was associated with the combined effect of chemical crosslinking and the formation of PVA crystallites induced by freeze–thaw cycles. The increased crosslinking density restricts polymer chain mobility and reduces the free volume available for water diffusion, leading to a lower equilibrium swelling capacity compared to the non-crosslinked system [27].

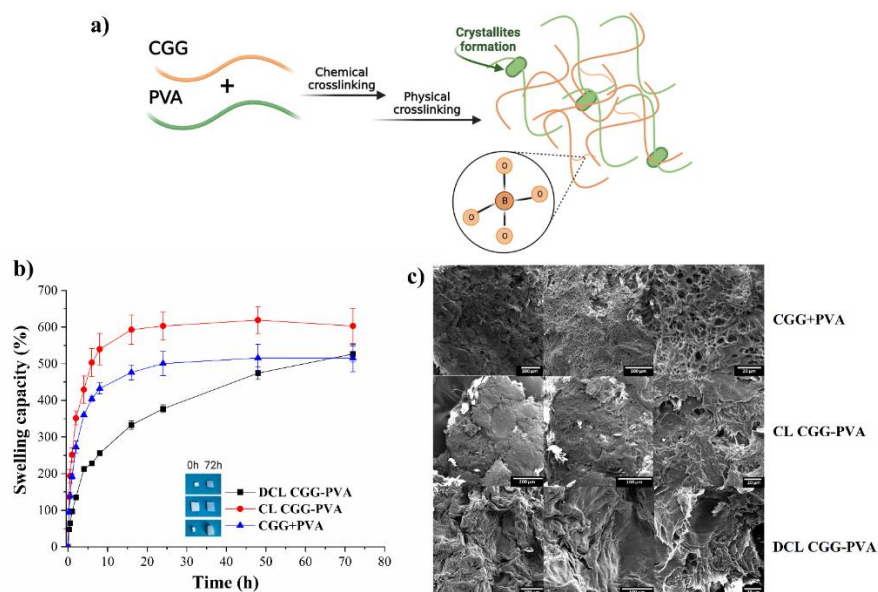


Fig. 2. Characterization of polyvinyl alcohol–cationic guar gum hydrogels: **(a)** schematic representation of hydrogel formation via physical and chemical crosslinking; **(b)** swelling profiles (St vs. time) of the different hydrogels, presented as mean $\pm$ confidence interval ($n = 3$); **(c)** SEM images showing the morphology of the hydrogels, highlighting differences in porosity and network compactness between non-crosslinked, chemically crosslinked, and doubly crosslinked systems.

The Raman and FT-IR spectra (Fig. 3(a) and 3(b)) presented the characteristic bands of PVA and CGG in all hydrogel systems, indicating that no major changes in the chemical structure of the polymers occurred during the crosslinking processes. No distinct peaks attributable to B–O–C bonds were identified in the spectra.

This may be due to the overlap of signals from the polymer matrix and the relatively low concentration of borax, which limits the detectability of these interactions. However, the presence of such interactions is supported indirectly by the observed changes in swelling behavior, morphology, and mechanical properties, which indicate an increase in crosslinking density in the chemically and doubly crosslinked hydrogels.

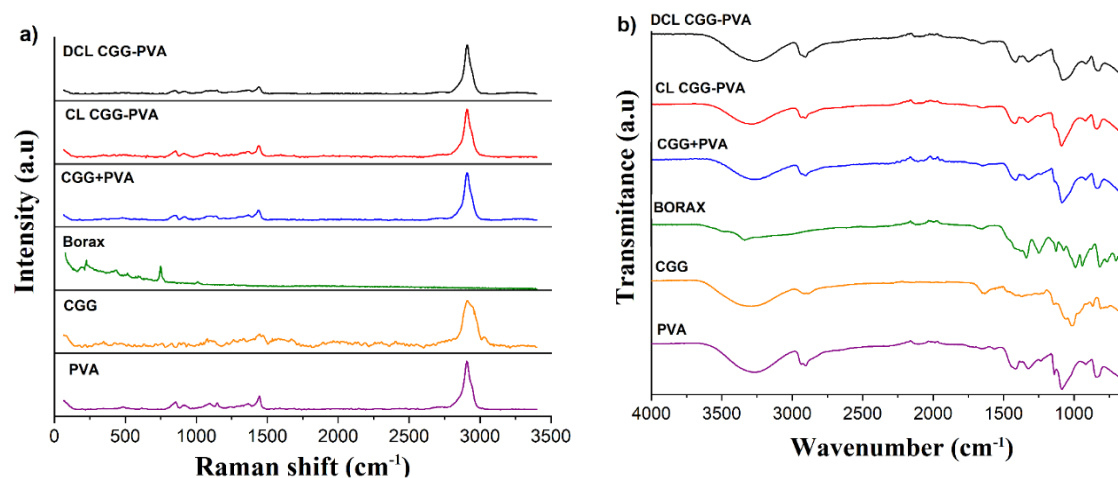


Fig. 3. Spectroscopic characterization of hydrogels: (a) Raman spectra and (b) FTIR spectra of the different formulations.

As depicted in Fig. 4(a), the raw materials, Borax, PVA, and CGG, exhibited a prominent thermal signal at 140, 220, and 170 °C, respectively [28–30]; however, the signals from Borax and CGG were not detected in HGs thermograms. The thermal pattern may be explained by the formation of chemical crosslinking between Borax and CGG, which causes the CGG chains to unfold, leading to polymeric molecular dispersion. On the other hand, the PVA thermal signal is maintained in all HGs; this is associated with both the concentration of PVA in the HG and the formation of crystallites by the F-T cycles.

The relative crystallinity of PVA decreased with the addition of CGG by approximately 78 % relative to pure PVA in the CGG + PVA mixture. This effect was attributed to CGG interfering with the regular organization of the PVA chains, occupying the potential sites for crystal formation and generating a more heterogeneous and amorphous matrix [12]. In the case of CL CGG-PVA, the polymeric network generated by the chemical bonds reduces the mobility of the chains, producing a decrease in relative crystallinity of approximately 90 % compared with pure PVA. However, in DCL CGG-PVA, the freeze-thaw cycles allowed a degree of physical reorganization of the PVA chains, favoring the partial formation of crystalline domains. Nevertheless, crystallinity remained limited by the presence of chemical crosslinking and CGG, resulting in an overall 82 % decrease compared to pure PVA. Taken together, these results show that both the presence of CGG and chemical crosslinking decrease the PVA crystallinity, while F–T cycles allow a partial recovery of the crystalline organization [22]. The loss of crystallinity makes the materials more flexible and deformable.

In the case of DTA (Fig. 4(b)), the signals for CL CGG-CL PVA at approximately 225 °C and 325 °C are more prominent and broader than the control HGs. This supports the observations described concerning the effect of chemical and physical crosslinking. These signals are also mainly associated with PVA. The presence of CGG in the different HGs can be considered to generate a thermally stable structure by shifting the PVA signal observed at 275 °C to value around 325 °C.

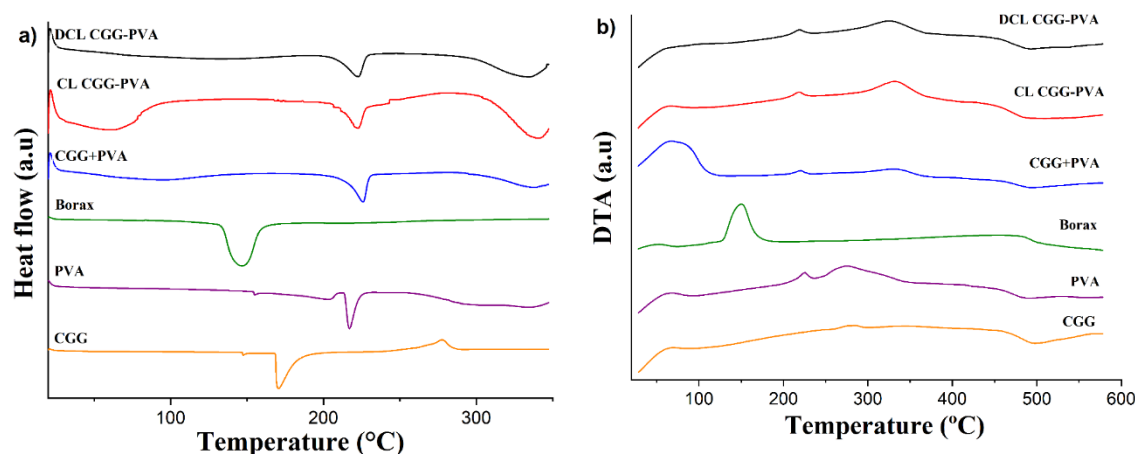


Fig. 4. Thermal characterization of hydrogels: (a) thermograms showing the thermal transitions of raw materials and hydrogels; (b) DTA curves highlighting the effect of crosslinking on thermal stability.

Conclusions

A doubly crosslinked (DCL) PVA–CGG hydrogel was formulated and characterized, revealing favorable physicochemical and mechanical properties. The optimized formulation, achieved with 0.1% borax, 2.0 % cationic guar gum, three freeze/thaw cycles, and three hours of freezing, combines chemical and physical crosslinking mechanisms, resulting in a hydrogel with enhanced tensile strength (34.16 kPa), compact morphology, reduced porosity, controlled swelling (~300 %), and partial recovery of crystallinity. These properties indicate a clear improvement compared to non-crosslinked and singly crosslinked systems. The obtained tensile strength falls within the range reported for certain soft tissues such as skin, ~10–100 kPa, depending on anatomical location and testing conditions, suggesting potential suitability for low-load soft tissue applications. In addition, the hydrogel exhibited stability and flexibility under aqueous conditions, which are desirable features for biomedical applications. These results indicate that the developed hydrogel may be suitable for applications involving low mechanical stress, such as superficial or skin-related uses. However, further studies are required to fully validate its performance in tissue engineering applications, including biocompatibility, drug-loading capacity, and *in vivo* behavior.

The results demonstrate that the tensile strength of the hydrogels is governed by the combined effect of physical and chemical crosslinking. The factorial design identified freeze–thaw cycles and borax as significant factors, while the structural characterization revealed a denser and less porous network in the doubly crosslinked system. These features are directly associated with reduced swelling and enhanced tensile strength, confirming that the dual crosslinking strategy is an effective approach to improve the mechanical properties of PVA–CGG hydrogels.

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