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Abstract: Chitosan hydrogels have emerged as promising materials for biomedical applications due to their biocompatibility, biodegradability, and tunable rheological properties. This study investigates the shear-thickening–shear-thinning (ST-ST) transition in chitosan hydrogels, a phenomenon often misinterpreted as mechanical oscillation or experimental deviation. The ST-ST transition, characterized by a shift from shear-thickening to shear-thinning behavior within a specific shear rate range, was systematically explored in hydrogels prepared with varying molar masses, degrees of acetylation, crosslinking densities, preparation methods, and aging conditions. Rheological analyses were conducted across shear rates ranging from 0.03 s⁻¹ to 1.5 s⁻¹ at temperatures of 22°C, 23°C, and 37°C. Results reveal that the ST-ST transition is significantly influenced by pH, molarity, and chitosan concentration, while thermal aging exhibits a comparatively minor effect. These findings provide critical insights into the rheological behavior of chitosan hydrogels, enabling the optimization of their formulation for advanced biomedical applications, including drug delivery systems and tissue engineering scaffolds. This study underscores the importance of understanding the ST-ST transition for tailoring the mechanical properties of chitosan-based hydrogels to meet specific biomedical requirements.

Keywords: Chitosan; hydrogel; ST-ST transition; Dilatant behavior; Rheology; Biomedical applications.

1. Introduction

Shear-thickening, or dilatancy, is a phenomenon characterized by a continuous increase in apparent viscosity with the rate of deformation. Despite its importance, shear-thickening is often challenging to observe due to several factors, including its frequent confusion with mechanical oscillations or experimental deviations [1,2]. This behavior was first hypothesized by Reynolds, with significant developments made later by Hoffmann, who established the foundational theory for understanding shear-thickening. Over time, this theory has been adapted to various polymeric systems, and alternative models have been proposed to explain atypical behaviors specific to each system. Recent advancements have integrated shear-thickening with viscoelasticity, leading to the identification of shear-thinning–shear-thickening (ST-ST) transitions. While considerable attention has been given to the opposite sequence, where shear-thickening emerges in pseudoplastic fluids at high shear rates, relatively few studies [3–8] focus on the dilatancy-to-pseudoplasticity sequence. This discrepancy arises from the narrow range in which dilatancy manifests, often overshadowed by pseudoplasticity at higher shear rates [9–17]. However, when analyzed within a restricted shear rate range (0.01 s⁻¹ to 2 s⁻¹), the ST-ST transition becomes clearly distinguishable (see Figure 1).
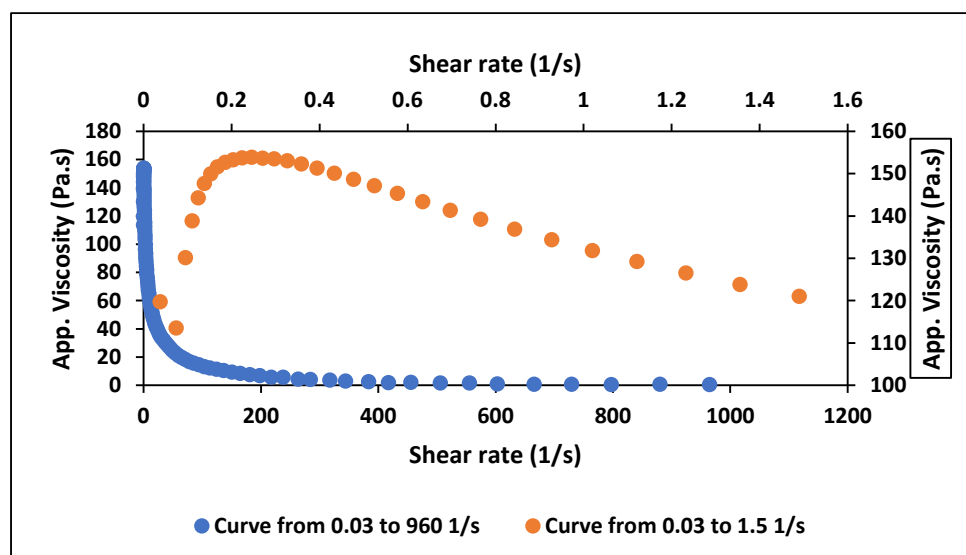
Figure 1. Apparent viscosity versus shear rate curves for a chitosan hydrogel, presented within two distinct shear rate ranges.

Hydrogels, three-dimensional polymer networks capable of absorbing substantial amounts of water without dissolving, have gained significant attention due to their versatility in various applications, including biomedical engineering, drug delivery, and tissue regeneration. The rheological properties of hydrogels are influenced by factors such as polymer composition, cross-linking density, and solvent nature. In particular, the shear-thickening–shear-thinning (ST-ST) behavior of hydrogels offers valuable applications in fields where controlled shear rates are critical, such as drug delivery, tissue engineering, and ophthalmic materials. Additionally, ST-ST behavior can improve the texture and mouthfeel of food products and enhance the sensory experience of personal care formulations like shampoos and lotions. Understanding the factors that influence ST-ST behavior is critical for designing hydrogels with tailored rheological properties for diverse biomedical, food, and cosmetic applications.

The primary objective of this study was to investigate the shear-thickening–shear-thinning (ST-ST) transition in chitosan hydrogels, a class of biocompatible and biodegradable materials with significant potential for applications in biomedical engineering, drug delivery, and tissue regeneration. Specifically, we aimed to analyze this transition at shear rates below 1 s^{-1}, focusing on the influence of key parameters such as hydrogel pH, the molarity of the pH-modifying solution, chitosan concentration, and accelerated thermal aging conditions. By systematically examining these factors under constant temperature, this work provides a deeper understanding of the rheological behavior of chitosan hydrogels, contributing to the optimization of their properties for advanced biomedical applications.

2. Materials and Methods

2.1. Samples Qx.y and Qx.yP Preparation

2.1.1. Materials

Chitosan (CS) with a molecular weight of 639 kDa and a degree of acetylation of 4% was supplied by Northeastern Biomaterials Evaluation and Development Laboratory - CERTBIO (Campina Grande, Brazil). Acetic acid (CH_3COOH) and citric acid ($C_6H_8O_7 \cdot H_2O$) were purchased from Química Moderna (Barueri, Brazil). Lactic acid ($C_3H_6O_3$), sodium hydroxide micropearls (NaOH) were acquired from Neon (Suzano, Brazil) and genipin 98 % and % ethanol were supplied by Sigma Aldrich.

2.1.2. Preparation of Hydrogels

The hydrogels were prepared to obtain compositions with 2.5; 5.0; 7.5; and 10.0% chitosan (w/w), named as Q2.5, Q5.0, Q7.5 and Q10.0, respectively, in a mixture of acids initially formed by 40% acetic acid and 20% lactic acid in distilled water. The compositions were subjected to magnetic stirring for 1 h at 500 rpm. After this period, 4% citric acid was added in a w/w ratio of the acid mixture, maintaining the stirring for another 1h. At the end of the process, the samples were subjected to manual stirring and filtered through a 200 mesh to eliminate possible particulates. The hydrogels were then centrifuged using a Novatecnica NT 835 Benchtop Macro Refrigerated Centrifuge after 48 h of preparation, at 3000 rpm for half an hour, and kept refrigerated.

2.1.3. Preparation of the Crosslinking Solution

The solution was prepared by weighing 1.7 mg of solid genipin and diluting it under magnetic stirring for 30 min in 2 ml of distilled water, then 96% ethanol was added to obtain an 8:2 ethanol/water solution with 0.75 mM solute concentration.

In the hydrogels, the solution was added superficially (by dripping) after their extrusion, with the aim of optimizing the permanence of structure, since it would promote crosslinking in the outermost layer. The crosslinked samples were named Q2.5GP, Q5.0GP, Q7.5GP and Q10.0GP. Table 1 shows the prepared compositions.

Table 1. Formulations of Qx.y and Qx.yP hydrogels.

	Sample	Raw Materials				
		Acetic Acid (v/v)	Lactic Acid (v/v)	Citric Acid (v/v)	Chitosan (w/v)	Genipin
	Q2.5	40%	20%	4%	2.5%	-
	Q5.0	40%	20%	4%	5.0%	-
	Q7.5	40%	20%	4%	7.5%	-
Content	Q10.0	40%	20%	4%	10.0%	-
	Q2.5GP	40%	20%	4%	2.5%	0.75 mM
	Q5.0GP	40%	20%	4%	5.0%	0.75 mM
	Q7.5GP	40%	20%	4%	7.5%	0.75 mM
	Q10.0GP	40%	20%	4%	10.0%	0.75 mM

2.2. Samples xMy.z Preparation

2.2.1. Materials

High molar mass chitosan (>400 KDa; degree of acetylation (GA) of 3%; Genetic heritage with registration number AEBD12D) and deionized water, supplied by the Northeast Biomaterials Assessment and Development Laboratory – CERTBIO. Acetic acid (CH_3COOH) and citric acid ($C_6H_8O_7.H_2O$) were purchased from Química Moderna (Barueri, Brazil). Lactic acid ($C_3H_6O_3$) and sodium hydroxide micropearls (NaOH) were acquired from Neon (Suzano, Brazil). The FTIR of these samples is shown in Figures 5a e 5b.

2.2.2. Preparation of hydrogels

The synthesis of chitosan hydrogel was conducted using a methodology adapted from [18]. Initially, two acidic solutions were prepared and subsequently combined to dissolve the chitosan. The first solution comprised 40% (v/v) acetic acid, 20% (v/v) lactic acid, and 40% (v/v) deionized water. Concurrently, the second acidic solution was prepared as a 4% (w/v) aqueous solution of citric

acid. Following the preparation of these acidic solutions, a final solution was formulated by mixing 3% (v/v) of the citric acid solution with 97% (v/v) of the previously prepared acetic and lactic acid mixture. Chitosan was then dissolved in the resultant acidic solution at a concentration of 5% (w/v), with continuous stirring for 4 hours at room temperature (25°C) until complete homogenization was achieved. The compositions of these hydrogels are shown in Table 2.

Table 2. Composition of hydrogels xMy.z.

	Sample	pH	Chitosan (% w/v)
	3M0.53	2.8	5.26
	3M0.98	4	4.10
Content	3M1.26	4.8	2.78
	10M0.51	2.7	5.27
	10M0.84	4	4.77
	10M1.40	5.3	3.79

Subsequently, aqueous solutions of sodium hydroxide at concentrations of 3M and 10M were produced and dripped onto the resulting hydrogel, under mechanical agitation, until different samples with different pH values were obtained for rheological analysis and properties comparison, as suggested by Richa [19]. Finally, all the samples of the hydrogel were distributed into syringes and, then, centrifuged at 2000 rpm for 15 minutes to remove bubbles.

2.3. Preparation of unexposed (A0) and exposed for 3 months (A3M) hydrogels

2.3.1. Materials

Medium molar mass chitosan (247.65 KDa; degree of acetylation (GA) of 13%; Genetic heritage with registration number AEBD12D) and deionized water, supplied by the Northeast Biomaterials Assessment and Development Laboratory - CERTBIO. Acetic acid (CH_3COOH), glycerin ($C_3H_8O_3$) P.A/ACS and sodium hydroxide (NAOH) in microbeads, supplied by Neon® Suzano, São Paulo - Brazil.

2.3.2. Preparation of hydrogels

The chitosan hydrogel was obtained and its degradation was evaluated in times of 0, and 3 months, under primary packaging storage conditions. The chitosan hydrogel was obtained by dissolving 6 g of chitosan in 150 ml of a 2% (v/v) aqueous acetic acid solution, under mechanical stirring at 400 rpm for 1 hour. After dissolution, 1% of the chitosan mass was added as a plasticizer. Table 3 shows the data for the formulation used.

Table 3. Composition of hydrogels AO and A3M.

| Raw material	$C_6H_{11}NO_4$ (% w/v)	$C_2H_4O_2$ (% v/v)	$C_3H_8O_3$ (% w/v)
Content	4.0	2.0	0.04

2.3.3. Thermal Degradation

The thermal degradation stability study followed RDC No. 318/2019, which establishes the criteria for conducting Stability Studies of Active Pharmaceutical Ingredients. To measure accelerated stability, the samples were subjected to pre-established conditions in a chamber (40 ± 2°C and 75% ± 5% relative humidity), in a climatic chamber manufactured by Ethiktechnology.

2.4. Chemical characterization for all Samples

The chemical composition of the chitosan hydrogel and chitosan powder were evaluated. To characterize the chemical composition, Fourier Transform Infrared (FTIR) spectroscopy was employed. The spectra of the samples were recorded over a range of 650 to 4000 cm^{-1}, with 16 scans at resolution of 4 cm^{-1}. These measurements were conducted using the Spectrum 400 FT Mid-IR spectrometer by Perkin Elmer. The data are shown in Figures 2, 3 and 4.
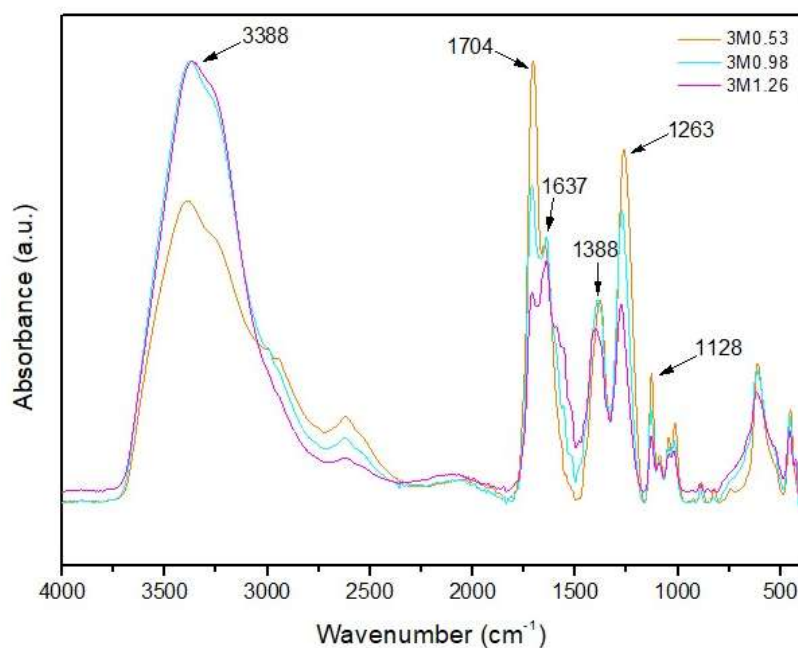
a)
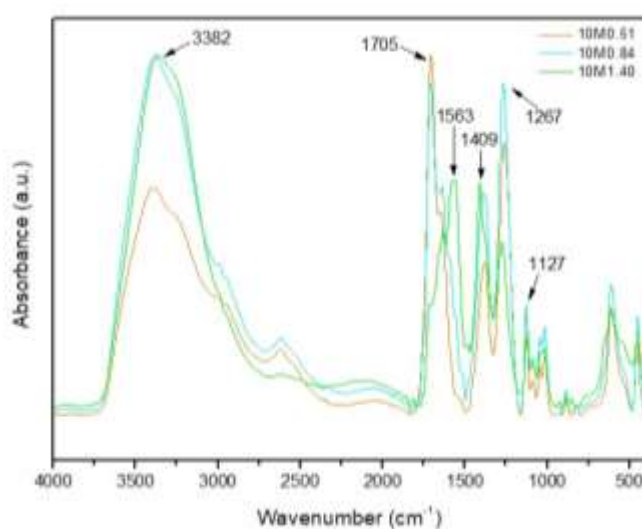
b)

Figure 2. Chemical composition by FTIR of a) 3Mx.y and b) 10Mx.yz samples.
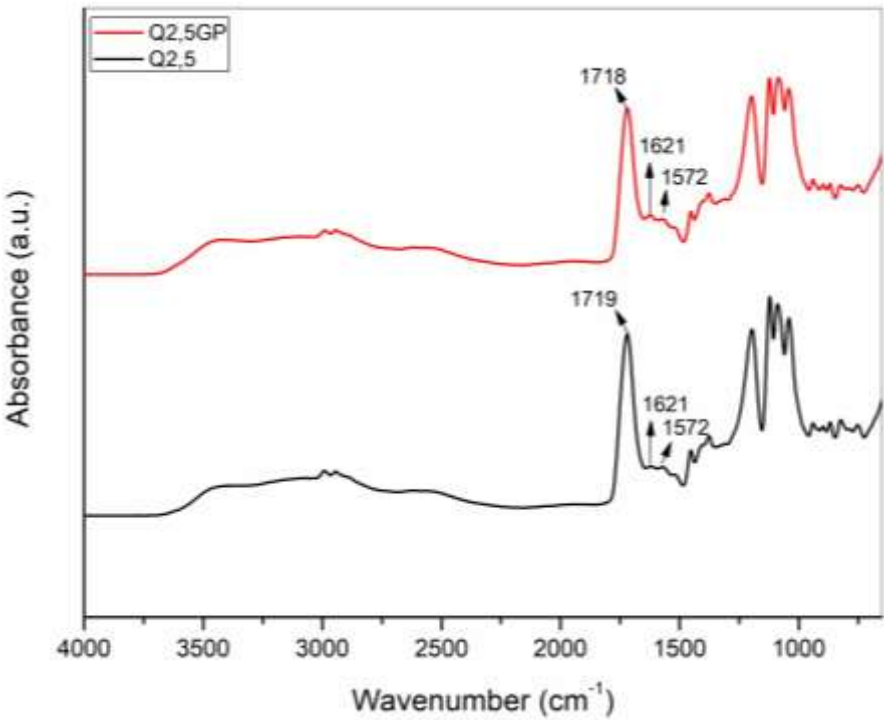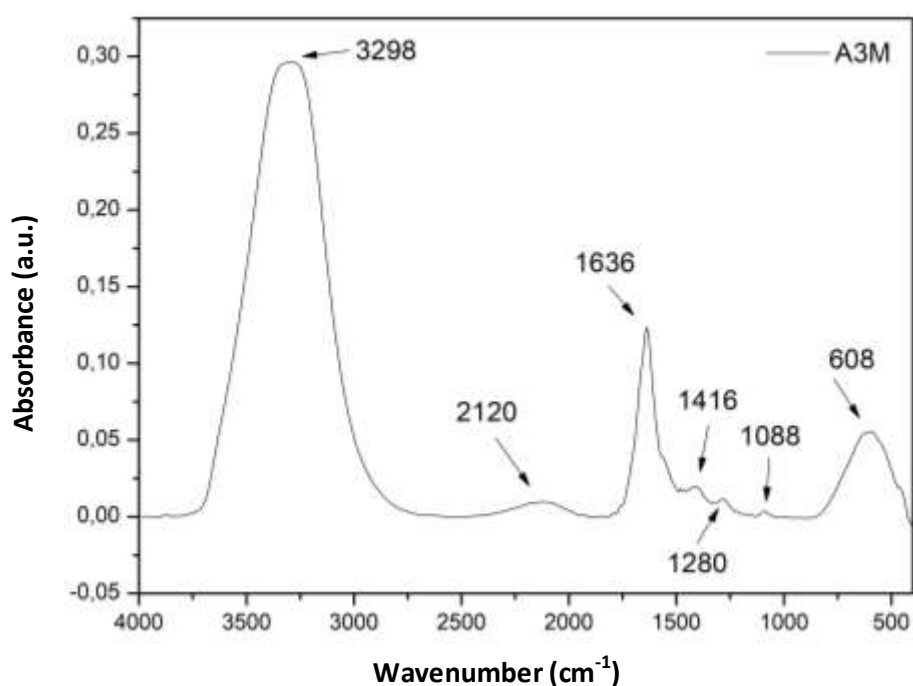
a)
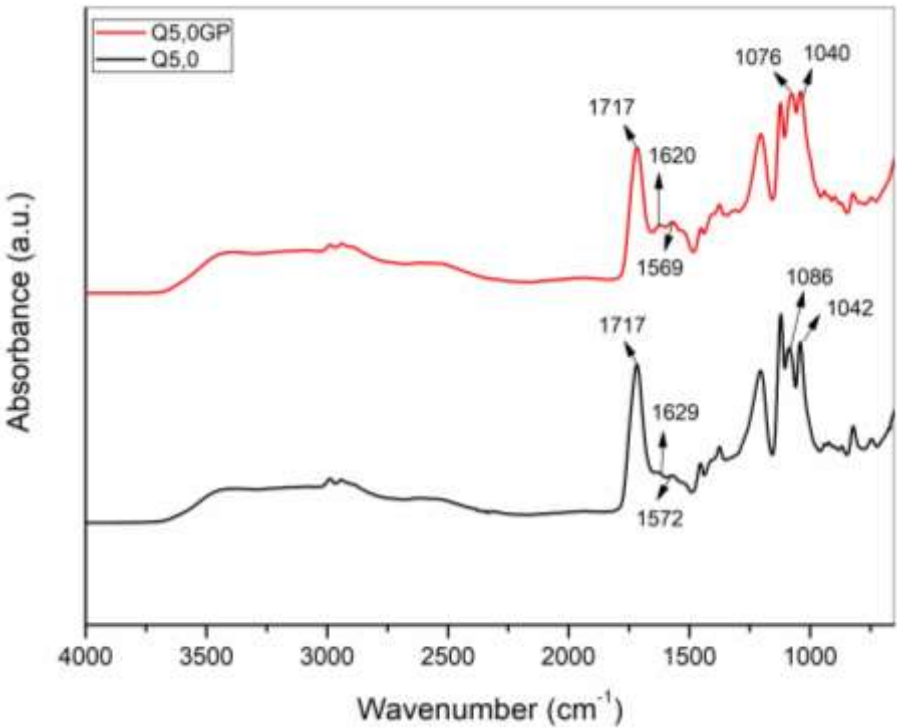
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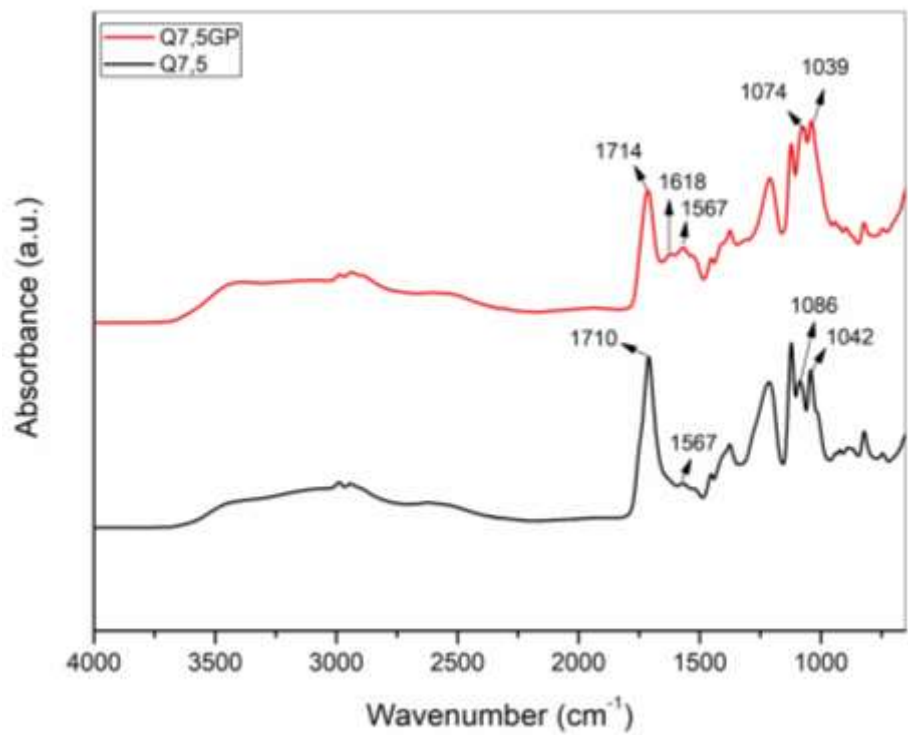
c)
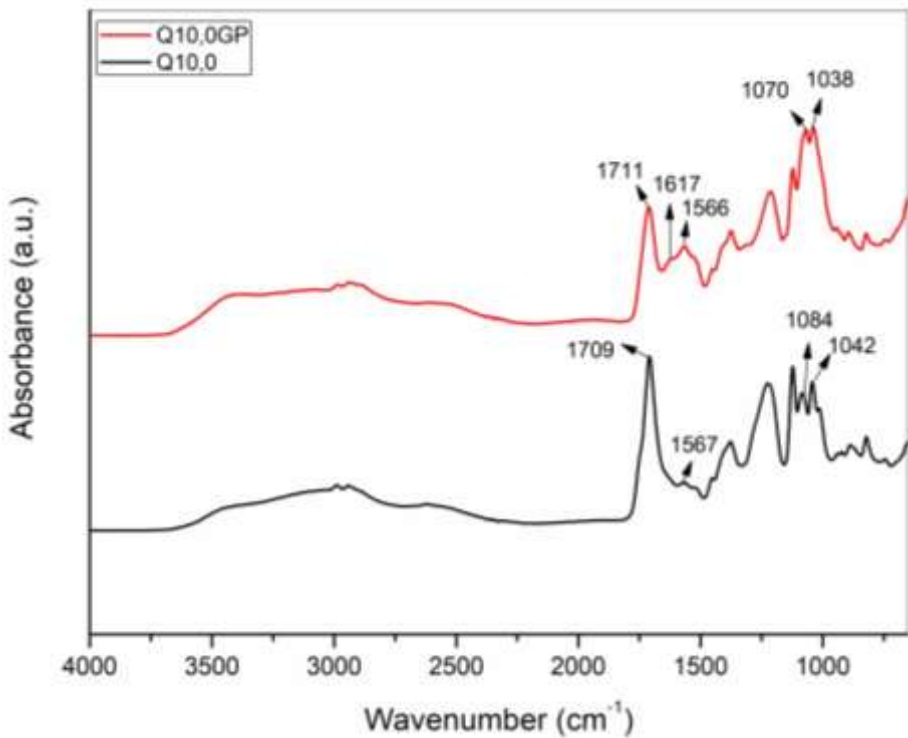
d)

Figure 3. Chemical composition by FTIR of a) Q2.5 and Q2.5P, b) Q5.0 and Q5.0P, c) Q7.5 and Q7.5P and d) Q10.0 and Q10.0P samples.
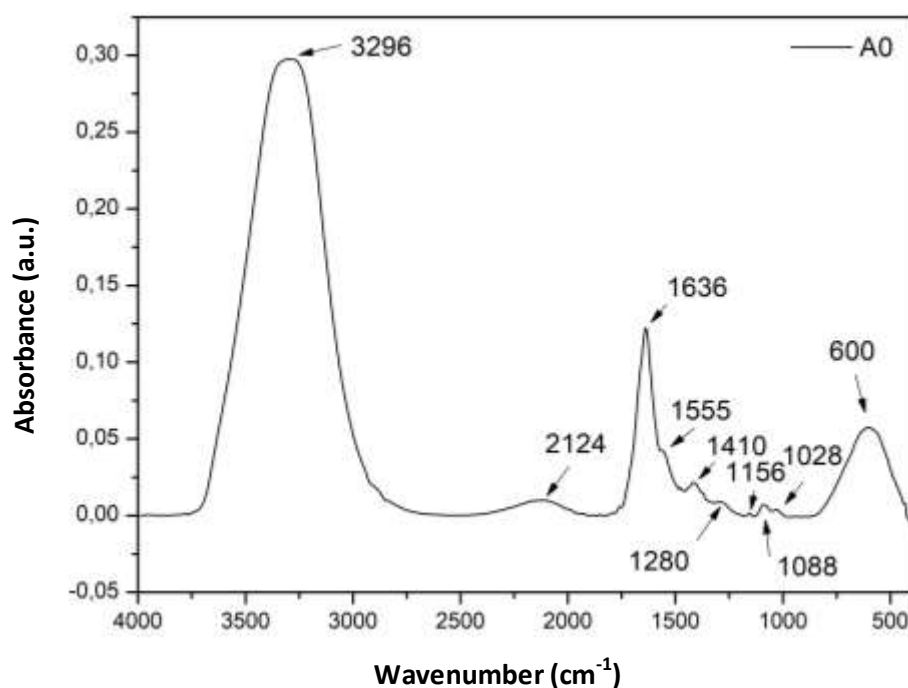
a)

b)

Figure 4. Chemical composition by FTIR of a) unexposed (A0) and b) exposed (A3M) samples.

2.5 Rheological Analysis for all Samples

The samples of hydrogel were rheologically characterized using a HAAKE™ MARS™ rheometer (Thermo Fisher Scientific), equipped with a PP35TiL rotor with plate-plate geometry and a gap of 0.5mm, in a shear rate range between $0.01s^{-1}$ up to $3s^{-1}$, at 22°C, 23°C or 37°C, depending on the application that the hydrogel would have.

3. Results

When analyzing Figures 5a and b, a reduction in the critical shear rate for the ST-ST transition of around 40% is observed for the samples crosslinked with genipin with 2.5% and 5.0% chitosan in relation to the non-crosslinked samples with the same concentration. From 5.0% chitosan onwards, there is practically no difference in the shear rate at which the change from dilatant to pseudoplastic behavior occurs, $\dot{\gamma}_C$. In other words, as the chitosan concentration increases, the effect of crosslinking becomes negligible in the ST-ST transition. The use of chemical cross-linking agents, such as glutaraldehyde or genipin, can significantly influence the rheological properties of chitosan hydrogels. A higher degree of cross-linking can lead to a more rigid structure, which may exhibit shear-thickening at lower shear rates. Since the genipin concentration was the same for all samples, the relationship between the degree of crosslinking and the chitosan mass decreased with increasing chitosan concentration in the hydrogel. Thus, the critical shear rate was expected to undergo little modification at higher chitosan contents when comparing data from non-crosslinked and crosslinked samples.

a)

b)
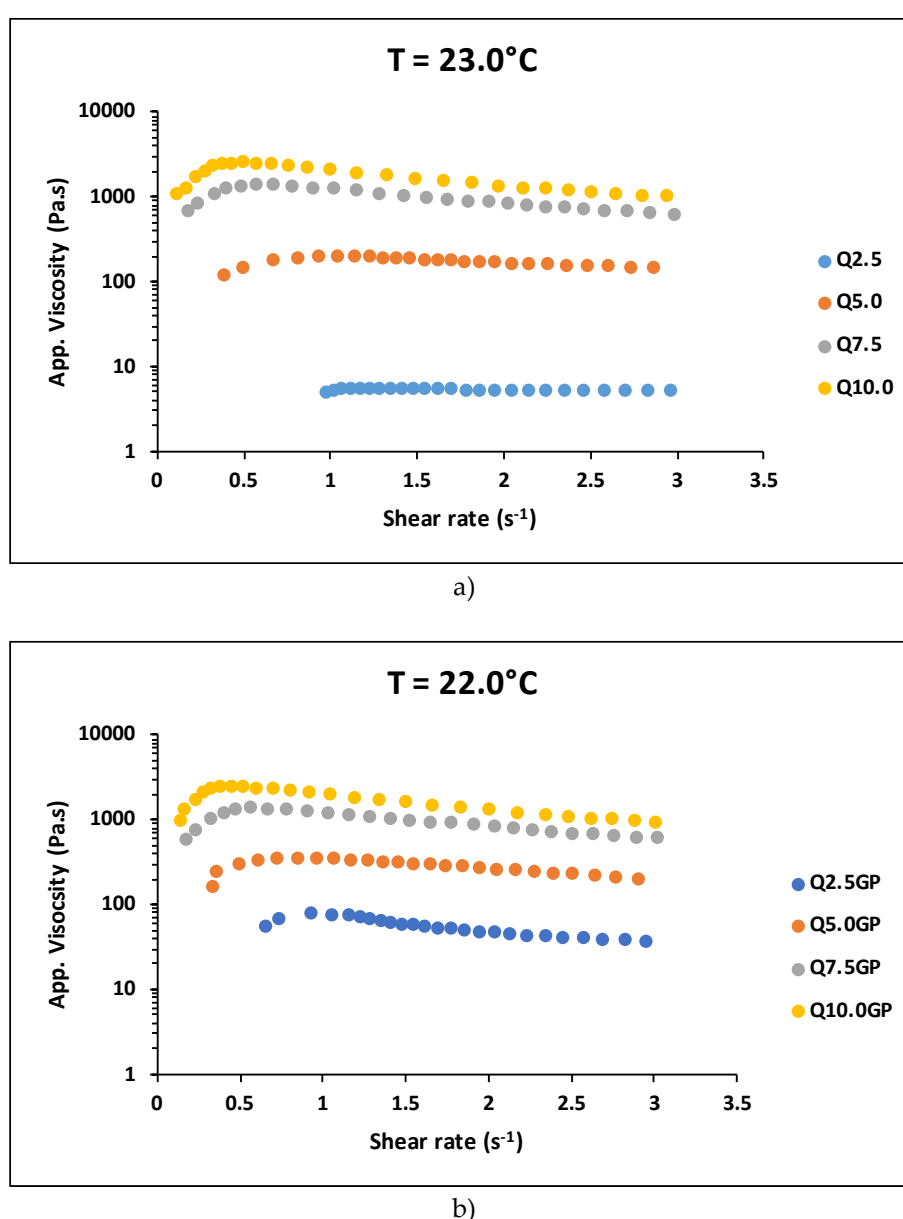
Figure 5. ST-ST transition for chitosan hydrogel with 400KDa molar mass and 80% deacetylation degree for a) non-crosslinked and b) crosslinked samples.

Here, the concept of pHred, a quantity that relates the pH to the concentration of chitosan in the hydrogel, was used as a way to analyze the effects of these two variables on the rheological behavior of the hydrogel. pHred is obtained by the ratio of the hydrogel's pH to the chitosan concentration (%w/v). Increasing molarity brings the apparent viscosity versus shear rate curves closer together, makes the sol-sol transition (ST-ST) in chitosan hydrogels with similar pHred values for 3M and 10M more evident, and significantly reduces the critical shear rate value (see Figure 6a,b). The higher the molarity, the higher the zero-shear apparent viscosity. A higher zero-shear apparent viscosity can delay the onset of the ST-ST transition. This occurs because the fluid needs to overcome a higher initial resistance to flow, requiring greater shear stress, even at lower critical shear rates, before initiating shear-thinning behavior.

a)

b)
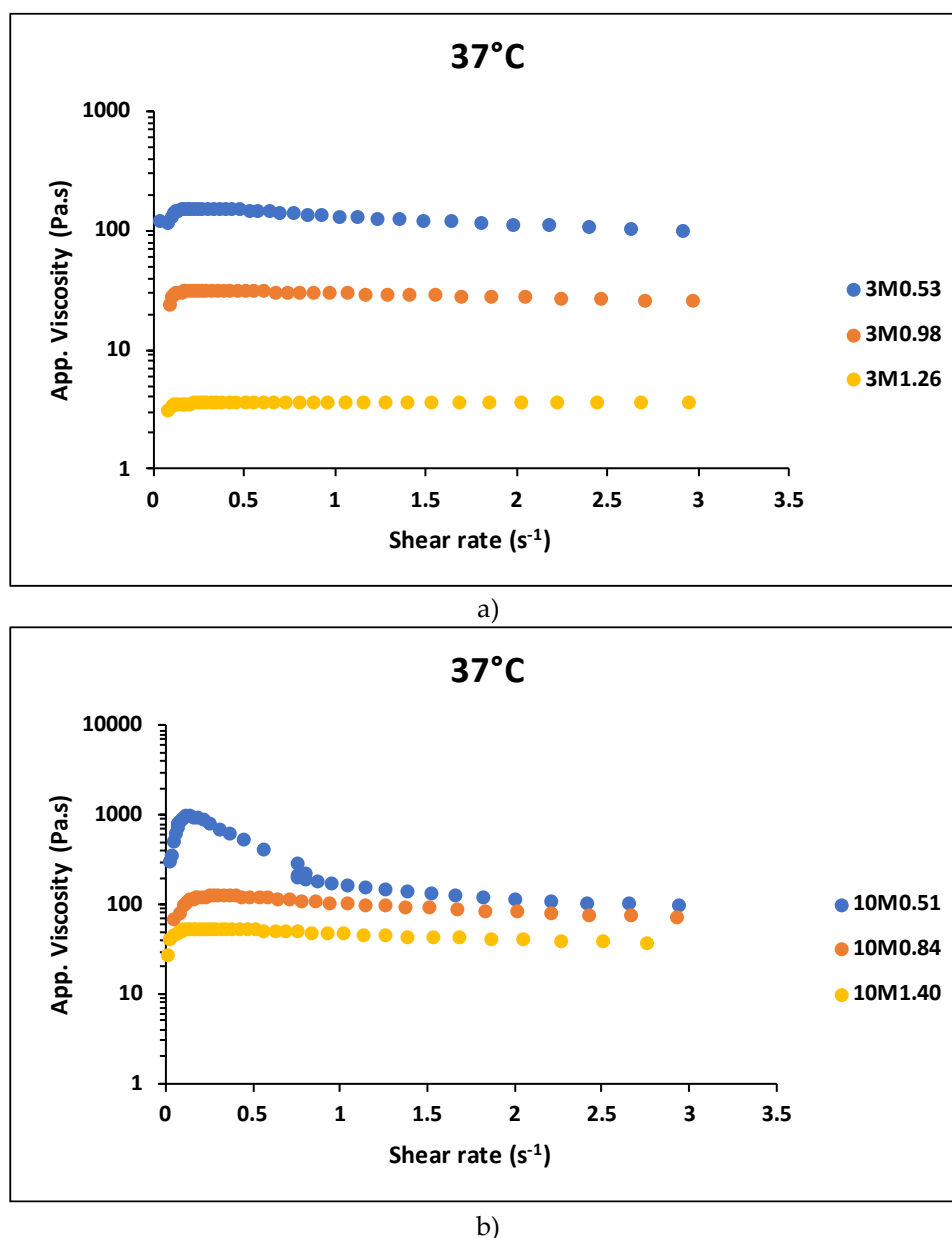
Figure 6. Effect of molarity a) 3M and b) 10M of pH modifying solution on ST-ST transition for chitosan hydrogel with different pHred.

The influence of thermal aging of chitosan hydrogels on their rheological properties is being analyzed in an ongoing work from which some results have already been processed. In Figure 7, it can be seen that aging for 3 months inside the primary packaging at 40°C and 70% humidity caused a decrease of around 10 decades in the viscosity of the hydrogel. This decrease in

viscosity, however, did not provide an ST-ST transition at very different critical shear rates (0.21s^{-1} for A0; 0.19s^{-1} for A3M), as observed in the increase in viscosity due to molarity, shown in Figures 3a e b. In the case of thermal aging, the unexposed sample with higher viscosity required a higher shear stress (0.0815 Pa for A0; 3.6922 Pa for A3M) and not a higher shear rate. This is probably related to the difference between the indices n estimated for the two samples in the dilatant region. Contrary to what was observed for the pseudoplastic regions, no sample presented a dilatant region adjusted by the power law. Thus, we will refer to the degree of departure from Newtonian behavior only as index n_D, for dilatant region and n_P, for pseudoplastic one. n_D was estimated by Equation 1:

$$\eta(\dot{\gamma}) = \eta_0(\dot{\gamma} - \dot{\gamma}_0)^{n_D-1} \; for \; \dot{\gamma} > \dot{\gamma}_0 \qquad (1)$$

Where: η_0 is the initial shear-viscosity and $\dot{\gamma}_0$ is the shear rate correspondent to this initial shear-rate viscosity at dilatant region.

While the A0 sample has $n_D = 1.07$, the A3M sample has $n_D = 1.22$, being, therefore, more dilatant than the unexposed sample. For the same initial apparent viscosity, a more dilatant fluid will present a greater increase in apparent viscosity in the same shear rate range, for shear rate higher than 1.0, presenting a greater resistance to flow than the less dilatant fluid. Thus, the balance between initial apparent viscosity and the power law index can justify the fact that both samples present the same critical shear rate for the ST-ST transition.
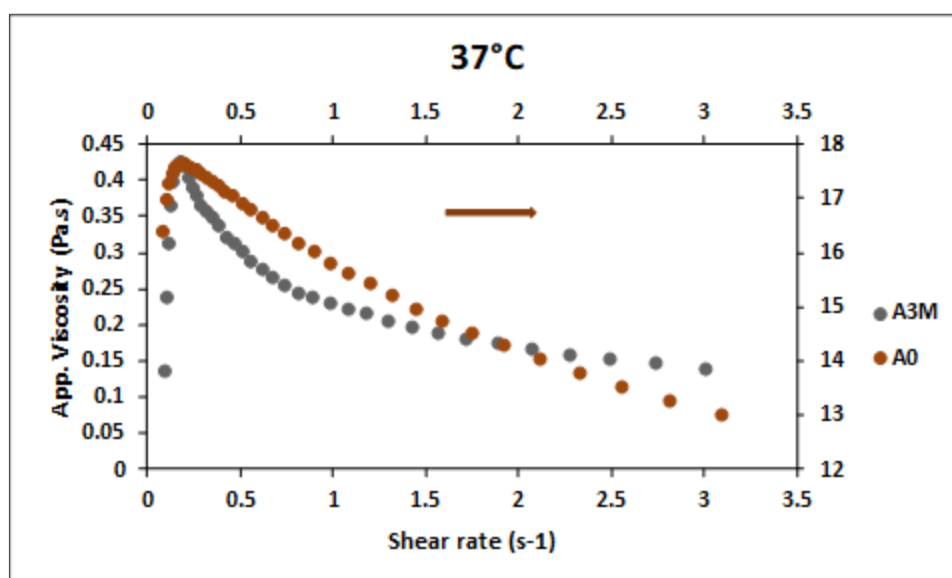

Figure 7. Influence of thermal aging on the ST-ST transition.

Regardless of molarity, the ST-ST transition has a sharper peak the lower the n_P value, regardless of the n_D value. For the same pH, n_D increases and n_P decreases with increasing chitosan concentration in non-crosslinked hydrogels. For crosslinked gels, it was observed that above 2.5% chitosan, the n_D and n_P values fluctuate little in relation to the average, remaining within the average ± the standard deviation. These n_D and n_P behaviors need to be observed in other systems that present the shear-thickening - shear-thinning transition so that more informed conclusions can be drawn.

4. Conclusions

From the results presented in this work, it can be concluded that the complex rheological behavior of chitosan hydrogels, particularly the shear-thickening (dilatant) to shear-thinning (ST-ST) transition, which is challenging to observe due to its frequent confusion with mechanical oscillations or experimental deviations. This transition is more evident in specific shear rate ranges and is less common than the reverse (shear-thinning to shear-thickening). Chitosan hydrogels, known for their applications in biomedical engineering, drug delivery, and tissue regeneration, exhibit ST-ST

behavior under low shear rates, making them suitable for controlled applications. The ST-ST transition is primarily influenced by factors such as pH, molarity, and chitosan concentration, rather than thermal aging, with crosslinking agents like genipin enhancing rigidity and promoting shear-thickening at lower shear rates. As chitosan concentration increases, the effect of crosslinking on the transition becomes negligible, while higher molarity of the pH-modifying solution makes the ST-ST transition more visible, decreases the critical shear rate, and increases zero-shear viscosity, delaying the transition onset. Thermal aging affects viscosity but does not significantly alter the critical shear rate, requiring higher shear stress instead. The rheological behavior, characterized by indices such as n_D (dilatant region) and n_P (pseudoplastic region), helps understand the departure from Newtonian behavior and flow resistance. Overall, understanding ST-ST behavior enables the design of tailored hydrogels for applications in drug delivery, tissue engineering, food texture improvement, and personal care products, emphasizing the importance of controlling specific parameters to achieve desired material properties.

The following abbreviations are used in this manuscript:

MDPI	Multidisciplinary Digital Publishing Institute
DOAJ	Directory of open access journals
TLA	Three letter acronym
LD	Linear dichroism

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