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Determination of Swelling Kinetics and Diffusion Mechanisms of Chemically Crosslinked Porous Chitosan Hydrogels

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Abstract - Chitosan hydrogels have gained popularity in a variety of industrial applications due to their biocompatibility, biodegradability, and various physicochemical features. Understanding these hydrogels' swelling dynamics and diffusion processes is crucial to improve their efficiency in drug delivery, tissue engineering, and wound healing applications. This work aims to examine the chemically crosslinked porous chitosan hydrogels in swelling and diffusion processes. The swelling kinetics of the hydrogels were investigated using Fick's diffusion mathematical model to determine the effects of different molecular weights on its swelling behavior at pH: 2.0, 5.6 and 7.4. It was observed that the swelling percentages of hydrogels prepared with low molecular weight chitosan and 1% glutaraldehyde were higher. Chitosan hydrogels cross-linked with glutaraldeyhde exhibited Super Case II Diffusion according to Fick's laws of diffusion. In addition, optical microscopy was used to analyze pictures of porous chitosan hydrogels that were generated using two different molecular weight chitosan.

Keywords: hydrogel, freeze-drying, Fick’s law, swelling kinetic, diffusion coefficient

Kimyasal Olarak Çapraz Bağlı Gözenekli Kitosan Hidrojellerin Şişme Kinetiği ve Difüzyon Mekanizmalarının Belirlenmesi

Öz - Kitosan hidrojelleri biyouyumlulukları, biyobozunurlukları ve çeşitli fizikokimyasal özelliklerinden dolayı çeşitli endüstriyel uygulamalarda popülerlik kazanmıştır. Bu hidrojellerin şişme dinamiklerini ve difüzyon süreçlerini anlamak, ilaç salınımı, doku mühendisliği ve yara iyileştirme uygulamalarındaki etkinliklerinin arttırılması açısından çok önemlidir. Bu çalışma kimyasal olarak çapraz bağlı gözenekli kitosan hidrojellerde şişme ve difüzyon süreçlerini incelemeyi amaçlamaktadır. Hidrojellerin şişme kinetiği, pH: 2.0, 5.6 ve 7.4’ te kitosanın farklı moleküler ağırlıklarının şişme davranışı üzerindeki etkilerini belirlemek için Fick Kanunu difüzyon matematiksel modeli kullanılarak araştırıldı. Düşük molekül ağırlığında kitosan ve %1 lik glutaraldehit ile hazırlanan hidrojellerin şişme yüzdeleri daha yüksek olduğu görüldü. Glutaraldehit ile çapraz bağlanan kitosan hidrojelleri, Fick'in difüzyon yasalarına göre Süper Durum II Difüzyonu gösterdi. Ayrıca iki farklı molekül ağırlıklı kitosan ile hazırlanan porous kitosan hidrojellerin optik mikroskop ile görüntüleri incelendi.

Anahtar kelimeler: hidrojel, dondurarak kurutma, Fick Yasası, şişme kinetiği, difüzyon katsayısı

1. Introduction

Hydrogels are polymeric materials with a hydrophilic structure that allows them to absorb large amounts of water into their three-dimensional networks. Natural polymers including proteins (collagen and gelatin) and polysaccharides (chitosan, starch, alginate, and agarose) can form hydrogels. Hydrogel-based products are widely used in various industrial, and environmental applications [1]. Hydrogels are often produced by cross-linking biodegradable polysaccharides including starch and chitosan. These natural polymers possess distinctive characteristics such as biocompatibility, biodegradability, low prices, and rapid gelation, owing to their hydrophilic nature[2]. The swelling characteristics of hydrogels are determined by the polymer’s solvent compatibility, cross-linking degree, and its nature. [3]. The deacetylation degree (DD) is critical for changing the swelling characteristics of chitosan for a variety of applications. The deacetylation

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degree indicates the percentage of free amino groups in the chitosan molecule. The degree of deacetylation is a crucial factor that influences the behavior of chitosan in terms of its physicochemical characteristics, including reactivity, crystallinity, and swelling degree[4], [5].

Chitosan is a copolymer composed of glucosamine and N-acetylglucosamine repeat units, with the repeat units defined by the degree of deacetylation of crustacean shell chitin [6]. Chitosan's deacetylation degree determines the ratio of D-glucosamine to N-acetyl-d-glucosamine units in polymer chains. Chitosan is defined as DD > 50%, while chitin is defined as DD < 50% [7], [8]. Chitosan is soluble in dilute acids at acidic pHs. However, it is not soluble at pH 7.4, non-protonated chitosan may absorb huge volumes of water. The swelling characteristic of chitosan, even in the absence of chemical cross-linking, may be explained by the swelling theory of polymer networks, which includes crystalline structures and physical entanglements[4], [5]. According to Zhou et al., the molecular weight and the degree of chitosan deacetylation have strong influence on the pH value, turbidity, viscosity, and thermosensitive properties of chitosan-based hydrogels crosslinked with glycerophosphate [9]. Although, chitosan has been used for many years in a variety of fields, including agriculture, health, sensors, wastewater treatment, metal removal, and cosmetics. It has specific limitations when used as a scaffold, especially in controlled fertilizer, or drug release applications. Here, chemical modification has been proven to overcome these constraints, cross-linked chitosan hydrogels have thus become increasingly important in relevant recent research on drug, fertilizer release, and tissue engineering. Modifying chitosan improves its intrinsic properties such as biocompatibility, chemical versatility, biodegradability, and low toxicity. These adjustments can be made to fit in a specific application. Chitosan's physical and chemical properties can be effectively and practically enhanced for its use in practical applications by crosslinking with crosslinking agents such as sodium tripolyphosphate or glutaraldehyde [10]. Physical hydrogels are hydrophilic structures formed by non-covalent cross-links from ionic, hydrogen, Van Der Waals, or hydrophobic interactions, whose formation depends on thermodynamic parameters like temperature, pH, and ionic strength. The primary drawbacks of physically cross-linked systems are potential mechanical instability and the possibility of system breakdown caused by extremely pH-sensitive swelling [11], [12]. Sodium tripolyphosphate (STPP) is used as a ionic physical crosslinker. STPP-based hydrogels are non-toxic and have low mechanical strength, while they have high swelling capacity [13]. However, chemical cross-linking's irreversible gelation creates stable, mechanically strong hydrogels with resistance to dissolution, making them ideal for chitosan applications due to their physicochemical stability and resistance to extreme pH conditions[14]. The main disadvantage of this system is that most of the cross-linkers used for the cross-linking process are relatively toxic and their effects on the living body are not fully known due to the lack of data on their biocompatibility. The most used chemical crosslinkers in studies on chitosan hydrogels are dialdehydes (such as glutaraldehyde or glyoxal) and genipin. Dialdehydes allow direct reaction in aqueous media, under mild conditions and without the addition of auxiliary molecules such as reducers, which is advantageous in terms of biocompatibility. However, the use of these cross-linkers that exhibit toxic properties requires an additional purification and verification step before application [15]. As mentioned above, chemically cross-linked hydrogels exhibit superior mechanical strength and reduced swelling degree compared to physically cross-linked hydrogels. Chitosan-based hydrogels exhibit different characteristics in swelling behavior at various pH conditions. Mathematical modeling of swelling is critical to understanding the behavior and application of hydrogels under various environmental circumstances[16].

Several mathematical models are used to describe the kinetics of a hydrogel’s swelling, t among which, the dominant model is Fickian diffusion, that describes the dispersion of a liquid into the gel matrix as the hydrogel swells or collapses. This model demonstrates a linear increase in the swelling fraction with the square root of time until it reaches 0.4 for diffusion exponential. Additionally, the swelling curve never exhibits a sigmoidal shape. The second model, also known as collective diffusion, establishes a connection between the stress gradient and swelling of the gel as well as the network. None of these two models can adequately explains the significant sigmoidal swelling curves that occur due to large volume changes and are often used to describe non-Fickian diffusion. The Fickian diffusion is characterized by the occurrence of sigmoidal swelling when the movement of the gel surface is precise [16]. The swelling dynamics of hydrogels can be categorized as either diffusion-controlled (Fickian) or relaxation-controlled (non-Fickian) [3]. In this study, glutaraldehyde was preferred as a very reactive chemical crosslinker. Glutaraldehyde is easier to obtain and less costly. The formation of hydrogel using glutaraldehyde occurs more rapidly. However, the crosslinker of glutaraldehyde has toxic properties. Therefore, this disadvantage of glutaraldehyde eliminated by washing the unbound glutaraldehyde from the hydrogel environment after the cross-linking process. Different molecular weight chitosan was used to prepare hydrogels at varying glutaraldehyde concentrations. Hydrogels' swelling properties were examined for their diffusion coefficient and percentages equilibrium swelling. The order of kinetics was further examined using the Fickian diffusion mathematical model. The purpose of this study was to produce porous gels using freeze treatment to examine how the microstructure of the gels affects their swelling process. The effect of the change in the molecular weight of chitosan on the swelling kinetics and optical properties of the hydrogels was investigated.

2. Materials and Methods

Low and medium molecular weight chitosan with a deacetylation degree of at least 75% was obtained from Sigma-Aldrich. Other chemicals including acetic acid (glacial) 100% anhydrous, hydrochloric acid (puris ≥37%), sodium hydroxide (puris 98-100%), glutaraldehyde (25% solution in water) for analysis along with other chemicals obtained from Sigma Aldrich chemicals, disodium hydrogen phosphate (sodium phosphate dibasic) (Na_2HPO_4) purity ≥99.0%, potassium phosphate monobasic (KH_2PO_4) purity ≥99.5%, and disodium citrate (purum p.a., ≥99.0%) were also provided.

The buffer solutions (pH: 2.0 and 7.4) were prepared based on the compositions provided in the Merck laboratory handbook [17]and their precision was verified using a pH meter. The composition and proportions of the buffer solutions are shown in Table 1. Only distilled water was used to prepare the pH:5.6 solution. When required, 0.1 M solution of NaOH and 0.1 M solution of HCl were used to adjust the pH of the solution to desired pH.

Table 1. Chemicals and their ratios used in preparing buffer solutions

pH	Chemicals used in solution preparation and their usage amounts
2.0	0.1 M Disodium citrate (C6H7O7Na2) – 0.1 M Hydrochloric acidt (HCl) 30.2 mL (C6H7O7Na2) + 69.8 mL HCl is completed to 1 L with distilled water.
7.4	0.067 M Potassium dihydrogen phosphate – 0.067 M Disodium hydrogen phosphate Prepare a solution by combining 19.7 mL of KH2PO4 and 80.3 mL of Na2HPO4 with distilled water to a total volume of 1 L.

2.1. Hydrogel Preparation

Figure 1 illustrates the procedural stages for manufacturing chitosan hydrogels cross-linked with glutaraldehyde through a chemical approach. 2 grams of chitosan (2% w/v) were prepared in 100 mL acetic acid (2% w/v) solution. After chitosan was dissolved in acetic acid, the air bubbles were eliminated by using an ultrasonic bath. Then, 1% glutaraldehyde solution was prepared from 25% glutaraldehyde solutionHydrogels were synthesized by adding glutaraldehyde solution at various concentrations ranging from 1% to 10% into solution, depending on the quantity of chitosan [8]. After the hydrogels were frozen in the freezer at -18°C, they were dried with a lyophilizerto form a porous structure. Freeze-drying process was performed with using Labconco FreeZone Freeze-Dry System (cold trap temperature: -40 °C, vacuum degree: ≤30 Pa).

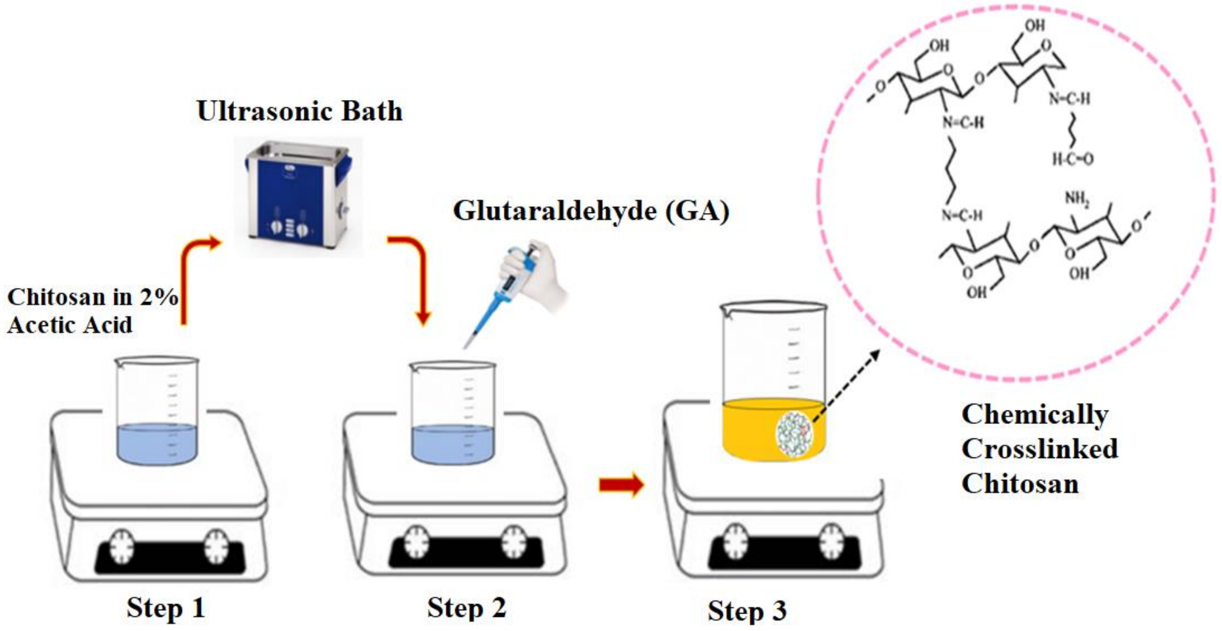

Figure 1. Preparation procedure of chitosan hydrogels

2.2. Swelling Ratio

The swelling ratios of the hydrogels were determined according to Jin et. al.[18]. The gravimetric method was employed to evaluate the gels' swelling under various circumstances at room temperature. Initially, the gel's mass was measured, and then, it was placed in the media solution. The hydrogels were kept 6 hours in the media solution. The media solution was pH:2.0, 5,6 and 7.4. Periodically, the hydrogel was removed from the media solution, and it was dried to eliminate any remaining water on its surface. Once the hydrogel's mass was measured, it was placed back into the solution [18]. As the water molecules penetrate the gel, they encounter the cross-linkers' resistance in the network structure after a certain point and this is known as the elastic resistance. The moment when this resistance, which affects the swelling in the opposite direction, and the osmotic pressure force acting in favor of the swelling are equalized, the swelling reaches its maximum [19]. Equation 1 is used to determine the hydrogels' water content when they reached their maximum swelling value at this equilibrium moment.

$$Eq_w = \frac{m_d - m_0}{m_0} * 100 \tag{1}$$

Eq_w; maximum swelling percentage of the hydrogel at equilibrium.

m_d ; hydrogel weight at equilibrium.

m_0 ; hydrogel dry weight.

2.3. Swelling kinetics and diffusion mechanism

The Fickian diffusion model, which is widely used in modeling the absorption behavior of hydrogels, is explained by the second-order kinetic equation given below [10], [16], [20].

$$\frac{dS}{dT} = k_s\,(S_{eq} - S)^2 \tag{2}$$

$^{dS}/_{dT}$: swelling rate; k_s: swelling rate constant; S_{eq}: the swelling value at the time of equilibrium; S: refers to the swelling value at time t.

The mechanism of swelling proceeds from the zero order and is expressed by the Fick's law equation given below.

$$F = k\,.\,t\ \frac{M_t}{M_d} \tag{3}$$

F is the ratio of the solvent amount absorbed by the hydrogel at t moment to the amount of solvent absorbed at the equilibrium, M_t; the amount of solvent absorbed at t moment, M_d; the amount of solvent absorbed at the equilibrium, t; the diffusion time, n; the diffusion exponent and k is a characteristic constant that varies according to the polymer's structure. By applying the logarithm to this equation, the diffusion exponent, n, is calculated. The parameter "n" facilitates the identification of the diffusion type. This value will give an idea of the diffusion of the solvent into the gel or gel into the solvent [18]. To determine the nature of diffusion mechanism which the diffusion of water into the chitosan hydrogels follows according to Akakuru and Isiuku [10]

$$\log F = \log k + n.\log t \tag{4}$$

The value of n is calculated by the log(t) graph's slope, drawn against the log(F) value at a time when 60% of the solvent is absorbed by the polymer network ($F < 0.60$), and thus, the diffusion mechanism is determined [10], [16].

2.4. Optical microscopy

Both the visible light images, and the chitosan hydrogels' morphologies prepared at different molecular weights and glutaraldehyde (GA) concentrations were examined by using SOIF MD50 model optical microscope.

3. Results and Discussion

Swelling ratios of the hydrogels were assessed via water absorption. Hydrogels with 1, 3, 5, 7, and 10 wt.% GA were immersed in water to determine their swelling ratios (Fig. 2 and Fig. 3). Such hydrogels, cross-linked with GA, reached maximum swelling at the end of 6 hours. Both L-Mw and M-Mw chitosan gels showed a decrease in %s of swelling values with increased GA concentrations at all different pH mediums. The hydrogel prepared with a lower concentration of cross-linker (1 wt.%) exhibited more swelling compared to the one with a higher percentage of cross-linker (10 wt.%), respectively.

Chitosan hydrogels cross-linked with GA showed higher swelling values compared to non-crosslinked chitosan gels. It can be said that this is because gels with low cross-linking density have a more permeable structure. Zielińska et al. reported a similar result [21]. Silva et al. reported that chitosan membranes with low cross-link ratio (1 wt. % of GA) achieved a higher degree of equilibrium swelling compared to non-crosslinked chitosan, arguing that low crystallinity increases the accessibility of water molecules. Silva et al. observed that the increase in the cross-linking amount (10 wt. % and 20 wt. % of GA) was effective in reducing the degree of equilibrium swelling [22]. Similarly, Wegrzynowska et al. found that neat chitosan films left into the solvent medium exhibited a swelling degree that is twice as low as the cross-linked ones [23]. In cationic gels, less protonation of free amino groups at high pH values (pH>6) increases the hydrophobicity along the chitosan chain. The decrease in the ionization and electrostatic repulsion effect at the basic environment causes shrinkage, and decrease in swelling equilibrium values by reducing the pore area through which the gel absorbs water [24]. Hamedi et al. reported that chitosan hydrogels have low swelling values because they do not cause protonation at neutral and basic conditions [15].

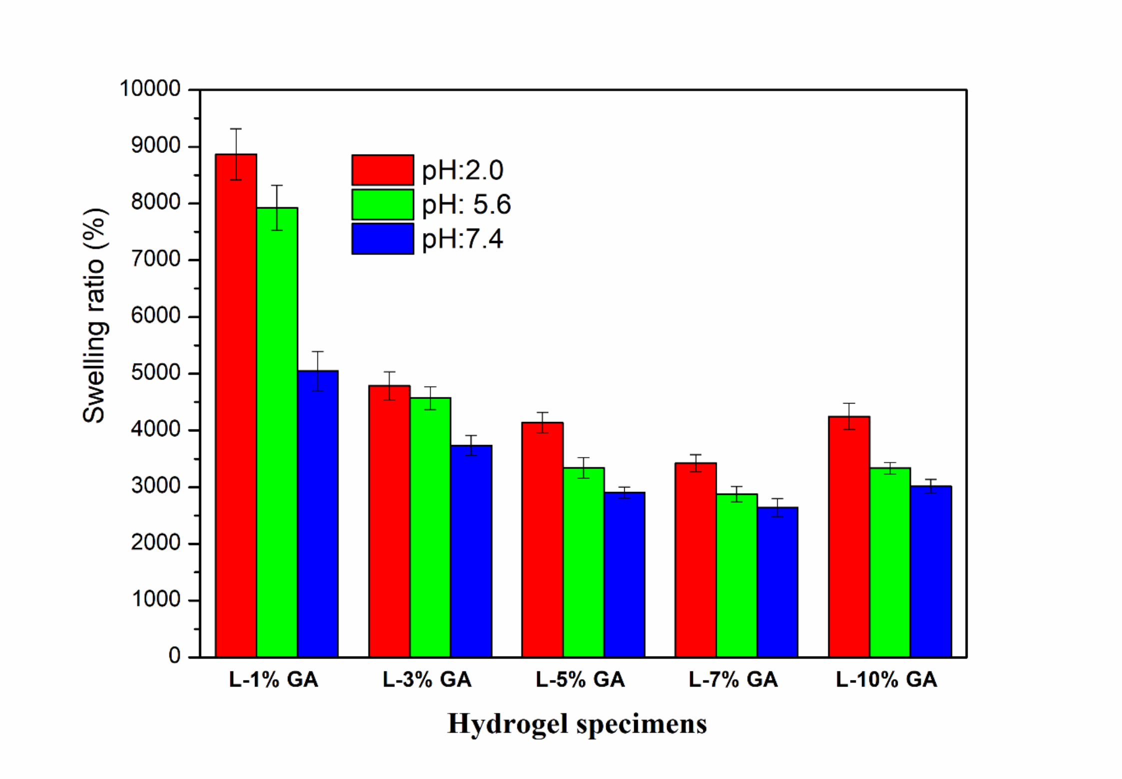

Figure 2. Swelling percentages of low molecular weight chitosan (L-) hydrogels crosslinked with different amounts of glutaraldehyde (GA)

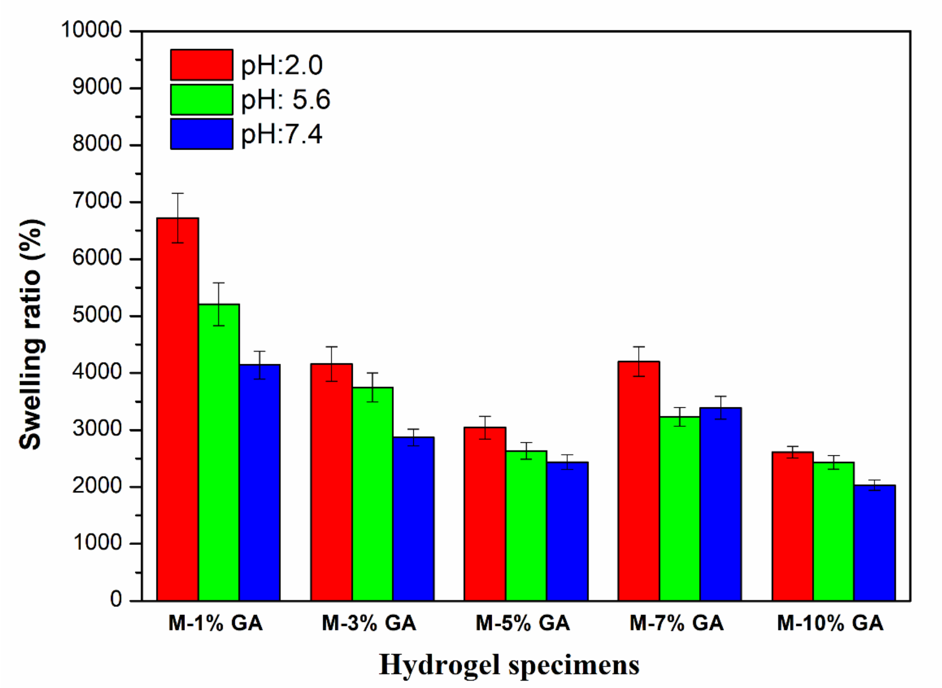

Figure 3. Swelling percentages of medium molecular weight chitosan (M-) hydrogels crosslinked with the different amounts of glutaraldehyde (GA).

On the other hand, it was observed that the swelling values decreased noticeably with the increasing molecular weight. Gupta et al. prepared microspheres with chitosan in three different molecular weights: low, medium and high, and examined their swelling properties. Chitosan chains with a greater molecular weight are longer and more entangled, which reduces swelling ability by increasing resistance to chain mobility and hydration when dispersed in water. They concluded that the increase in molecular weight showed a lower swelling degree because it caused strong intermolecular interactions. The study reveals that higher molecular weight chitosan has reduced swelling due to increased interchain interactions and reduced chain mobility [6].

Table 2 demonstrates the highest water absorption capacity per gram of hydrogel at various concentrations of GA. At pH 2, one gram of hydrogel containing 1 wt.% of GA absorbs ~90 times of its weight in water, while one gram of hydrogel containing 10 wt.% of GA by weight exhibited a maximum water absorption corresponding to ~44 times of its weight.

Table 2. The maximum swelling ratio (g/g) of the hydrogels.

	Absorbed water (g)/ g of hydrogel for low molecular weight chitosan.			Absorbed water (g)/ g of hydrogel for medium molecular weight chitosan.		
GA (%)	pH:2.0	pH: 5.6	pH: 7.4	pH:2.0	pH: 5.6	pH: 7.4
1	89.7	80.3	59.3	68.2	53.1	41.4
3	48.9	46.7	37.0	42.6	38.5	29.1
5	42.3	34.4	29.5	31.4	27.3	24.9
7	35.2	29.8	26.1	43.0	33.3	33.8
10	43.5	34.3	29.6	27.1	25.3	19.8

Once cross-linked structures are immersed in an appropriate solvent, they expand as the solvent permeates their network. This scenario continues until the rate at which the solvent enters the network structure is the same as the pace at which it is released. The moment at which inflation reaches its highest value is known as the equilibrium point. Generating swelling curves of cross-linked polymers that demonstrate swelling behavior is highly significant for elucidating the kinetics of swelling and the diffusion mechanism of [11].

Swelling kinetics were investigated to better understand the swelling characteristics and diffusion mechanisms of hydrogels that reached the equilibrium at swelling point. The swelling curves of cross-linked polymers exhibiting swelling behavior is extremely important in explaining the swelling kinetics and the diffusion mechanism. The relationship between the diffusion exponent (n) and the diffusion mechanisms were shown in Table 3 [10].

Table 3. The relationship between diffusion exponent (n) and the diffusion mechanism.

Diffusion Exponential (n)	**Diffusion Mechanism**
$n \leq 0.5$	Fick Type Diffusion
$0.5 < n < 1$	Non-Fick Type Diffusion
$n \geq 1$	Super case II Diffusion

Graphs of the swelling behavior of L-Mw and M-Mw chitosan hydrogels containing different concentrations of GA in distilled water, pH 2.0 and 7.4 environments are presented in Figure 4.

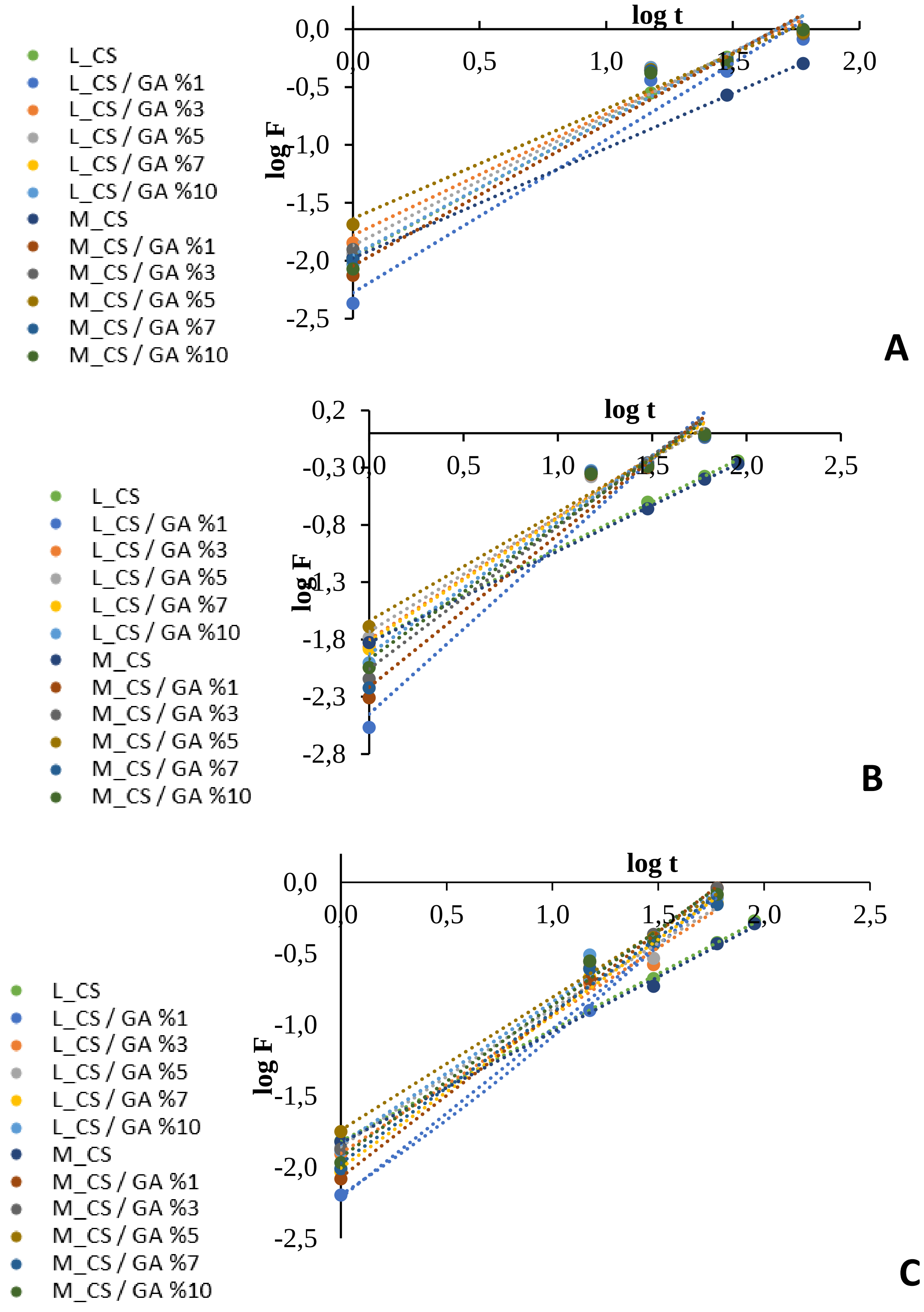

Figure 4. Swelling behavior of chitosan hydrogels cross-linked with GA in (A) Distilled water (B) pH 2.0 and (C) pH 7.4 according to Fick's Law

Because of the thermodynamic compatibility of the polymer chains and water, when a polymer network meets an aqueous medium, it begins to swell. The cross-linked webs' retraction force balances the swelling force, and when these two forces are equal, the swelling reaches the equilibrium. Since the polymer networks' thermodynamic behavior cannot be certainly predicted, no theory can predict the diffusion mechanism, as well. Fickian diffusion analysis, on the other hand, allows making realistic evaluations [25]. Both the diffusion exponent (n) of chitosan hydrogels was determined at pH: 2.0, 5.6 and 7.4, respectively, and their diffusion mechanisms were examined. The 'n' values of pure chitosan hydrogels without GA were in the range of $0.5<n<1$ based on the data presented in Table 4 [18].

Table 4. Diffusion parameters of chitosan hydrogels (pH 2.0, pH: 5.6/distilled water and pH 7.4) cross-linked by GA

Specimens	**n**			**k**			**R^2**		
	pH: 2.0	**pH: 5.6**	**pH: 7.4**	**pH 2.0**	**pH: 5.6**	**pH 7.4**	**pH 2.0**	**pH: 5.6**	**pH 7.4**
L-CS	0.813	0.968	0.786	1.820	1.972	1.819	0.9997	0.9993	0.9997
L-CS/1% GA	1.481	1.321	1.186	2.450	2.277	2.214	0.9538	0.9652	0.9965
L-CS/3% GA	1.068	1.049	0.962	1.801	1.780	1.902	0.9705	0.9700	0.9915
L-CS/5% GA	1.001	1.116	0.949	1.731	1.869	1.852	0.9775	0.9694	0.9930
L-CS/7% GA	1.072	1.164	1.071	1.816	1.955	2.006	0.9697	0.9702	0.9956
L-CS/10% GA	1.155	1.164	1.001	1.928	1.953	1.842	0.9669	0.9657	0.9825
M-CS	0.799	0.949	0.779	1.829	1.978	1.831	0.9999	0.9999	0.9978
M-CS/1% GA	1.329	1.222	1.150	2.217	2.045	2.071	0.9631	0.9676	0.9993
M-CS/3% GA	1.240	1.071	1.032	2.059	1.837	1.852	0.9658	0.9698	0.9954
M-CS/5% GA	0.949	0.946	0.933	1.639	1.636	1.740	0.9773	0.9758	0.9985
M-CS/7% GA	1.276	1.149	1.057	2,130	1.928	1.971	0.9614	0.9734	0.9899
M-CS/10% GA	1.171	1.189	1.067	1.972	2.001	1.931	0.9687	0.9732	0.9900

This means that their swelling behavior is non-Fickian, in which the diffusion rate of the solvent into the gel is greater and faster than the polymer chains' relaxation rate. The swelling rate of gels of this type is determined by the rate of relaxation of polymer chains. Chitosan hydrogels cross-linked with GA appear to have $n \geq 1$ value in all three media with different pHs. This situation, called as superposition diffusion, means that both the diffusion, and the relaxation rate have the same effect on the swelling rate.

The high number of ionic groups at pH 2 has led to a higher diffusion rate compared to other different media. Among the cross-linked samples, M-CS/GA 5% exhibited non-Fickian type diffusion behavior, unlike its other counterparts. This condition is thought to be related to the sol content. Since NH_2 groups that participate in the cross-linking reaction have less interest in water than the other groups that do not participate in the reaction, as they affect the swelling in a decreasing direction.

An optical microscope was used to analyze both the images using 40× magnification lenses and morphologies of chitosan hydrogels that were produced at various molecular weights and GA concentrations under visible light.

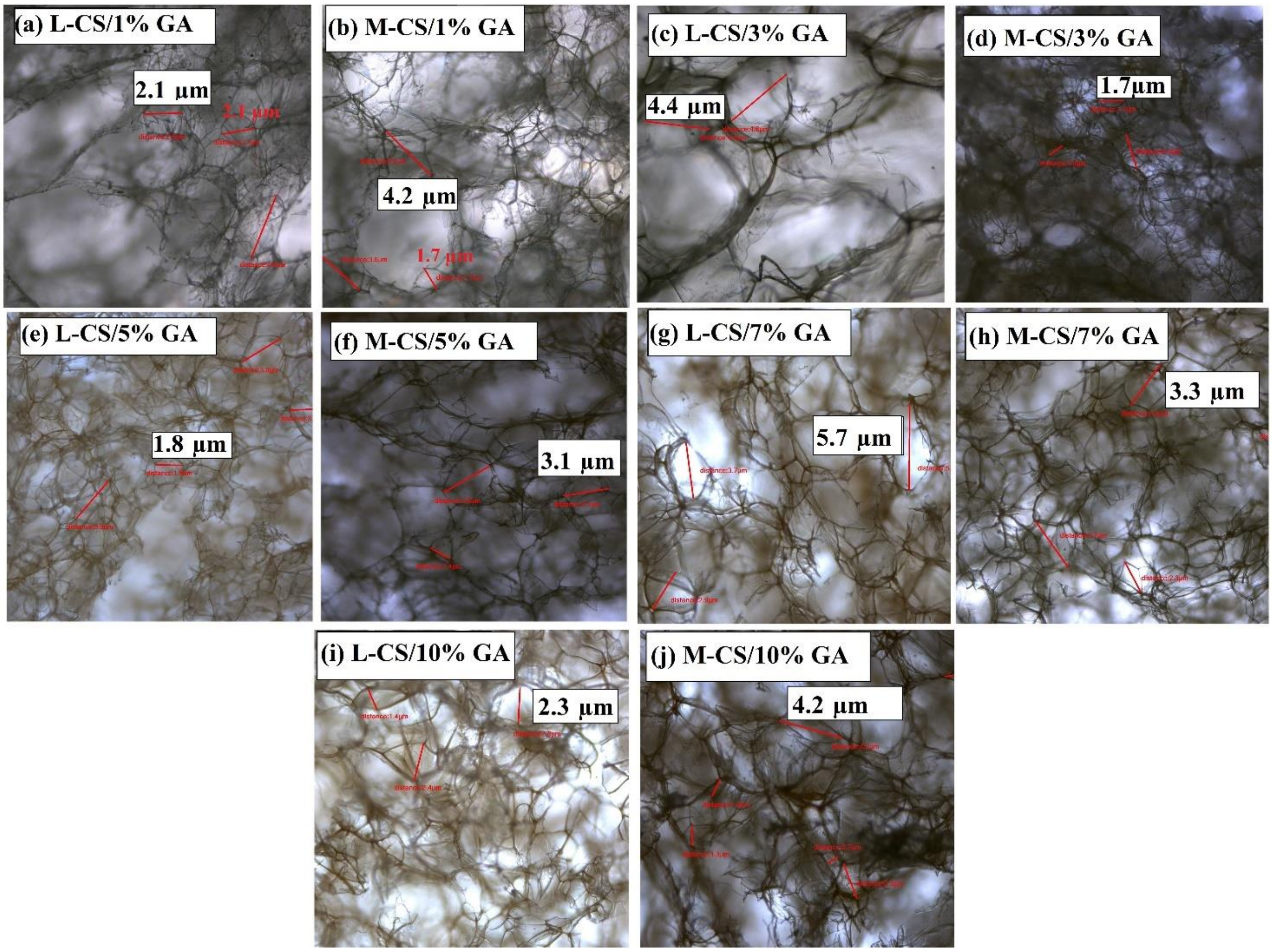

Figure 5. Optical microscope images of cross-linked chitosan hydrogels with GA at different ratios

Optical microscope images of the dry chitosan hydrogels cross-linked with 1-3-5-7-10% GA by weight is shown in Figure 5. It can be observed that hydrogels' pore sizes decrease as the cross-linking ratio in the hydrogel matrix increases. This situation directly affects such gels' swelling behavior**.** Mirzaei et al. analyzed the relationship between the pore sizes and swelling values by cross-linking chitosan hydrogels that were used as drug delivery systems with GA at different ratios. The experimental results revealed that pore diameters were decreased from 500 µm down to 100 µm upon increasing the GA ratio from 0.068% to 0.30%, and thus the equilibrium swelling values were observed to decrease from 1200% down to 600% [26] [26]. M-CS-3% and L-CS-7% hydrogel specimens seem to have larger pore sizes than expected, which is associated with the fact that the sol content of these gels is higher than the other ones. As a matter of fact, during the swelling trials, it was reported that the groups with high sol content exhibited high swelling values due to absorbing more water. Additionally, hydrogels prepared with medium molecular weight chitosan appear to be opaquer. It is thought that the increase in molecular weight causes the increase in entanglements, resulting in a decrease in light transmittance.

4. Conclusions

The swelling values exhibited significant decrease along with increasing in molecular weight. The hydrogel formulated with lower concentration of cross-linker demonstrated a greater extent of swelling in comparison to the hydrogel containing a higher proportion of cross-linker for both different molecular weight chitosans. The findings indicate that the level of cross-linking had a significant impact on the degree of swelling. 1% GA cross-linked chitosan-based hydrogels showed the highest swelling percentage. The swelling ratio (g/g) of low molecular weight chitosan hydrogels crosslinked with 1% GA was measured as 89.7, 80.3 and 59.3 for pH: 2.0, 5.6 and 7.4, respectively. However, the lowest swelling percentages were observed in hydrogels prepared with 10% GA and medium molecular weight chitosan. Maximum swelling ratio (g/g) of medium molecular weight chitosan hydrogels crosslinked with 10% GA was determined as 27.1, 25.3 and 19.8 for pH: 2.0, 5.6 and 7.4, respectively.

As the molecular weight of chitosan increase from low to medium molecular weight, there is often a corresponding alteration in the size and chain structure of the molecule. The alterations have the potential to impact the physical characteristics of chitosan, thereby influencing its diffusion coefficient. As the molecular weight increased, the diffusion coefficient (k) of chitosan generally decreased. Because diffusion of larger molecules may be more difficult. The absorption and release of solvent by a gel is commonly explained by a straightforward process that is regulated by diffusion, which is known as Fick's law of diffusion. The diffusion coefficient generally showed an inverse relationship with molecular weight. The diffusion mechanism of porous low and medium molecular weight chitosans, which were synthesized without the addition of crosslinks, was identified as non-Fick Type. The diffusion mechanism of all hydrogels produced with GA, except for the M-CS/5% GA hydrogel, was determined as Super CASE II.

Based on the optical microscope images, this shows that the increased GA amount reduces the pore size in the gel structure and leads to reduced water-holding capacity. Generally, low molecular weight chitosan formed a more homogeneous structure, while medium molecular weight chitosan tended to form larger pores.

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Conflict of Interest: This study was produced from the YL thesis entitled " Synthesis of low and medium molecular weight chitosan based hydrojels, characterization and investigation of biodegradability properties" by Hanife Songül KAÇOĞLU, which was accepted in 2022.

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