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Salicylaldehydediol Grafted onto Chitosan: Characterization and Their Film Properties

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Abstract: The concentrations of linker group effect different physicochemical features of the biopolymer, including thermal stability, shape, swelling, and water solubility. Herein, three novel chitosan (CH) based films (CHSD1-3) have been prepared by a facile method for their film characteristics. Thus, amphiphilic salicylaldehydediol (SD) was synthesized from hydrophilic glycidol and salicylaldehyde in high yield and regioselectivity. CHSD1-3 films were prepared by the imine condensation reaction of polymeric chitosan backbone and various ratios of SD linker. The reaction takes place with high conversation and amazingly mechanically resistant thickness films without using any plasticizer that exhibits low water solubility and low swelling ratios at pH > 3, which can be suggested as thin layer protecting systems for medical devices. Chitosan-salicylaldehydediol biopolymer films were characterized by Fourier transform infrared (FT-IR) spectroscopy, differential scanning calorimetry (DSC), and X-ray diffraction (XRD) methods. The FT-IR, DSC, and XRD results show a clear linkage of the SD group to the chitosan backbone, high thermal stability of the films, and a change in the original nature of chitosan, respectively. Scanning Electron Microscopy (SEM) observations have also supported the successful grafting of the SD group onto the chitosan.

Keywords: Chitosan film, salicylaldehyde, grafts copolymer, swelling, Schiff bases.

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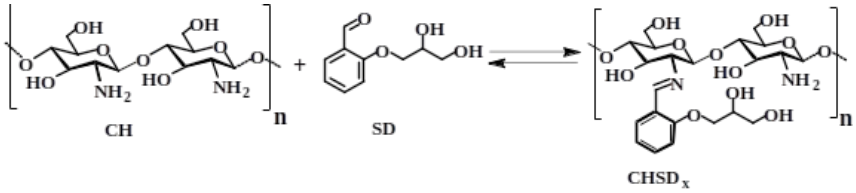
INTRODUCTION

Chitin is the main substance of arthropods and is a polymeric structure formed by the bonding of a highly acetylated glucosamine unit from the β-1,4 place (1). The partial deacetylation of chitin results in the formation of CH is resembled to the cellulose. The difference between them is a primary amine functional group instead of one of the hydroxyl functional groups in the cellulose structure (2). The high cohesion energy of CH caused by strong intermolecular hydrogen bonds prevents chitin from dissolving in many typical solvents such as alcohols, water, and dilute acids (2). Because of this situation, it can be a fundamental problem for the handling and use of the kit. However, the significantly different reactivity of the NH_2 group at position C2 and the OH groups at positions C6 and C3 at the structure of the CH both increase the selectivity of the CH and make it more attractive to chemists.

The biggest cause of environmental pollution is the great deal of plastic materials derived from petroleum due to their decomposition. Therefore, environmentally friendly bio-based polymeric materials such as chitosan have received increasing attention as an alternative to petroleum-derived materials. Biodegradable and biocompatible of bio-based polymeric materials can be used as edible films in the food industry to protect them from water or oxygen. They are functional compounds used to both improve the quality and extend the shelf life of foods (3). Wound healing and hemostatic properties of chitosan make chitosan films as wound healing materials (4). Thus, chitosan films are prepared by the solution moulding method. Both natural chitosan and cross-linking chitosan films have been prepared for various purposes. Cross-linking improves the mechanical and physical behavior of chitosan, such as moisture holding capacity, thermal stability, tensile strength, color, waterproof feature, etc. (5-7). Cross-linked films have been used for oral mucosal (6), transdermal and sublingual (8), and periodontal (9) drug release vehicles.

Chitosan Schiff bases are synthesized by the NH_2 group of CH with aldehydes/ketones. The first CH Schiff base has been synthesized by S. Hirano et. al. by reacting with various aldehydes (10). Then many examples have been reported for various purposes (11,12). Among them are those derived primarily from salicylaldehyde and its nitro derivatives, which are used as a film (13), antitumor reagent (14), and hydrogels (15), as well as chirooptical switches. Imine bond formation over the CH backbone occurs with a relatively low yield in aqueous solutions, but this is increased in hydrogel or solid-state film synthesis (13). Many amazing characteristics and potential of Schiff bases, such as chemical reactivity, formability (films, gels, beads, and membranes), chelating ability, and biological activity, make them suitable for many application fields in pharmaceutics, drug and protein delivery, sensors, wound healing, bio-sorbents, and food packaging (17).

The poor solubility of CH limits the use of it in biological and other applications (10). Thus, modification of CH by reversible reaction of amino groups with aldehydes improves its aqueous solubility by disrupting the H-bonding network of CH (3,18). Herein, a series of chitosan-based biopolymers (CHSD1-3) have been prepared to overcome the poor solubility of CH to promote its physicochemical characteristics for use in the biomedical field, such as drug delivery, bactericidal films, swelling and self-healing as reported (19). Therefore, amphiphilic linker group SD having additional hydroxyl groups compared to the salicylaldehyde has been synthesized from salicylaldehyde and reactive hydrophilic glycidol by an atom-economy method in high yield and regioselectivity (20). CH-based films were prepared through an imine condensation reaction between the SD and NH_2 groups of CH by an environmentally friendly pathway in methanol. CHSD1-3 were obtained by applying a SD ratio of 0.6 to 1 to the CH (Scheme 1). Thermal stability and physical characteristics, swelling, and surface morphology of biopolymer films have been investigated comparatively to encourage us to use them as thin layer protecting systems for biomedical applications.



Scheme 1: Synthesis of modified chitosan (X = 0.6, 0.8, 1.0).

MATERIALS AND METHODS

Materials

Salicylaldehyde, ethanol, acetone, and acetic acid were purchased from Carlo Erba, and chitosan (low molcular weight, deacetylation degree ≥75%) from Sigma-Aldrich without purification. All reactions were carried out with dry solvent in an inert nitrogen environment.

Characterization of Films

The melting point was recorded by the Gallenkamp model apparatus. For FT-IR spectra and ^{1}H (400 MHz) NMR spectra, Perkin-Elmer-100 and Bruker AV-400-HPD FT-NMR were

used, respectively. For morphological analysis of CH and CHDSs and analysis X-ray diffraction (XRD), SEM FEI-Quanta-250-FEG and Bruker-AXS-D8 Advance diffractometer were used, respectively. In addition, for film thickness (µm), DSC analysis and elemental analysis, a digital micrometer (Blue Technology, Miernik Grubosci Lakieru), TGA Shimadzu DSC-60 instrument, and Carlo-Erba-1108 were used, respectively.

Synthesis of 2-[(2,3-dihydroxy)-1-propoxy]benzaldehyde (SD)

Salicylaldehyde 1.22 g (10 mmol) was reacted with 0.74 g (10 mmol) 2.3-epoxypropane-1,2-diol (glycidol) and was reacted to give SAD 1.8 g (91%) yield. The progress of the reaction was checked by TLC [hexane: EtAc (1:5)]. After the reaction mixture was evaporated, it was crystallized with hexane and ethyl acetate. The product was dried under vacuum at room temperature. M.p.: 91.1-93 °C**,** IR (cm^{-1}); 3345, 3200, 2935, 2871, 1593, 1485, 1456, 1400, 1288, 1242, 1190, 1163, 1102, 1044, 981, 954, 834, 758, 682, 673, 526. ^{1}H NMR ($CDCl_3$); 10.3(s, 1H); 7.80-7.78(dd, 1H); 7.59-7.55(m,1H); 7.12-7.08(m,1H); 7.02-7. (d,1H); 4.24-4.15(m,3H); 3.89-3.85(m, 2H); 3(bs,2H). ^{13}C NMR ($CDCl_3$); 190.5, 160.3, 136.2, 130.8, 124.8, 121.2, 112.8, 70.34, 69.95, 63.5. Anal. Calc. for $C_{10}H_{12}O_4$, C: 61.22, H:6.12. Found; C:61.51, H:6.28.

Preparation of CH-SD Films

CH (0.5 g) was dissolved by stirring in distilled water (25 mL) containing 1% (v/v) acetic acid. Various concentrations of SD (0.3g, 0.4g, and 0.5g) were dissolved in 5 mL of methanol. Each SD solution was added to the prepared CH solution and stirred under inert atmosphere at 50 °C for 5 hours. The film was obtained by pouring 2 mL of the reaction mixture into a 4 cm diameter plastic mold. The molds were dried at room temperature for 2 days. After evaporation of the solvent in the open air, the resulting film was soaked in 1 N NaOH solution for 1 hour to free it from acetic acid, then the films were washed with water until neutral. Finally, the resulting films were dried in a manifold at 25°C for 24 h to obtain CH/SD ratio 1/0.6,1/0.8 and 1/1 (CHSD1, CHSD2 and CHSD3), respectively (Figure 1).

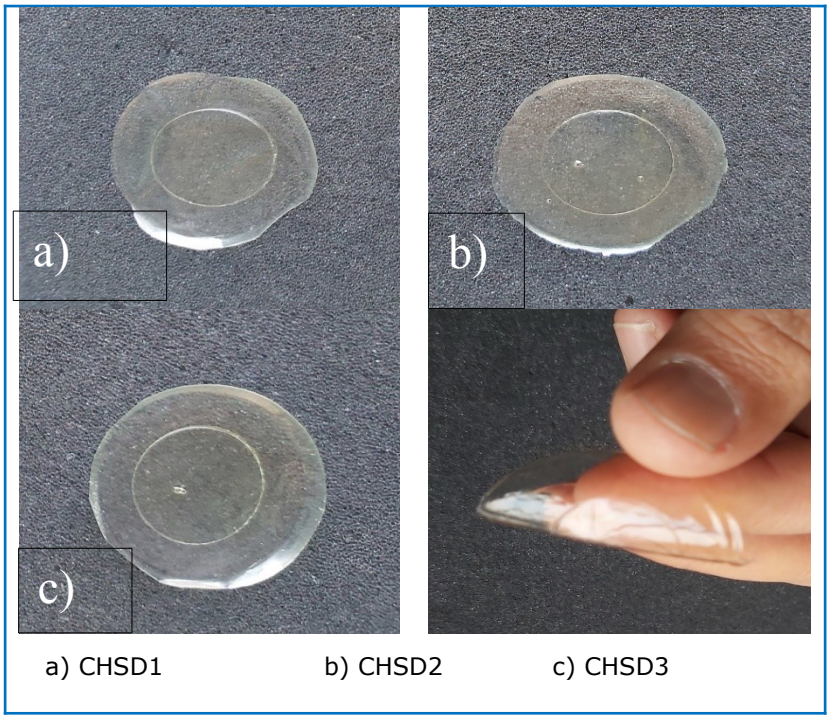


Figure 1: Samples of CHSDs.

Swelling Ratio (SR)

Dry film samples (W_0) with a diameter of 4 cm were weighed to measure the swelling rate of the films. The films were added to a beaker containing 25 mL of distilled water and incubated at 25 °C for an hour, after the films

were removed. After that, the films were dried superficially using filter paper and weighed (W). The swelling ratio was calculated with the equation SR = $(W-W_0)/W_0$.

Water Solubility (WS) and Thickness

Films were processed as follows:

1 Weighed after drying at 105 °C for 24 hours (Wi).

2 It was immersed in beakers containing 50 mL of distilled water at room temperature and left for 24 hours.

3 It was dried again at 105 °C for 24 hours and weighed (Wf),

4 WS was calculated according to the formula:

WS (%) = $(W_i-W_f)/W_i$ x 100, where Wi = Initial Dry Weight (g) and W_f = Final Dry Weight (g).

Film thickness (μm) was determined on three samples CH/SD ratio, averaging the measurements at five points for each film using a digital micrometer (Blue Technology, Miernik Grubosci Lakieru). Average thickness was calculated from randomly selected measurements at five different points on each film.

Scanning Electron Microscopy (SEM)

The surface morphology of the film sample was examined with the FEI Quanta 250 FEG model SEM. Before observation, the films were cut into small pieces and mounted on metal grids with adhesive tape.

X-Ray Diffraction (XRD)

The crystalline characters of CHSDs were evaluated by XRD using Ni-filtered Cu Kα radiation in the 2θ range from 12° to 60°. The X-ray analyses were carried out on CH powder and CHSD1-3 films.

RESULTS AND DISCUSSION

Chitosan is formed from glucosamine and N-acetylglucosamine monomers. NH_2 groups in CH may exhibit polycationic properties that handle electrostatic interactions in anionic systems. The presence of NH_2 and OH groups improves the solubility of CH, resulting in its biocompatibility. As indicated in Scheme 1, CH undergoes the Schiff's base reaction with SD having additional hydrophilic groups when compared with salicylaldehyde, resulting in good yields and promised properties such as swelling, thickness, and water solubility (13). The FT-IR spectra of biopolymer films clearly indicate the grafting of linker group to the CH backbone. Surface morphology and thermal stability have been measured by SEM and DSC data, respectively.

Fourier-Transform Infrared Spectroscopy Analysis

The condensation reaction between CH and the SD linker was investigated using FT-IR spectra. Figure 1 illustrates the FT-IR spectra of CH and biopolymer films. The broad peak at 3358-3288 cm^{-1} was assigned to various O-H and N-H stretching vibrations at CH. This is slightly shifted to lower frequency as a broad signal at 3288 cm^{-1} in the case of CHSD1-3 films that are evident for grafting of the SD group. This changing indicated the formation of additional hydrogen bonding by the SD linker group. Peaks in the spectra of CHSDs centered between 1630 and 1600 cm^{-1} show the frequency of the C=N stretching vibration of the imine bond of biopolymer films, which shifted higher in frequency than the CH spectrum. This is strongly evident for imine bond formation in CHSDs. Parallel outcomes can be seen from previously reported literatures (13-16).

The characteristic vibration of carbonyl and the C-H stretching vibration of the aldehyde group at 1670 and 2847 and/or 2750 cm^{-1} were missing in polymer spectra that also support the effective imine linkage of salicylaldehyde diol with the CH backbone. Absorption band at 2095 cm^{-1} (C-H stretching vibration of the benzene ring) and bands at roughly 1449 and 1486 cm^{-1} (benzene skeleton vibration) emerged with increasing of salicylaldehyde diol content. Furthermore, the band appeared at 1243 and 751 cm^{-1} showing the phenyl ether peak and ortho substituted of benzene ring of salicylaldehyde diol. The additional new peaks in the biopolymer films spectra are also described by the Schiff base condensation when compared to the CH spectrum.

Scanning Electron Microscopy Analysis

SEM images were used to examine the surface morphologies of CHSD films (Figure 3). CHSD films showed a rough and heterogeneous surface. The reason for the rough surface of CHSD films should be attributed to the ratio of SD groups to give the heterogeneity to the biopolymer structure. The CHSD1 and CHSD2 films showed a less rough surface than CHSD3 due to the higher grafting ratio of the SD group. The SD linker group ratio influences differences in appearance on the CHSD1-3 samples, which

are most likely caused by hydrogen bonding. This result is supported by a previous report that a flaky nature with a smooth surface of prepared films was attributed to the stronger hydrogen bond interaction when compared with CH (21).

Thermal Performance of CHSDs

Thermal degradation and transition behaviors of films were studied by DSC technique. Figure 4 shows DSC curves for dried CHSD1, CHSD2, and CHSD3 samples. There is a common endotherm appearing at around 100 °C corresponds to a weight loss process, which it is reasonable to assume a represented loss of water, while the exotherm at about 300 °C gives the temperature of decomposition of CH. These thermograms indicate that the samples were not dried completely and there was still some water in the structure. It is known that CH polysaccharide has a disordered structure and a strong affinity for water, allowing it to be quickly hydrated into solid form (22).

XRD Patterns of CHSD

A valuable insight on the structure of chitosan films can be seen from X-ray diffraction (XRD) patterns (Figure 5). CH is a semi-crystalline form with two main peaks at 2θ=14.50° and 20° (21), indicating inter- and intra-molecular hydrogen bonds in the presence of free amino groups. Additionally, biopolymer film patterns show that the strong peak appeared at 14.50° while the peak near 20° disappeared when compared with CH. This demonstrated the amorphous structure of CHSD films. Many other researchers have noticed that the conjugation of SD could destroy chitosan's semi-crystalline structure(23)(24). The covalent connections between CH and SD dramatically decreased hydrogen bonds in CH and inhibited the molecular mobility of CH chains, resulting in the creation of an amorphous state in CHSDs (23). The CHSDs had broader and weaker peaks, indicating that the addition of SD to CH resulted in a significant decrease in the crystallinity of the final products. This is attributed to chitosan's intermolecular H-bonding being damaged during the grafting step. The appeared peaks related to imine groups indicate that amino groups have been converted to imine groups (25). XRD patterns of CHSDs analyses were carried out on CH powder, and the CH/SD ratio was 1/1, 1/0.8, and 1/0.6 for CHSD3, CHSD2, and CHSD1, respectively.

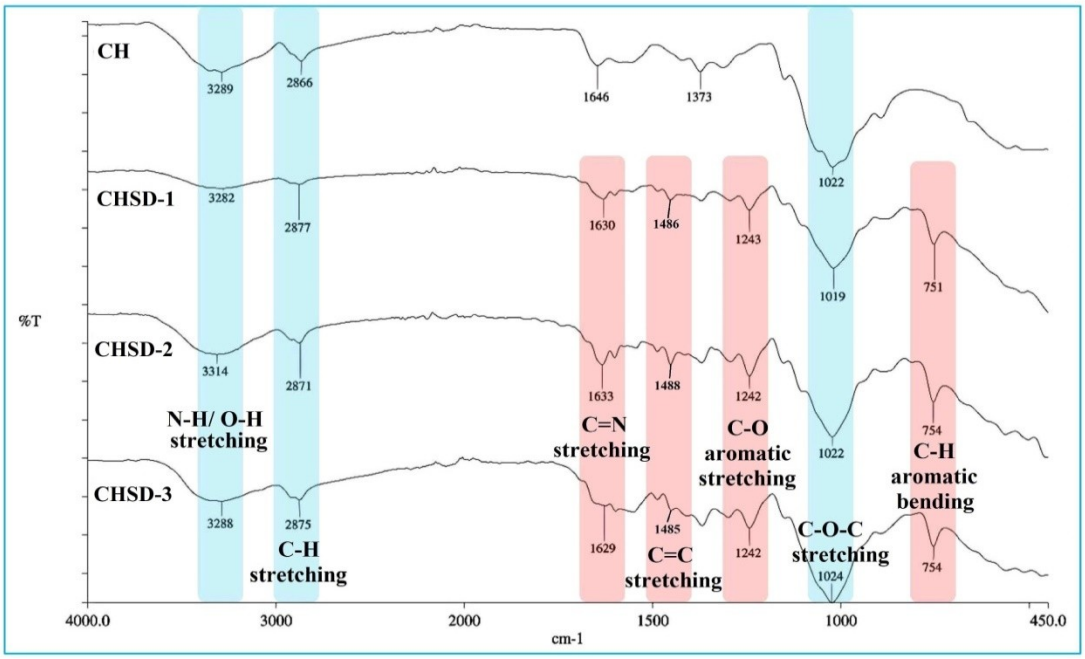


Figure 2: IR spectra of CH and CHSD1-3.

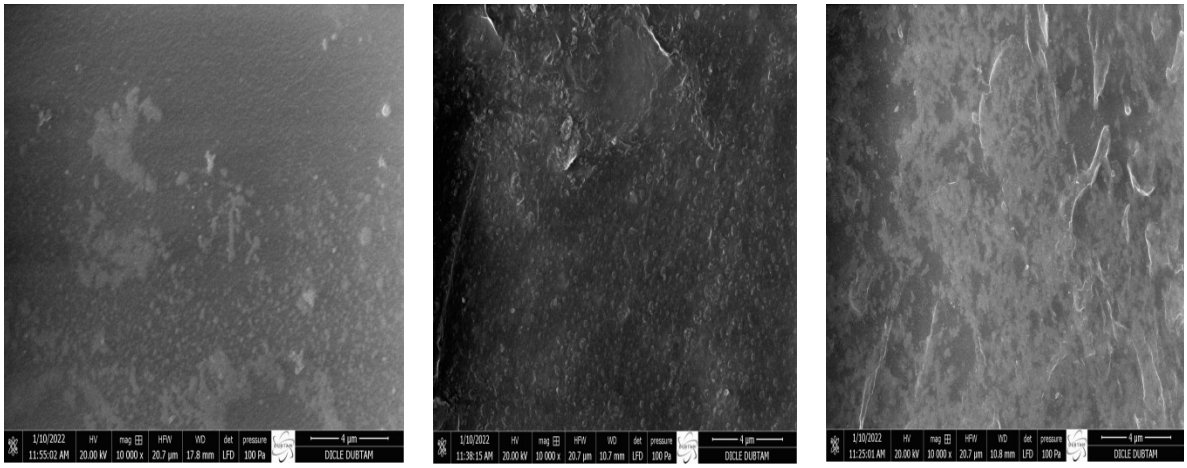


Figure 3: SEM Micrographs of CHSD1-3 films.

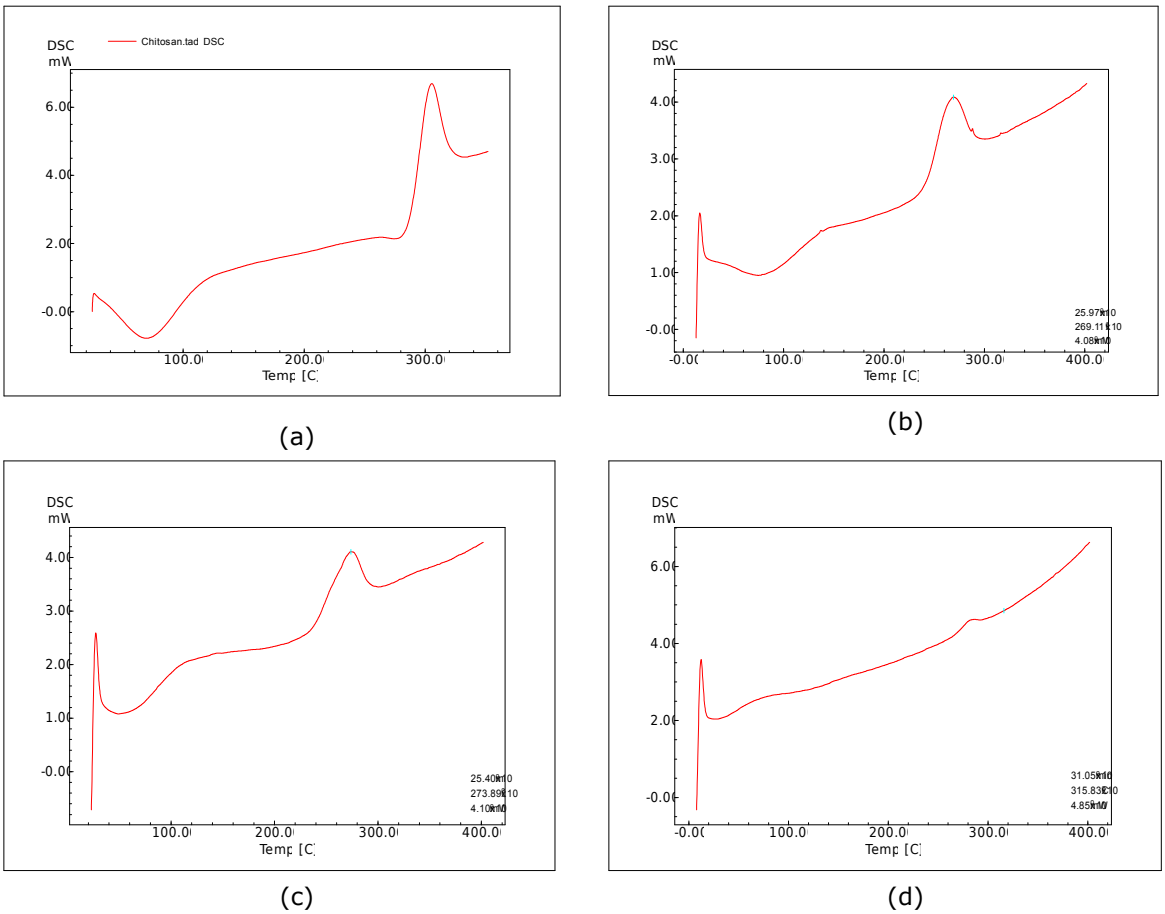


Figure 4: DSC thermogram of CHSDs (a:CH, b:CHSD1, c:CHSD2, d:CHSD3).

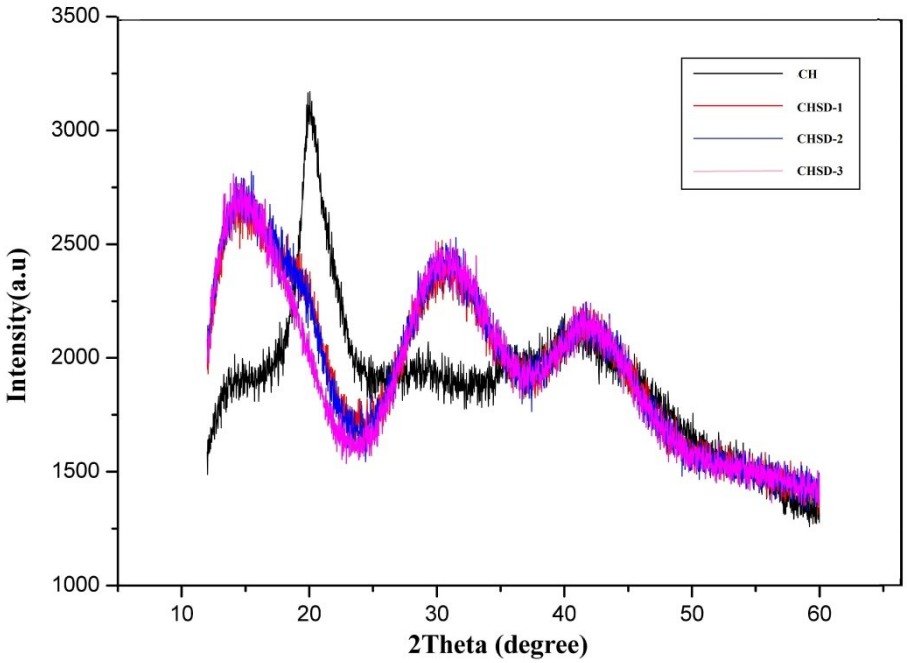


Figure 5: XRD of CHSD1-3.

Swelling Ratio

The swelling ratio is one of the main important criteria for biopolymeric films. CH is a water-retaining natural hydrophilic polymer having OH and NH_2 functional groups. The degree of swelling ratio has been determined for CHSD films in different pH conditions and is shown in Figure 6. Films submerged at pH 3 have a greater water uptake rate than the upper pH values. CHSD1 and 2 have more water uptake than CHSD3 due to the lower SD contents, which have low electrolytic media at pH 3. However, at higher pHs, all CHSD films exhibit approximately the same water uptake capacity. Primary NH_2 groups in the polymer backbone protonated into ammonium form at pH below 6.5, causing better swelling capacity. This might be due to the increased hydrolysis of imine bonds at pH 3, which allows the main NH_2 groups of CH to retain water molecules again. As a result, the deacetylation degree of CH and acidity of iminium ions effect the water solubility and swelling ratio of films (26,27). Thus, SD linked CHSD films with low water uptake make them good materials for many biological purposes.

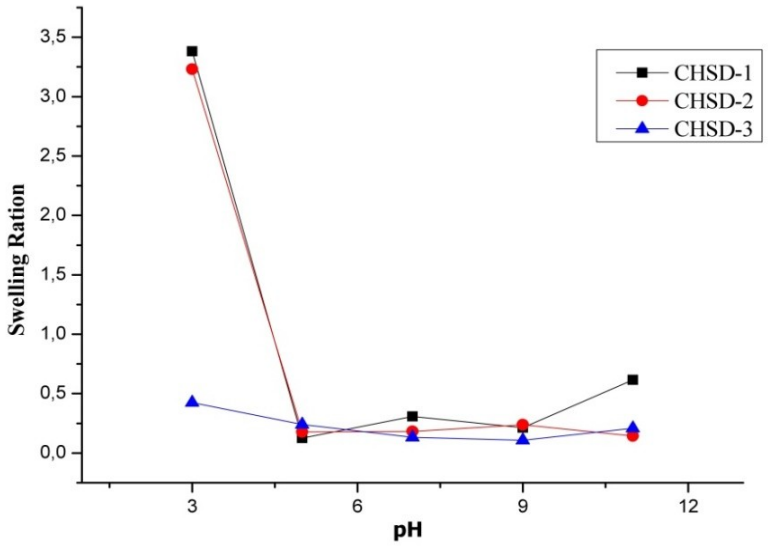


Figure 6: Effect of pH on the degree of swelling of the CHDSs.

Water Solubility and Thickness

The water solubility and thickness of biopolymer films are shown in Table 1. Film thickness and water solubility increased significantly with increasing SD concentrations. The interactions between OH groups and CH (including hydrogen bonding and hydrophobic force) increased, resulting in tighter OH group binding to CH. Due to the presence of OH groups in the molecular structures, OH groups may operate as a bridge, interacting with more than one CH molecule. The decreased distance between CH molecules, the film structure became more compact, raising thickness and water solubility (28). As a result, the thickness and water solubility of films order is CHSD3 > CHSD2 > CHSD1.

Table 1: Thickness and water solubility of films.

Samples	Thickness (µm)	Water Solubility (%)
CHSD1	84 ± 10	9.09 ± 1.8
CHSD2	88 ± 10	9.77 ± 1.8
CHSD3	95 ± 10	10.6 ± 1.8

CONCLUSION

In conclusion, we have reported the synthesis, characterization, and physicochemical properties of chitosan-based films formed by dynamic imine linkage of amphiphilic salicylaldehydediol and chitosan. The reaction takes place with high conversation and mechanically resistant thickness films without using any plasticizer. The linker group concentrations affect somewhat difference physicochemical features of the biopolymer films. All of them shown low swelling, water solubility and properly thickness values. Based on the above-mentioned features, the new chitosan-based films may be utilized for a wide range of biomedical applications, including tissue engineering, wound healing, antimicrobial, and coating applications.

DECLARATION OF COMPETING INTEREST

The authors note that they have no known competing financial interests or personal ties that might have influenced the research presented in this study.

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