SAKARYA ÜNİVERSİTESİ
FEN BİLİMLERİ ENSTİTÜSÜ
DERGİSİ

Sakarya University Journal of Science
SAUJS

e-ISSN 2147-835X Founded 1997 Period Bimonthly Publisher Sakarya University
http://www.saujs.sakarya.edu.tr/en/

Title: Preparation and Characterization of Biocompatible Membranes Based on TiO2 Nanoparticul

Authors: Gülşen TAŞKIN ÇAKICI

Recieved: 2021-07-13 00:00:00

Accepted: 2021-11-01 00:00:00

Article Type: Research Article

Volume: 25
Issue: 6
Month: December
Year: 2021
Pages: 1376-1385

How to cite
Gülşen TAŞKIN ÇAKICI; (2021), Preparation and Characterization of Biocompatible Membranes Based on TiO2 Nanoparticul . Sakarya University Journal of Science, 25(6), 1376-1385, DOI: https://doi.org/10.16984/saufenbilder.971191
Access link
http://www.saujs.sakarya.edu.tr/tr/pub/issue/66341/971191

Sakarya University Journal of Science 25(6), 1376-1385, 2021

Preparation and Characterization of Biocompatible Membranes Based on TiO$_2$ Nanoparticul

Gülşen TAŞKIN ÇAKICI*[1]

Abstract

In this study, biocompatible composite membranes of sodium alginate/hydroxypropyl methylcellulose (NaAlg/HPMC) based on nano-titanium dioxide (n-TiO$_2$) were prepared. Regarding the preparation processes of these membranes, the amount of citric acid [5%, 15%, 30% (w/w)] added to the NaAlg/HPMC blend, the crosslinker type (glutaraldehyde, acetone/water with glutaraldehyde, CaCl$_2$), and the amount of n-TiO$_2$ [5%, 15%, 20% (w/w)] were studied and optimum conditions were determined. When the equilibrium swelling values were examined, it was observed that the one with the least swelling was the CaCl$_2$ crosslinked membrane. Fourier Transform Infrared (FTIR) Spectroscopy, Differential Scanning Calorimetry (DSC), and Scanning Electron Microscopy (SEM) were used to characterize the modified crosslinked membranes. The FTIR analysis results showed the formation of hydrogen bonds between the hydroxyl groups of the HPMC and NaAlg polymer chains. The DSC analysis showed the existence of single glass transition temperature (Tg) which indicated the compatibility and physical interaction between the NaAlg and HPMC polymer chains for NaAlg / HPMC mixtures.

Keywords: sodium alginate, hydroxypropylmethylcellulose, nanoparticle TiO$_2$, nanocomposite membrane

1. INTRODUCTION

Today, biodegradable polymers are used especially in shopping bags, food packaging products, agricultural films, and medical instruments. The area, tension, and morphology of the surface of a material are extremely important in terms of biodegradation and colonization of microorganisms on the polymer surface [1]. Different structures can be created using natural-built reinforcement elements based on lignocellulose (starch, wheat stalks, rice halves, cellulose fibers) to meet specific criteria for polymers, to improve mechanical properties, and to cut prices [2]. In general, blend mixtures, which are prepared using the molecular hydrogen bonds formed by two or more polymers, are used in this regard [3]. Petroleum derivatives-polymers are dominantly used in the production of large quantities of plastics worldwide. Because these plastics are not biodegradable, they cause serious environmental problems such as soil poisoning, toxic gases emitted during incineration in landfills. Today, the increase in the use of petroleum-derivative synthetic polymers such as polyethylene (PE), polypropylene (PP),

---

* Corresponding author: gtaskin@cumhuriyet.edu.tr

[1] Sivas Cumhuriyet University, Yıldızeli Vocational School, Chemistry and Processing Technologies
ORCID: https://orcid.org/0000-0001-7564-9777

polystyrene (PS), which are not biodegradable, causes environmental pollution. Therefore, the importance of using biodegradable polymers is increasing day by day.

NaAlg, a biocompatible polymer with good film-forming ability, is used in biomedical applications such as drug release, cell encapsulation systems, tissue and organ regeneration [4-7]. HPMC, a hydrophilic and biocompatible polymer, is widely used in many fields such as drug release, building materials, adhesives, cosmetics, agriculture, and textile [8]. It is a potential polymer used in biomedical applications thanks to its excellent bioavailability and very low toxicity. In the literature, NaAlg and HPMC are generally available in the form of hydrogels, tablets, and matrix systems. Mujtaba and Kohli [9] prepared matrix tablets based on HPMC and NaAlg and examined the release of cefpodoxime. Okeke and Boateng [10] examined the development of tablets and films prepared from HPMC and NaAlg as a mucosadive system on the buccal mucosa for nicotine treatment. Yadava et al. [11] analyzed in vitro diclofenac sodium with gel beads prepared with NaAlg/HPMC/liquid paraffin.

Besides the advantages of biocompatible polymers, they also have some disadvantages such as low mechanical and thermal properties. Recently, polymer nanocomposite technology is used to eliminate these disadvantages of biocompatible polymers [12]. For this purpose, biocompatible nanocomposite polymers are prepared using nanoparticles such as organic and inorganic nanoclay, silicate, TiO_2, and graphene [13]. Kim et al. reported that the mechanical and thermal properties of biodegradable nanocomposite polymers were improved by using graphene nanoparticles [14]. Yun et al. used Chitosan, PVA, and TiO_2 nanoparticles to prepare a nanocomposite film and examined their effects on mechanical and thermal properties [13]. In their study, Işık et al. entrapped commercially obtained ZnO and TiO_2 nanoparticles in calcium alginate beads and carried out adsorption and photochemical experiments to decolorize Reactive Red 180 [15]. Thomas et al. studied the photocatalytic performance of the nanocomposites they synthesized in Sr^{2+} ion crosslinked alginate/carboxymethyl cellulose gels using TiO_2 and graphene nanoparticles [16]. TiO_2 is a nanomaterial of great interest for reasons such as lower costs, high photocatalytic performance, high chemical stability, non-toxicity, and biocompatibility [17-19]. Various polymer/ TiO_2 nanocomposite structures are also available in the literature [20,21].

Chemical cross-linking in the preparation of polymeric materials can affect some properties of polymeric materials such as swelling, drug release, permeability, and chemical stability. Different cross-linking agents are needed to understand the interactions between membrane material and cross-linking agents. For example, glutaraldehyde, epichlorohydrin, Ca^{+2} ions, citric acid, sodium benzoate, boric acid are used as cross-linking agent in typical cross-linking method [22]. The cross-linking improves performance and resistance of biopolymer films.

In this study, the nanocomposite membranes produced from NaAlg and HPMC biocompatible polymers were prepared using n-TiO_2 nanoparticles. Membranes with high mechanical strength have been prepared by using various types of crosslinkers. Depending on their morphological properties, biocompatible membranes have been obtained that can be an alternative in medicine and drug release studies. The hydrophilicity and water absorption tendencies of the membranes were determined by swelling studies. The prepared membranes were characterized by Fourier Transform Infrared (FTIR) Spectroscopy, Differential Scanning Calorimetry (DSC), and Scanning Electron Microscopy (SEM).

2. EXPERIMENTAL

2.1. Materials

Sodium alginate (NaAlg), glutaraldehyde (GA), hydroxypropyl methylcellulose (HPMC), and titanium di oxide (TiO_2) (<100nm particle size) were purchased from Sigma-Aldrich (Germany). Calcium chloride ($CaCl_2$) and citric acid (CA) were all supplied from Merck (Germany).

Hydrochloric acid (HCl) and acetone were provided by Merck (Germany).

2.2. Membrane Formation

Prepared by casting method, NaAlg-HPMC and NaAlg-HPMC -TiO_2 composite membranes were dried at 40 °C for 24 hours. For crosslinked process, membranes were immersed in the crosslinking solution for 24 h.

2.3. Techniques Used in The Characterization of Membranes

2.3.1. FTIR Analysis of Membranes

The prepared NaAlg, HPMC, NaAlg/HPMC/CA-30, and NaAlg/HPMC/CA-30/TiO_2-20 membranes were characterized by FTIR spectroscopy. Measurements were performed using a spectrophotometer (Bruker Mode: Tensor II) with potassium chloride pellets.

2.3.2. DSC Analysis of Membranes

DSC analysis of the prepared membranes was performed by DSC Q2000 V24.11 Build 124.

2.3.3. Scanning Electron Microscope (SEM)

For SEM analysis, the dried crosslinked membranes were sputtered with gold in vacuum and then observed under a microscope (TESCAN MIRA3 XMU).

2.4. Determination of Swelling Percentages of Prepared Membranes

The swelling values in water were examined to determine the water absorption tendencies of the crosslinked membranes. The membranes were immersed in water for 24 hours at room temperature. The residual liquid was removed from the swollen membranes and then weighed, dried in an oven and weighed again. Swelling degree percentages (SD%) of the membranes were calculated using Equation (1).

$$SD\%=\frac{Ww-Wd}{Wd}\ x100 \qquad (1)$$

where, W_w and W_d are the wet and dry masses of the membranes, respectively.

3. RESULTS AND DISCUSSION

3.1. Optimum Conditions for The Preparation of Membranes

Prepared membranes from a blend of nanoparticle added HPMC and NaAlg polymers and the effect of crosslinker type on the membrane properties have not been tested before this. Table 1 summarizes some the work done so far.

Table 1 Studies of NaAlg, HPMC and TiO_2 in the literature

Formulation	**Polymer**	**Crosslinking**	**Purpose**	**Ref.**
Composite hydrogel	NaAlg-HPMC	Ca^{+2} ions	Drug release	[23]
Emulsified gel beads	Sodium alginate/ HPMC/ liquid paraffin	Ca^{+2} and Zn^{+2} ions	Drug release	[11]
In situ gelling	NaAlg-HPMC	Ca^{+2} ions	Ophthalmic delivery system	[24]
Matrix tablet	NaAlg-HPMC-microcrystalline cellulose	magnesium stearate	Drug release	[25]
Hydrogel beads	NaAlg-HPMC	Ca^{+2} ions	Drug release	[7]
Films and wafers	NaAlg-HPMC	-	The buccal delivery nicotine.	[10]
Film	HPMC-TiO_2-bovine bone collagen	-	Active packaging in the food industry	[26]
Hydrogel	NaAlg-Pt/TiO_2	Ca^{+2} ions	Photodegradation activity	[27]
Membrane	NaAlg-TiO_2	water/acetone (30:70) 2.5 ml GA, 2.5 ml HCl	Pervaporation	[28]

In this study, HPMC and NaAlg blend aqueous solutions were first prepared in 1:1(w/w) ratio with citric acid (CA). Different amounts of CA (5, 15, and 30 mass % on the weight of HPMC) were added in the polymer blend solution. These blend solutions were designated as NaAlg/HPMC/CA-5; NaAlg/HPMC/CA-15; and NaAlg/HPMC/CA-30, respectively. The CA added to the polymer solution was used to facilitate crosslinking of HPMC [29]. The possible cross-linking mechanism was given in Figure 1. Predetermined amount of blend solution was cast onto glass plates and left for drying at 40 °C for 24 hours (Figure 2). The crosslinked membranes were prepared by immersing the dried membranes in crosslinking solution for 24 h. Then finally they were washed with distilled water and dried.

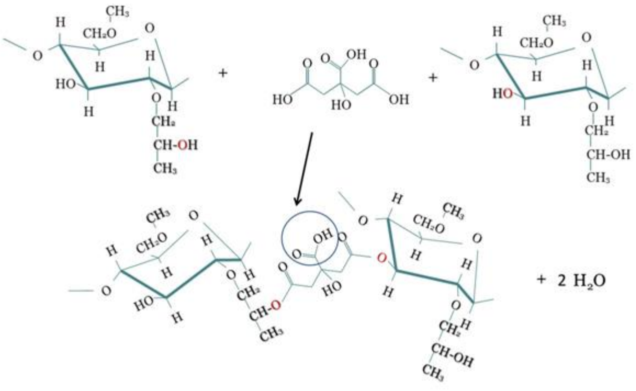

Figure 1 Crosslinking of HPMC with citric acid

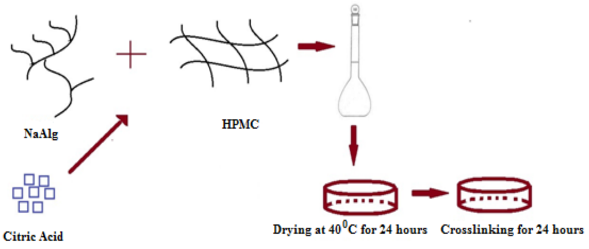

Figure 2 Preparation of NaAlg and HPMC blend solution and membranes

Secondly, nanocomposite solutions were prepared by adding n-TiO_2 (5,15 and 20 mass %) in NaAlg/HPMC blend solutions including citric acid (30 mass %). These solutions were coded NaAlg/HPMC/CA-30/TiO_2-5, NaAlg/ HPMC/ CA-30/ TiO_2-15, and NaAlg/HPMC/CA-30/TiO_2-20, respectively. Predetermined amount of nanocomposite blend solution was cast onto glass plates and left for drying at 40 ºC for 24 hours (Figure 3). The crosslinked nanocomposite membranes were prepared by immersing the dried membranes in crosslinking solution for 24 h. Then finally they were washed with distilled water and dried.

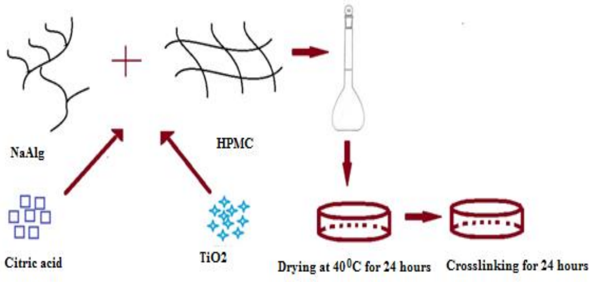

Figure 3 Preparation of NaAlg / HPMC / CA-30/TiO_2 nanocomposite polymer solution and membranes

Figure 4 NaAlg / HPMC / CA-30/ TiO_2 nanocomposite membrane

As seen in Figure 4, a homogeneous membrane was obtained. The membranes obtained were hard but not fragile and easily degradable. They were durable enough to be an alternative especially in transdermal drug systems.

3.2. Effect of Crosslinker Type on The Membrane Morphology

Water-soluble polymers are crosslinked with the help of some crosslinking agents. Crosslinked hydrophilic polymers are especially used for controlled-release preparations. Cross-linking is carried out using heat or chemical binding agents such as glutaraldehyde, formaldehyde, and diacid chloride. Heat denaturation is not suitable for heat-resistant substances. The type of cross-linking agent and the duration of cross-linking are important for the mechanical strength of polymeric materials used in drug release studies [22].

The effect of the cross-linking agent on the strength and morphology of the membranes was investigated by changing the crosslinking type ($CaCl_2$ solution, glutaraldehyde (GA) solution, and acetone/water solution containing 2.5 mL GA and 2.5 mL HCl). The possible cross-linking mechanism was given in the Figures 5 and 6.

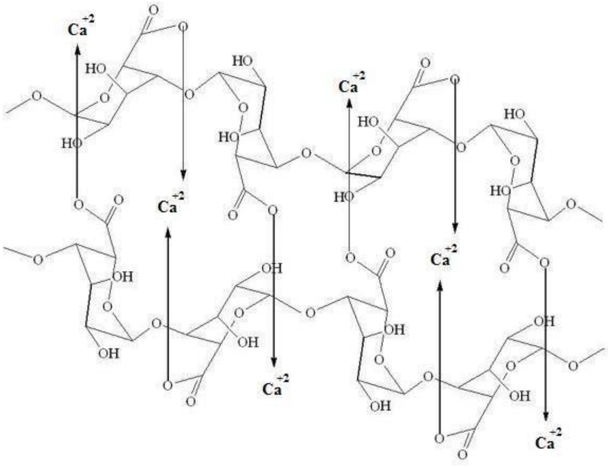

Figure 5 Crosslinking of NaAlg with $CaCl_2$ [30]

Calcium ions bind to carboxyl and hydroxyl groups in the alginate solution.

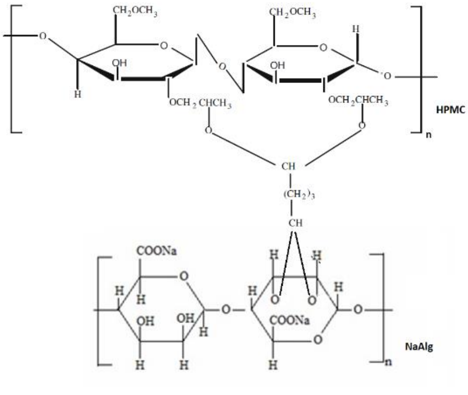

Figure 6 Crosslinking of NaAlg/HPMC blend with GA [31,32]

3.3. Membrane Characterization

3.3.1. FTIR Studies

Figure 7 showed the FTIR spectra of the NaAlg, HPMC, NaAlg/HPMC/CA-30, and NaAlg/HPMC/ CA-30/TiO_2-20 membranes, which were uncrosslinked by $CaCl_2$, GA, and acetone/water solution.

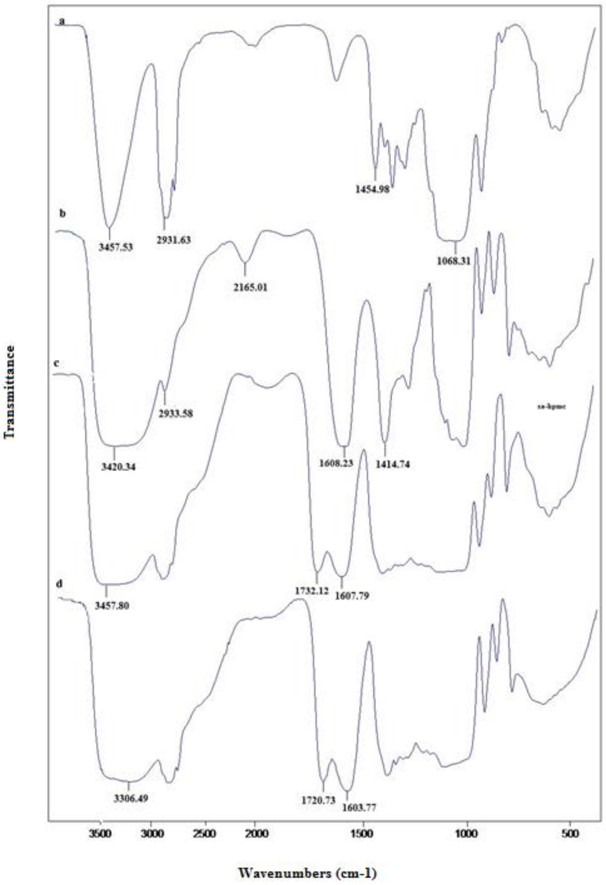

Figure 7 FTIR spectra of membranes [(a) HPMC (b) NaAlg (c) NaAlg/HPMC/CA-30 (d) NaAlg/HPMC/ CA-30/TiO_2-20]

The spectrum of the HPMC membrane (Figure 7a) showed peaks at around 3457.53 cm^{-1} wide band –OH stretching, 2931.63 cm^{-1} band –CH stretching, 1068.31 cm^{-1} band –CO stretching, and 1456 cm^{-1} band CH_3 asymmetric bending vibration [33]. The spectrum of NaAlg (Fig.7b) showed peaks at around 2933.58, 1608.23, 1414.74 and 3420.34 cm^{-1} indicating the stretching vibrations of aliphatic C–H, COO− (asymmetric), COO− (symmetric), and -OH, respectively [34]. The spectrum of NaAlg/HPMC-30 (Fig.7d) showed peaks at around 3457.80, 1607.79 and 1413.04 cm^{-1} indicating the stretching vibrations of -OH, COO− (asymmetric), COO− (symmetric), respectively. The change in these wave values indicates that the intermolecular hydrogen bonds in NaAlg and HPMC blend are formed [33,34]. Furthermore, the presence stretching of carbonyl in the 1723.12cm^{-1} band (C=O) is thought to result from the esterification of hydroxyl groups of HPMC with carboxylic acid groups of citric acids [35]. There is a strong shift in -OH stresses with the addition of TiO_2. This can be attributed to the occurring of hydrogen bond between the n-TiO_2 and polymer molecules [16].

3.3.2. DSC Studies

DSC results of uncrosslinked membranes using $CaCl_2$, GA, and acetone/water solution were given in Figure 8. HPMC showed a wider endothermic peak due to its more amorphous structure than NaAlg. In the NaAlg/HPMC/CA-30 blend, the expansion of the endothermic peak can be attributed to the polymers' having a different degree of crystallization, as well as the polymer –polymer interaction.

The most important factor that determines whether a polymer will crystallize is its geometric structure or chain configuration. NaAlg contains at least three different polymer segments (poly(b-D-mannopyranosyluro-nate), poly(a-L-guluopyranosyluronate), and segments with alternative sugar units. Due to these segment shapes, it has very a weak and small melting peak at 201.15 ºC. In the NaAlg/HPMC blend, the decrease in this melting peak can be attributed to the rigid molecular chain of NaAlg, which affects the overall chain mobility in the blend and crystal growth rate [34].

The reason why a single Tg was observed in the Figure 8 (c and d) may be due to the miscibility of NaAlg and HPMC with TiO_2.

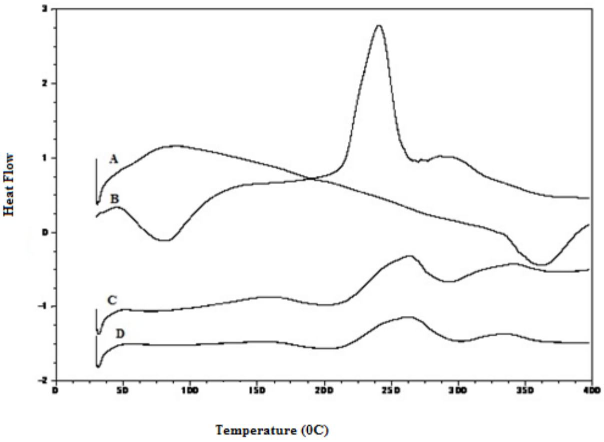

Figure 8 DSC results of membranes [(A) HPMC, (B) NaAlg, (C) NaAlg/HPMC/CA-30, (D) NaAlg/HPMC/CA-30/TiO_2-20]

3.3.3. SEM Studies

In order to investigate the surface morphology of the crosslinked NaAlg/HPMC/CA-30 and NaAlg/HPMC/ CA-30/TiO_2-20 membranes, SEM micrographs were taken and given in the Figures 9 and 10, respectively. Significant morphological differences were observed in SEM images of the membranes depending on the crosslinker used. The surface of the membranes crosslinked with $CaCl_2$ was rough and spongy, while those crosslinked with GA and acetone/water solution had a non-porous and smoother structure. This morphological difference can be attributed to the tighter crosslinking of $CaCl_2$ (crosslinker) membranes.

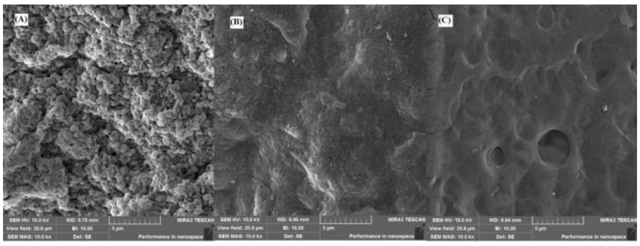

Figure 9 SEM micrographs of NaAlg/HPMC/CA-30 membranes crosslinked with (a) $CaCl_2$, (b) GA, and (c) acetone/water solution

The morphology of NaAlg/HPMC/CA-30 membranes changed depending on the amount of TiO_2 present in the polymer matrix. As can be seen in the images, there are many aggregates or particles dispersed on the top surface, showing that TiO_2 particles tend to form aggregates and are dispersed into the polymer blend matrix [36]. In Figure 10, the aggregation of n-TiO_2 particles was attributed to the tendency of nanoparticles to form aggregates due to their high surface energy [37].

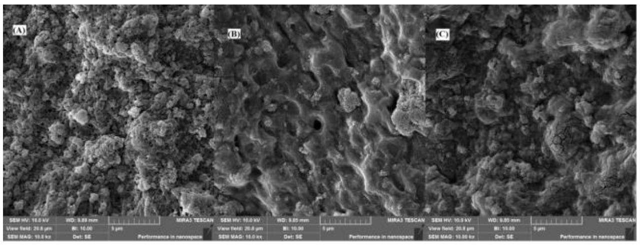

Figure 10 SEM micrographs of NaAlg/HPMC/CA-30/TiO_2-20 membranes crosslinked with (a) $CaCl_2$, (b) GA, and (c) acetone/water solution

3.3.4. Swelling Measurements

The results of swelling experiments for crosslinked NaAlg/HPMC membranes were shown in the Tables 2 and 3. $CaCl_2$ solution, glutaraldehyde (GA) solution, and acetone/water solution containing 2.5 mL GA and 2.5 mL HCl were used as crosslinker. Swelling rates were calculated by averaging at least 5 trials.

Table 2 shows that the membranes crosslinked with $CaCl_2$ have fewer swelling percentages than the membranes crosslinked with other solutions. This can be attributed to the increase in crosslink density and the formation of a more frequent network structure in the membranes. High cross-linking causes a low swelling percentage [38].

Table 2 Swelling percentages of NaAlg/HPMC/ CA membranes

MEMBRANE	$CaCl_2$	Acetone/Water	GA
NaAlg/HPMC/CA-5	210.5	391.8	401.7
NaAlg/HPMC/CA -15	230 .0	239.1	342.3
NaAlg/HPMC/CA -30	171.1	415.5	458.9

The addition of TiO_2 to the polymer matrix not only increased the interaction between hydroxyl groups on the polymer chains, but also reduced the hydrogen bonding effect between the polymer chains. Therefore, the decrease in SD is due to the good dispersion of TiO_2 polymers.

Table 3 Swelling percentages of NaAlg/HPMC/ CA-30/ TiO_2 membranes

Membrane	$CaCl_2$	Acetone/Water	GA
NaAlg/HPMC/CA-30/ TiO_2-5	208.1	345.9	387.8
NaAlg/HPMC/ CA-30/ TiO_2-15	202.5	227.7	334.6
NaAlg/HPMC/ CA-30/ TiO_2-20	139.4	403.4	448.6

4. CONCLUSION

Nanocomposite films were successfully synthesized from NaAlg, HPMC, and TiO_2 nanoparticles using the solutions of $CaCl_2$, GA, and acetone/water with GA as a crosslinker. The prepared membranes were characterized by FTIR, DSC, and SEM. The FTIR results showed strong hydrogen bonds between polymer and nanoparticle. In the DSC results, single Tg temperature showed strong polymer-polymer and polymer-TiO_2 interactions and the blend was miscible. SEM micrographs showed that TiO_2 was evenly dispersed in the NaAlg/HPMC blend. The biocompatible nanocomposite films prepared in this study have qualities that can be an alternative to other films used in the field of medicine.

Funding

This study is supported by Sivas Cumhuriyet University Scientific Research Projects Coordination Unit. Project Number: YMYO-005.

The Declaration of Conflict of Interest/Common Interest

No conflict of interest or common interest has been declared by the authors.

Authors' Contribution

The author solemly performed the computations and wrote the manuscript.

The Declaration of Ethics Committee Approval

The author declare that this document does not require an ethics committee approval or any special permission.

The Declaration of Research and Publication Ethics

The authors of the paper declare that they comply with the scientific, ethical and quotation rules of SAUJS in all processes of the article and that they do not make any falsification on the data collected. In addition, they declare that Sakarya University Journal of Science and its editorial board have no responsibility for any ethical violations that may be encountered, and that this study has not been evaluated in any academic publication environment other than Sakarya University Journal of Science.

REFERENCES

[1] E. Chiellini and R. Solaro, “Biodegradable polymeric materials,” Advanced Materials, vol. 8, pp. 305-313, 1996.

[2] M.T. Taghizadeh and N. Sabouri, “Biodegradation behaviors and water adsorption of poly(vinyl alcohol)/starch/carboxymethyl cellulose /clay nanocomposites,” International Nano Letters, vol. 51, pp. 1-8, 2013.

[3] Y Sun, Z. Shao, P. Hu, Y. Liu and T. Yu, “Hydrogen bonds in silk fibroin-poly(acrylonitrile-co-methyl acrylate) blends: FT–IR study,” Journal of Polymer Science Part B: Polymer Physics, vol. 35, pp. 1405-1414, 1997.

[4] N. Reyes, I Rivas-Ruiz, R. Domínguez-Espinosa and S. Solís, “Influence of immobilization parameters on endopolygalacturonase productivity by hybrid Aspergillus sp. HL entrapped in calcium alginate,” Biochemical Engineering Journal, vol. 32, pp. 43–48, 2006.

[5] B.L. Seal, T.C. Otero and A. Panitch, “Polymeric biomaterials for tissue and organ regeneration,” Materials Science and Engineering, vol. 34, pp. 147–230, 2001.

[6] M.R. Rasmussen, T. Snabe and L.H. Pedersen, “Numerical modelling of insulin and amyloglucosidase release from swelling Ca-alginate beads,” Journal of Controlled Release, vol. 91, pp. 395–405, 2003.

[7] A. Nochos, D. Douroumis and N. Bouropoulos, “In vitro release of bovine serum albumin from alginate/HPMC hydrogel beads,” Carbohydrate Polymer, vol. 74, pp. 451–457, 2008.

[8] N. Pekel, F. Yoshii, T. Kume and O. Güven, “Radiation crosslinking of biodegradable hydroxypropylmethylcellulose,” Carbohydrate Polymer, vol. 55, pp. 139-147, 2004.

[9] A. Mujtabaa and K. Kohli, “In vitro/in vivo evaluation of HPMC/alginate based extended-release matrix tablets of cefpodoxime proxetil,” International Journal of Biological Macromolecules, vol. 89, pp. 434–441, 2016.

[10] O.C. Okeke and J.S. Boateng, “Composite HPMC and sodium alginate based buccal formulations for nicotine replacement therapy,” International Journal of Biological Macromolecules, vol. 91 pp. 31–44, 2016.

[11] S.K. Yadava, J.S. Patil, V.J. Mokale and J.B. Naik, “Sodium alginate/HPMC/liquid paraffin emulsified (o/w) gel beads,by factorial design approach; and in vitro analysis,” Journal of Sol-Gel Science and Technology, vol.71, pp. 60–68, 2014.

[12] I. Armentano, M. Dottori, E. Fortunati, S. Mattioli and J.M. Kenny, “Biodegradable polymer matrix nanocomposites for tissue engineering: A review,” Polymer Degradation and Stability, vol. 95, pp. 2126 -2146, 2010.

[13] Y-H. Yun, J-W. Yun, S-Do Yoon and H-S. Byun, “Physical properties and photocatalytic activity of chitosan-based nanocomposites added titanium oxide nanoparticles.,” Macromolecular Research, vol. 24, pp. 51-59, 2016.

[14] H.W. Kim, A.A. Abdala and C.W. Macosko, “Graphene/ Polymer nanocomposites,” Macromolecules, vol. 43, pp. 6515-6530, 2010.

[15] Z. Isik, Z. Bilici, S. Konen Adiguzel, H.C. Yatmaz and N. Dizge, “Entrapment of TiO_2 and ZnO powders in alginate beads: Photocatalytic and reuse efficiencies for dye solutions and toxicity effect for DNA damage,” Environmental Technology & Innovation, vol. 14, pp. 100358, 2019.

[16] M. Thomas, T.S. Natarajan, M.U.D. Sheikh, M. Bano and F. Khan, “Self-organized graphene oxide and TiO_2 nanoparticles incorporated alginate/ carboxymethyl cellulose nanocomposites with efficient photocatalytic activity under direct sunlight,” Journal of Photochemistry and Photobiology A: Chemistry, vol. 346, pp. 113-125, 2017.

[17] A.L.I. Olad, S. Behboudi and A. Entezami, “Preparation, characterization and photocatalytic activity of TiO_2/ polyaniline core-shell nanocomposite,” Bulletin of Materials Science, vol. 35, pp. 801–809, 2012.

[18] J. Bouclé, S. Chyla, M.S.P. Shaffer, J.R. Durrant, D.D.C. Bradley and J. Nelson, “Hybrid solar cells from a blend of poly(3-hexylthiophene) and ligand-capped TiO_2 nanorods,” Advanced Functional Materials, vol.18, pp. 622–633, 2008.

[19] S.S. Mano, K. Kanehira, S. Sonezaki and A. Taniguchi, “Effect of polyethylene glycol modification of TiO_2 nanoparticles on cytotoxicity and gene expressions in human cell lines,” International Journal of Molecular Sciences, vol. 13, pp. 3703–3717, 2012.

[20] S. Chaudhari, T. Shaikh and P. Pandey, “Review on polymer TiO_2 nanocomposites,” International Journal of Engineering Research and Applications, vol. 3, pp. 1386–1391, 2013.

[21] S. Mallakpour and A. Barati, “Optically active poly(amide-imide)/ TiO_2 bionanocomposites containing L-isoleucine amino acid moieties: synthesis, nanostructure and properties,” Polymer-Plastics Technology and Engineering, vol. 52, pp. 997–1006, 2013.

[22] H.M.C. Azeredo and K. W. Waldron, “Crosslinking in polysaccharide and protein films and coatings for food contact-A review. Trends in,” Food Science & Technology, vol. 52, pp.109-122, 2016.

[23] Y. Hu, S. Zhang, D. Han, Z. Ding, S. Zeng and X. Xiao, “Construction and evaluation of the hydroxypropyl methyl cellulose-sodium alginate composite hydrogel system for sustained drug release,” Journal of Polymer Research, vol. 25, pp.148, 2018.

[24] Z. Liu, J.Li, S. Nie, H. Liu, P. Ding and W. Pan, “Study of an alginate/HPMC-based in situ gelling ophthalmic delivery system for gatifloxacin,” International Journal of Pharmaceutics, vol. 315, pp. 12–17, 2006.

[25] A. Mujtaba, M. Ali and K. Kohli, “Statistical optimization and characterization ofpH-independent extended-release drug delivery ofcefpodoxime proxetil using Box–Behnken design”, Chemical Engineering Research and Design, vol. 92, pp. 156–165, 2014.

[26] X. Shao, H. Sun, R. Zhou, B. Zhao, J. Shi, R. Jiang and Y. Dong, “Effect of bovine bone collagen and nano-TiO_2 on the properties of hydroxypropyl methylcellulose films,” International Journal of Biological Macromolecules, vol. 158, pp. 937–944, 2020.

[27] P. Chen and X. Zhang, "Fabrication of Pt/TiO_2 Nanocomposites in Alginate and Their Applications to the Degradation of Phenol and Methylene Blue in Aqueous Solutions," Clean, vol. 36 no. (5–6), pp. 507 – 511, 2008.

[28] K. Mallikarjuna Reddy, M. Sairam, V. Ramesh Babu, M. C. S. Subha, K. Chowdoji Rao and T. M. Aminabhavi, "Sodium alginate-TiO_2 mixed matrix membranes for pervaporation dehydration of tetrahydrofuran and isopropanol," Designed Monomers and Polymers, vol. 10, no. 4, pp. 297–309, 2007.

[29] L.M. Pedro, G.D. Bloisi and D.F.S. Petri "Hydroxypropylmethyl cellulose films crosslinked with citric acid for control release of nicotine," Cellulose, vol. 22, pp. 3907–3918, 2015.

[30] F. Kurşun, "Grafting of itaconic acid on sodium alginate and use of graft copolymer in drug delivery systems", Kırıkkale University, Kırıkkale,Turkey, (2008).

[31] E. Kondolot Solak, "Preparation and characterization of IPN microspheres for controlled delivery of naproxen," Journal of Biomaterials and Nanobiotechnology, vol. 2, pp. 445-453, 2011.

[32] B. YerriSwamy, C. Venkata Prasad, C.L.N. Reedy, B. Mallikarjuna, K. Chowdoji Rao and M.C.S. Subha, "Interpenetrating polymer network microspheres of hydroxypropyl methyl cellulose/poly (vinyl alcohol) for control release of ciprofloxacin hydrochloride," Cellulose, vol. 18, pp. 349-357, 2011.

[33] C. Ding, M. Zhang and G. Li, "Preparation and characterization of collagen/hydroxypropyl methylcellulose (HPMC) blend film," Carbohydrate Polymer, vol. 119, pp. 194-201, 2015.

[34] S.T.M. Mruthyunjaya, B. Ramaraj and Siddaramaiah, "Thermal and morphological properties of SA/HPMC blends," Journal of Applied Polymer Science, vol. 112, pp. 2235–2240, 2009.

[35] S. Kondaveeti, T.C. Damato, A.M. Carmona-Ribeiro, M.R. Sierakowski and D.F.S. Petri, "Sustainable hydroxypropyl methylcellulose /xyloglucan/gentamicin films with antimicrobial properties," Carbohydrate Polymer, vol. 165, pp. 285-293, 2017.

[36] G.T. Padma, T. Subba Rao and B.N.K. Chandra, "Preparation, characterization and dielectric properties of sodium alginate/titanium dioxide composite membranes," SN Applied Sciences, vol. 1:75, 2019.

[37] Y. Tai, J. Qian, Y. Zhang and J. Huang, "Study of surface modification of nano-SiO_2 with macromolecular coupling agent," Chemical Engineering Journal, vol. 141, pp. 354-361, 2008.

[38] K. Tomihata and Y. Ikada, "Crosslinking of hyaluronin acid with water-soluble carbodiimide," Journal of Biomedical Materials Research; 37: 243-251, 1997.