Characterization of Polyvinyl Alcohol/Gelatin Blend Hydrogel Films for Biomedical Applications

S. M. Pawde, Kalim Deshmukh

Department of Physics, Institute of Chemical Technology, University of Mumbai, Matunga, Mumbai 400019, India

Received 4 December 2007; accepted 30 March 2008
DOI 10.1002/app.28454

ABSTRACT: In the present investigation, attempt was made to prepare blend hydrogel by esterification of polyvinyl alcohol with gelatin. The blend hydrogel was further converted into films by the conventional solution-casting method. These films were characterized by FTIR, DSC, and X-ray diffraction studies. The refractive index and viscosity of different composition of the blends were measured in the solution phase of the material. The mechanical properties of the blend films were measured by tensile test. Swelling behavior of the blend hydrogel was also studied. The FTIR spectrum of the blend film indicated complete esterification of the free carboxylic group of gelatin. The DSC results indicate that the addition of gelatin with PVA changes the thermal behavior like melting temperature of PVA, which may be due to the miscibility of PVA with gelatin. The interaction of gelatin with PVA molecule changes the crystallite parameters and the degree of crystallinity. The crystallinity of the blend film was mainly due to gelatin. The comparison of viscosity indicated an increase in the segment density within the molecular coil. The results revealed the changes observed in the properties of the gel, and it enhances the gel formation at viscoelastic phase of the material. The blend film had sufficient strength and water-holding capacity. The results obtained indicated that the blend film could be used for various biomedical applications such as wound dressing and drug-delivery systems. © 2008 Wiley Periodicals, Inc. J Appl Polym Sci 109: 3431–3437, 2008

Key words: PVA; gelatin; FTIR; DSC; XRD

INTRODUCTION

Hydrogels belongs to a class of one of the most significant polymeric materials being used for various biomedical and pharmaceutical applications.[1] Hydrogels are indeed very versatile materials and have found widespread application in various technological areas such as artificial implantation,[2] swelling controlled drug delivery system,[3] artificial skin development,[4] wound dressing,[5] and humidity sensors.[6] Among various synthetic hydrophilic polymers used in the preparation of hydrogels, PVA has a prime position in biomaterials science because of its inherent nontoxicity, noncarcinogenicity, good biocompatibility, and desirable physical properties such as rubbery or elastic nature and a high degree of swelling in aqueous solutions. PVA hydrogels have gained wide biomedical applications in articular cartilage replacement[7] as a pharmaceutical release agent,[8] reconstructive (vocal cord) surgery,[9] and drug-delivery systems.[10]

PVA is a linear polymer, and it can easily be crosslinked by irradiation[11] or bifunctional group containing chemical agents such as glutaraldehyde,[12] boric acid,[13] and hexamethylene disocyanate.[14] Although PVA can be crosslinked using glutaraldehyde, great care must be taken when choosing a crosslinking agent, because it can evoke an immune response within the body. Fortunately, PVA has unique properties that allow it to be crosslinked without the use of a chemical agent. However, traditional methods of crosslinking suffer from several disadvantages, such as lack of precise control over crosslinking, toxic effect of the crosslinker, and loss in bioactivity of entrapped agent. Hydrogel based on blends of PVA with biological macromolecules are known as bioartificial polymeric materials and have been extensively evaluated as potential matrices for the release of human growth hormone and other macromolecular drugs.[15]

Gelatin widely found in nature and is the major constituent of skin, bones, and connective tissue can easily be obtained by a controlled hydrolysis of the fibrous insoluble protein, collagen.[16] The denatured type of collagen, gelatin, has been used in medicine as a plasma expander wound dressing, adhesive, and absorbent pads for surgical use.[17] Recently, gelatin has been demonstrated to exhibit activation of microphage[18,19] and high-hemostatic effect.[20] Consequently, it has been used in a wide variety of wound dressings[21,22] and as a biomaterial in tissue engineering. The presence of higher levels of pyrrolidines in gelatin results in the formation of stronger gels.[23]

Correspondence to: S. M. Pawde (smpawde@udct.org).

Journal of Applied Polymer Science, Vol. 109, 3431–3437 (2008)

The strength of the gelatin film is due to the presence of triple helixes. The greater the triple helix content, the higher the strength of the film and lower swelling property in water.[24] Considering the film-forming property, a PVA/gelatin blend film was thought to be a good candidate for artificial skin.

Thus, the selection of gelatin as another component for preparation of the blend hydrogel rest up on two reasons. First, gelatin is a connective tissue protein, well known for its non toxic, nonirritant and biodegradability properties, and good living body compatibility and therefore has been widely used in food, pharmacology, and cosmetic applications.[25] Second, the formation of specific intermolecular interaction through hydrogen bond of two or more polymers is responsible for the observed mixing behavior and properties of the blends.[26] The selection of gelatin is also justified with this point of view. Hence, in this study, attempts were made to develop blend hydrogel film by esterifying the hydroxyl group of PVA with the carboxyl group of gelatin. The experiments were designed to measure the effect of various compositions of PVA/gelatin blends on viscosity, refractive index, and effect of crystallization over gel formation. Attempts were also made to characterize the blend films by various analytical techniques such as FTIR, X-ray diffraction (XRD), differential scanning calorimetry (DSC), tensile strength, and swelling studies.

EXPERIMENTAL

Materials

PVA powder used in this work was obtained from S.D. Fine Chemicals, Mumbai, India. The molecular weight of PVA is 125,000 g/mol, and its degree of saponification is 86–89%. Gelatin used in this work was purchased from Rankem Ranbaxy Fine Chemicals, Mumbai, India, and used without further purification. Hydrochloric acid (HCL) was obtained from Merck, Mumbai, India. Double-distilled water was used throughout the study.

Gel and film preparation

The preparation of the hydrogel has been described elsewhere.[27] PVA powder with different compositions (w/w) of gelatin was dissolved in 25 mL distilled water. Concentrated HCL (0.05mL) was added, and the resulting dispersion was stirred (using an overhead stirrer at 100 ± 5 rpm) at 60°C for half an hour to carry out esterification reaction between PVA and gelatin. The thick dispersion so obtained was converted into films by conventional solution-casting method. The blend films of thickness (40–50 μm) were washed thoroughly with distilled water to remove HCL and kept in vacuum desiccators so as to use them for further study.

Characterization

The FTIR spectroscopy of PVA/gelatin blend hydrogel films was performed by ATR-FTIR Spectrophotometer (Paragon 500 Model, PerkinElmer, Beaconsfield, Buckinghamshire, UK) in the wave number range 400–4000 cm^{-1} with resolution of 4 cm^{-1}. The FTIR spectrum was taken in a transmittance mode.

The thermal analysis was performed using a (PerkinElmer DSC-7, Norwalk, CT) differential scanning calorimeter operating on UNIX platform at a heating rate of 10°C/min under nitrogen flow of 0.5 kg/cm^2 in a temperature range of 50–350°C. The weight of the sample was 8.50 mg.

The X-ray diffraction of the films were recorded using a Bruker D8 advance X-ray diffraction meter (Rigaku, Japan, Tokyo) with ''Ni-filtered'' Cu Kα radiation of wavelength $\lambda = 1.54060$ Å with a graphite monochromator. The scan was taken in the 2θ range, 5–60° with a scanning speed and step size of 1°/mm and 0.01°, respectively. The percentage crystallinity was measured by formula given elsewhere.[28]

The refractive index was measured using Abbe's Refractometer (Milton Roy Company, USA) for different compositions of PVA/gelatin blend solutions.

The viscosities of the solution were measured using capillary Oswald viscometer and Ubbelohde viscometer. The latter has the advantage that the measurement is independent of the amount of solution in the viscometer measurements, and series of concentration can easily be made by successive dilutions. These measurements were carried out at room temperature of 30°C.

The tensile strength and % elongation of PVA/gelatin blend films of thickness (40–50 μm) were tested on a LLOYD made LR10K Universal Tensile Machine (UTM). Thin film of length 4 cm and width 1 cm (ASTM D 638) was gripped between the two jaws of the tensile machine. The cross head speed was kept at 5 mm/min. The average value was determined from the set of minimum 10 repeats.

Swelling behavior

The film was immersed directly in buffers of pH 1.4 and 5.4 (prepared as per Indian Pharmacopoeia 1996, Ministry of Health and Social Welfare, New Delhi, India) at room temperature for 72 h; after that the swollen product was dried at 30°C under vacuum to a constant weight. The equilibrium percentage swelling of the product was calculated as follows:

$$\%\ \text{Swelling} = [(W_e - W_d)/W_d] \times 100 \qquad (1)$$

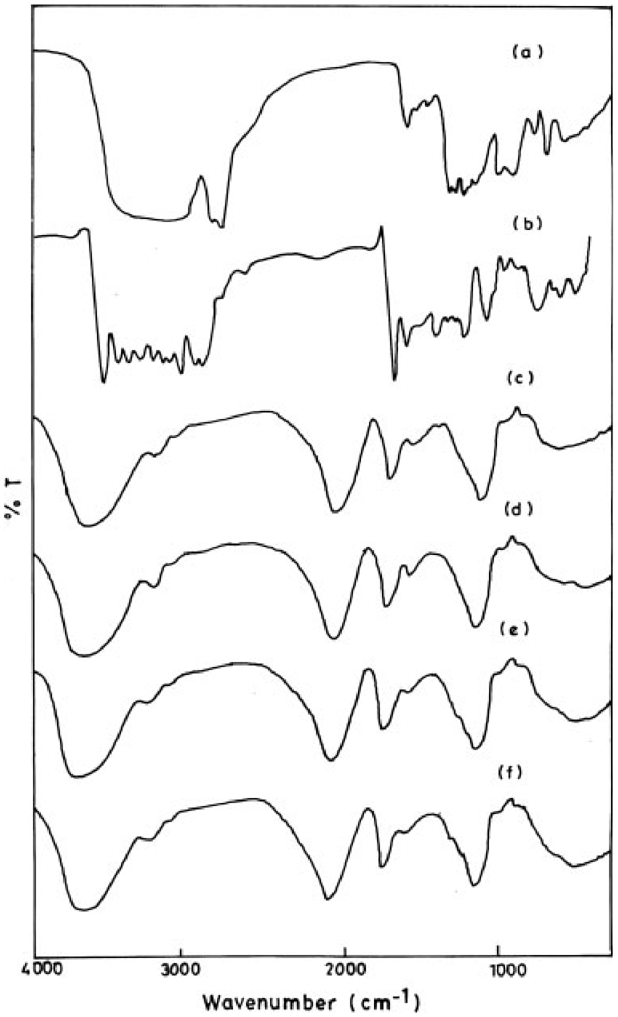

Figure 1 FTIR spectroscopy of PVA, gelatin, and PVA/gelatin blend hydrogel film. (a) 100/0, (b) 0/100, (c) 98/02, (d) 95/05, (e) 93/07, and (f) 85/15.

where W_e is the weight of the product after hydration for 48 h, and W_d is the weight of the dried product.

RESULTS AND DISCUSSION

FTIR spectroscopy

FTIR is of importance in the study of the molecular structure. The width and intensity of the spectrum bands, as well as the position of the peaks, are all sensitive to environment changes and to the conformation of macromolecules on the molecular level. Intermolecular interaction occurs when different polymers are compatible, so that the FTIR spectrum of the blend is different from those of pure polymers, which is advantageous to the study of the extent of polymer compatibility. The FTIR spectrum of PVA/gelatin blend hydrogel film is shown in Figure 1. The FTIR spectra of PVA show a broad peak around 3425 cm^{-1} indicating stretching of hydroxyl groups and peaks at 2923 cm^{-1} and 2850 cm^{-1} corresponds to C—H stretching. The C—C and C—O stretching vibration was observed at 1144 cm^{-1}. The band for C—O stretching and O—H bending was observed at 1096 cm^{-1}. The corresponding bending and wagging of CH_2 vibrations and C—H wagging are at 1438 cm^{-1} and 1378 cm^{-1}, respectively.[29,30] The FTIR spectrum of gelatin show that the region of 3000–3600 cm^{-1} and 1100–1700 cm^{-1} contain the most potentially useful information bearing on the structure of gelatin. The band identified as *N*—H stretching vibrations are considered to be hydrogen bonded.[31] The existence of two or more frequencies for the same band might be interpreted as indicating two different types of hydrogen bond. The frequency *N*—H band was observed at 3360 cm^{-1} that is a characteristic of the collagen fold.[32] The spectrum of gelatin also show the peaks at 3450 cm^{-1} and 3423 cm^{-1} due to *N*—H stretching of secondary amide, C=O stretching at 1680 cm^{-1} and 1640 cm^{-1} *N*—H bending between 1550 cm^{-1} and 1500 cm^{-1}, *N*—H out of plane wagging at 670 cm^{-1} and C—H stretching at 2922 cm^{-1} and 2850 cm^{-1}. The FTIR spectrum of the blend film shows a peak at 3398 cm^{-1} indicating the presence of a hydroxyl group with polymeric association and a secondary amide. The peaks at 1088 cm^{-1} and 1277 cm^{-1} indicated the C—O stretching of secondary alcoholic groups and ester. The spectra of the blend hydrogel film also show a peak at 1635 cm^{-1} indicating the presence of a secondary amide group. The peak of the gelatin at 1680 cm^{-1} shifted to a higher wave number indicating the formation of an esterified product (after esterification bond length is shortened, resulting in the shift of the peak to a higher wave number). Therefore, it can be concluded that all the free carboxylic groups of gelatin have been esterified.

Thermal analysis

The thermal characterization of prepared hydrogel was investigated by recording of DSC thermograms of PVA, gelatin, and blend hydrogel. Figure 2 shows the behavior of glass transition temperature (T_g) with gelatin content for various compositions of PVA/gelatin blend hydrogel. The glass transition temperature for PVA was observed at 92°C. In case of gelatin, the glass transition temperature (T_g) reported has been explained by the block copolymer model for amino acid content of gelatin.[33] The glass transition temperature of gelatin occurs at 60°C and is associated with the glass transition of α amino acid blocks in the peptide chain. The glass transition temperature of the blend hydrogel was found to be decreased as the wt % of gelatin was increased. Figure 3 shows the melting thermograms for PVA,

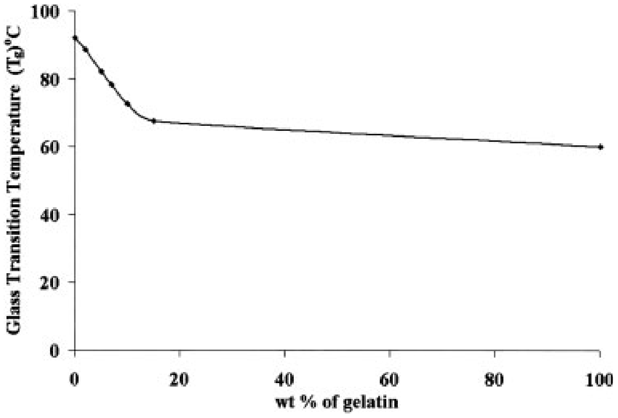

Figure 2 The dependence of glass transition temperature on gelatin content for the blend hydrogel.

gelatin, and blend hydrogel. In case of PVA, a sharp melting endotherm at 229°C was observed. The thermogram of pure gelatin shows an endothermic peak at 220°C, which marks the transition from the glass to rubber state (T_g).[34–36] It is also clear from the thermograms in Figure 3(b–d) that a melting endotherm of the blend hydrogel appears in the region 223–227°C, and this may be assigned to the melting of PVA crystals. The observed value is slightly lower than the melting temperature of pure PVA (229°C), and this may be explained by the fact that the presence of gelatin acts as an impurity and lowers the melting point of PVA.[37] The melting temperatures at high gelatin content were dependent on the gelation of gelatin. The depression of melting temperatures that can be considered to be due to the miscibility of PVA and gelatin molecules.

X-ray diffraction studies

Figure 4 presents the X-ray diffraction pattern of PVA, gelatin, and their blend hydrogel films. It shows a relatively sharp and broad peak at 2θ = 19.56° (d = 4.5347 Å) indicating the semicrystalline nature of PVA, which contains crystalline and amorphous regions. Two typical peaks on 2θ = 7.6° (d = 5.6881 Å) and 18° (d = 2.4344 Å) were observed for gelatin.[25] In case of blend hydrogel film, various sharp peaks were observed. The diffraction intensities of gelatin at 7.6° decreased drastically in the blend. The unchanged nature of a peak at 2θ = 18.96° for 2 wt % of gelatin indicates that the crystallinity is nearly the same as that of pure PVA. Table I shows 2θ values, d-spacing, and crystallinity percentages obtained by X-ray diffraction. From these data, one can notice that at small angles the first-order diffraction shifts to lower angles in comparison to pure PVA. It is obvious that the percentage crystallinity of the blend hydrogel film was found to decrease as the gelatin content is increased,[38] which can explain that intermolecular interaction destroyed the regularity of gelatin. From this, we can infer that the crystallinity of the blend film is mainly due to the gelatin rather than PVA. Therefore, it can be concluded that the good miscibility existed between PVA and gelatin molecules due to the strong interaction from the intermolecular hydrogen bonds.

Refractive index

The refractive index (RI) of a material is the factor by which electromagnetic radiation is slowed down (relative to vaccum) when it travels inside the material. Refractive index is a suitable state parameter being directly correlated to the material density. The refractive index values in polymers are around 1.3–1.6 almost comparable to silica glass. Refractive index measurements are very effective for the evaluation of extent of reaction in polymer solutions. Figure 5 shows the variation of refractive index with

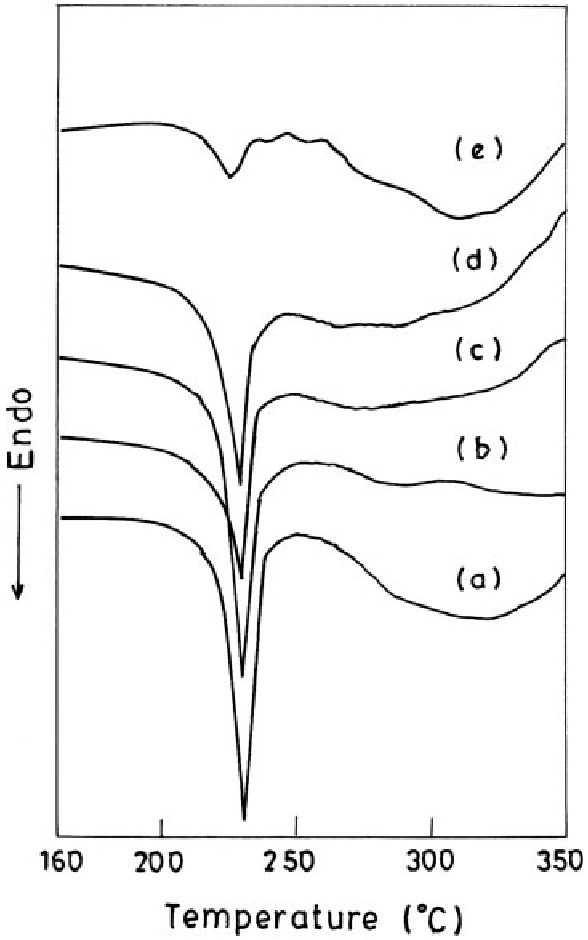

Figure 3 Melting thermograms of PVA, gelatin, and PVA/gelatin blend hydrogel. (a) 100/0, (b) 95/05, (c) 90/10, (d) 85/15, and (e) 0/100.

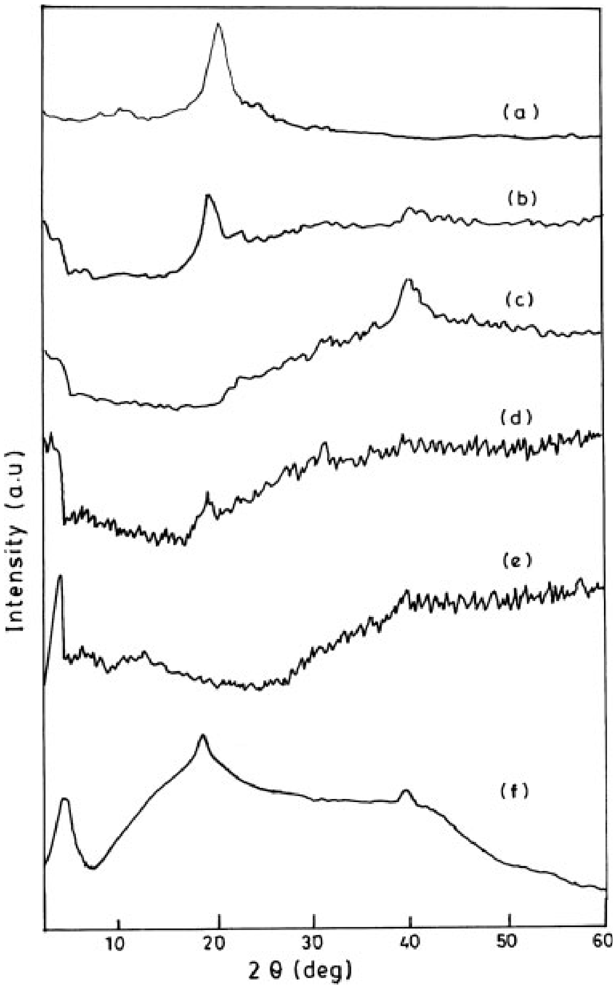

Figure 4 X-ray diffraction patterns of PVA, gelatin, and PVA/gelatin blend hydrogel films. (a) 100/0, (b) 98/02, (c) 95/05, (d) 90/10, (e) 85/15, and (f) 0/100.

gelatin content for different compositions of PVA/gelatin blend solutions. It was observed that the refractive index of PVA/gelatin blend decreases with increase in the gelatin content. The refractive index measurement can have correlation with the electrical properties of the gel. Hence, there was a need to measure the refractive index for the different % wt of the crosslinking agent. Also by fusing polymers having proper refractive index bifocal contact lens can be constructed.

Viscosity measurements

Because of the simplicity and accuracy of its measurements, viscosity has been regarded as a valuable characteristic of polymer solution since the very beginning of polymer science. The viscosity of polymer solutions is an involved function of many interacting variables, such as molar mass, structure and conformation of polymer molecules, polymer concentration, polymer solvent interaction, solvent viscosity, and shear rate. In this study, the blend solutions of PVA/gelatin were prepared in distilled water (Effux Time for Distilled Water is $t_o = 23$),[39] and different parameters of viscosity were measured. Table II shows the name, symbols, and defining equations of different viscosity parameters. The variation of different type of viscosities with gelatin content was shown in Figure 6, and it was observed that the viscosity decreases with increase in gelatin content. This indicate that some interaction has taken place among the two polymers, which results in an increase in segment density within the molecules, which, in turn, results in a smaller hydrodynamic volume and a lower intrinsic viscosity.[40]

TABLE I
X-ray Diffraction Results for Pure PVA, Gelatin, and PVA/Gelatin Blend Hydrogel Films

PVA/gelatin blends with different compositions (w/w)	2θ values	$d = (n\lambda/2\sin\theta)$ Å	% Crystallinity
100/0	19.56	4.5347	75.12
98/02	18.96	4.9406	73.34
95/05	17.21	5.1680	68.72
93/07	16.72	5.2966	63.39
90/10	16.33	5.4209	59.36
	39.48	2.2810	
85/15	16.25	5.4488	56.42
0/100	7.6	5.6881	62.56
	18	2.4344	

Mechanical properties of blend films

Because polymer materials such as films may be subjected to various kinds of stress during being used. The study of the mechanical properties is of primary importance for determining the performance of the materials. The tensile strength and % elongation at break of pure and blend hydrogel films were plotted as a function of the gelatin content are

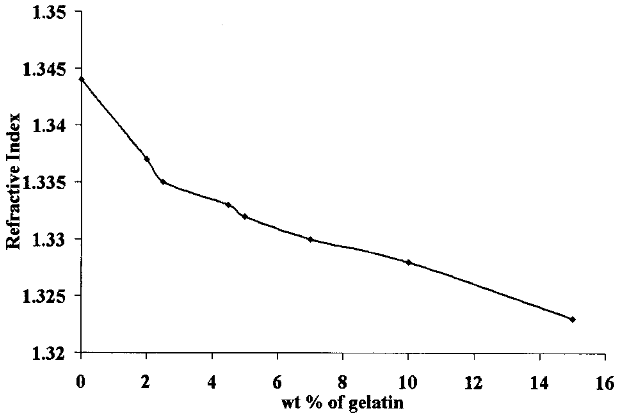

Figure 5 The dependence of refractive index on gelatin content for the blend solution.

TABLE II
Name, Symbols, and Defining Equations of Different Kind of Viscosities

Common name	Recommended name	Symbols and defining equations
Relative viscosity	Viscosity ratio	$\eta_r = \eta/\eta_0 = t/t_0$
Specific viscosity	–	$\eta_{sp} = \eta_r - 1 = (\eta - \eta_0)/\eta_0 = (t - t_0)/t_0$
Reduced viscosity	Viscosity number	$\eta_{red} = \eta_{sp}/c$

shown in Figures 7 and 8, respectively. The tensile strength of PVA film was found to be 22.31 ± 1.51 (MPa), while the strength of the gelatin film was found to be 17.51 ± 0.52 (MPa). The strength of the blend film was found to be 37.63 ± 1.51 (MPa) with increase in the gelatin content up to 15 wt %. The remarkable increase in the tensile strength of the blend films indicated the presence of intermolecular interaction between PVA and gelatin molecules. The % elongation at break of PVA film was found to be 10.96 while that of gelatin film was found to be 7.86. The % elongation at break of the blend film was found to increase with increase in the gelatin content. The strength of the film is due to the presence of triple helix, presented in the gelatin. The greater the triple helixes content higher the strength of the film. So, these films could be used for wound covering, as it can withstand some frictional stresses during day to day activities. The films are stitched around the wound surface so as to cover the wound. If there are any frictional stresses, the film absorbs the energy without breaking and thus protects the wound.[41]

Swelling behavior

Generally, the chemical structure and aggregate structure can both affect the water absorbability of polymers. Taking the chemical structure in to account, PVA/gelatin blend hydrogel can increase the water absorbability because of the hydrophilic nature of PVA and gelatin. Figure 9 shows the variation of % swelling for blend hydrogels. The results shows that the % swelling decreased with increase in the gelatin content until 2 wt %, then increases gradually up to 5 wt %, then again decreases with increase in the gelatin content until 10 wt % and suddenly increases up to 15 wt % of gelatin. As expected, the addition of gelatin to PVA resulted in higher water uptake. This result seems to explain the behavior of improving the elongation at break of the blend material as resulting from the plasticizing effect of water absorbed in the films. The water retention capacity of the blend hydrogel was around 250–260% of the dried weight, so that it can be considered as super absorbent. From the FTIR results for PVA/gelatin blend hydrogel film, it was clear that the whole carboxylic group of the gelatin has been esterified but the free amino groups are present. From this fact, it can be hypothesized that these

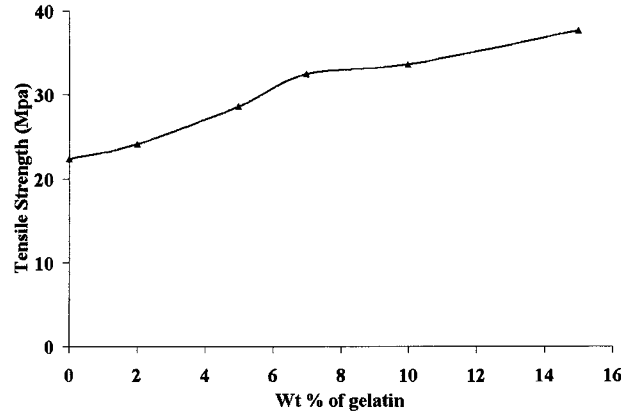

Figure 7 The dependence of tensile strength on gelatin content for the blend hydrogel film.

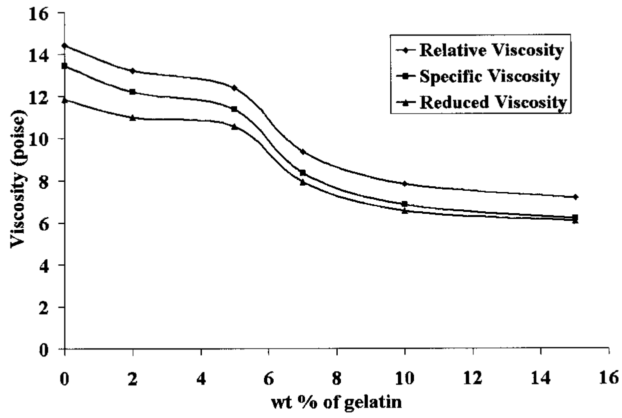

Figure 6 The dependence of viscosities on gelatin content for the blend solution.

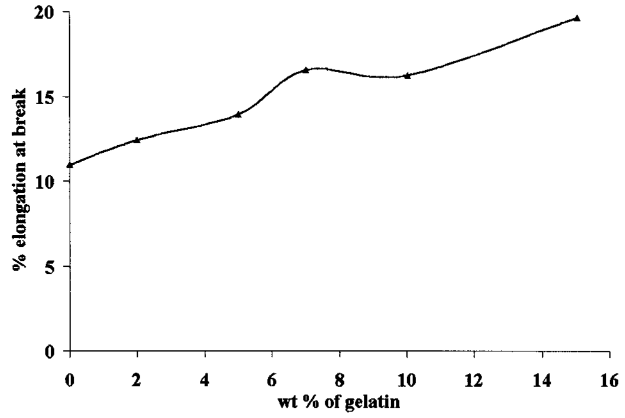

Figure 8 The dependence of % elongation at break on gelatin content for the blend hydrogel film.

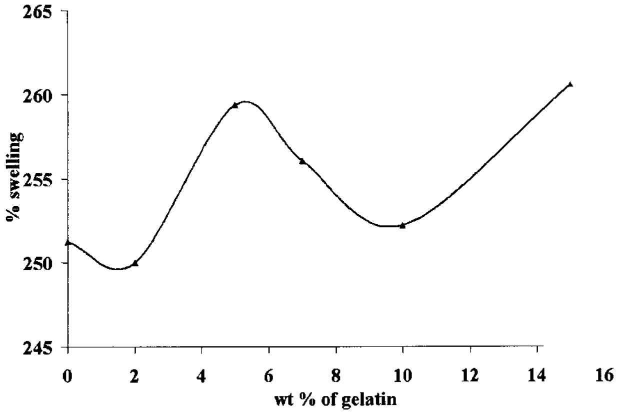

Figure 9 The dependence of % swelling on gelatin content for the blend hydrogel.

free amino groups play an important role in water uptake because of their hydrophilic nature.

CONCLUSION

The PVA/gelatin blend hydrogel films were prepared by esterification of the hydroxyl group of PVA with the carboxylic group of gelatin and characterized by various analytical techniques. The FTIR analysis indicated that the whole carboxylic group of the gelatin has been esterified but the free amino groups are present. The DSC results show depression in the glass transition temperature and melting temperature of PVA, which can be considered to be due to the miscibility of PVA and gelatin molecule. The XRD results indicate that due to interaction of gelatin with PVA chains, the structural repositioning take place, which leads to decrease in the crystallinity with increase in gelatin content. The refractive index of PVA/gelatin blend solution decreases with increase in gelatin content. The viscosity of PVA/gelatin blends also decreased with increase in the gelatin content. The tensile strength of the films revealed that the films can be used as wound covering as it can withstand some frictional stresses during day-to-day activities. Therefore, this crosslinked gel could be used as synthetic cartilage in synovial joints. The gel obtained was found to be super absorbent, hence it could be of use for various medical applications, such as drug-delivery system and moist wound dressings.

References

1. Hoffman, A. S. Adv Drug Deliv Rev 2002, 43, 3.
2. Fung, L. K.; Saltzmann, W. M. Adv Drug Deliv Rev 1997, 26, 209.
3. Ruiz, J.; Mantecon, A.; Cadiz, V. J Appl Polym Sci 2002, 85, 1644.
4. Mao, J.; Zhao, L.; De Yao, K.; Shang, Q.; Yang, G.; Cao, Y. J Biomed Mater Res 2003, 64, 301.
5. Fakirov, S.; Sarac, Z.; Anbar, T.; Boz, B.; Bahar, I.; Evstatiev, M.; Apostolov, A. A.; Mark, J. E.; Kloczkowski, A. Colloid Polym Sci 1996, 274, 334.
6. Rauen, K. L.; Smith, D. A.; Heinemann, W. R.; Sehuin, R.; Stoughton, P. Sens Actuators B 1993, 17, 61.
7. Masuda, M. In Polyvinyl Alcohol; Finch, C. A., Ed.; Wiley: New York, 1992.
8. Casone, M. G.; Barbani, N.; Maltini, S.; Lazzeri, L. Polym Int 2001, 50, 1241.
9. Laporte, R. J. Hydrophilic Coating for Medical Devices; Tehnomic Publishing: Lancaster, PA, 1997.
10. Peppas, N. A.; Mongia, N. K. Eur J Pharm Biopharm 1997, 43, 51.
11. Razzak, M. T.; Darwis, D.; Zainuddin, S. Radiat Phys Chem 2001, 62, 107.
12. Rajmires, P. A.; Milella, E. J Mater Sci Mater Med 2002, 13, 119.
13. Hennink, W. E.; Van Nostrum, C. F. Adv Drug Deliv Rev 2002, 54, 13.
14. Shafee, E. E.; Naguib, H. F. Polymer 2003, 44, 1647.
15. Cascone, M. G.; Maltinti, S. J Mater Sci Mater Med 1999, 10, 301.
16. Lihong, F.; Yumni, D.; Ronghua, H.; Qun, W.; Xiaohui, W.; Lina, Z. J Appl Polym Sci 2005, 96, 1625.
17. Young, S.; Sung, R. H.; Young, N. L.; Kang, W. S.; Moon, H. P.; Young, S. N. Biomaterials 1999, 20, 409.
18. Anderson, J. M.; Miller, K. N. Biomaterials 1984, 5, 5.
19. Tabata, Y.; Ikada, Y. J Pharm Pharmacol 1987, 39, 698.
20. Chvapil, M. J Biomater Mater Res 1982, 16, 245.
21. Neumann P. M.; Zur, B.; Ehrenreich, Y. J Biomed Mater Res 1981, 15, 9.
22. Takahashi, H.; Miyoshi, T.; Boki, K. Tokushima J Exp Med 1993, 40, 169.
23. Full, D. O.; Scott, A. Food Hydrocolloids 2003, 17, 207.
24. Bigi, A.; Panzarvolta, S.; Rubini, K.; Biomaterials 2004, 25, 5675.
25. Payne, J. A.; Mecormick, A. V.; Francis, L. F. J Appl Polym Sci 1999, 73, 553.
26. Sun, Y.; Shao, Z.; Hu, P.; Liu, Y.; Yu, T. J Polym Sci Part B: Polym Phys 1997, 35, 1405.
27. Pal, K.; Banthia, A. K.; Majumdar, D. K. Biomed Mater 2006, 1, 85.
28. Manjunath, B. R.; Venkatraman, A.; Stephan, T. J Appl Polym Sci 1973, 17, 1091.
29. Selim, M. S.; Seoudi, R.; Shabaka, A. A. Mater Lett 2005, 59, 2650.
30. Joo, S. E.; Hun, L. Y.; Chul, C. S. J Appl Polym Sci 2004, 91, 2407.
31. Lixing, D.; Jun, L.; Eisuke, Y. J Appl Polym Sci 2002, 86, 2342.
32. Gustarson, K. H. The Chemistry and Reactivity of Collagen; Academic Press: New York, 1956.
33. Gruber, E.; Soehendra, B.; Schurz, J. J Polym Sci Symp 1974, 44, 105.
34. Sarti, T.; Scandola, M. Biomaterials 1995, 16, 758.
35. Fraga, A. N.; Williams, R. J. J. Polymer 1985, 26, 113.
36. Tanaka, T.; Ohmishi, S.; Yamaura, K. Polym Int 1999, 48, 811.
37. Bajpai, A. K.; Saini, R. Polym Int 2005, 54, 1233.
38. Bhajantri, R. F.; Ravindrachary, V.; Harisha, A.; Crasta, V.; Nayak, S. P.; Poojary, B. Polymer 2006, 47, 3591.
39. Van Wazer, J. R.; Lyons, J. W.; Kim, K. Y.; Colwell, R. E. Viscosity and Flow Measurement: A Laboratory Handbook of Rheology; Wiley: New York, 1963; Chapter 1.
40. Young, R. J.; Lovell, P. A. Introduction to Polymers; Stanley Thorne: Scotland, UK, 2004; p 195.
41. Kunal, P.; Ajit, K. B.; Dipak, K. M. AAPS Pharm Sci Tech 2007, 8, E1.