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Polyvinyl Alcohol-Polyethylene Oxide-Carboxymethyl Cellulose Membranes for Drug Delivery

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ABSTRACT: The purpose of this research was to develop blends of poly(vinyl alcohol) (PVA)-poly(ethylene oxide) (PEO) and carboxymethyl cellulose (CMC) by two approaches: solvent casting and freeze-drying to develop membranes for various biomedical applications. The PVA/PEO/CMC blends in different compositions of 90/10/20, 80/20/20, 70/30/20, 60/40/20, and 50/50/20 were prepared and were coated on polyester (PET) nonwoven fabric and were subsequently freeze-dried (FD). The influence of PEO concentration on the blend membranes was investigated and characterized by X-ray diffraction (XRD), differential scanning calorimetry, and attenuated total reflectance-fourier transform infra-red (ATR–FTIR) techniques. The water vapor transmission rate (WVTR), swelling behavior, and surface morphology of the FD membranes was also investigated. It was observed that an increase of PEO concentration in blends makes the membranes more fragile. However, the coating of this blend on PET fabric helps in developing the stable membrane. Swelling of the membranes decreased with the increase in the PEO concentration. XRD showed decrease in crystallinity with increase in concentration of PEO. Morphological studies showed a highly porous structure with interconnected pores. The total porosity of the membranes was found to be in the range 89–92%. The FD membranes were found to have WVTR in the range 2000–3000 g/m^2/day. A model drug, ciprofloxacin hydrochloride was also incorporated in the matrix and drug release was studied. The antimicrobial nature of the membranes was monitored against *E. coli* by zone of inhibition method. © 2013 Wiley Periodicals, Inc. J. Appl. Polym. Sci. 129: 3728–3736, 2013

KEYWORDS: biomaterials; blends; drug delivery systems

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INTRODUCTION

Wound healing is the body's natural healing process, which involves several series of events, such as haemostasis, inflammation, granulation tissue formation, and remodeling. Modern wound dressings are designed in such a way that these will provide proper healing environment to the wound. In wound care, the focus has been shifted towards the hydrogels that can be used as wound dressings and drug delivery systems.[1,2] The ideal wound dressings should maintain moist environment for proper and quick healing. It should be easy to remove, absorb exudates, should be biocompatible, allows water vapor permeation, and exhibits antimicrobial nature. Hydrogels provide moist environment to the wound in which healing is faster than that in a dry environment.[3] Hydrogels can be prepared by several methods out of which blending process is simple, most common and effective way to prepare hydrogels with desired properties.[4,5] Several synthetic and natural polymers such as poly(vinyl alcohol) (PVA), poly(ethylene oxide) (PEO), polyvinyl pyrrolidone (PVP), and chitosan can be used to prepare hydrogels.

PVA is a well known polymer used in several biomedical applications. It is nontoxic, biocompatible, noncarcinogenic, and has high degree of swelling in aqueous solvents.[6,7] PEO, on the other hand, has interesting features for biomedical and pharmaceutical applications such as wound dressings,[8–10] drug delivery systems,[11,12] and hemodialysis membranes.[13,14] In this study, PEO is added to PVA because of its flexible nature, biocompatibility, and antiadhesion properties. CMC and PEO both separately and in combination exhibit antiadhesion properties.[15,16] Therefore, the membranes incorporating PEO and CMC can be easily removed from the wound without causing any trauma to the patients. Vigilon dressing composed of water and crosslinked PEO is nonadherent, permeable to water vapor and oxygen and promote better wound healing than other occlusive dressings.[17] LUOFUCON^{TM} medical hydrogel dressing is composed of moderately crosslinked PEO and PVA, provides moist

environment, effectively absorb exudates, semi transparent, and can be removed easily.[18] AquaMed is a leading manufacturer of PEO/PVP hydrogels, which has good adhesive properties without debriding wounds.[19] PVA and PEO hydrogels were cross-linked using electron beam irradiation and it was observed that these hydrogels caused faster healing as compared to gauze dressing and easily removed from the wound without causing any trauma to the patient.[20] PEO/PVA blend hydrogel films were evaluated for toxicity and healing effect and it has been observed that these hydrogels did not induce toxic effects on mice.[21] PEO and kappa-carrageenan (KC) hydrogel system shows better swelling behavior and gel strength and it may be used as wound dressing material.[8] Nanofibers based on poly(ethylene glycol)-*g*-chitosan blended with PEO have been fabricated by electrospinning and have potential to be used as tissue engineering scaffolds, drug carriers, and wound dressings.[9] Electrospun chitosan/PEO membranes containing silver nanoparticles were prepared and investigated for strong antimicrobial action.[10] Interpenetrating network (IPN) membranes of sodium alginate and PVA prepared by solvent casting method have been developed for transdermal delivery of the antihypertensive drug prazosin hydrochloride. These membranes were permeable to water vapor, exhibited drug release upto 24 h and were safe for skin as observed in skin irritation and histopathology test.[22] Chitosan/PVA/cloisite® 30B nanocomposite membranes were prepared by solvent casting technique and used as drug carrier for delivery systems of anticancer drug, curcumin.[23]

In earlier studies, it has been found that PVA and PEO form incompatible and immiscible blends. Therefore, CMC has been added to the blend solution as a compatibilizer, which helps in increasing miscibility between the polymers because of the formation of H-bonds and has been found to be an interesting approach to develop a compatible PVA/PEO system.[24] In the present work, solutions with varying PEO concentration were prepared and PET nonwoven fabric was used as a support layer for the freeze-dried (FD) blend membranes. Coating this composition on a fabric to develop a dressing material is a novel approach. A model drug, ciprofloxacin hydrochloride, is also incorporated into PVA/PEO/CMC blend solution and FD. This drug is a third generation fluoroquinolone and has broad spectrum of activity, low toxicity, relatively stable under heat condition, and fewer side effects.[25–27] It kills bacteria by interfering with the enzymes that cause DNA to rewind after being copied, which stops synthesis of DNA and protein.

As concluded in previous work, PVA/PEO/CMC blend membranes having 20% CMC may be taken as optimized concentration of CMC in all blend solutions for further studies.[24] The influence of PEO concentration on the air-dried (AD) and FD blend membranes with PET as support layer was studied using various characterization techniques. The FD membranes were evaluated for swelling behavior, surface morphology, and water vapor transmission rate (WVTR). With ciprofloxacin hydrochloride as the antimicrobial agent, the *in vitro* drug release behavior and the antibacterial action of the membrane against *E. coli* was also investigated.

EXPERIMENTAL

Materials

PVA (DP = 1700–1800 and molecular weight 1,15,000) and carboxymethyl cellulose (CMC) sodium salt of high viscosity were received from Loba Chemie, Mumbai, India. PEO of molecular weight 3,00,000 was supplied by Sigma Aldrich. Ciprofloxacin hydrochloride is a biochemical reagent (used as model drug) and was purchased from Central Drug House, New Delhi. Deionized water was used for all experiments. Nonwoven Polyester (PET) fabric (39.52 GSM) supplied by Uniproducts (India), New Delhi, was used as supporting base for FD samples. Deep freezer and freeze-drier −80°C supplied by Ilshin, South Korea were used for the cryogenic experiments.

Preparation of Membranes

PVA was dissolved in deionized water under constant stirring at 70°C to achieve a homogeneous solution. PVA solution was brought to room temperature and then cast on a petri dish. The drying was carried out at room temperature and the membrane was dislodged carefully and then kept for further drying in vacuum oven for 2 h at 80°C. PVA/PEO/CMC in desired proportions 90/10/20, 80/20/20, 70/30/20, 60/40/20, and 50/50/20 were dissolved in deionized water using magnetic stirrer for 8 h at 70°C. The total polymer concentration was maintained to be 5% by weight. After complete dissolution, two approaches i.e. solvent casting and freeze-drying were used to prepare blend membranes. In solvent casting, the blend solutions were cast on petri dish and dried at room temperature, similar to the procedure followed for pure PVA membrane preparation.

In freeze-drying, blend solutions were poured onto PET nonwoven fabric and the whole system was placed in deep freezer at −82°C for 24 h followed by freeze-drying at −82°C for 12 h, followed by drying in vacuum oven at 80°C for 4 h. Ciprofloxacin hydrochloride (1% of polymer weight) was dissolved, under stirring in the optimized blend solution to make it completely homogeneous and FD by the above given procedure.

Miscibility Studies

The transparency of polymer solutions having different ratios of PVA/PEO/CMC was measured by UV-Visible spectrophotometer (Perkin Elmer Lambda 35 UV-Visible Spectrophotometer). The percentage transmittance of solutions was measured in the range of 300–900 nm.

Morphology Study

The surface morphology of FD membranes was studied using STEREOSCAN 360 (Cambridge Scientific Industries), scanning electron microscope (SEM), after coating them with silver. All the samples were predried under vacuum prior to the SEM.

Attenuated Total Reflectance-Fourier Transform Infra Red Spectroscopy (ATR-FTIR)

ATR-FTIR spectroscopy of thin membranes of samples was recorded on a Perkin–Elmer spectrophotometer in the wave number range of 650–4000 cm^{-1} in transmittance mode.

Density Measurements

Density of the FD membranes was measured by taking into account the thickness of films of same size by thickness tester and by measuring the weight of the sample on an

analytical balance. The density was obtained by the following expression.[28]

$$\text{Density} = \frac{\text{weight (g)}}{\text{volume (cm}^3\text{)}} \quad (1)$$

Porosity Measurements

The porosity of the FD membranes was estimated by the following formula.[29]

$$\text{Porosity (\%)} = \left(1 - \frac{d}{d_p}\right) \times 100 \quad (2)$$

where d and d_p are the densities of the FD membrane and the AD membrane, respectively, having similar concentration of PVA/PEO/CMC.

Differential Scanning Calorimetry (DSC)

The DSC studies on the samples were carried out on a Perkin-Elmer DSC-7 system. Vacuum-dried samples were loaded, and the thermograms were run in the 50–250°C range under nitrogen atmosphere at a heating rate of 10°C/min. The melting temperature was obtained as the peak of the thermogram.

In high temperature DSC, all samples were heated from 50 to 150°C at a heating rate of 10°C/min, kept for 5 min at 150°C, cooled to 50°C at the same rate, and kept for 5 min at 50°C. Then, the samples were reheated from 50 to 350°C at 10°C/min. The first heating scan, which was carried to remove the residual water and the second scan, was carried out to see the transition.

X-Ray Diffraction (XRD)

XRD patterns of the samples were recorded in the 2θ range of 5°–40° on a Phillips X-ray diffractometer equipped with a scintillation counter. CuKα radiation (wavelength, 1.54 Å; filament current, 30 mA; voltage, 40 kV) is used for the generation of X-rays. The degree of crystallinity of samples was assessed from the XRD pattern by separating the amorphous and crystalline parts under the diffraction pattern using following expression.[30]

$$\text{Degree of crystallinity (\%)} = \frac{A_{cr}}{A_{cr} + A_{am}} \times 100 \quad (3)$$

where A_{cr} is the area under crystalline peak and A_{am} is the area under amorphous portion.

Swelling Measurements

Swelling measurements were carried out by weighing the FD samples and then immersing in phosphate buffer saline (PBS) pH 7.4. The tubes were then kept in a water bath at 37°C. The samples were removed after required period of time and blotted free of moisture by pressing gently between filter paper and weighed on an analytical balance. The swelling of the sample was calculated using following equation.[7]

$$\% \text{ Swelling} = \frac{W_s - W_d}{W_d} \times 100 \quad (4)$$

where W_d and W_s are the weight of dry and swollen membranes, respectively.

Water Vapor Transmission Rate

WVTR across the membranes was determined according to the ASTM method E398-03. WVTR tests were carried out using an automatic water vapor permeability testing machine Lyssy L80-5000 (PBI Dansensor, Denmark) at 38°C and 10/15% RH. WVTR of films was measured using aluminum sample cards.

Drug Release Studies

The release of ciprofloxacin hydrochloride from drug loaded membrane was studied by UV-Vis Spectrophotometer. The drug loaded FD membrane having PVA/PEO/CMC/Ciprofloxacin hydrochloride in ratio 80/20/20/1 was immersed in 20 ml PBS (pH 7.4), in a water bath at 37°C. At appropriate time intervals, 5 ml aliquot was withdrawn, and replaced with fresh PBS. The amount of drug released was measured at the absorbance of 268 nm from the calibration plot of the optical density versus drug concentration. The experiment was performed in triplicate.

Antimicrobial Studies

Antimicrobial nature of AD drug loaded membrane having PVA/PEO/CMC/drug in ratio 80/20/20/1 was examined by zone of inhibition test method. The PVA/PEO/CMC AD membrane without drug was used as control. The antibacterial activity was determined against gram-negative bacteria, *E. coli*. In this method, colonies of *E. coli* (ATCC 35218) obtained from an overnight culture were suspended in Muller Hinton Broth (MHB) and the turbidity was adjusted to 0.5 McFarland standards. Of this suspension, 200 μL was spread on Muller Hinton Agar (MHA) plates to obtain a semiconfluent growth. Different membranes were then placed on the inoculated medium and the plates were kept for incubation for 24 h at 37°C and the zone of inhibition were observed the next day.[31]

RESULTS AND DISCUSSION

It is observed that when blend solution having PVA/PEO/CMC was lyophilized and FD leaves a porous matrix, which is fragile and breaks into pieces [Figure 1(a)]. Therefore, PET fabric is used as the support layer to the FD membrane. It provides mechanical strength to the membrane as shown in Figure 1(b) and helps in the formation of thin and light weight structures that can be further used as wound dressings.

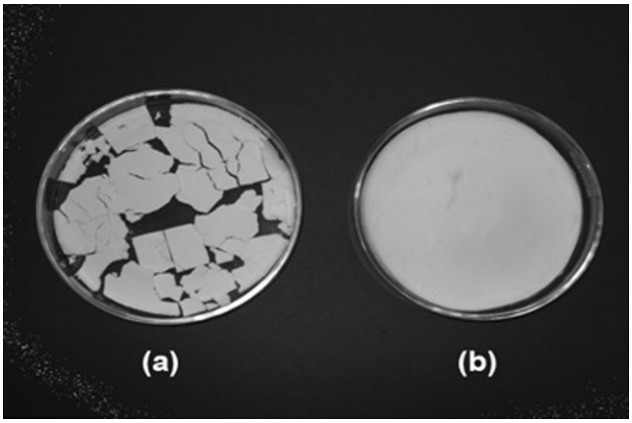

Figure 1. FD membranes of the PVA/PEO hydrogel (a) without PET fabric (b) with PET fabric.

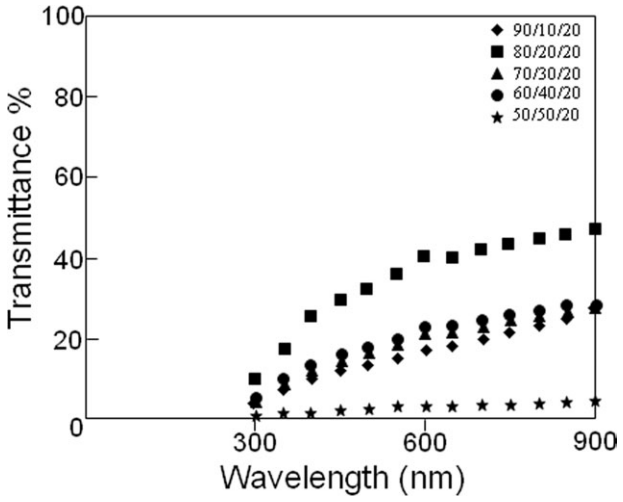

Figure 2. Transmittance % of pure and blend solutions having PVA/PEO/CMC in ratio 90/10/20, 80/20/20, 70/30/20, 60/40/20, and 50/50/20.

The blend solutions having PVA/PEO/CMC in ratio 80/20/20 possessed more transmittance as compared to other compositions. Figure 2 shows that the transmittance for 80/20/20 composition was 47% at 900 nm. However, all the other blend solutions having PEO concentration 10, 30, 40, and 50% possessed lower transmittance values 28%, 27.6%, 28.4%, and 4.6% at 900 nm, respectively and exhibited translucence as compared to blend solution having PVA/PEO/CMC in ratio 80/20/20. Thus, it can be inferred that at 20% PEO concentration the polymers in the blend solutions interact more. This miscibility between polymers may be due to the formation of hydrogen bonds between the hydroxyl groups of CMC with ether groups of PEO and hydroxyl groups of PVA. As the concentration of PEO increased to 50% in the blend solution transparency decreased to a much lower value i.e. 4.6%. This may be due to the incompatible and immiscible nature of PVA and PEO as discussed in our previous publication.[24]

In previous work, it was observed that PVA and PEO induce phase separation as a result of which pore developed even in the AD membranes.[24] CMC is added to the PVA/PEO blends; it interacts with the polymers and pores morphology changes from elongated to spherical. The aim of the present work is to study the morphology of the FD membranes with respect to the increase in the concentration of PEO in blends. SEM micrographs presented in Figures 3–5 showed the morphology of top, bottom, and cross-section of the FD composite membranes, respectively. As illustrated in Figures 3–5, the method of freeze-drying leads to porous morphology of the blend membranes. As PEO concentration was varied from 10 to 20% keeping CMC content constant, it is observed that size of pores increases that can be observed from SEM of bottom side of the membranes. On further increasing the PEO concentration, porosity can be observed but the shape and size of pores cannot be determined accurately. SEM of cross-section of membranes showed three-dimensional porous structure together with good interconnections between the pores. It seems that the surface and bottom morphology is governed by the exposure of the membrane interface to the glass surface, and hence we do not see a huge difference in the porous structure. The real difference is evident from the bulk structure, which shows much wider and non homogeneous porous structure. Furthermore, the shapes and size of pores vary considerably throughout the membrane. Thus, the porous morphology present in the membranes provide channels for fluids to move from the wound and also enable the free transport of oxygen to the wound to promote breathability for healing.

The variation of density with the PEO content of membranes is presented in Table I. There is a decrease in density as the PEO

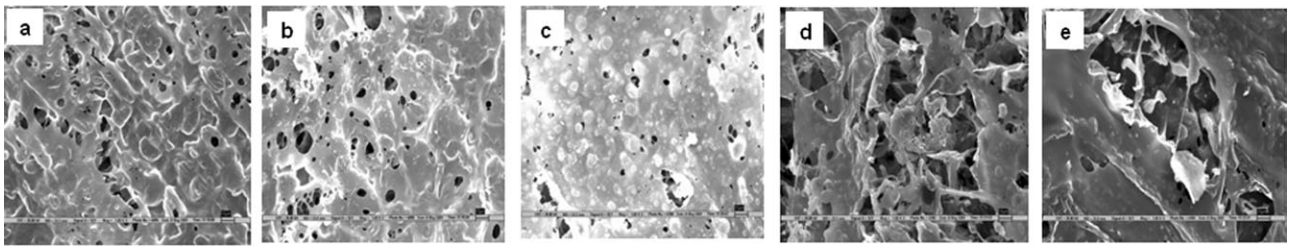

Figure 3. SEM micrographs of the top side of FD membranes having PVA/PEO/CMC in ratio (a) 90/10/20; (b) 80/20/20; (c) 70/30/20; (d) 60/40/20; and (e) 50/50/20 at ×1800.

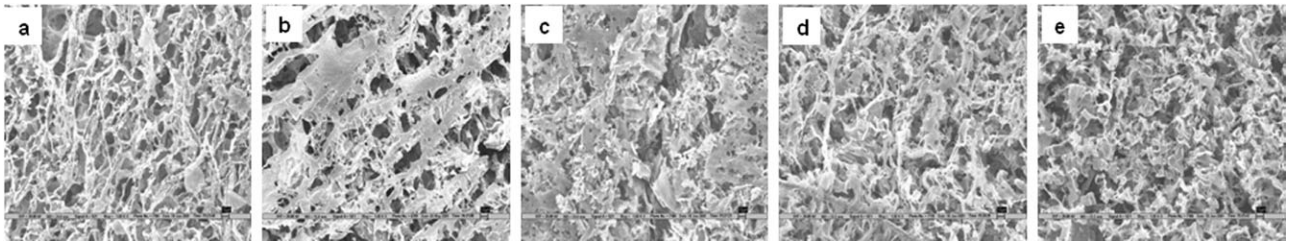

Figure 4. SEM micrographs of the bottom side of FD membranes having PVA/PEO/CMC in ratio (a) 90/10/20; (b) 80/20/20; (c) 70/30/20; (d) 60/40/20; and (e) 50/50/20 at ×1000.

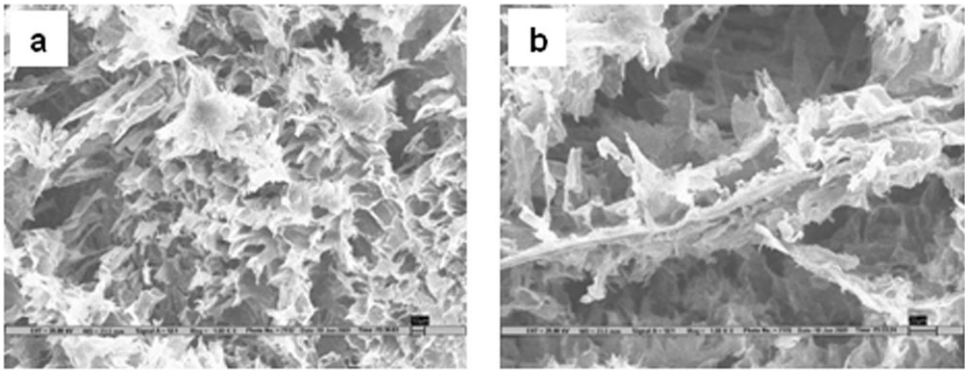

Figure 5. SEM micrographs of the cross-section of FD membranes having PVA/PEO/CMC in ratio (a) 90/10/20 and (b) 80/20/20 at ×1000.

content in both AD and FD membranes increases. Density of AD membranes varies in the range of 1.22 ± 0.05 g cm^{-3} for membrane having PVA/PEO/CMC in ratio 90/10/20 and 0.77 ± 0.09 g cm^{-3} for membrane with 30% PEO content. Density of FD membranes varies in the range of 0.089 ± 0.04 g cm^{-3} for membrane having PVA/PEO/CMC in ratio 90/10/20 and 0.069 ± 0.01 g cm^{-3} for membrane with 40% PEO content. This decrease in density may be attributed to the increase in phase separation between PVA and PEO with the increase in PEO content in the membranes.

The porosity of FD membranes at varying PEO concentration is presented in Table II. The porosity of the membranes shows similar values with the increase in the PEO content i.e. it varies from $92.7 \pm 0.5\%$ for membrane having PVA/PEO/CMC in ratio 90/10/20 and $89.8 \pm 0.9\%$ for membrane having PVA/PEO/CMC in ratio 70/30/20. These results do not reflect the observation from the SEM studies, where the enhanced incompatibility of the moieties due to PEO addition shows much larger pores. Maybe the density approach of porosity determination is not able to differentiate all types of pores including dead ends and interstices along with the three-dimensional porosity in an efficient manner.

The ATR-FTIR spectra of blend membranes with 20% CMC and variable ratio of PVA/PEO have been presented in Figure 6. There is strong evidence i.e. the peak in the range 3200–3400 cm^{-1}, which is not present in the PEO but is present in PVA, to establish clear hypotheses for the hydrogen bonds formation between PVA, PEO, and CMC, which favors blending between the pure polymers at all different ratios.[24] IR peak ranges which are of interest in this spectrum are C—O—C asymmetric stretch at 1087–1099 cm^{-1}, —OH broad peak in the range 3290–3400 cm^{-1} and —CH stretching vibration in the range 2875–2920 cm^{-1}. The intensity of the peak at 1087–1099 cm^{-1} (characteristic peak of ether group) increases with the increase in PEO concentration. It is interesting to note that these peaks in the spectrum of blend membrane shift a little. The IR spectra of blends showed all the characteristic peaks of PVA, PEO, and CMC and it is also interesting to note that the intensity of all peaks corresponding to PEO decreases as the concentration of PEO decreases in the blend membranes. Although there is no appreciable shift in the peak position at 1598 cm^{-1}, the intensity of the peak increases as the concentration of PVA decreases from sample a to e. This is because of the decrease in the available number of hydroxyl groups in blend to interact with the carboxylate ions of CMC. Thus, it can be inferred that CMC interacts more with PVA than with PEO[24,32,33] and as the concentration of PVA decreases more carboxylate ions become free as a result of which intensity of this peak increases.

XRD patterns of the blends and the pure components are presented in Figures 7 and 8. The diffraction peaks for the pure PVA appeared at 2θ 14.1°, 16.9°, and 19.0° characteristic of PVA.[24] It has been observed in previous publication that as

Table I. Influence of Concentration of PEO on Density and Crystallinity of Blend Membranes Having Different Compositions

Composition (PVA/PEO/CMC)	Density (g cm^{-3}) AD films	Density (g cm^{-3}) FD films	Crystallinity (%) by XRD
100/0/0	1.28 ± 0.08	0.086 ± 0.05	48.6
0/100/0	[a]	[a]	50.3
0/0/100	[a]	[a]	17.4
90/10/20	1.22 ± 0.05	0.089 ± 0.04	42.5
80/20/20	1.06 ± 0.07	0.088 ± 0.02	34.7
70/30/20	0.77 ± 0.09	0.078 ± 0.01	33.9
60/40/20	[a]	0.069 ± 0.01	26.5
50/50/20	[a]	[a]	21.3

[a]Sample preparation was difficult so not able to calculate density.

Table II. Influence of Concentration of PEO on Porosity; WVTR; and % Swelling of Blend Membranes Having Different Compositions

Composition (PVA/PEO/CMC/drug)	Porosity (%)	WVTR (g/m^2/day)	% Swelling
90/10/20 (FD)	92.7 ± 0.5	2989	1058
80/20/20 (FD)	91.7 ± 0.8	2319	952
70/30/20 (FD)	89.8 ± 0.9	2095	648
60/40/20 (FD)	–	2062	503
50/50/20 (FD)	–	–	192
80/20/20 (AD)	–	506.4	–
80/20/20/1 (AD)	–	374.2	–

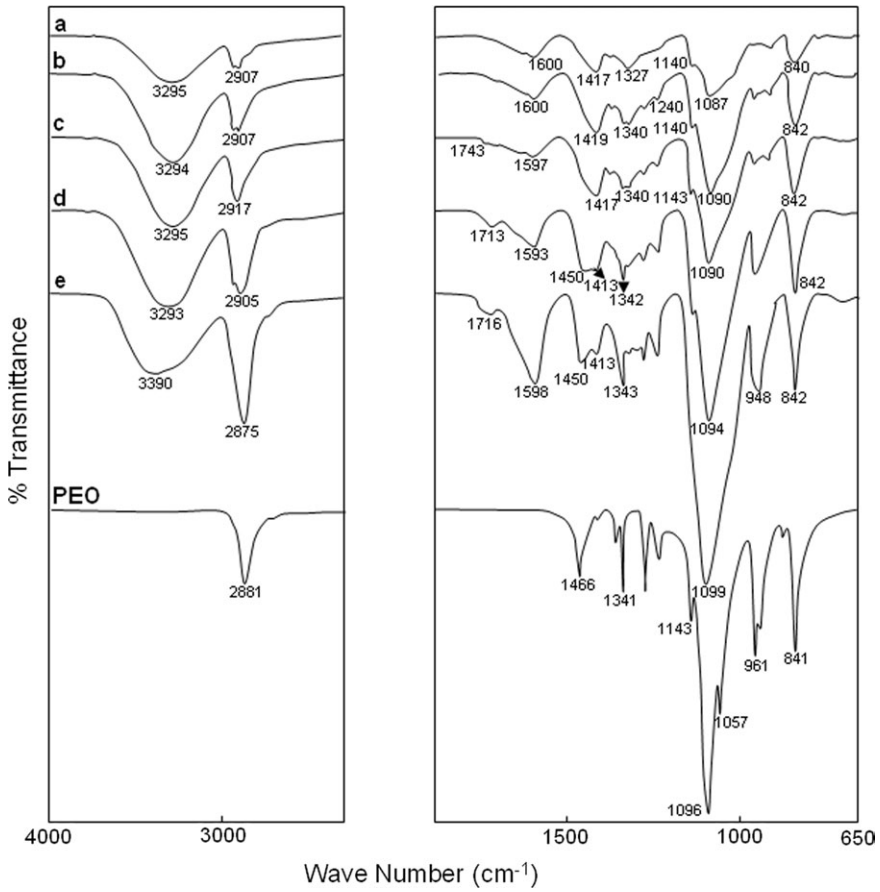

Figure 6. ATR-FTIR of samples having 20% CMC and variable amounts of PVA/PEO (a) 90/10; (b) 80/20; (c) 70/30; (d) 60/40; and (e) 50/50.

CMC is added to the blends of PVA and PEO having PVA/PEO/CMC in ratio 90/10/20, all crystalline peaks of pure PVA and PEO get merged and show only one single diffraction around 19.6°, which is near to the characteristic sharp peak of PEO suggesting that CMC has strong interaction with PVA, but very little interaction with PEO.[24] In Figure 7, as the PEO concentration increases from 10 to 50%, a new peak at 23.4° develops along with peak at 19.6°, both of these are characteristic peaks of PEO thus showing that as more and more PEO is added to the blend solution, the system miscibility decreases. The crystallinity of blend membranes decreases from 42.5 to 21.3% as the concentration of PEO in PVA/PEO/CMC system varies from 10 to 50% (Table I), which is ascribed to the destruction of regularity of pure polymers.

Figure 8 shows the XRD patterns of ciprofloxacin hydrochloride, membrane having PVA/PEO/CMC in ratio 80/20/20 with and without drug. Ciprofloxacin hydrochloride, showed typical crystalline peaks at 2θ 8.9°, 11.6°, 19.3°, 24.6°, 26.6°, and 29.4° because of its close molecular packing and regular crystallization.[34] It can be seen that drug loading in the membrane changed the diffraction pattern of the membrane, it is clear that after the addition of drug to the membrane having PVA/PEO/CMC in ratio 80/20/20, the diffraction intensity of control membrane without drug decreased at 23.2°; also a new diffraction originated at 26.8°. These results indicate that the addition

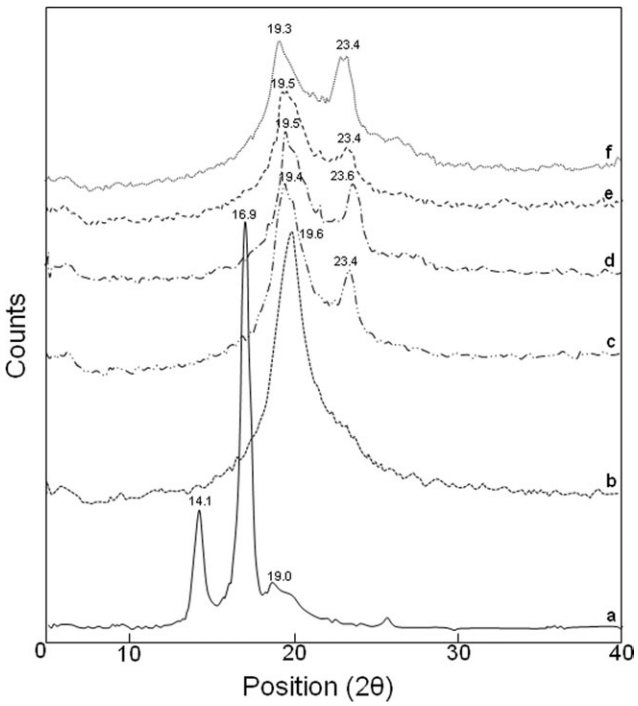

Figure 7. XRD patterns of (a) pure PVA and samples having 20% CMC and variable amounts of PVA/PEO (b) 90/10; (c) 80/20; (d) 70/30; (e) 60/40; and (f) 50/50.

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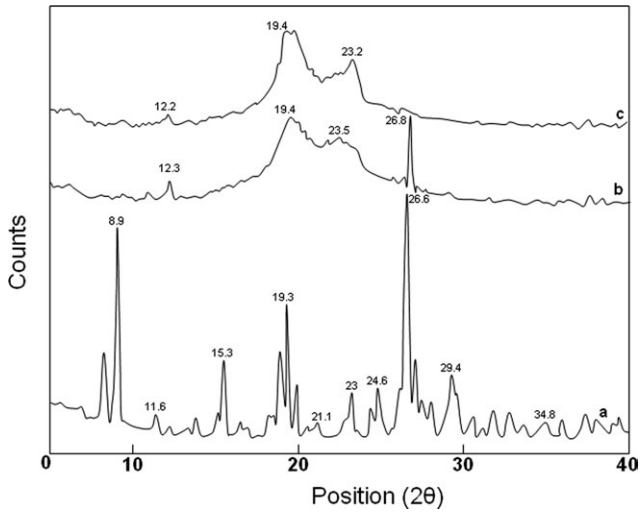

Figure 8. XRD patterns of (a) ciprofloxacin hydrochloride and AD membranes having PVA/PEO/CMC in ratio 80/20/20 (b) with drug, (c) without drug.

of ciprofloxacin hydrochloride destroyed the ordered packing of the polymer blends.

DSC thermograms of PVA and blends with various concentrations of PEO are presented in Figure 9. The pure PVA sample gives a relatively large melting endotherm with a peak maximum (T_m) at 222.8°C. The addition of PEO in different ratios to the blends of PVA/PEO/CMC having 20% CMC shows significant change in the melting temperature [Figure 9(a–e)]. The shape of thermograms under the melting peak of pure PVA remains almost identical for all membranes.

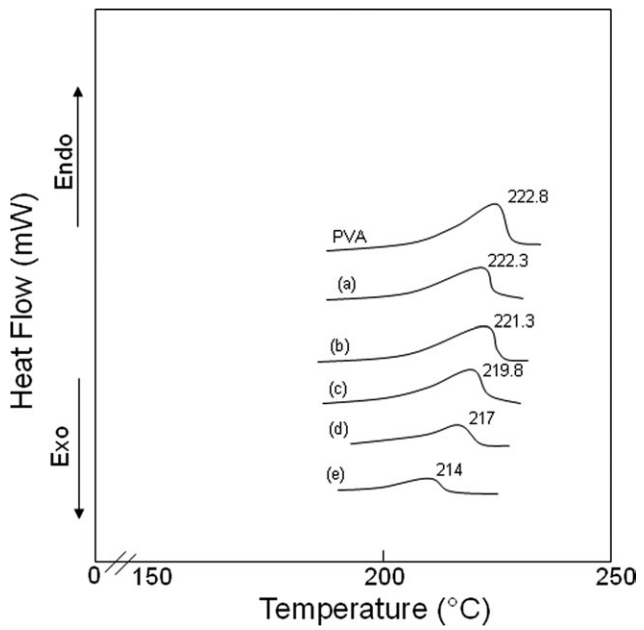

Figure 9. DSC curves showing the melting peaks of PVA; and samples having 20% CMC and variable amounts of PVA/PEO (a) 90/10; (b) 80/20; (c) 70/30; (d) 60/40; and (e) 50/50.

The influence of PEO concentration on the swelling of blend membranes is given in Table II. The greater the increase of PEO in the blend membranes, the lower the swelling was. It seems that these membranes have high and enough swelling to be used as a suitable dressing even for high exudating wounds.

WVTR of the different membranes, both AD and FD, are presented in Table II. It has been reported that an ideal wound dressing should maintain the ideal rate of WVTR i.e. 2000–2500 g/m^2/day so that both excessive dehydration and build up of exudates can be controlled.[35] High value of WVTR would lead to dehydration of wound and result in adhering of dressing to the wound surface, which will ultimately cause trauma at the time of removal of the dressing. The values of WVTR for FD membranes in Table II were close to the range appropriate for maintaining a proper fluid balance on the wound surface. The increase in the concentration of PEO in the PVA/PEO/CMC blend decreases the transmission rate from 2989 to 2062 g/m^2/day, which may be compared with the decrease in swelling of blend membranes with increase in the concentration of PEO from 10–40%. It is clear from the table that out of all compositions, the blend membrane having PVA/PEO/CMC in ratio 90/10/20 has high WVTR value not appropriate for maintaining a proper fluid balance whereas all other compositions have WVTR values in the ideal range. It is also investigated that the AD membrane having PVA/PEO/CMC in ratio 80/20/20 have WVTR 506.4 g/m^2/day, which decreases to 374.2 g/m^2/day with the addition of drug in the matrix.

The cumulative amount of ciprofloxacin hydrochloride release behavior from the wound dressing having PVA/PEO/CMC/drug in ratio 80/20/20/1 as a function of time is shown in Figure 10. The calibration plot for concentration versus optical density was prepared by solutions having different amounts of drug and measuring their optical density at 268 nm using UV-Vis spectrophotometer (Figure 10 inset). A straight line is obtained for ciprofloxacin hydrochloride. The drug release starts immediately and continues upto 10 h, beyond which it levels off. This leads to the conclusion that the dressing can be changed after every day so that the wound site will remain infection free till the wound heals completely. In drug containing matrix, about 99

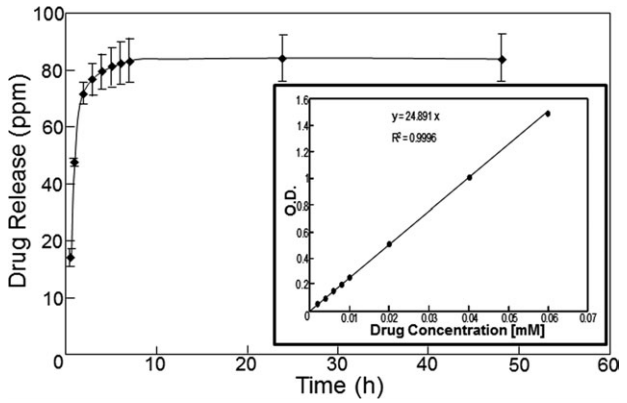

Figure 10. Drug release profile of ciprofloxacin hydrochloride from the FD blend membrane having PVA/PEO/CMC/drug in ratio 80/20/20/1; (inset) Calibration plot of ciprofloxacin hydrochloride at 268 nm.

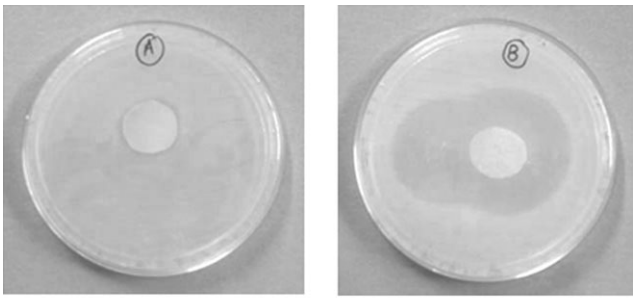

Figure 11. Antimicrobial activity of membranes (a) without drug, and (b) with drug against *E. coli* (ATCC 35218) by zone of inhibition method.

ppm of drug was released in 4 h, and the release then becomes constant. It can be said that the drug release from the system depends on the drug loaded matrix. Here, the matrix is PVA/PEO/CMC, which swells as soon as it come in contact with aqueous medium and causes a quick burst release of drug at the wound site thus making the site infection free.

The antibacterial nature of membrane loaded with ciprofloxacin hydrochloride drug was investigated qualitatively by zone of inhibition against gram-negative *E. coli* (Figure 11) and it is also compared with the control membrane without drug having PVA/PEO/CMC in ratio 80/20/20. Clear zone of inhibition can be observed in membrane loaded with drug and no zone of inhibition is observed in the control membrane. Therefore, from drug release and antibacterial studies it can be said that the membrane loaded with drug can also incorporate antibacterial nature to the polymeric FD membrane so formed.

CONCLUSION

PVA/PEO/CMC blend membranes having PET nonwoven fabric as the support layer and ciprofloxacin hydrochloride drug as antibacterial agent were prepared by two approaches of solvent casting and freeze-drying. It is observed that as the concentration of PEO increases in the blend membranes, the crystallinity decreases significantly. DSC data showed significant shifts in the melting temperature of PVA with increase in PEO content. It was observed that the membrane with PVA/PEO/CMC in the ratio 80/20/20 possesses excellent light transmittance and water vapor evaporation as compared with the other compositions. Therefore, the ratio 80/20/20 of PVA/PEO/CMC can be optimized for further studies.

The FD membranes have three-dimensionally interconnected porous morphology, which provides channels for fluids to move from the wound. The WVTR results show that these membranes exhibit high rate of moisture transmission of the order of $\sim$ 2000 g/m^2/day. These membranes showed enough swelling in PBS and so can be recommended for exudative wounds. The drug release continued upto 10 h suggesting that the dressing so formed can be changed after every day so that the wound site will be infection free till the wound heals completely. Moreover, the zone of inhibition in the drug incorporated membranes signifies that the drug is effectively releasing out in the medium and inhibits the growth of microorganisms. Thus, this system could be used as a very promising antibacterial wound dressing.

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