Skin-Compatible Carbopol Electrospun Fiber Membranes with pH-Dependent Rheological Properties for Biomedical Applications

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Properties of pH-responsive electrospun nanofibers incorporated with biocompatible/degradable Carbopol, commonly used in pharmaceuticals and personal care products, are reported. Sonication of Carbopol dispersions prior to electrospinning leads to uniform incorporation into fibers of the host polymer polyvinylpyrrolidone. The hydration behavior is strongly influenced by pH conditions, forming a viscous network at higher pH. Since Carbopol is more responsive to higher pH, at pH > 6 increasing Carbopol concentration leads to increased uptake volume of buffer solution, faster uptake rate and complete gel formation. The physical spreadability (resulting from a combination of viscoelastic properties and the structural polymer network) of the hydrated fibers is evaluated for multiple Carbopol concentrations and pH conditions. At low starting pH of 4, increasing the Carbopol amount results in slightly increasing viscosity while maintain solution pH. On the other hand, at high starting pH of 8 increasing Carbopol concentrations result in significant reduction in the pH of the buffer solution, which in turn decreases the viscosity of the gel and increases its spreadability. These findings provide guidelines for rational designs of pH responsive Carbopol fibers for various applications, including drug delivery, wound dressing, contraceptive devices, and prevention of sexually transmitted diseases.

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1. Introduction

"Smart" materials that change their properties upon exposure to external stimuli, such as temperature,^[1] pH,^[2] light,^[3] specific chemicals,^[4] or biological agents,^[5] have attracted much attention due to their potential for versatile use in many applications.^[6] In particular, pH-responsive materials^[2a] are of significant importance in biomedical applications, such as drug delivery,^[7] tissue engineering,^[8] wound healing,^[9] and diagnostics,^[10] because of their ability to physically and chemically respond to pH changes within the physiological range, as well as pH-changing medical conditions, such as gastro-intestinal drug release,^[11] wounds^[12] and cancers.^[9a]

While conventional pH-responsive materials provide a very useful set of properties, nanostructured pH-responsive materials can deliver additional functionality.^[13] Polymeric nanofiber membranes produced by electrospinning represent a versatile platform for biomedical applications due to high surface-to-volume ratio, high

porosity, self-supporting structure (no substrate), numerous possible materials options, various fiber structures, and easy incorporation of functional materials.^[14] The extremely high surface area in conjunction with a highly porous structure amplifies the sensitivity to external stimuli and accelerates external stimuli to react with pH-responsive molecules, leading to much faster responsiveness than that of the equivalent bulk material. For example, pH-responsive coaxial fiber membranes consisting of two different Eudragit materials provided $\approx 30 \times$ faster response to external pH changes than that of equivalent cast films.^[2b] Also, blended fibers with self-immolative polymer (SIP) and polyacrylonitrile (PAN) exhibits $\approx 25 \times$ faster depolymerization rate compared to a cast film upon the triggering condition.^[15]

Polyelectrolytes have been utilized as a pH-responsive material because their polymer chains can be charged by acquiring or releasing protons, upon hydrating with responding pH solutions.^[13] Among them, anionic polyacrylic acid (PAA) has been popularly investigated because of its pH responsiveness and a simple molecular structure. PAA can be directly electrospun into micro/nanofibers or mixed with other polymers for enhanced pH responsiveness. Vats et al.^[16] investigated the solvent

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mixture for electrospinning of PAA, especially in water-ethanol mixture at different ratios, which is closely related to the viscosity of the solution for electrospinning. The solution viscosity reached the maximum at a water-to-ethanol molar ratio of $\approx 2:1$. Li and Hsieh^[17] directly electrospun PAA into fibers and obtained water-insoluble PAA fibers upon heat-induced crosslinking process with β -cyclodextrin. Crosslinked PAA fibers strongly presented pH-responsive swelling ratio of 2 and 17 in buffer solutions with pH of 2 and 7, respectively. Anionic PAA can also be blended with cationic polyelectrolytes, such as chitosan and polyallylamine hydrochloride (PAH), to form the polyelectrolyte complexation, presenting reversible action of swelling/deswelling based on the surrounding pH condition.^[1a,18]

Carbopol 974P NF is a commercially available polyacrylic acid polymer - (CH2-CHCO2H)n - highly cross-linked with allyl pentaerythritol. Because of its very high viscosity, it has been used as a liquid thickening, extended release, bioadhesion or stabilizing agent. Additionally, the low toxicity of Carbopol makes it a very versatile mucosal- and skin-compatible material for use in oral health and topical applications.^[19] However, its crosslinked nature prevents Carbopol from being conventionally electrospun into a nanofiber platform. Because Carbopol is not soluble in most solvents, the electrospinning of Carbopol has not yet been reported. Here, we have successfully produced Carbopol nanofibers by uniformly incorporating Carbopol particles into a host polymer (polyvinylpyrrolidone - PVP), and demonstrated pH-responsive properties of electrospun Carbopol nanofiber membranes. First, fiber formation and related surface morphologies were characterized and then optimized based on the ratio of Carbopol and PVP. Finally, the pH-dependent hydration properties and rheological properties have been fully evaluated and discussed.

2. Results and Discussion

2.1. Electrospinning of Carbopol Incorporated Fibers

Electrospinning with CP974P is very challenging because it is not dissolved in organic solvents and forms a thick gel-phase in aqueous solution even at very low concentration < 1 wt.%. Owing to the solubility issue, CP974P powders were dispersed in organic solvents without dissolution. Because CP974P is a hydrophilic powder that contains carboxylic acid groups (-COOH) with lower density (\approx 1.2 g cc⁻¹) than the solvent (e.g., trifluoroethanol (TFE) \approx 1.4 g cc⁻¹) it remains suspended in solvent for days. However, some CP974P particles do coalesce, as shown in Figure S1a (Supporting Information) (left vial). To dissociate the aggregates, the CP974P-added suspension was agitated in a sonication bath, resulting in very fine and uniform dispersions, as shown in the right sample vial of Figure S1a (Supporting Information). After sonication, the host polymer material was added and dissolved into the solution, which can further enhance the dispersity of CP974P in solution because of the increased solution viscosity. SEM observations of the resulting electrospun fiber membranes clearly indicate that CP974P solutions without the sonication process leads to the presence of large aggregates within the fiber network (Figure S1b, Supporting Information), while sonicated solution provided much finer distribution of CP974P powders without large aggregates (Figure S1c, Supporting Information).

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To optimize the CP974P incorporated electrospun fibers, several host polymers (PVP, PEO, and a (4:1) blend of PVP/HPMC) were investigated in different concentrations, as shown in Figure S2 (Supporting Information). All polymers including PVP, PEO, and PVP/HPMC blend were successfully electrospun into CP974P-containing nanofibers (Figure S2a-c, Supporting Information). The solution of PEO in TFE solution was too viscous to be electrospun when high molecular weight PEO (down to 200 kDa) was utilized, while lower MW (100 kDa) PEO could not be electrospun stably. To achieve stable PEO electrospinning, a mix of 3% 100 kDa and 3% 200 kDa PEO were dissolved into a solution. HPMC was also not readily electrospinnable alone due to excess bead formation even with very viscous HPMC solutions. To improve the electrospinnability, HPMC was blended with other electrospinnable polymers. PVP presenting excellent electrospinnability with CP974P is known as a safe excipient for human use with a low toxicity and irritation potential.^[19] Different concentrations of CP974P and PVP at the fixed 1:2 wt. ratio were evaluated to obtain stable fiber formation. For PVP 4% (Figure S2d, Supporting Information), beaded fibers with very thin diameter (<1 µm) were formed, resulting in poor incorporation of CP974P particles within fibers and very weak mechanical integrity. Starting at PVP concentrations of 6%, the electrospun fiber membranes present good mechanical stability and can be handled easily (Figure S2e, Supporting Information). At PVP 8%, the fiber diameter became thicker (average of $3.75 \,\mu m$) with more uniform CP974P particle distribution and fewer aggregates outside the fiber body (Figure S2f, Supporting Information). We have also measured the particle sizes of CP974P in both liquid and dry states using a scanning electron microscopy (SEM) and dynamic light scattering (Zetasizer Nano-ZS, Malvern Pananalytical), respectively (Figure S3, Supporting Information). To observe the particle in the dry state, we cast the diluted Carbopol dispersions in TFE solvent onto a heated glass slide and dry it before coating the Carbopol particles with sputtered gold for SEM observation. The measured average diameter of the dried CP974P particles was $\approx 1.6 \,\mu m$. Interestingly, Carbopol particle diameter in the liquid state presented an average diameter of $\approx 4 \, \mu m$ (more than twice as large as in the dried state), while the polydispersity index in the liquid state was 0.4. The difference in particle size between the wet and dry conditions is possibly due to the swelling and relaxation of hydrophilic Carbopol particles although they are not dissolving in TFE solvent, leading to the increased hydrodynamic diameter in the liquid state.

Fiber formation with different weight ratios of PVP to Carbopol have been evaluated. The concentration of PVP was kept constant at 8% while the Carbopol concentration was varied from 0% to 8%. In the absence of Carbopol, very uniform PVP fibers were obtained (**Figure 1a**). At low Carbopol concentrations in solution (PVP/Carbopol ratios of 8:1 and 8:2) it resulted in embedded particles within fiber body (Figure 1b,c). At higher Carbopol concentrations (PVP/Carbopol ratios of 8:4 and 8:8) very noticeable presence of Carbopol particles were observed (Figure 1d,e). It is important to point out that even in the case where Carbopol particles represent \approx 50% of the fiber mass the membrane still provides good mechanical integrity for easy handling.

Table 1 summarizes fiber diameter (obtained by analyzing SEM microphotographs), the effective pore diameter (measured using capillary flow porometry), and membrane porosity

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Figure 1. SEM observation of electrospun fibers with different PVP to Carbopol ratios: a) no Carbopol (PVP-only); b) 8:1; c) 8:2; d) 8:4; e) 8:8. PVP concentrations were fixed at 8%.

(obtained from density measurements). These values are plotted them in Figure S5 (Supporting Information) as a function of Carbopol concentration. As an increasing amount of Carbopol is incorporated into the fibers, the average fiber diameter increases, from $\approx 2.4~\mu m$ for the PVP-only case to $\approx 3.4~\mu m$ for the 8:8 PVP/Carbopol ratio. Because the fiber surface becomes increasingly rougher with higher Carbopol concentration the average membrane pore size (as measured by capillary flow porometry) increases from $\approx 6~\mu m$ (no Carbopol) to $\approx 9~\mu m$ (equal PVP and Carbopol), while the resulting membrane porosity increases slightly from $\approx 88\%$ to $\approx 90\%$.

2.2. pH-Dependent Hydration Properties of PVP/Carbopol Electrospun Fibers

The hydration properties of Carbopol fiber membranes were first evaluated by measuring the water contact angle (WCA) on membranes with different buffer solutions with pH from 4 to 8. WCA cannot be measured on PVP due to fast absorption, therefore polycaprolactone (PCL)/Carbopol fiber membranes have been used instead of PVP/Carbopol membranes for WCA measurements. All pH buffer solutions presented similar contact angles on PCL-only membrane. However, when Carbopol is incorporated into fiber membranes, the water droplet was also quickly absorbed into the membrane, leading to an apparent WCA of ≈0° (Figure S4a, Supporting Information). Therefore, instead of WCA, the absorption speed rate was quantified (Figure S4b, Supporting Information). Interestingly, more basic solutions presented slower absorption speed rates because Carbopol instantly swells in basic condition, forming a viscous barrier. For a similar reason, a pH 4 droplet forms a larger spreading area than that of pH 8, as shown in Figure S4c (Supporting Information). Figure S4d (Supporting Information) illustrates the conversion from dry membrane to hydrogel for a 100 mg PVP/Carbopol (1:1 wt. ratio) membrane upon insertion into a 400 mL of pH 8 buffer solution.

Although WCA and absorption rate measurements on Carbopol fiber membranes show a trend of Carbopol effect, these results do not fully represent the hydration properties of PVP/Carbopol membranes. Therefore, hydration behavior of PVP/Carbopol fibers was evaluated by immersing the membrane into buffer solution and monitoring the mass change over time, as shown in Figure 2. In this immersion approach, the different wicking characteristics over time are clearly observed. As seen in the photos of Figure 2a, at pH 4, the Carbopol was not hydrated and the membrane retained its powder color of white. In contrast, at pH 8, PVP/Carbopol membrane quickly absorbed the liquid and turns into a translucent hydrogel by hydration. After immersion for 20 min the total amount of absorbed liquid is \approx 19x times of the membrane dry mass as shown in Figure 2b. At pH 4, there was a rapid increase in membrane mass ($\approx 10x$ the membrane dry mass) in the first 1–2 min, but only slightly increased after that.

 Table 1. Characteristics of Carbopol incorporated PVP fibers.

PVP to Carbopol wt. ratio	Fiber Diameter [µm]			Porosity [%]		
	Average	Std. Dev.	Maximum	Average	Minimum	
8:8	3.38	1.11	9.96	8.99	6.96	89.9
8:4	3.37	0.69	9.11	8.37	5.94	88.4
8:2	3.44	0.85	8.31	7.63	5.15	87.4
8:0.8	2.82	0.60	7.16	6.52	4.53	88.2
8:0	2.42	1.10	6.83	6.25	4.97	87.7

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Figure 2. Evaluation on hydration behavior of PVP/Carbopol (8:8) fiber membranes immersed into acidic and basic buffer solutions: a) photos of membranes after immersion; b) absorption properties over time in different pH buffer solutions.

While this immersion approach was successful at determining broad differences in liquid absorption depending on pH, careful sample handling is required to obtain consistent results because the immersed membranes can lose some mass by dissolving into the solutions.

To eliminate the issue of membrane mass loss in solution, a new approach has been developed, as illustrated in Experimental section. Using this approach, the effect of solution pH and Carbopol concentrations in fibers was accurately evaluated by assessing the mass change of membranes and the wicking speed of buffered pH solutions. The absorbed mass of the membranes was shown to increase with pH (Figure 3), as well as with Car-

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bopol concentration (Figure 4). For example, at pH 4 and 8, after a duration of 120 min the PVP/Carbopol fibers at 8:8 ratio absorbed 400 mg in pH 4 solution and \approx 1500 mg in pH 8 solution. This represents a total uptake of $\approx 10 \times$ and $\approx 40 \times$ the mass of the starting (dry) membrane weight in pH 4 and 8 solutions, respectively. The effective hydration rate for the 8:8 PVP/Carbopol membranes was ≈ 0.9 and ≈ 9.6 mg min⁻¹ in pH 4 and 8 solutions, respectively. In contrast, PVP/Carbopol fibers with 8:2 ratio only absorbed \approx 4 and 12x of the membrane mass after 120 min in pH 4 and 8 solutions, respectively. The relative absorbed hydration mass (mass of absorbed buffer to mass of starting membrane, see Equation (3), Supporting Information) of membranes with different PVP/Carbopol ratios from 8:8 to 8:0 is shown as a function of solution pH in Figure 4b. The hydration mass ratio is equivalent to normalized fluid uptake ($\mu L mg^{-1}$) because the buffer solution is > 98% water. As the amount of Carbopol in the fiber increases, the ability of the fiber to absorb buffer increases correspondingly. Consequently, higher Carbopol concentration in fibers leads to larger absorption capacity and faster hydration rate at higher pH conditions.

2.3. pH-Dependent Rheological Properties of PVP/Carbopol Fibers

The effect of Carbopol concentration in pH 4 and 8 solutions on the work of shear is shown in **Figure 5**a for membranes with varying PVP/Carbopol ratios. This is an important consideration for determining the spreadability of the membranes in the gel phase.



Figure 3. Absorbed buffer mass versus hydration time for membranes with different PVP to Carbopol ratios in solutions with: a) pH 4; b) pH 8. (n = 3).



Figure 4. Mass absorption after 120 min as a function of buffer solution pH for membranes with several PVP:Carbopol ratios: a) absorbed fluid mass; b) ratio of absorbed mass normalized to starting (dry) membrane mass. (n = 3).

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Figure 5. Resulting work of shear a) and solution pH b) of PVP/Carbopol composite fiber membranes as a function of Carbopol concentration in pH 4 and 8 buffer solutions.

When the fiber membrane is combined with increasing volume fractions of pH 4 buffer, the work required to spread the resulting gel decreases from 4.5 to 3.5 N-s. As the carboxylic acid groups of Carbopol remain protonated under such acidic conditions, these results are consistent with decreasing interactions within the 3D Carbopol network with increasing polymer dilution. In contrast, the work of shear increases monotonically after Carbopol/PVP fiber membranes are exposed to pH 8 buffer. In the presence of small buffer volumes that generate a gel phase comprised of high Carbopol concentrations, the results from these experiments demonstrate limited changes in viscoelastic gel properties with pH 4 buffer (work of shear clustered between \approx 4.5 and 5.5 N-s). In contrast, when Carbopol/PVP fiber membranes were combined with pH 8 buffer, the force required to spread the gel phase dramatically increased. This behavior underlines the consequences of pH-dependent swelling of Carbopol as a result of deprotonated carboxylic acid functional groups. Interestingly, this behavior was more pronounced in the presence of larger volume fractions of this alkaline buffer solution. In general, it is reported^[2a] that viscoelastic properties of CP974P hydrogels in the presence of a basic pH environment demonstrate a positive correlation with Carbopol concentration. The observations from our experiments, however, confirm the opposite effect whereby the greatest work of shear was measured for the gel phase that contained the lowest CP concentration.

To explore further this unexpected gel behavior, the pH value of the gel phase that was established after combination of the

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dry fiber membrane with various volume fractions of pH 4 and 8 buffer solutions was quantified using an ion-sensitive field effect transistor pH sensor. The results summarized in Figure 5b show that the gel phase pH value in the presence of the acid (pH 4) buffer solution remains constant and is independent of the respective PVP/Carbopol mass ratio of the fiber membrane. This supports the earlier conclusion that viscoelastic properties of the gel phase under acidic conditions is primarily dominated by the Carbopol concentration of the gel phase (i.e., work of shear is directly related to gel phase Carbopol concentration). Combination of PVP/Carbopol fiber membranes with alkaline (pH 8) buffer solutions, however, demonstrates a significant dependence between Carbopol concentration of the gel phase and corresponding gel phase pH value. If the gel phase comprises a greater Carbopol concentration, the results from these measurements suggest a greater acid buffer capacity that limits pH changes of the gel phase. In the presence of lower Carbopol concentrations, the gel phase pH value increases more dramatically due to a reduced acid buffer capacity. Consequently, the swelling behavior increases due to the presence of a greater number of carboxylate groups within the polymer network.

For example, the high Carbopol concentration of 20% in the pH 8 buffer solution at relatively low volume provides a strong acidic buffer capacity lowering the solution pH to \approx 4.0, while providing a relatively low work of shear (\approx 5 N-s). As the volume of the pH 8 buffer increases, the Carbopol concentration in solution decreases leading a gradual increase in the solution pH. At low Carbopol concentration of 1%, the solution pH has increased to \approx 6 and the work of shear is significantly increased to 8 N-s, as the acid buffer capacity is weakened and the carboxylic molecules are deprotonated.

3. Conclusion

We have successfully demonstrated pH-responsive electrospun PVP fibers highly loaded with Carbopol 974P NF. Because of the insolubility of Carbopol in organic solvents, Carbopol powders were uniformly dispersed in solution prior to electrospinning. High proportion of Carbopol (up to 50%) can be successfully electrospun into fibers. Electrospun PVP/Carbopol fiber membranes are mechanically stable and able to be handled without tearing even at 50% Carbopol loading into fibers. The pH-responsive properties of PVP/Carbopol fibers are obtained by measuring hydration behaviors and spreadability of the resulting gel phase at different pH values and different PVP to Carbopol ratios. Upon hydration, the initially dry PVP/Carbopol membranes are converted into a gel phase that exhibits physicochemical properties influenced by the amount of Carbopol present in the membrane and the pH value of the buffer solution. It was observed that Carbopol has two dominant effects - on one hand, increasing Carbopol concentrations in the gel phase formed during combination of PVP/Carbopol fiber mats with pH 4 buffer solutions increases the viscosity of the gel. In the presence of alkaline buffer, however, the presence of increasing Carbopol concentrations enhances the acidic buffer capacity of the gel phase, which reduces viscoelastic properties of the gel phase.

The pH-dependent transformation of dry PVP/CP974P fiber mats into a hydrogel that exhibits tailored viscoelastic properties and low toxicity indicates that Carbopol incorporated PVP fiber

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Figure 6. Electrospinning of CP974P-incorporated PVP nanofiber membrane: a) multi-nozzle electrospinning of CP974P/PVP solution on large flat collector; b) single-nozzle electrospinning on rotating drum collector; c) large electrospun CP974P/PVP (8:8) membrane.

membranes have a great potential usage for many bio/medical applications, including mucosal administration and extended drug delivery.

4. Experimental Section

Materials: Polyvinylpyrrolidone (PVP) 1.3 MDa, polyethylene oxide (PEO) 200 kDa, hydroxypropyl methylcellulose (HPMC) 20 kDa and 0.825 mm thick cellulose fiber sample pad sheets (CFSP223000) were purchased from MilliporeSigma (Burlington, MA). Carbopol 974P National Formulary (NF) (hereafter referred to as CP974P or Carbopol) was generously provided by Lubrizol (Wickliffe, OH). Trifluoroethanol (TFE) (99.8% "extra pure") was purchased from Fisher Scientific (Waltham, MA), and colorless buffered solutions of pH 4, 5, 6, 7, and 8 were purchased from Carolina Biological Supply (Burlington, NC).

Fabrication of Carbopol Fibers: Carbopol-incorporated nanofibers have been produced using the electrospinning technique. Electrospinning extracts nanofibers from a viscous polymeric solution by applying a high electric field drawing droplets into fibers. Electrospinning solution with Carbopol was prepared by dispersing Carbopol powders in TFE solvent. To dissociate some aggregates, the Carbopol dispersed solution was treated in a sonication bath (Fisher Scientific FS-60H ultrasonic cleaner) for 30 min. Then, the host polymer, PVP, was added to the solution. The solution vials were stirred overnight to fully dissolve PVP using a rotator RKVSD (Appropriate Technical Resources, Laurel, MD) at 25 rpm. Although Carbopol itself forms a stable dispersion in TFE solvent, added viscosity by the host polymer further enhances the stability of Carbopol particles in solution. No sign of precipitation was observed after 24 h. Once fully dissolved, the homogenous suspension is loaded into a NE-1000 syringe pump and continuously fed to the 18 G nozzle (inner diameter 0.8-1.0 mm) with a constant flow rate. Positive high-voltage bias was applied to the nozzle, and negative (or ground) to the drum collector rotating at 100 RPM. The resultant strong electric field produces a CP974P-dispersed liquid jet ejected from the nozzle, which experiences vigorous whipping and stretching actions due to the dominating charge repulsion force within the jet. Finally, solidified CP974P electrospun fibers were collected on the rotating drum collector.

Electrospinning was also carried out using the Professional Lab Device electrospinning machine (DOXA Microfluidics, Malaga, Spain) for generating large sample membranes (**Figure 6**). High throughput of CP974P fiber production is available using either a multi-nozzle source (Figure 6a) and/or a rotating drum collector (Figure 6b). A CP974P fiber membrane in the size of $\approx 30 \times 60$ cm obtained using the drum collector is shown in Figure 6c. All electrospinning parameters used for samples in this report are listed in **Table 2**.

Evaluation of Hydration Characteristics: Liquid-uptake testing was first attempted by submersion, but it was found that the membrane dissolves into solution rapidly and cannot maintain the mechanical integrity, preventing accurate evaluation. A new method was conceived as illustrated in Figure 7. A cellulose wick pad was laser cut to the width of a glass slide such that the ends of the membrane overhang each end of the slide to a final size of 25 \times 110.25 mm. The laser was operated at the power of 30 W with 6 cm $\rm s^{-1}$ head velocity. The glass slide-cellulose pad assembly was then placed on a laser-cut acrylic support such that the slide was suspended above a bath of buffered pH solution, with each end of the cellulose wick pad below the level of the fluid, allowing it to wick the fluid across its top surface. This assembly was allowed to wick for 5 min for full saturation. Upon removal from the bath all excess droplets were wiped from the assembly and the mass, $m_{wick(wet)},$ was taken. Pieces of PVP/CP974P fiber membrane were also laser cut to the size of the slide (25 \times 75 mm) and their dry mass, m_{membrane(dry)}, were recorded. A piece of PVP/ CP974P dry membrane was then placed on top of the wet wick, and the whole assembly returned to the bath for predetermined testing times of 15, 30, 60, 90, or 120 min. After wicking, the assembly was removed and dried of excess droplets and weighed as before ($m_{wick+membrane(wet)}$). Buffered solutions of pH 4, 5, 6, 7, and 8 were evaluated for all CP974P to PVP ratios. Using this approach, the amount of absorbed buffer solution, $m_{\text{buffer absorbed}}, \text{can}$ be measured accurately by eliminating the possible variation caused by the loss of the sample membrane in solution, calculated using Equation (1).

 $m_{buffer \ absorbed} = m_{wick+membrane(wet)} - m_{wick(wet)} - m_{membrane(dry)}$ (1)

Evaluation of Spreadability: To quantify pH-dependent changes in structural and viscoelastic properties of hydrated fiber membranes, the spreadability of the polymeric gel phase that resulted from exposure of dry fiber membranes with increasing volume fractions of pH 4 or 8 buffer solutions was measured using the TA-XTPlus texture analyzer (Stable Microsystems, Surrey, UK) equipped with a parallel glass plate assembly as outlined in Figure 8. For a single measurement, two layers of fiber membranes were immobilized on the lower glass plate using a compression ring with a circular opening in the center that allowed fluid exposure to a membrane surface area of 9 cm². Reproducible fluid administration was accomplished by spraying 70 to 1720 µL of pH 4 or 8 buffer solution from a constant distance of 37 mm onto the membrane surface. To rapidly expose the entire membrane surface to the applied fluid, the buffer solution was applied using a plastic syringe fitted with a MAD Nasal Intranasal Mucosal Atomization nozzle (Teleflex, Wayne, PA) that creates a fine mist of fluid particles ranging from 30-100 µm in size. After a 5 min incubation period at room temperature, the coaxially aligned upper glass plate was lowered at a test speed of 0.1 mm s⁻¹ until a maximum load force of 5 N was reached. Each experiment was performed in triplicate using fresh membrane samples. The area under the force-distance curve is equivalent

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Table 2. List of samples and electrospinning parameters.

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Figure ID	Host polymer			CP974P Conc. [wt.%]	Voltage [kV]	Flow rate [mL h ⁻¹]
	Material	Molecular Weight [Da]	Conc. [wt.%]	-		
Figure 4d; Figure S4f (Supporting Information)	PVP	1.3 м	8	4	10	2.0
Figure S4b (Supporting Information)	PEO	200 К	6	3	11	1.8
Figure S4c (Supporting Information)	PVP / HPMC	1.3 м / 24 К	4 / 1	2.5	12	1.9
Figure S4d (Supporting Information)	PVP	1.3 м	4	2	12	1.5
Figure <mark>S4e</mark> (Supporting Information)	PVP	1.3 м	6	3	10	1.8
Figure <mark>4</mark> a	PVP	1.3 м	8	0	10	1.8
Figure 4b				1	10	2.0
Figure <mark>4c</mark>				2	10	2.0
Figure <mark>4</mark> e				8	9	2.0
Figure 5	PVP	1.3м	8	8	spinneret 9.5 collector	2.5
Figure 6				4	2	
Figure 7				2		
				0.8		
				0.0		



Figure 7. Electrospun membrane liquid uptake measurement: a) crosssectional schematic of the wicking testing setup illustrates fluid drawn up a cellulose pad (green) by wicking; electrospun membrane (red) is placed on the wet cellulose surface and allowed to hydrate; b) photograph of the wicking test setup with three test membranes loaded into an acrylic testing rig, sitting in a basin of buffered pH solution.

to the total work done to spread (or shear) the polymeric gel phase.

Evaluation of Buffer Capacity: Buffer capacity of Carbopol fiber membranes was assessed by measuring the pH value of the gel phase established after exposure of dry fiber membranes with increasing volume fractions of pH 4 or 8 buffer solutions using the DeltaTrak Pocket ISFET pH Meter, which is equipped with an ion-sensitive field effect transistor pH sensor and an integrated temperature sensor (DeltaTrak, Inc., Pleasanton, CA). Measurements were performed in duplicate at room temperature.

Evaluation of Membrane Pore Size: The pore size distribution of electrospun fiber membranes comprised of different CP974P and PVP mass ratios was quantified experimentally using capillary flow porometry as described by Reichman and colleagues.^[20] Briefly, the fiber membrane was inserted into the Porometer 3G sample holder (25 mm diameter, Anton Paar, Ashland, VA) and wetted using two drops of low surface tension pore filling solution (Porofil). After a 5 min incubation period, the flow of nitrogen was measured against the applied pressure to calculate the pore size of the most constricted part of through pores in the membranes following the Young–Laplace equation. Experiments were performed in triplicate and the minimum, maximum, and mean pore size was calculated from the pressure/flow diagrams using the manufacturer-supplied 3GWin2 v2.3.6 permeability software, plotted in Figure S5 (Supporting Information).

Other Experimental Procedures: All mass measurements were taken using a Denver Instruments PI-225D digital balance (Bohemia, NY). Membrane thickness was measured using a model 543–792 absolute digital indicator mounted on a model 215-151-10 comparator stand (Mitutoyo, Aurora, IL). The thickness, area, and mass of a membrane was used to calculate average densities of bulk polymer ($\rho_{bulk polymers}$) and membrane ($\rho_{membrane}$), from which porosity was calculated from Equation (2).

$$Porosity = \frac{\rho_{bulk \ polymers} - \rho_{membrane}}{\rho_{bulk \ polymers}} \times 100 \ (\%) \tag{2}$$

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Figure 8. Spreadability assessment of the gel phase established after exposure of electrospun fiber mats to various volume fractions of pH 4 or 8 buffer solutions: a) schematic of measurement process, b) customized test probe & stage setup.

For SEM observation, fiber samples were coated with thin gold layer using Denton Desk V sputter (Moorestown, NJ) for 60 s under 40 mA current and 50 mTorr pressure. Gold coated samples were imaged using an EVEX Mini-SEM SX-3000 (Princeton, NJ) with an acceleration voltage of 20 kV. Carbopol fiber membrane and cellulose wicking pad were cut using a Universal Laser Systems VLS3.60DT 50 W CO2 laser cutter (Scottsdale, AZ).

Membranes were characterized by determining the average thickness, average fiber diameter, and average mass cm⁻². The thickness was determined by cutting a \approx 3 cm wide strip of membrane parallel to the axis of rotation of the drum collector. The thickness gauge was then used to measure 8 points evenly spaced along the length of the strip and averaged to find average thickness. Areal density was determined by dividing the mass of the membrane and by the membrane's area. Fiber diameter was determined by use of on-screen verniers in the SEM.

Dispersion settling tests were performed to evaluate the stability of CP974P dispersion during the typical electrospinning process times from solution preparation to fiber formation (circa 12 h). To do so, a standard 8:8 suspension was prepared as well as a second sonicated vial containing only CP974P and TFE for comparative control. The vials were left undisturbed on a benchtop in the lab. They were tilted once per day over the course of a week and the bottoms of the vials observed.

Supporting Information

Supporting Information is available from the Wiley Online Library or from the author.

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Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Keywords

carbopol, electrospinning, nanofiber, pH responsive hydrogel, skin compatibility

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