Ultra-fast self-gelling powder mediate robust wet adhesion to promote healing of gastrointestinal perforations

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Abstract

Achieving strong adhesion of bioadhesives on wet tissues remains a challenge and an acute clinical need due to the interfering interfacial water and lack of adhesive–tissue interactions. Herein we report a self-gelling and adhesive polyethyleneimine and polyacrylic acid (PEI/PAA) powder, which can absorb interfacial water to rapidly form a physically crosslinked hydrogel *in situ* within two seconds due to strong physical interactions between the polymers. Furthermore, the physically crosslinked polymers can diffuse into the substrate polymeric network to enhance wet adhesion on various tissues. Superficial deposition of PEI/PAA powder can effectively seal damaged porcine stomach and intestine despite excessive mechanical challenges. We further demonstrate the use of PEI/PAA powder as sealants to enhance the treatment outcomes of gastric perforation in a rat model. Owing to their strong wet adhesion, excellent cytocompatibility, adaptability to fit complex target sites, and easy synthesis, we believe that the PEI/PAA powder are promising bioadhesives with a wide array of biomedical applications.

Introduction

Adhesive hydrogels that can strongly adhere to wet tissues have been widely used in wound dressings,^{1–5} hemostatic agents,^{6–10} wearable devices,^{11–13} drug delivery systems,^{14, 15} and tissue engineering,^{16–21} owing to their strong adhesion, excellent biocompatibility, good permeability, high deformability, and tunable mechanical properties. Two main hydrogel design strategies have been adopted to achieve adhesion on wet tissues: adhering prefabricated adhesive hydrogels^{22–29} on wet tissues and forming adhesive hydrogels on wet tissues *in situ* from precursor solutions.^{7, 8, 30–32} For the first strategy, polymers containing adhesive functional groups in the hydrogel network need to diffuse through the tissue interfacial water to bond with the tissues. However, most adhesive hydrogels are stabilized by chemical crosslinking, which restricts polymer diffusion, thereby leading to weak tissue–hydrogel contact and bonding. For the second strategy, monomers or macromers containing the adhesive functional groups in the precursor solutions also need to diffuse through interfacial water to bond with tissues while undergoing rapid polymerization. However, the short gelation time and the chemically crosslinked hydrogel networks hamper the effective contact and bonding between the hydrogels and tissues. Therefore, the tissue interfacial water and the lack of polymer dynamics in hydrogel network are key hurdles to achieving robust adhesion between hydrogels and wet tissues.

Recent studies have developed adhesives that can remove or absorb interfacial water to form tight contact with tissues.^{6, 33–37} Cui et al. reported a hyperbranched polymer adhesive containing a hydrophobic backbone and hydrophilic side branches with catechol groups.⁶ Upon contacting water, the hydrophobic chains self-aggregate to form coacervates, which displace the interfacial water and promote catechol group exposure, leading to tight contact and strong adhesion between the adhesives and tissues. Yuk et al. prepared a dried double-sided tape by dehydrating hydrogels containing carboxylic acid and *N*-hydrosuccinimide ester groups.³⁶ The dried tape absorbs interfacial water and forms effective covalent bonds and strong adhesion on the tissues. Han et al. prepared dynamic hydrophobic hydrogels,

which repel interfacial water to form tight contact, effective hydrophobic interactions, and strong adhesion on wet substrates.³⁷ Therefore, removing interfacial water on wet tissues is an effective approach to achieving strong wet adhesion. On the other hand, Yang et al. developed a topological adhesion strategy to promote interfacial adhesion by using stitching polymer solutions.³⁸ Upon spreading the stitching polymer solution between two soft materials, the polymer molecules can diffuse into the polymer network of both the materials to form a new network, leading to strong adhesion between the two soft materials.

Herein we report a polyethyleneimine/polyacrylic acid (PEI/PAA) powder that can *in-situ* form physically crosslinked hydrogels on wet tissues within two seconds by absorbing interfacial water. Furthermore, the physically crosslinked polymers can diffuse into substrate polymeric network to enhance wet adhesion on various tissues, such as chicken skin, porcine heart, and mucosa of porcine stomach and intestine. We demonstrated that the PEI/PAA powder can effectively seal damaged porcine stomach and intestine *in vitro* and promote healing of gastric perforation in a rat model. The advantages of the adhesive PEI/PAA powder including low cost, adaptability to fit irregular-shaped target sites, easy delivery by assistive devices, strong adhesion, and excellent cytocompatibility make it a promising adhesive biomaterial for use in a wide array of medical applications.

Results

Preparation and properties of PEI/PAA powder. Self-gelling and adhesive polyethyleneimine/poly (acrylic acid) (PEI/PAA) powder were prepared by freeze-drying and grinding PEI/PAA complexes,^{39–41} which were prepared by mixing equal volume of aqueous PEI (M_w ca. 70,000, 10 wt%) and PAA (M_w ca. 240,000, 10 wt%) solutions (Fig. 1a and Supplementary Fig. 1). Addition of water or PBS to the obtained PEI/PAA powder that were deposited into different shapes resulted in the rapid formation of hydrogels of the same shape without any additional preparation steps (Fig. 1c and Supplementary Movie 1). As a comparison, we prepared chemically crosslinked PEI-cPAA hydrogels by free radical polymerization of acrylic acid (AA) in the presence of PEI and a chemical crosslinker. However, the dried powder of chemically crosslinked PEI-cPAA hydrogels cannot form a bulk hydrogel after hydration (Fig. 1b, Supplementary Fig. 2 and Supplementary Movie 2). To further study the self-gelation of PEI/PAA powder, we first observed the changes that occurred while the powder was turned into a hydrogel by using a microscope. The PEI/PAA powder rapidly absorbed water and swelled to connect with each other to form a bulk hydrogel (Fig. 1d and Supplementary Fig. 3). The gelation of PEI/PAA powder upon hydration was completed in 2 s, which is much faster than the time required for gelation of fibrin gel (approximately 10 s) (Fig. 1e and Supplementary Fig. 4).

We next studied the crosslinking mechanisms of PEI/PAA hydrogel. Fourier transform infrared (FTIR) spectra of PEI, PAA, and PEI/PAA gels are shown in Fig. 1 f. The carboxylic acid ($-\text{COOH}$) peaks at 1695 cm^{-1} in PAA and the amine group ($-\text{NH}_2$ or $-\text{NH}$) peaks in PEI at 1585 cm^{-1} shifted to 1708 cm^{-1} and 1546 cm^{-1} in PEI/PAA gels, respectively. The shifting of the characteristic carboxylic acid and amine

group peaks in PEI/PAA gel without generating new characteristic peaks indicated that PEI and PAA are crosslinked through physical interactions, such as hydrogen bonding and electrostatic interaction, instead of covalent bonds. Dynamic oscillatory rheological studies were performed to compare the rheological properties of the PEI/PAA hydrogels with those of the chemically crosslinked PEI-cPAA hydrogels. The storage modulus (G'), loss modulus (G''), and loss factor ($\tan \delta = G''/G'$) of the PEI/PAA hydrogels were depended on frequency and temperature, whereas those of the chemically crosslinked hydrogels were independent of both the parameters (Fig. 1g and Supplementary Fig. 5). These results further indicated that the PEI/PAA hydrogels are only crosslinked through physical interactions.

Finally, we investigated the polymer diffusion during the PEI/PAA hydrogel formation. We prepared fluorescent PEI_{FITC}/PAA powder by labeling 20% of the added PEI with fluorescein isothiocyanate (FITC) and monitored its self-gelation process upon hydration by using confocal microscopy (Fig. 1h). Initially, fluorescent regions in the PEI_{FITC}/PAA powder were dispersed. After absorbing water, the fluorescent regions expanded due to swelling of the powder until the whole hydrogel was fluorescent, and this indicated the diffusion of polymers during the formation of the physically crosslinked hydrogel. It should be noted that only 20% of the PEI was labeled with FITC, and therefore, we expect the diffusion of polymers should be more rapid and significant than that observed in the confocal imaging. As a comparison, we then observed the changes occurring in the chemically crosslinked PEI_{FITC}-cPAA gel powder (100% of the PEI was labeled with FITC) upon hydration. The diffusion of polymers was limited by chemical crosslinking as evident from the fluorescent regions that remained separate even after being incubated at 37 °C for 12 h (Supplementary Fig. 6). These results showed that polymer diffusion also plays an important role in the self-gelation of PEI/PAA powder. Owing to the strong physical interaction between PEI and PAA and the diffusion of physically crosslinked polymers, the dispersed PEI/PAA powder can absorb water and swell to connect with each other to form physically crosslinked hydrogels within 2 seconds of hydration.

We next studied the factors affecting the mechanical properties of PEI/PAA hydrogel. PEI_x/PAA_y powders were prepared using varying mass ratios (x: y) of PEI (M_w ca. 70,000) and PAA (M_w ca. 240,000). PEI₃/PAA₇ and PEI₅/PAA₅ powders formed hydrogels, while the other formulations formed coacervates (Fig. 1i). In addition, the powders prepared with low molecular weight PEI (M_w ca. 1800) and PAA (M_w ca. 3000), formed coacervates instead of hydrogels after absorbing water (Supplementary Fig. 7). Moreover, the tensile properties of the PEI₅/PAA₅ hydrogels improved over time (Fig. 1j and Supplementary Fig. 8). After incubating at 37 °C for 30 min, the failure elongation and tensile strength of the PEI₅/PAA₅ hydrogels were 702% and 57.1 kPa, respectively. Thus, the PEI₅/PAA₅ powder prepared using 50% PEI (M_w ca. 70,000) and 50% PAA (M_w ca. 240,000) was used in subsequent experiments.

In addition, PEI/PAA powder showed good cytocompatibility. The viability of gastric epithelial cells after being co-incubated with either PEI/PAA hydrogels or control medium for 7 days was greater than 95% with no statistically significant differences between the samples. The live gastric epithelial cells were

stained green and exhibited a spindle like morphology in all samples (Fig. 1k). These results indicated that PEI/PAA powder was cytocompatible.

Wet adhesion mechanism of PEI/PAA powder. We next evaluated the wet adhesive properties of PEI/PAA powder. PEI/PAA powder deposited on wet substrates can absorb interfacial water quickly to form physically crosslinked hydrogel *in situ* (Fig. 2a). We first assessed the water absorption of prefabricated hydrated PEI/PAA hydrogels prepared from PEI/PAA powder, dried chemically crosslinked PEI-cPAA gel, and PEI/PAA powder by recording weight change of aqueous Rhodamine B solution on a glass plate before and after applying the different test materials. The dried PEI-cPAA gel and the PEI/PAA powder absorbed most of the solution, but the prefabricated PEI/PAA hydrogel only absorbed approximately 50% of the solution (Fig. 2d). This result showed that the PEI/PAA powder and the dried PEI-cPAA gel can quickly absorb substantial amount of interfacial water to form tight contact with substrates, while the contact of the prefabricated hydrated hydrogel with substrate was limited by the interfacial water (Fig. 2a-c).

We next studied the interactions between the adhesives and substrates. We spread PEI/PAA powder on a poly (acrylamide) (PAAm) hydrogel and immersed them in water for 30 days, and examined the cross-sections of the obtained hydrogels by SEM. There was a dense interface layer (approximately 20 μm) with no notable gap between the PAAm and *in situ*-formed PEI/PAA hydrogels. The element composition of C, N, O, and H of the interfacial gel was between that of the PAAm and PEI/PAA gels (Supplementary Fig. 9). In contrast, both the dried PEI-cPAA gel and prefabricated PEI/PAA hydrogel adhered to the PAAm hydrogels showed obvious gaps between the adhesives and the substrates because their adhesion was hampered by the chemically crosslinked network and interfacial water, respectively (Fig. 2d). Moreover, the adhered PEI_{FITC}-PAA powder can diffuse into the PAAm hydrogel network as evidenced by the increasing fluorescence in the PAAm hydrogel substrate over time (Fig. 2e). These findings together demonstrated that the PEI/PAA powder can effectively absorb interfacial water to form physically crosslinked hydrogels *in situ*, and the physically crosslinked polymers can diffuse into the substrate network to further promote adhesive–substrate interactions, resulting in the enhanced wet adhesion.

Strong adhesion of PEI/PAA powder on wet tissues. To demonstrate the potential applications of the PEI/PAA powder, we first investigated the adhesion of PEI/PAA powder using the PAAm hydrogel and animal tissues as the substrates *in vitro*. When PEI/PAA powder were spread on a PAAm hydrogel, the PEI/PAA hydrogel formed *in situ* within 2 s can strongly adhere to the PAAm hydrogel substrate without minimal detachment upon repeated bending and stretching of the substrate even after being immersed in deionized water for 30 days (Fig. 3a and Supplementary Movie 3). Moreover, the PEI/PAA powder also can form hydrogels *in situ* on chicken skin and porcine heart. The PEI/PAA hydrogels strongly adhered to these tissues despite distorting, bending, or water flushing even after being immersed in PBS for 12 h (Fig. 3b, c, Supplementary Movie 4 and Supplementary Movie 5). Further, PEI/PAA powder deposited on the mucosa of porcine stomach and intestine can form hydrogels *in situ*, which strongly adhered on the tissues even after being immersed in the simulated gastric fluid (SGF) and simulated intestinal fluid (SIF) for 12 h, respectively (Fig. 3d, e, Supplementary Movie 6 and Supplementary Movie 7).

We next evaluated the adhesion performance of different adhesives on chicken skin by using the lap shear test (Supplementary Fig. 10). The PEI/PAA powder showed an adhesion stress of 70.4 kPa, which was much higher than that of the prefabricated hydrated PEI/PAA hydrogel (18.2 kPa), dried PEI-cPAA gel powder (20.2 kPa), and fibrin gel (37.8 kPa) (Fig. 3f). Moreover, the PEI/PAA powder showed excellent adhesion on various tissues including porcine liver, stomach, intestine, and heart (Fig. 3g). The adhesion of PEI/PAA powder increased with increasing temperature because of the enhanced polymer diffusion with increasing temperature (Fig. 3h). The PEI₅/PAA₅ powder showed the highest shear strength among all the formulations, and this can be attributed to the best mechanical and therefore cohesion property of the PEI₅/PAA₅ powder-formed hydrogel (Fig. 1i and Fig. 3i).

In addition, PEI/PAA powder can seal damaged porcine stomach (1.5 cm-long strip wound) filled with SGF and damaged porcine small intestine (5 mm diameter circular wound) filled with SIF (Fig. 4a, b, Supplementary Movie 8 and Supplementary Movie 9). The damaged tissues sealed by the PEI/PAA powder showed higher bursting pressure than tissues sealed by fibrin gels (Fig. 4c, d). Next, we adhered a stretchable strain sensor on the damaged intestine using an *in situ* formed PEI/PAA hydrogel (Fig. 4e). The PEI/PAA hydrogel supported the tight adhesion of the foil strain sensor on the dynamic and curved surface of the beating porcine small intestine and enabled the electrical measurements of tissue shrinking and expansion (Fig. 4f and Supplementary Movie 10). These results showed that the PEI/PAA powder can seal the damaged tissues and serve as a versatile platform to attach wearable and implantable devices onto wet and dynamic tissues.

Enhanced healing of gastric perforation by PEI/PAA powder treatment. To further demonstrate that the PEI/PAA powder can be used as sealants to treat gastrointestinal perforation, we used an *in-vivo* rat gastric perforation model^{42–44} (Fig. 5a). A 5-mm vertical perforation was made at the gastric antrum using a scalpel, allowing the gastric lumen to open into the abdominal cavity. The gastric perforations were disinfected with iodophor and closed by using a non-absorbable suture, fibrin gel, or PEI/PAA powder. On day 7 after the treatment, macroscopic investigation revealed that the wounds treated with the suture and the PEI/PAA powder showed better macroscopic healing than the fibrin gel treatment group (Fig. 5b). Hematoxylin-eosin (H&E) staining showed that the gastric perforations sealed with the PEI/PAA powder were completely bridged with the regenerated mucosa (Fig. 5c). Importantly, the PEI/PAA hydrogel formed *in situ* still tightly adhered to the stomach wall on day 7 after the treatment (Fig. 5d). In contrast, perforations treated with the suture and fibrin gel showed clear gaps in the mucosa. We also examined the expression of proliferating cell nuclear antigen (PCNA, a proliferation marker of G1/S phase) and CD31 (a marker for endothelial cell and angiogenesis) to assess the re-epithelialization of the gastric wound. The perforations treated with the PEI/PAA powder showed the highest percentage of PCNA-positive epithelial cells and the highest blood vessel density in the granulation tissue as evidenced by CD31 staining of all the tissue samples (Fig. 5e, f). Taken together, these results showed that the PEI/PAA powder can seal and promote healing of gastric perforations *in vivo*.

Discussion

In this work, we prepared self-gelling and adhesive PEI/PAA powder. Owing to the strong physical interactions between the polymers and free polymer diffusion, the PEI/PAA powder can directly form physically crosslinked hydrogels by absorbing water without additional crosslinking agents. Superficially deposited PEI/PAA powder can absorb interfacial water to form tight contact with various wet substrates. Furthermore, the physically crosslinked polymers can diffuse into the polymeric network of the wet substrates to further promote wet adhesion. Therefore, spreading PEI/PAA powder on various tissues, such as chicken skin, porcine heart, and mucosa of porcine stomach and intestine resulted in strong adhesion on these wet tissues over a prolonged time period. Moreover, such adhesive PEI/PAA powder can effectively seal and promote healing of damaged tissues *in vivo* and facilitate attachment of medical devices. Owing to the strong adhesion and easy preparation of PEI/PAA powder, we believe that these powder are an ideal candidate for several applications, such as wound healing, hemostatic agents, wearable devices, and drug delivery.

Materials And Methods

Materials. Polyethyleneimine (PEI, M_w ca. 70,000 and M_w ca. 1,800) aqueous solution (50 wt%), potassium persulfate (KPS), *N,N'*-methylenebisacrylamide (BIS), acrylamide (AAm) and acrylic acid (AA) were purchased from Aladdin (China). Poly (acrylic acid) (PAA, M_w ca. 240,000 and M_w ca. 3,000) aqueous solution (25 wt%) and fluorescein isothiocyanate (FITC) were purchased from J&K Scientific (China). Calcein-AM, propidium iodide, and trypsin were purchased from Sigma (USA). Dulbecco's modified eagle medium (DMEM) and fetal bovine serum were purchased from Gibco (USA). Penicillin and streptomycin were purchased from Hyclone (USA). PEI_{FITC} was prepared by mixing 1 g PEI with 10 mg FITC in a mixed solution of DMSO and water at room temperature in the dark for 24 h. The mixture was purified by dialysis. Fibrin gel was purchased from Beixiu Biotechnology Co., Ltd (China).

Non-absorbable suture was purchased from Ethicon, Johnson & Johnson, Somerville (New Jersey, USA). Anti-proliferating cell nuclear antigen (PCNA) mouse polyclonal antibody and anti-CD31 mouse polyclonal antibody were purchased from Santa Cruz Biotechnology (Texas, USA). Anti-mouse IgG and peroxidase-labeled streptavidin were purchased from Vector Laboratories (California, USA). Diaminobenzidine (DAB) solution was purchased from Dako (Glostrup, Denmark).

PEI/PAA powder preparation. We mixed 10 wt% PEI (M_w ca. 70,000) and 10 wt% PAA (M_w ca. 240,000) aqueous solution in the following ratios: 1:9, 3:7, 5:5, 7:3 and 9:1. Additionally, we mixed 10 wt% PEI (M_w ca. 70,000 or 1800) and 10 wt% PAA (M_w ca. 240,000 or 3000) in a 5:5 volume ratio. The mixtures were immediately immersed in liquid nitrogen for about 15 min without pouring out any liquid and freeze-dried to remove water. Finally, the dried solids were ground to obtain PEI/PAA powder using a mortar and pestle. The PEI/PAA powders were prepared by mixing 5:5 PEI (10 wt%, M_w ca. 70,000) and PAA (10 wt%, M_w ca. 240,000) aqueous solutions, unless otherwise stated. PEI_{FITC} was used to prepare PEI_{FITC}/PAA powder as indicated.

Lap shear test. Lap shear tests were performed using a Kinexus rheometer with custom clamps at a crosshead speed of 3 mm min^{-1} . For lap shear tests (Fig. S12), different adhesives were sandwiched between two tissues with an adhesion area of $2 \text{ cm} \times 1 \text{ cm}$. The adhesion stress was calculated as follows: Adhesion stress = $F_{\text{max}}/(wl)$, where F_{max} was the maximum force, and w and l were the width and length of the adhesion area). Three specimens per condition were tested to ensure the reliability of the data.

Bursting pressure test. Bursting pressure tests were performed according to previous reports.²² As shown in Fig. 4c, tissues with a penetrating defect were fixed on a cylinder, and attached to a syringe pump and a pressure monitor through a three-way stopcock. The whole device was then filled with PBS. Five minutes after the adhesives were applied, pressure was applied via the pump at a speed of 2 mL min^{-1} . A rapid pressure decrease was considered the bursting pressure.

Animal models. Animal experiments were conducted according to the guidelines of the Animal Ordinance (Chap. 340), Department of Health, Hong Kong. The study was approved by the Animal Experimentation Ethics Committee of the Chinese University of Hong Kong (12-052-MIS). Animal experiments are shown in Fig. 5a. After fasting for 12 h, the rats were anaesthetized by intraperitoneal administration of ketamine (80 mg per kg of body weight), and their stomachs were exposed along the midline abdominal incision. A 5-mm vertical perforation was then made at the body of the stomach using a scalpel. The wounds were disinfected with iodophor first. Forceps were used to grasp the opposing wound edge, and then applying fibrin gel or PEI/PAA powders until gelation *in situ* achieved. A positive control group with closing wounds by suturing was also set. All experiments were performed under sterile conditions. The rats returned to a normal diet after 36 h and were given standard care and regular monitoring. Five female wild-type Sprague-Dawley rats (200 ~ 250 g) were used for the PEI/PAA powder group, and three for suture and fibrin gel groups, respectively.

Macroscopic observation and tissue preparation. Rats were euthanized 7 days after surgery. The stomachs were opened along the lesser curvature to observe wound healing. Macroscopic images revealing wound approximation were taken. The tissues adhered with PEI/PAA hydrogel were immersed in liquid nitrogen for 15 min and freeze-dried. Cross sections of the tissue-hydrogel were observed by SEM. Other tissues were fixed in phosphate-buffered formalin for 24 h, dehydrated, and embedded in paraffin.

Histological assessment. Paraffin-embedded samples were cut into $5\text{-}\mu\text{m}$ sections, which were dewaxed using xylene and dehydrated using gradient alcohol. Then, the slides were stained with hematoxylin-eosin (HE) according to established protocols. Histological analysis was conducted by a blinded pathologist to assess the healing of gastric perforations.

Immunohistochemistry. Immunohistochemistry was performed to detect PCNA (a cell proliferation marker) and assess regenerated blood vessels (CD31) in the gastric wound. These methods are described in the Supplementary Information.

The authors declare that all relevant data of this study are available from the corresponding authors.

Declarations

Competing interests

The authors declare no competing interests.

Author contributions

X.P., X.X and L.B. conceived and designed the experiments. X.P. performed the materials preparations and characterization. X.P., X.X. and X.X. conducted the experiments of animal studies. X. Y., B. Y., P. Z. and W. Y. provided suggestions. X.P. and L.B. wrote the paper. All authors commented on the manuscript.

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Figures

Figure 1

Preparation and properties of PEI/PAA hydrogel. a Schematic illustration of polyethyleneimine/polyacrylic acid (PEI/PAA) powder and PEI/PAA hydrogel preparation. b Schematic illustration of chemically crosslinked PEI-cPAA hydrogel preparation and the swelling of the dried gel powder. c Heart, C, U, H and K-shaped PEI/PAA hydrogels formed upon adding water to the PEI/PAA powder deposited on the glass plates. d The process of changing from dispersed PEI/PAA powder to bulk hydrogel. e Gelation time of the PEI/PAA powder upon absorbing water as determined by rheological analysis. f FTIR spectra of PEI, PAA, and dried PEI/PAA gel. g The storage modulus (G') and loss modulus (G'') as a function of frequency of the physically crosslinked PEI/PAA hydrogels and chemically

crosslinked PEI-cPAA hydrogels. Strain = 1% and T = 25 °C. h Confocal microscopy images of polymer diffusion in PEI/PAA hydrogel. i Storage modulus (G') and loss modulus (G'') of PEI/PAA hydrogels/coacervates prepared with varying mass ratios of large molecular weight PEI and PAA. j Typical tensile stress vs. strain curves of the PEI5/PAA5 hydrogels incubated at 37 °C. k Live/Dead staining (left) and cell viability (right) of gastric epithelial cells after being co-incubated with hydrogel or positive control media for 7 days (n=5).

Figure 2

Wet adhesion of the PEI/PAA powder. a-c Schematic illustration for wet adhesion of PEI/PAA powder (a), dried chemically crosslinked PEI-cPAA gel (b), and prefabricated hydrated PEI/PAA hydrogel (c). d Water absorption of three test materials. e SEM images of PAAm hydrogel adhered with three test materials. f Confocal microscopy images of the diffusion of the physically crosslinked polymers in the deposited PEI/PAA powder into the PAAm hydrogel substrate.

Figure 3

The adhesion of PEI/PAA powder on various wet substrates/tissues. a-e Adhesion of PEI/PAA powder on a wet poly (acryl amide) (PAAm) hydrogel (a), chicken skin (b), porcine heart (c), and the mucosa of porcine intestine (d) and stomach (e) before and after immersion in various aqueous solutions. f Adhesion stress of different adhesives on wet chicken skin. g Adhesion stress of PEI/PAA powder on various tissues. h Change in adhesion stress on skins after being incubation at different temperature. i, Adhesion stress of different PEI_x/PAA_y powders on skins. All scale bars are 1 cm.

Figure 4

The wound sealing and device-anchorage capability of PEI/PAA powder. a, b The PEI/PAA powder effectively sealed a 1.5 cm-long strip wound in a porcine stomach filled with simulated gastric fluid (SGF) (a) and a 5 mm diameter circular wound in a porcine small intestine filled with simulated intestinal fluid (SIF) (b). c Schematic illustration for the bursting pressure test. d Bursting pressure of stomach and intestine sealed by either fibrin gel or PEI/PAA powder. e Adhesion of a stretchable strain sensor on a damaged porcine small intestine. f Electrical resistance (R/R_0) measured by the PEI/PAA hydrogel-adhered strain sensor over several cycles. The gray and white shades indicate inflation and deflation, respectively.

Figure 5

Enhanced sealing and healing of gastric perforations by the PEI/PAA powder. a A schematic illustration and photos of the surgical procedures performed to seal gastric perforations. b, c Macroscopic photos (b) and Hematoxylin-eosin (H&E) staining (c) of gastric wounds acquired on day 7 after treatment with sutures, fibrin gel, or PEI/PAA powder (original magnification: $\times 20$ for top, $\times 40$ for bottom). d Photographs and SEM images of PEI/PAA hydrogel adhered on the stomach wall. e Representative images and quantification of staining against proliferating cell nuclear antigen (PCNA) at high power field (HPF, original magnification $\times 400$, hematoxylin counterstain). f Representative images and quantification of staining against the angiogenesis marker, CD31 at high power field (HPF, original magnification $\times 200$, hematoxylin counterstain).

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