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Closed-Loop Theranostic Hydrogel-Electronics Patch for Chronic Wound Management

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Abstract: Chronic diabetic wounds present a significant clinical challenge due to antibiotic abuse and limited understanding of the wound microenvironment. Real-time monitoring of key biomarkers in the wound microenvironment can provide critical insights into wound status and guide therapeutic interventions. In this study, we developed an intelligent wound patch by integrating a near-infrared (NIR)-responsive photothermal antibiotic-releasing hydrogel (PPQTA) with a multichannel electrochemical biosensor array, which takes sensor monitoring-guided precise drug administration as its core. The sensing module can continuously monitor the key biomarkers in the wound in situ with high sensitivity and strong anti-interference capability within the physiological range (pH: 4–9; uric acid: 0–700 μ M; glucose: 5–30 mM), providing a quantitative basis for drug release. The PPQTA hydrogel can release drugs on demand *via* NIR irradiation based on the sensing results, achieving 100% antibacterial efficacy against both Gram-negative and Gram-positive bacteria. Experiments in a diabetic rat wound model confirmed that this patch can monitor the dynamic changes of biomarkers in situ and guide drug administration within 7 days. After terminating drug administration on day 4, the bacteria in the wound were effectively eliminated on day 5, and the wound healing process was significantly promoted. By combining real-time diagnostics with responsive therapy, this patch offers a closed-loop strategy for personalized management of diabetic chronic wounds.

Keywords: Wearable bioelectronics; Flexible biosensing; Theranostic hydrogel; Closed-loop wearable patch; Chronic diabetic wounds; Wound management.

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Introduction

The healing of chronic wounds, a complex biological process involving inflammation, proliferation, and remodeling stages [1-3], is severely impaired in diabetic patients. Hyperglycemia can lead to prolonged inflammation, making these wounds difficult to heal and often resulting in severe complications such as amputation or death [4-6]. Conventional wound management relies heavily on gauze dressings, which require visual assessment and wound culture tests by healthcare providers [7]. This approach, however, is subjective, time-consuming, and lacks the capability for real-time monitoring of the wound's dynamic physicochemical microenvironment. Consequently, it often leads to the irrational use of antibiotics, accelerating the development of antibiotic resistance and increasing infection-related morbidity and mortality rates [8]. Therefore, there is an urgent need for the development of smart wound dressings that enable real-time monitoring of the wound microenvironment and on-demand therapeutic intervention.

Hydrogels have emerged as promising candidates for advanced wound dressings due to their excellent hydrophilicity, good biocompatibility, and unique three-dimensional porous structure that facilitates drug loading [9-11]. Although hydrogel-based dressings have shown progress in chronic wound treatment, most current systems are limited to monitoring a single wound biomarker, failing to provide a comprehensive assessment of the wound status [12-14]. The wound healing process involves multiple dynamically changing parameters, making multi-indicator monitoring critical for accurate diagnosis and treatment guidance [15-19]. Furthermore, the ability to trigger responsive drug release based on wound monitoring data is essential for effective infection control and treatment.

Among various stimulus-responsive hydrogels, photothermal hydrogels have garnered significant attention for on-demand drug delivery systems. Their advantages include rapid response, remote controllability, minimal invasiveness, and high spatiotemporal resolution [20, 21]. Specifically, near-infrared (NIR)-induced photothermal hydrogels exhibit strong NIR absorption and excellent photothermal conversion capabilities. These materials can convert light energy into heat, inducing structural changes that facilitate controlled drug release [22-24]. This

approach not only enhances therapeutic efficacy but also significantly reduces side effects [14, 25].

Herein, we report an integrated wireless smart wound patch that combines multi-parameter sensing with NIR-responsive drug delivery. A double-network structured hydrogel (PPQTA) was developed by incorporating tannic acid (TA)-Fe nanoparticles and quaternary ammonium chitosan (QCS) into a poly(N-isopropylacrylamide) (PNIPAM) matrix. This hydrogel exhibits excellent near-infrared responsiveness, high deformation capability, and strong antibacterial properties, enabling precise and non-contact controlled drug release. Simultaneously, a wearable multichannel electrochemical biosensor array with miniaturized flexible electrodes was designed for simultaneous real-time continuous monitoring of key wound biomarkers (pH, uric acid, and glucose). It can accurately track the inflammatory state during the wound healing process, and more importantly, provides a quantitative guidance basis for the initiation and termination of drug release. Through the synergistic integration of the PPQTA hydrogel and the wearable bioelectronic device, this intelligent patch achieves real-time in situ monitoring of multiple parameters and non-contact NIR-controlled drug release in the chronic wound model of diabetic rats, effectively accelerates wound healing, and demonstrates the promising application potential of this intelligent patch in practical clinical scenarios.

Results

Design of the Wireless Chronic Wound Treatment Management System

In the design of this intelligent wound patch, a double-layer structure is adopted, consisting of a multimodal biosensor array and an antibiotic-laden photothermal hydrogel, which is deeply integrated with a custom flexible printed circuit board (FPCB) to create an intelligent system with both monitoring and therapeutic functions (Fig. 1a, b). While the chronic wound is infected with bacteria, the real-time dynamic changes in pH, uric acid, and glucose levels in the exudate will be recorded by the biosensor array. The data is then uploaded to a mobile device via Bluetooth and onward to the cloud (Fig. 1c). Based on a multi-parameter comprehensive analysis of the wound's healing stage, if necessary, the antibiotic-releasing hydrogel system can be activated through near-

infrared (NIR) light irradiation to achieve on-demand drug release, thereby accelerating wound healing (Fig. 1b). This photothermal hydrogel employs PNIPAM as the matrix and incorporates tannic acid-iron nanoparticles as the photothermal conversion material, exhibiting excellent NIR responsive performance (Fig. 1d). The introduction of QCS and acrylamide (AAM) effectively enhances the hydrogel's adhesiveness and lower critical solution temperature (LCST), ensuring precise drug release control under NIR irradiation (Fig. 1d). Notably, both the wound patch and FPCB exhibit excellent flexibility (Fig. S1; Fig. S2 for the circuit principle). The patch, consisting of an electrode layer and hydrogel, hidden beneath the FPCB and can directly contact the chronic wound. The total thickness of the device was merely 6.5 mm. The pre-reserved hollow structure on the circuit board provides a channel for NIR light to penetrate into the hydrogel, further ensuring the precise regulation of drug release (Fig. 1e). This integrated design ultimately achieves a closed-loop management technology for chronic wound monitoring and therapeutic intervention.

Preparation and characterization of electrode arrays and hydrogels

The smart patch consisted of a flexible electrode array and a controllable antibiotic-releasing hydrogel. The electrode array was based on a PET membrane and included three sets of electrochemical electrodes (Fig. 2a). The detailed geometric dimensions of the single electrode were shown in Fig. S3. Among them, the uric acid (UA) sensor and glucose (Glu) sensor adopted a three-electrode system, consisting of carbon working electrode, carbon counter electrode, and Ag/AgCl reference electrode. It is important to note that the UA sensor and Glu sensor shared the same carbon electrode and Ag/AgCl reference electrode, whereas the pH sensor used a separate two-electrode system, consisting of a different carbon working electrode and an Ag/AgCl reference electrode. From the exploded diagram, it could be seen that all electrodes were modified layer by layer to achieve different wound monitoring and therapeutic function (Fig. 2a). All the solutions used for modifying the electrodes are shown in Fig. 2b. To reduce the impedance of the pH sensor electrode, a layer of microspherical gold nanoparticles (AuNPs) was electrochemically deposited on the carbon electrode surface by cyclic voltammetry (CV) (Fig. S4a, b) [26]. Then, a thick

fibrous polyaniline (PANI) layer was further electrochemically deposited on the AuNPs layer (Fig. 2c, d) [27]. For the UA sensor, a non-enzyme design was used for the working electrode, and a composite material of reduced graphene oxide and gold nanoparticles (rGO/AuNPs) was electrochemically deposited by CV (Fig. 2e) [28]. SEM images clearly showed that the gold nanoparticles were evenly distributed on the reduced graphene oxide (rGO) nanosheets (Fig. 2f). The working electrode of the Glu sensor consists of a conductive layer, a transducer layer, and an enzyme layer. First, a layer of AuNPs was deposited on the carbon electrode by constant voltage as the conductive layer (Fig. S4c, d); then, a platinum (Pt) layer was deposited on the AuNPs-modified layer by constant voltage as the transducer layer (Fig. 2g); and finally, a thin layer of glucose oxidase (GOx) was coated as the enzyme layer, completing the three-layered electrode architecture (Fig. 4e) [29, 30].

During the preparation of the controllable antibiotic-releasing hydrogel, poly N-isopropylacrylamide (PNIPAM), a temperature-responsive polymer, was combined with TA-Fe nanoparticles to fabricate a NIR -responsive hydrogel system, enabling on-demand precise wound therapy (Fig. 2i) [31]. As shown in Fig. 2j, the PNIPAM@TA-Fe solution is in a viscous liquid state before crosslinking. After 3 minutes of UV light exposure, NIPAM and AAM undergo chemical crosslinking to form the first primary network of the hydrogel (PP). A small amount of QCS further constructs a secondary network through non-covalent interactions (PPQ). The TA-Fe complex acts as a “molecular bridge” connecting the first primary network and the second network via hydrogen bonding interactions formed with both networks, ultimately establishing a structurally robust 3D network of the composite hydrogel (PPQT) (Fig. 2i). The swelling procedure is shown in Fig. S5, all the hydrogels achieved swelling equilibrium at about 48 h. Pure PNIPAM (P) showed the lowest swelling ratio due to hydrophobic isopropyl side chains. The addition of AAM increased the swelling via hydrogen bonding between amide groups and water molecules. QCS incorporation gave PPQ the highest swelling, as quaternary ammonium groups bound water through electrostatic. TA-Fe nanoparticles reduced the PPQT swelling ratio by interacting with QCS quaternary ammonium groups, increasing crosslinking density and

tightening the network. The freeze-dried PPQT hydrogel exhibited a typical interconnected porous structure, which facilitates efficient drug release [32-34]. With the addition of QCS and TA-Fe nanoparticles, the tensile strain (PPQ $\approx$ 35.60 kPa, PPQT $\approx$ 41.01 kPa) and tensile strength (PPQ $\approx$ 436.78 %, PPQT $\approx$ 549.26 %) of the PPQT hydrogel were significantly enhanced (Fig. S6a, b). The incorporation of QCS and TA-Fe enhances the mechanical properties of the hydrogel and improves its structural stability. Fig. 2k demonstrates the favorable adhesion performance of PPQT hydrogel on various substrates, including wet tissue, iron, and glass, alongside its excellent ductility and stretchability (Fig. S7). To quantitatively characterize the adhesion strength of the hydrogel, we conducted a peel shear test between the pig skin and the hydrogel. The results showed that with the addition of Chitosan Quaternary Ammonium Salt and TA-Fe nanoparticles, the hydrogel's adhesion strength was significantly improved (PPQ: 32 kPa; PPQT: 46 kPa) (Fig. S6c). Therefore, the prepared hydrogel exhibits mechanical properties and favorable tissue adhesion, which effectively prevents injury caused by detachment during application and thus meets the clinical requirements for wound dressings.

NIR-responsive drug release from hydrogels and their *in vitro* antibacterial characterization

To reduce the significant volume change of pure PNIPAM hydrogel at body temperature, hydrophilic molecules AAM was incorporated to increase its LCST (Fig. S8) [35]. When the AAM content is 1%, the hydrogel exhibited a small volume change between 33-37 °C, while at 40 °C, its volume shrank to 60 % of the original volume, while facilitates the rapid release of drugs [36-38]. The photothermal properties of PPQ hydrogels can be achieved by adding NIR-responsive TA-Fe nanoparticles. However, the enhancement effect of TA-Fe nanoparticles varies with different concentrations. Under near infrared light (NIR) (808 nm, 1 W/cm²) irradiation, the PPQT hydrogel without TA-Fe nanoparticles showed no response to the infrared light. As the concentration of TA-Fe nanoparticles increases, the photothermal performance of the PPQT hydrogel gradually improves (Fig. 3a, b). To ensure that NIR could provide appropriate driving energy to the PPQT hydrogel while avoiding potential burns caused by excessive heating during

the photothermal conversion process, the optimal concentration of TA-Fe nanoparticles was determined by comparison to be 200 $\mu\text{g/mL}$ (Fig. 3a, b). Similarly, the intensity of NIR also has a significant impact on the photothermal performance of the PPQT hydrogel. As shown in Fig. 3c, after irradiating hydrogel containing 200 $\mu\text{g/mL}$ TA-Fe nanoparticles with different power intensities (0.5 W/cm^2 , 1 W/cm^2 , 1.5 W/cm^2 , and 2 W/cm^2) for 10 minutes, the hydrogel temperatures were measured at 36.8 $^{\circ}\text{C}$, 41.6 $^{\circ}\text{C}$, 54.8 $^{\circ}\text{C}$, and 65.8 $^{\circ}\text{C}$, respectively. When the irradiation power was 0.5 W/cm^2 , the temperature of the hydrogel increased slowly; moreover, the volume change at this temperature was not conducive to enable rapid drug release (Fig. S8). However, when the irradiation power exceeded 1.5 W/cm^2 , the temperature of the hydrogel increased too rapidly and reached excessive levels, posing a risk of skin burns [39]. Therefore, the most suitable irradiation power is 1 W/cm^2 . Under the irradiation of NIR (1 W/cm^2), the temperature change of the hydrogel did not decrease significantly after four cycles, indicating that the photothermal properties of the hydrogel remained stable after repeated irradiation (Fig. 3d). During the NIR irradiation process, the photothermal drug (Antibiotic cefazolin)-controllable-release hydrogel (PPQTA) converts NIR light energy into thermal energy, thus increasing the local temperature. The rise in temperature leads to a change in the volume of the hydrogel, which in turn promotes the release of the drug from the hydrogel, achieving controlled drug release (Fig. 1d). The intensity of NIR regulates the temperature increment of hydrogels and further modulates the drug release kinetics. As shown in Fig. S9, the cumulative drug release increases positively with the elevation of NIR intensity. However, excessive intensity would raise the hydrogel temperature to approximately 50 $^{\circ}\text{C}$, while low intensity results in a drug release efficiency lower than 20%. Balancing release efficiency and thermal safety, an optimal intensity of 1 W/cm^2 was determined. As illustrated in Fig. 3e, under NIR irradiation, the cumulative drug release from the PPQTA hydrogel reaches 27.9% within 10 minutes, while the drug release is less than 5% after 30 minutes without irradiation, thereby validating the critical modulatory role of NIR in enabling controlled drug release.

To verify the antibacterial effect of the antibiotic-releasing hydrogel under light exposure, we

conducted an inhibition zone experiment with *Staphylococcus aureus* (*S. aureus*, Gram-positive) and *Escherichia coli* (*E. coli*, Gram-negative) (Fig. 3f). After incubation for 12 hours, the size of the inhibition zone was measured. The results showed that the PPQT hydrogel, which contains no drug, failed to form any inhibition zones, and its effect was consistent with the control group. In contrast, the drug-loaded PPQTA hydrogel successfully released the drug after NIR irradiation, significantly inhibiting the growth of *E. coli* and *S. aureus*, and forming clear inhibition zones. At this time, the diameter of the drug-loaded PPQTA hydrogel against *E. coli* and *S. aureus* was 3.07 ± 0.06 and 3.30 ± 0.20 cm, respectively. These results indicate that the excellent bacteriostatic effect of the PPQTA hydrogel stems from the successful release of the drug after NIR irradiation, rather than effect caused by photothermal damage. Further, the antibacterial properties of PNIPAM-based hydrogels of different components were studied by co-culture with *E. coli* and *S. aureus* under NIR irradiation by plate counting (Fig. 3g, i, Fig. S10, 11a). The results showed that only the drug-loaded PPQTA hydrogel exhibited significant antibacterial effects after NIR irradiation, with a marked decrease in bacterial survival rate. In the absence of NIR irradiation, PPQTA hydrogel did not show obvious antibacterial effect. Other components of PNIPAM-based hydrogels, regardless of NIR irradiation, did not significantly inhibit bacterial growth, and the bacterial survival rate did not change much. Furthermore, cyclic antibacterial effect tests were tested (against *S. aureus* and *E. coli*) (Fig. 3h, j, Fig. S11b). The results showed that both the control group and the PPQT hydrogel did not exhibit significant antibacterial effects (with or without NIR irradiation), and there was no obvious difference in sterilization effectiveness. However, the drug-loaded PPQTA hydrogel showed a significant difference in sterilization effectiveness under the presence or absence of NIR irradiation, with the antibacterial effect gradually increasing as the number of irradiation cycles increased (reaching 100 % in the third cycle). This further confirmed the significant drug-controlled release capability of the drug-loaded PPQTA hydrogel under NIR irradiation. The cytocompatibility of the PNIPAM-based hydrogel was evaluated through the CCK-8 method and L929 cells live/dead staining (Fig. S12a, b). The CCK-8 results displayed that the PNIPAM-based hydrogel maintained cell viability greater than 94.9 %, and the fluorescent

images of the cell live/dead staining showed no apparent cytotoxicity, suggesting that it has good biocompatibility. The hemolytic compatibility of the PNIPAM-based hydrogel was evaluated through an in vitro hemolysis test. Compared to the positive control group, the hemolysis rate of the PNIPAM-based hydrogel was lower ($< 0\%$), and the hemolytic effect was negligible, demonstrating its good hemocompatibility (Fig. S12c).

***In vitro* evaluation of the multiplex Biosensors for wound monitoring**

In order to obtain more comprehensive information about the chronic wound to provide more efficient treatment, we integrated pH, UA, and Glu sensors into the same chip to form a biosensor that can simultaneously monitor the chronic wound. We will conduct a detailed study on the sensing performance of the pH sensor, UA sensor, and Glu sensor, including sensitivity, linearity, reproducibility, repeatability, bending resistant and selectivity.

The stability of the reference electrode is crucial to the test results. To verify its stability, the reference electrode was tested for approximately 14 h in 10 mM NaCl solution. The results demonstrate that the reference electrode exhibits excellent long-term stability, ensuring reliable performance for subsequent tests (Fig. S13a). The pH sensor can effectively detect the deprotonation of H^+ through potentiometric analysis, enabling a reliable response to changes in H^+ concentration (Fig. 4a) [40, 41]. For the sensitivity of the pH sensor, the measured voltages during the pH range from 4 to 9 showed high consistency, indicating that the pH sensor has a stable response to H^+ . Its response time to H^+ was approximately 5 s (Fig. S14a). Moreover, the detection range covers the potential pH range of chronic diabetic wounds (Fig. 4b) [42-44]. The measured potential is linearly related to the pH value, with a sensitivity of -55.08 mV/pH and a correlation coefficient of 0.998, which confirms a near-Nernstian behavior. (Fig. 4c). After adding interferents such as K^+ , Na^+ , Mg^{2+} , Ca^{2+} , and NH_4^+ to the solution at pH=5.16, the potential of the pH sensor remained unchanged (Fig. 4d). Meanwhile, anti-interference tests were performed in simulated wound fluid (SWF). The results demonstrate that interfering substances exert negligible influences on the performance of the pH sensor under complicated environments, verifying its

selectivity (Fig. S15a). In addition, the pH sensor demonstrated good reproducibility and stability (Fig. S16a). During a 12 h test in solutions at pH=4.18, 6.99, and 8.89, the voltage variation was minimal, confirming its outstanding long-term stability (Fig. S13b).

UA was effectively detected and analyzed by differential pulse voltammetry (DPV), with the detection principle illustrated in Fig. 4e. This method applies a series of pulse voltages, causing UA to oxidize on the rGO/Au surface to form allantoin, while releasing electrons, resulting in a change in the current on the electrode surface [17, 28]. Fig. 4f shows the differential pulse voltammetry plot of the UA sensor for detecting UA within the concentration range of 0-700 μM . It can be observed that a clear oxidation peak of UA, with a sharp peak shape. The peak current increases regularly with the concentration. The peak current of the UA oxidation peak was linearly fitted with the corresponding UA concentration, resulting in the linear fitting curves shown in Fig. 4g. The sensitivity of the UA sensor was further calculated to be 0.018 $\mu\text{A}/\mu\text{M}$, with a correlation coefficient of 0.998, indicating a good linear relationship. After calculation, the resulting sensitivity was 0.573 $\mu\text{A}/(\mu\text{M} \cdot \text{cm}^2)$ ($S=k/A_{\text{eff}}$, where S is the sensitivity, k is the slope of the linear equation, and A_{eff} is the effective active area of the electrode). Based on this calibration curve, the limit of detection (LOD) was calculated to be 15.24 μM ($S/N=3$). In term of selectivity, tests were conducted with several possible interfering substances. DPV test was performed after adding AA, Glu, Lac, and Na^+ interferents to a 500 μM UA solution. The results, shown in Fig. 4h, indicate that the oxidation peak current did not change regardless of whether the interferents were added, confirming that the rGO/AuNPs modified layer exhibits excellent selectivity. Further verification was implemented in SWF, confirming that the UA sensor retains outstanding selectivity in complex environments (Fig. S15b). Furthermore, the UA sensor demonstrated good reproducibility (Fig. S16b). A series of 60 continuous DPV tests were performed in 500 μM UA solution, and the results showed that the oxidation peak remained consistent, further confirming its excellent stability (Fig. S13c).

The response principle of the Glu sensor to glucose is shown in Fig. 4i. when Glu comes into GOx, it is catalytically oxidized by GOx to form gluconic acid and hydrogen peroxide (H_2O_2) [45,

46]. Subsequently, H_2O_2 is rapidly decomposed into water (H_2O) under the action of Pt nanoparticles. The electrons generated during this process are recorded by the electrochemical workstation, generating a current signal. Accordingly, the response time of the Glu sensor to glucose was approximately 50 s (Fig. S14b). Fig. 4j shows the Glu sensor response to glucose at different concentrations in phosphate-buffered saline (PBS). With the increase of glucose concentration, the current signal increased regularly, and the maximum detection concentration was 30 mM, which was consistent with the possible range of glucose concentration in diabetic chronic wounds [47]. By performing a linear fit between the measured current signal and the corresponding glucose concentration, the sensitivity of the Glu sensor is calculated to be 32.05 nA/mM and a correlation coefficient of 0.997 (Fig. 4k). The resulting sensitivity was -1020.7 nA/(mM·cm²). Based on this calibration curve, LOD was calculated to be 2.18mM (S/N=3). In addition, the Glu sensor demonstrates good selectivity, showing negligible response to these interfering substances in wound exudates, such as Lac, UA, and Na⁺. Subsequent verification in SWF further confirms the excellent selectivity of the Glu sensor (Fig. S15c). The Glu sensor also exhibits good reproducibility, indicating that sensors with consistent performance can be fabricated (Fig. S16c). Meanwhile, during the 30-cycle stability test in a 5 mM low-concentration glucose solution, the current response of the sensor showed no significant decay with good signal consistency, indicating its outstanding cycling stability and further validating the reliability of its sensing performance (Fig. S13d). Furthermore, a long-term stability test was conducted for 12.5 h in a 20 mM high-concentration glucose solution. The results showed that the sensor's current response exhibited only slight drift and maintains a stable overall signal, demonstrating its good long-term stability (Fig. S13e).

As different wound locations necessitate distinct bending angles, the impact of mechanical deformation on sensor performance warrants systematic investigation. The results reveal that the sensor outputs under static fixed bending of 45° and 90° match the flat-state baseline data well (Fig. S17a-d). Following 30 repeated bending cycles, the calibration data showed no noticeable drift (Fig.S17e-g). Extending the test to 50 cycles, data fluctuations remained minimal, indicating

good mechanical flexibility and cyclic stability (Fig.S17h-j). Moreover, during dynamic bending from the unbent state to 90° , the sensor maintained stable readings (Fig. S18).

***In-situ* animal evaluation of the wearable intelligent wound patch**

To verify the functionality and efficacy of the wound monitoring and treatment system in wearable intelligent wound patch, we established full-thickness skin wounds on diabetic rats. The diabetes model in healthy rats was induced by intraperitoneal infection of streptozotocin (STZ), and a $12.5 \times 12.5 \text{ mm}^2$ wound was created on their back. The diabetic rats were randomly divided into four groups: the control group, the control + NIR group, the PPQTA group, and the PPQTA + NIR group. Throughout the healing process, we recorded relevant parameters of the wounds in the control group and hydrogel with light group (such as pH, UA, and Glu) to assess the therapeutic effect of the intelligent wound patch. The detailed experimental procedure is shown in Fig. 5a. During the experiment, representative photos of the wounds in all four groups of rats were taken and recorded from day 0 to day 10 (Fig. 5b, Fig. S19a). The relative wound area changes are shown in Fig. 5c and Fig. S19b. The experimental results indicated that all four groups had different degrees of wound healing, and the hydrogel light group had significantly better wound recovery on the third day than the other groups, especially the control group. By the 10th day, the wounds of the hydrogel light group had almost completely recovered, while the wounds of the other groups had poor recovery, and the relative area of the wound remained at more than 40% of the initial area. This indicated that the use of the hydrogel under light could more effectively release drugs, significantly promoting wound healing in diabetic rats and achieving faster and better therapeutic effects. The wound exudate was collected on the fifth day and wound infection status was measured using the plate count method (Fig. S20). The results showed that the hydrogel with light group had almost no bacterial colonies, indicating that under NIR (808 nm, 1 W/cm^2) irradiation, the PPQTA hydrogel could effectively inhibit or kill bacteria at the wound site. Furthermore, *in vivo* biocompatibility tests were conducted, and hematoxylin-eosin (H&E) staining were performed on major organs (heart, liver, spleen, lung and kidney) of rats on the 10th day. The

results showed that the histological morphology of the important organs in all groups was normal, with no pathological changes observed, indicating that the use of the hydrogel and sensors did not cause organ damage and demonstrated excellent biocompatibility (Fig. S21) [48].

To understand the changes in relevant parameters during the wound healing process, we continuously monitored the pH, UA and Glu of the wounds in the control group and the PPQTA + NIR group during the early healing state (Fig. 5e-g). As shown in Fig. 5d, schematic diagram of *in-situ* animal experiments. The monitoring results revealed that the pH value and UA concentration of wounds in the PPQTA + NIR group were consistently lower than those in the control group, with a faster declining rate (Fig. 5e-f). Previous studies have shown that bacterial infection can exacerbate the inflammatory response at the wound site, leading to an increase in uric acid concentration and a shift in pH from acidic to alkaline [25,49]. Although both groups still had certain inflammatory reactions on the third day, the pH value and UA concentration in the PPQTA + NIR group were significantly lower than those in the control group, indicating that the wounds receiving drug treatment achieved superior therapeutic effects and exhibited better recovery status during this period. In subsequent monitoring, the pH value of the PPQTA + NIR group approached neutrality on the fourth day and remained stable in the following days. The pH value of the control group was still as high as 8 on the fourth day, which was alkaline, indicating that the wound was still in a state of inflammation. It wasn't until the 6th day that the pH value of the control group gradually approached that of the PPQTA + NIR group, with the inflammation in the control group lasting longer. This indicated that the PPQTA + NIR group achieved drug release under NIR irradiation, which exerted a significant effect on inhibiting bacterial activity, consistent with the results in Fig. 5b and S20. According to the UA sensor data, both groups showed a trend of rising and then falling UA concentrations, likely due to the accumulation of UA at the wound site caused by infection or inflammation, which gradually decreased during the subsequent healing process (Fig. 5f) [50]. This result is consistent with the data from the pH sensor. Glucose concentrations in both groups did not change significantly over the course of the study, which was due to the fact that the hydrogel did not alleviate the glucose concentration in diabetes.

Nevertheless, the relevant results provide a research reference for the subsequent development of wound therapeutic systems with glucose-lowering functions. Therefore, from the perspective of the relative change of pH and UA, the PPQTA + NIR group achieved efficient bacterial eradication and effective inflammation control in wounds on day 4. At this point, drug release from PPQTA was automatically terminated accordingly, realizing the strategy of “stop drug delivery upon bacterial elimination” and fundamentally avoiding the overuse and abuse of antibiotics. By real-time monitoring of wound pH and UA, this sensing system can accurately and dynamically reflect the wound healing status, providing a reliable basis for personalized and precise theranostics of chronic wounds.

To further investigate the internal details and quality of wound healing, the skin tissue samples from the wounds of both the control group and the PPQTA + NIR group were collected on day 10 and subjected to H&E and Masson. The H&E results showed that the control group still exhibited visible residual scabs (composed of dry blood, serum, and exudate) at the wound site, while no such scab was observed in the PPQTA + NIR group (Fig. 5h). Besides, the tissue structure in the PPQTA + NIR group was more organized, with the presence of hair follicles and connective tissue observed (Fig. 5h). Furthermore, the Masson staining results revealed that the collagen fibers in the PPQTA + NIR group were denser and more regularly arranged compared to the control group, further confirming the positive therapeutic effect (Fig. 5i).

Discussion

In this study, we have developed an integrated smart wound patch that combines a PPQTA photothermal antibiotic-releasing hydrogel with a multichannel electrochemical biosensor for the management of chronic diabetic wounds. The patch system—comprising a customized mobile application, wearable electronic hardware, and the functionalized PPQTA hydrogel—delivers dual capabilities in real-time monitoring and on-demand therapy. Through its embedded biosensors, the system continuously tracks key wound exudate biomarkers (pH, UA, and Glu), allowing dynamic assessment of healing progress, precise regulation of the initiation and termination of drug release,

effective avoidance of antibiotic abuse, and accelerated wound repair. The engineered PPQTA hydrogel demonstrates controlled drug release under NIR irradiation, exhibits potent broad-spectrum antibacterial activity, and shows excellent biocompatibility, as confirmed by both *in vitro* and *in vivo* evaluations. Meanwhile, the multichannel biosensor array displays outstanding analytical performance, characterized by high stability and accurate quantification across physiological ranges: pH 4-9, UA 0-700 μ M, and Glu 5-30 mM. By merging real-time diagnostic monitoring with responsive therapeutic intervention, this smart patch system overcomes the limitations of conventional single-modality wound management. It not only expands the available strategies for chronic wound care but also provides a viable pathway toward a closed-loop medical platform that integrates continuous biomarker surveillance with targeted treatment. This work underscores the potential of combined sensing and therapy systems for personalized, effective wound care.

Methods

Reagents

Sodium chloride (NaCl), Boric acid (H_3BO_3), Phosphoric acid (H_3PO_4) were purchased from Innochem. Butvar B-90 Polyvinyl butyral (PVB), Methanol (CH_3OH), Aniline, Potassium chloride (KCl), Chitosan, Tetrahydrofuran (THF), Uric acid (UA), Magnesium chloride hexahydrate ($\text{MgCl}_2 \cdot 6\text{H}_2\text{O}$), Ascorbic acid (AA), L-lactic acid (Lac), Ferric chloride hexahydrate ($\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$), N-Isopropylacrylamide, Acrylamide, Tannic acid (TA), Streptozotocin (STZ), Cefazolin, Chloroplatinic acid solution ($\text{H}_2\text{PtCl}_6 \cdot x\text{H}_2\text{O}$) were procure from Aladdin. Glucose oxidase (GO_x), Glucose (Glu), Triton X-100 were obtained from Sigma-Aldrich. Acetic acid (CH_3COOH) was purchased from Macklin. Hydrogen tetrachloroaurate hydrate (HAuCl_4) was obtained from Alfa. Sodium hydroxide (NaOH) and nitric acid (HNO_3) purchased from DAMAO CHEMICAL REAGENT FACTORY. Graphene oxide (GO) was purchased from XFNANO Materials Tech Co., Ltd. (Nanjing, China). Lithium phenyl (2,4,6-trimethyl) benzoylphosphinate (LAP), Polyethe F127 Diacrylate (F127DA), Quaternary Ammonium Chitosan (QCS) were

purchased from *Engineering For Life*.

Fabrication of biosensors

pH sensor: First, a layer of AuNPs was deposited onto the working electrodes by 9 cycles of cyclic voltammograms (CVs) (-1.4 - 1.0 V) with a scan rate of 0.1 V S⁻¹ in a solution containing 0.1 wt% HAuCl₄ and 0.5 mM Na₂SO₄. Next, an appropriate amount of aniline solution (0.1M aniline and 1M HCl) was added to the electrode surface, and 24 CV cycles (-0.2 - 1.0 V, 0.1 V s⁻¹) were performed to form polyaniline (PANI) film.

UA sensor: A lay of rGO/Au was electrodeposited onto the electrodes by 5 cycles of CVs (-1.5 - 0.6 V) with a scan rate of 50 mV s⁻¹ in a solution containing 0.1 wt% HAuCl₄ and 0.8 mg/ml GO.

Glu sensor: First, a AuNPs was electrodeposited on the working electrode in a fresh solution containing 10 mM HAuCl₄ and 0.1 M KCl by at -0.3 V for 2000 s. Next, a platinum (Pt) was electrodeposition on the AuNPs layer in a solution containing 0.5 M HCl and 10 mM H₂PtCl₆ by at -0.3 V for 300 s. Finally, 7.5 µL of the Glu oxidase/chitosan mixed solution was dripped onto the Pt layer and dried in the ambient environment. A Glu oxidase/chitosan mixed solution was prepared by adding the glucose oxidase (GOx) solution (10 mg/mL in PBS) to chitosan solution (1 wt % chitosan in 2 % acetic acid) in a 1:1 volume, and then mixed carefully.

Reference electrode: 78.1 mg PVB and 50 mg NaCl were dissolved in 1 ml methanol and oscillated in ultrasonic bath for 30 min to obtain the reference membrane mixed solution. Then, the 2.5 µL reference membrane mixed solution was dripped onto the surface of the Ag/AgCl electrode.

***In-vitro* characterization of multiplex biosensors**

The biosensor was characterized using an electrochemical workstation (CHI660E).

1) pH sensors:

Sensitivity, linearity and reproducibility of the pH sensors: The pH sensors were tested in

Borat-Robison Buffer Solutions (BR, prepared from CH_3COOH , H_3PO_4 , H_3BO_3 and NaOH) with the pH value from 4.18-8.89.

Selectivity of the pH sensors: The solutions of different pH value were prepared with NaOH and HNO_3 , and 1mM KCl , 1mM NaCl , 1mM MgCl_2 , and 1mM NH_4Cl were added to the test solutions.

Stability of the pH sensors: The pH sensors performed open circuit potential tests for about 14 h in BR buffer solutions at pH=4.18, 6.99, 8.89.

2) UA sensors:

Sensitivity, linearity and reproducibility of the UA sensors: The UA sensors were tested in PBS solutions containing 0, 100, 200, 300, 400, 500, 600 and 700 μM UA. The voltage range of differential pulse voltammetry (DPV): -0.1-0.8 V; step: 4 mV; pulse width: 0.06 s; amplitude: 50 mV; pulse period: 0.5 s.

Selectivity of the UA sensors: The solution containing 500 μM UA was supplemented with 0.2 mM AA, 5.0 mM Glu, 1.0 mM Lac, and 1.0 mM NaCl as interfering substances. The voltage range of DPV: -0.1-0.8V ; step: 4 mV; pulse width: 0.06 s; amplitude: 50 mV; pulse period: 0.5s.

Stability of the UA sensors: The UA sensors were subjected to multiple consecutive tested in PBS solution containing 500 μM UA. The voltage range of DPV: -0.1-0.8V ; step: 4 mV; pulse width: 0.06 s; amplitude: 50 mV; pulse period: 0.5s.

3) Glu sensors:

Sensitivity, linearity and reproducibility of the Glu sensors: The Glu sensors were tested in PBS solutions containing 5, 10, 15, 20, 25 and 30 mM Glu. The initial voltage of chronoamperometry of -250 mV.

Stability of the Glu sensors: The Glu sensors were subjected to multiple consecutive tested in PBS solution containing 5 mM Glu. The initial voltage of chronoamperometry of -250 mV.

Stability of the Glu sensors: The Glu sensors were subjected to multiple consecutive tested in PBS solution containing 5 mM Glu. The initial voltage of chronoamperometry of -250 mV.

The SWF solution was prepared by dissolving 58.4 mg NaCl , 33.6 mg NaHCO_3 , 2.98 mg

KCl, 2.78 mg CaCl₂ and 0.33 g BSA in 100 mL deionized water.

Hydrogel precursor solution preparation process:

Preparation of Tannic acid-iron nanoparticles (TA-Fe): Under stirring conditions, 200 μ L FeCl₃ solution (25 mg/mL) was slowly added to 4.8 mL TA solution (5 mg) at a mass ratio of 1:1. After the reaction continued for 2 h, the mixture was centrifuged at 6000 rpm for 10 min. The precipitate was collected and washed 2-3 times with water. Finally, the precipitate was dried in a freeze dryer.

Preparation of mixture solution A: Under stirring conditions, 400 μ L/mL TA-Fe was mixed with 3% QCS by mass ratio and stirred until the solution became transparent and free of particulates, yielding Mixture Solution A.

Preparation of mixture solution B: In a solution containing 2.5% F127DA and 0.5% LAP, 50% NIPAM and 2% AAM were added sequentially by mass/volume ratio. After sonication and uniform mixing, mixture solution B was obtained. In the case of stirring, mix solution A and B in equal volumes.

Preparation of Drug-loaded Hydrogel Precursor Solution: A certain amount of Cefazolin was added to the hydrogel precursor solution (1.2 mg/mL). An appropriate amount of hydrogel precursor was dropped into the mold, followed by curing under UV light irradiation for approximately 3 min. Depending on the different components of the hydrogel, certain components are added or reduced during the synthesis process.

P: PNIPAM; PP: PNIPAM + AAM; PPQ: PNIPAM + AAM + QCS; PPQT: PNIPAM + AAM + QCS +TA-Fe; PPQTA: PNIPAM + AAM + QCS +TA-Fe + Antibiotic (Cefazolin)

Physical characterization of hydrogels

Morphological characterization: The microstructure of hydrogels was observed using a scanning electron microscope (S4800, Hitachi, Japan). Adhesion performance characterization: Fresh porcine skin was first immersed in saline to remove fat. The hydrogel was then applied to

the porcine tissue with a bonding area of 10 mm × 25 mm, and a tensile testing machine was used for stretching at a speed of 5 mm/min. Tensile property characterization: Hydrogel precursor solutions with different components is prepared, with 4 groups as follow: i. Pure PNIPAM hydrogel (P); ii. Copolymerized PAM on pure PNIPAM hydrogel (PP); iii. PP hydrogel incorporated with QCS (PPQ); iv. PPQ hydrogel added with TA-Fe (PPQT). The samples are tested using a tensile testing machine (n=3).

The biocompatibility characterization of the hydrogel

The sterilized hydrogel was extracted in serum-free DMEM culture medium at 37 °C for 48 h to prepare the extract. L929 cells were seeded into 96-well plates at a density of 3×10^4 cells/mL (100 μ l per well). After 10 h of culture to allow cell adhesion, the original culture medium was discarded and replaced with the hydrogel extracts of each group. Cytotoxicity was evaluated using a CCK-8 cell viability assay kit after 24 and 48 h of culture, respectively.

Live/Dead cell staining experiment

Seed L929 cells at a density of 6000 cells/well in a 48-well plate and culture for 10 hours under appropriate conditions. After 10 hours, discard the original culture medium and replace it with the hydrogel extract. After culturing for 1 day, 3 days, and 5 days, stain the cells using a live/dead cell staining kit.

Characterization of antibacterial properties of hydrogels

Antibacterial in vitro experiments: *E. coli* and *S. aureus* were used in the experiment, with 6 groups designed: Control group (NO NIR/NIR), P group (NO NIR/NIR), PP group (NO NIR/NIR), PPQ group (NO NIR/NIR), PPQT group (NO NIR/NIR), and PPQTA group (NO NIR/NIR). Each group was incubated with 500 μ L of 1×10^8 CFU/ml bacterial suspension. The NIR groups received 10 minutes of near-infrared (NIR) irradiation during the incubation, while the NO NIR groups underwent no NIR irradiation and were only incubated with the bacterial solution for 10

minutes. After incubation, the mixture was diluted 10^5 times, and 200 μL was plated on solid culture media, which were then incubated at 37 °C for 12 to 16 h. Each experiment was repeated 3 times.

Cyclic irradiation antibacterial experiment: In this experiment, *E. coli* and *S. aureus* were used, with 3 groups were designed: Control group, PPQT group, and PPQTA group. Each group was incubated with 500 μL of 1×10^8 CFU/ml bacterial suspension, and subjected to 1, 2, or 3 cycles of NIR irradiation (10 min per cycle). After incubation, the mixture was diluted 10^5 times, and 200 μL was plated on solid culture media, which were then incubated at 37 °C for 12 to 16 h. Each experiment was repeated 3 times.

Antibacterial zone experiment: In this experiment, *E. coli* and *S. aureus* were used, with 3 groups were designed: Control group, PPQT group, and PPQTA group. 200 μL of bacterial solution was inoculated onto solid culture medium, after which each group of hydrogel was placed on the surface of the medium. After 5 min of NIR irradiation, the petri dishes were incubated at 37 for 12 to 16 h.

Hemolytic characterization of hydrogel

This experiment included 7 experimental groups: Negative control group (PBS), Positive control group (0.1% Triton X-100), and Experimental Groups (P, PP, PPQ, PPQT, PPQTA). First, 100 mL of Alsever's solution (containing 2.05 g glucose, 0.80 g sodium citrate, and 0.42 g sodium chloride) was prepared and sterilized (10 min). Blood was then collected from the eye socket of mice, mixed with Alsever's solution at a 1:2 volume ratio, added with PBS, and centrifuged at 1500 rpm for 5 min (n=3). The supernatant was discarded. The red blood cell (RBC) suspension was diluted to 10% and 5%, and incubated with materials from different groups.

The specific treatment methods are as follows: 1) Negative control group: mix 0.25 mL of 10% red blood cell suspension with 0.25 mL PBS. 2) Positive control group: mix 0.25 mL of 10% red blood cell suspension with 0.25 mL of 0.1% Triton X-100. 3) Experimental group: mix 0.1 g hydrogel with 0.5 mL of 5% red blood cell suspension (n=3). All groups were incubated in a 37 °C for 1 h. After incubation, the hydrogel was removed, and the mixture was centrifuged at 2500 rpm

for 5 min. Finally, the ultraviolet absorbance was measured using a microplate reader. Hemolysis was calculated using the following formula:

$$\text{Hemolysis rate (\%)} = \frac{\text{Abs}_{504 \text{ nm}} (\text{experimental group}) - \text{Abs}_{540 \text{ nm}} (\text{PBS})}{\text{Abs}_{540 \text{ nm}} 0.1\% (\text{Triton X} - 100) - \text{Abs}_{540 \text{ nm}} (\text{PBS})} \times 100 \%$$

Drug Release Characterization of hydrogels

Hydrogel precursor solutions containing drug were prepared and divided into two groups. Following photocrosslinking, the hydrogels were submerged in PBS at 25 °C. Group 1 underwent cyclic NIR irradiation (808nm, 1 w/cm²), with each cycle consisting of 10 min irradiation followed by a 30 min rest period, repeated three times consecutively. Group 2 served as the control, maintained in PBS at 25 °C without NIR treatment. At predetermined time points, the concentration of released drug in the PBS was quantified using a UV-visible spectrophotometer.

Animal Experiments

The healthy male rats used in the experiment were purchased from Biouhan Technology (Jiangsu) Co., Ltd., with a body weight of approximately 250 ± 10 g. All rats underwent a 1-week acclimatization period before being administered the STZ solution. The STZ solution was prepared with a sodium citrate buffer and administered via intraperitoneal injection at a dose of 55 mg/kg to rats that had been fasted for 12 hours. During the process of constructing the diabetes model, blood glucose measurements were conducted on the rat tails at 3-day intervals over a total period of 9 days. The diabetes model was deemed successful when blood glucose levels consistently stabilized above 16.7 mM for 9 consecutive days. In the experiment, diabetic rats were anesthetized with isoflurane, and their dorsal fur was subsequently shaved. A 12.5 mm × 12.5 mm circular wound was then created on their back. Subsequently, 200 µL of activated *Staphylococcus aureus* (1 × 10⁸ colony-forming units/mL, CFU/mL) was inoculated onto the wound surface, which was designated as day 0. On the day 1, the rats were randomly divided into four groups (n=3 per group): the control group, the control + NIR group, the PPQTA group, and the PPQTA + NIR group. NIR groups was applied to the wound followed by 5 minutes of NIR light treatment (808

nm, 1 w/cm²) to release the drug and promote wound healing). For evaluating wound healing progression, wound microenvironmental parameters—including pH, uric acid, and glucose concentrations—were measured in the control and hydrogel (With NIR) groups using a custom wound monitoring system. Meanwhile, wound morphology was recorded using a digital camera, and ImageJ software was utilized to perform quantitative analysis of the wound area.

Data availability

The data supporting the main findings of this work are available within the paper and its Supplementary Information files. The raw datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

Author contributions

These authors contributed equally in this work. **K. L.** conducted the device fabrication and characterization, completed the overall experimental work, and wrote the initial draft of the manuscript. **B. Y.** performed the chemical synthesis, characterization, and was responsible for performance testing and optimization. **G. Y.** assisted with the cell and animal experiments. **C. L.** contributed to the research discussions, helped optimize the experimental design, and participated in manuscript revision. **G. Z.** assisted with data analysis and provided supervision of the research work. **Y. Z.** contributed to parts of the analysis for the device application demonstration. **Z. L.** supervised parts of the project's progress. **D. W.** contributed to the conceptualization of the work, provided funding support, critically reviewed and revised the manuscript. All authors read and approved the final manuscript.

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Conflict of Interest

All authors declare no financial or non-financial competing interests.

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Figure Captions

Figure 1. A wireless patch system for monitoring and treating chronic wounds in diabetes. a) Layered assembly schematic of the smart patch, showing the stacked structure of a flexible Polyethylene terephthalate (PET) substrate, an electrochemical biosensor array, an insulating layer, and a drug-loaded hydrogel layer. b) Schematic of the smart patch worn on a diabetic chronic wound. c) Schematic of the smart patch for real-time monitoring of glucose, uric acid, and pH values in infected diabetic foot wounds, as well as promoting wound healing. d) Schematic of the preparation process of the photothermal hydrogel and the photothermal drug release process. e) Photograph of the wireless wound monitoring system. f) Block diagram of the operational data transmission of the system.

Figure 2. Preparation and characterization of hydrogels and biosensors. a) Exploded view of the multichannel biosensor. b) Digital image of the reagent solutions used in sensor fabrication. Electrochemical deposition processes of c) Polyaniline (PANI), e) Reduced graphene oxide (rGO)/Au, and g) Platinum (Pt) on carbon-based working electrodes, performed using a three-electrode system at constant potential. SEM images of d) PANI-, f) rGO/Au-, and h) Pt-modified working electrodes, respectively. i) The structural schematic diagram of PPQT (PNIPAM + AAM + QCS + TA-Fe) hydrogel. j) Photographs of the PPQT hydrogel precursor solution before and after UV-light-mediated crosslinking, accompanied by Scanning electron microscopy (SEM) images of hydrogel. k) Adhesion performance characterization of the PPQT hydrogel.

Figure 3. Photothermal properties and in vitro characterization of hydrogels. a) Infrared thermal images of hydrogel containing Tannic acid-iron (TA-Fe) nanoparticles at different concentrations under near-infrared (NIR) (808 nm, 1.0 W cm^{-2}) irradiation. b) Temperature rises curves of hydrogels with different concentrations of TA-Fe nanoparticles under NIR (808 nm, 1.0 W cm^{-2}) irradiation. c) The corresponding temperature rise curve of PPQT hydrogel under different power irradiation. d) Cyclic response stability of PPQT hydrogel under NIR (808 nm, 1 W cm^{-2})

irradiation. e) The near-infrared responsive photothermal antibiotic-releasing hydrogel (PPQTA; PNIPAM + AAM + QCS +TA-Fe) achieved drug release via an “on-off” cycle combined with a nature release mode, sustained for 120 minutes, where “on” refers to the application of NIR irradiation, and “off” refers to the absence of NIR irradiation. f) Inhibition zone assays of drug-loaded and drug-free PPQT hydrogels under NIR irradiation against two common bacteria (*S. aureus* and *E. coli*). Evaluation of the bactericidal effect of PPQT and PPQTA hydrogels against *S. aureus* (g) and *E. coli* (i) by plate colony counting under both with and without NIR irradiation. The cyclic bactericidal effect of PPQT and PPQTA hydrogels against *S. aureus* (h) and *E. coli* (j) was evaluated under NIR irradiation.

Figure 4. *In vitro* characterization of the pH, Uric acid (UA), Glucose (Glu) sensors. a) Schematic of the pH sensor detection mechanism. b) The measured potential varied as the pH level decreased from 4 to 9 and then back to 4. c) The linear relationship between the potential detected by the pH sensor and the pH (n=3). d) Selectivity of pH sensors to K^+ , Na^+ , Mg^{2+} , Ca^{2+} and NH_4^+ . e) Schematic of the UA sensor detection mechanism. f) The current response curve of the UA sensor at UA concentrations ranging from 0 to 700 μM . g) The linear relationship between the current detected by the UA sensor and the UA concentration (n=3). h) Selectivity of UA sensors to Ascorbic acid (AA), Glu, Lac and Na^+ . i) Schematic of the Glu sensor detection mechanism. j) The current response curve of the Glu sensor at Glu concentrations ranging from 5 to 30 mM. k) The linear relationship between the current detected by the Glu sensor and the Glu concentration (n=3). l) Selectivity of Glu sensors to UA, Lactic acid (Lac) and Na^+ .

Figure 5. Rat wound monitoring and treatment. a) Schematic diagram of the detailed experiment for treating diabetic rat wounds and detection. b) Images of wound changes in non-treated/treated rats during the treatment process (0-10 days). c) Statistical analysis of wound area ratio during the wound healing process in rats. d) Image of the smart wound patch attached to the back of the rat. Continuous monitoring of three parameters during the wound process: e) wound surface pH, f)

uric acid concentration, and g) glucose concentration in non-treated/treated rats. Skin tissue sections showing h) Hematoxylin-eosin (H&E) staining and i) Masson's trichrome staining of wound sites after 10 days of treatment. Green arrows represented the hair follicles and connective tissue. The black scale bar: 500 μm , and the green scale bar: 100 μm .

Figure 1.

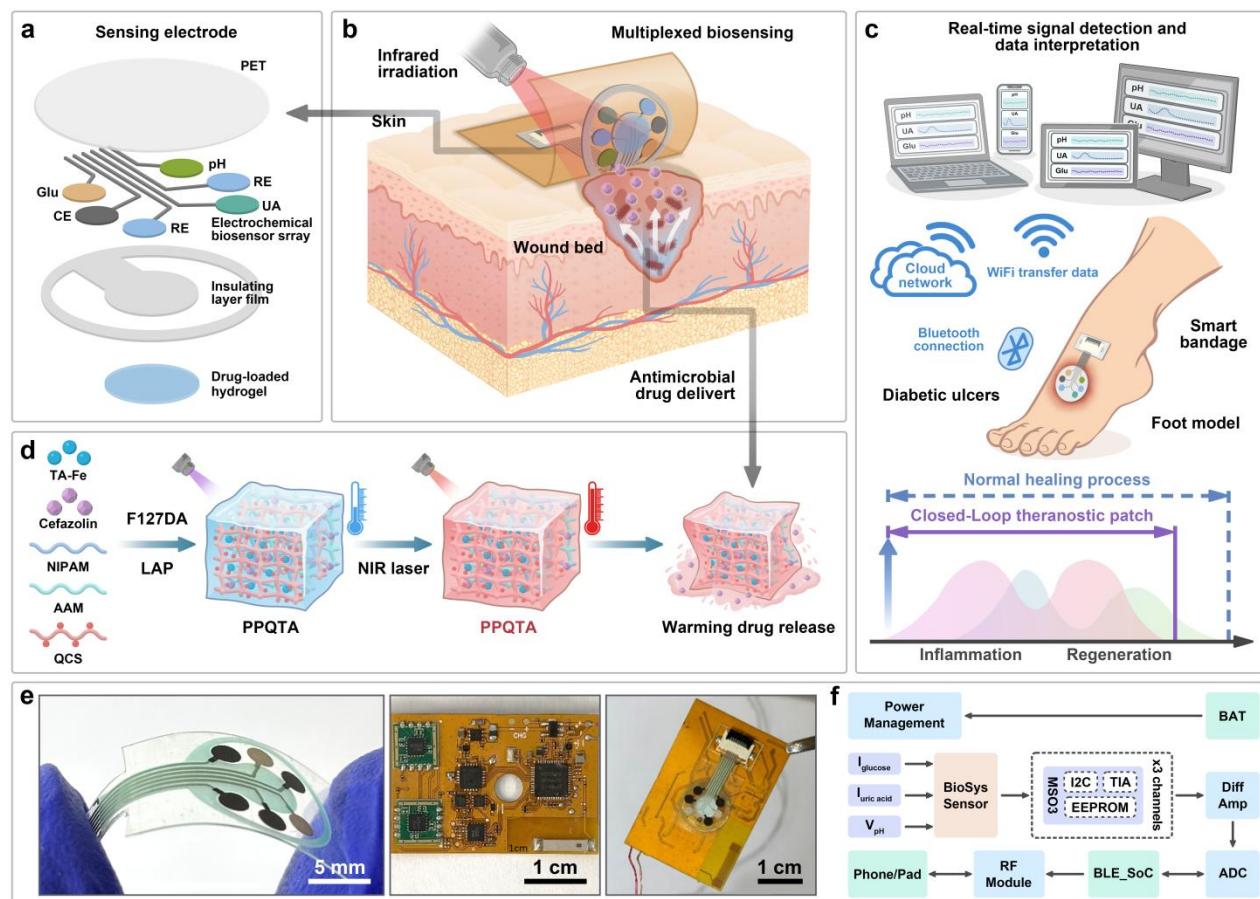


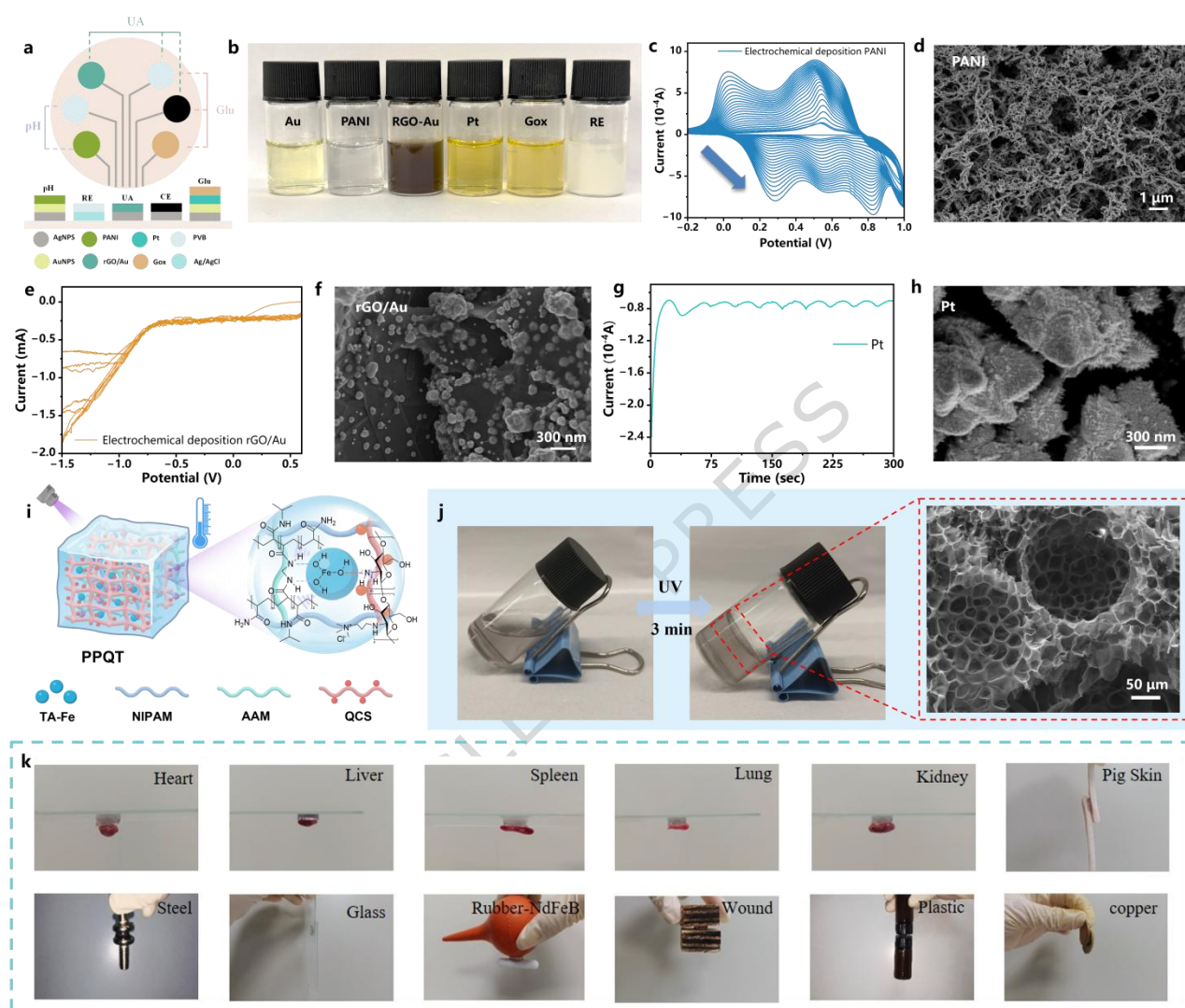
Figure 2.

Figure 3.

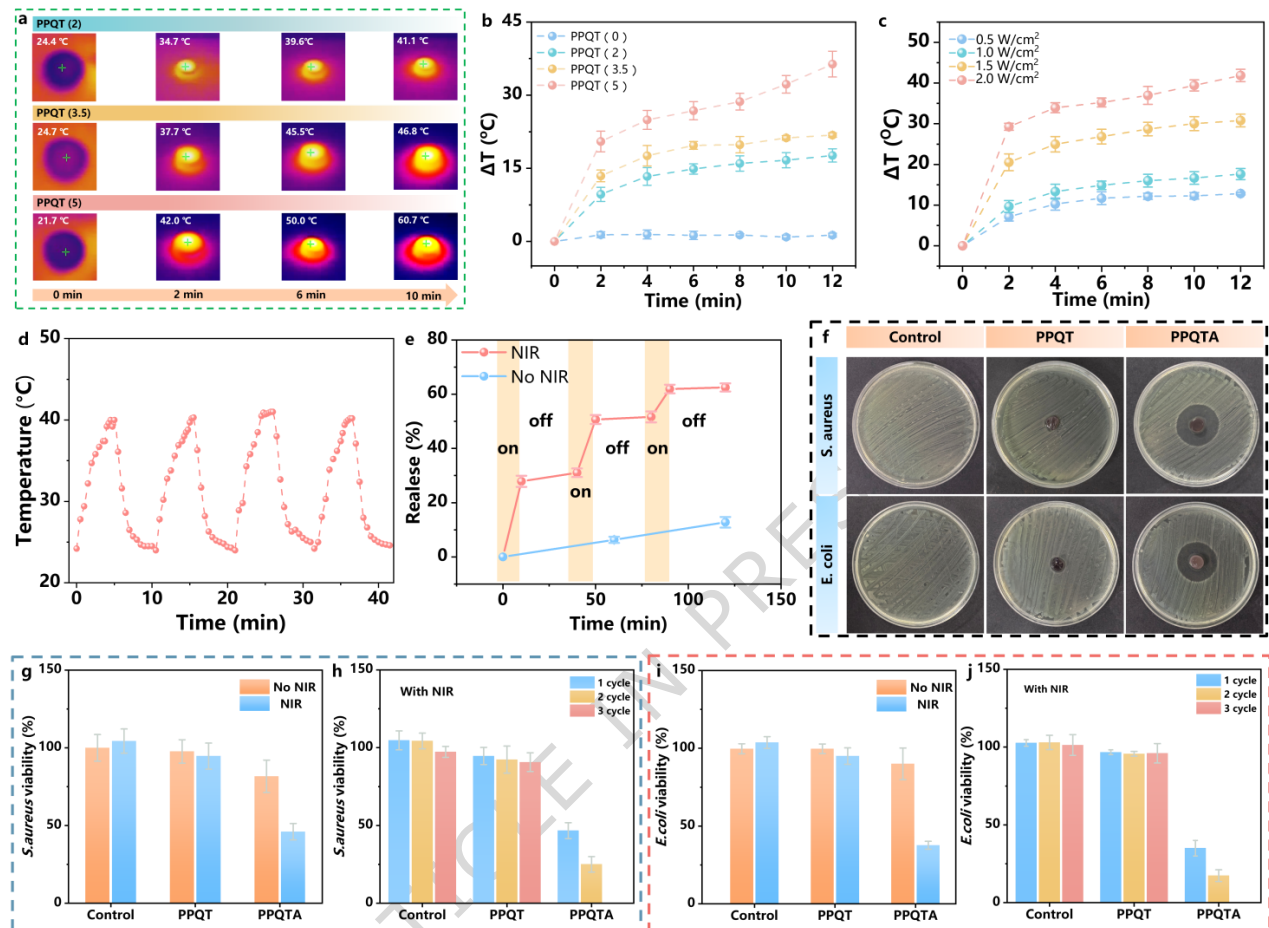


Figure 4.

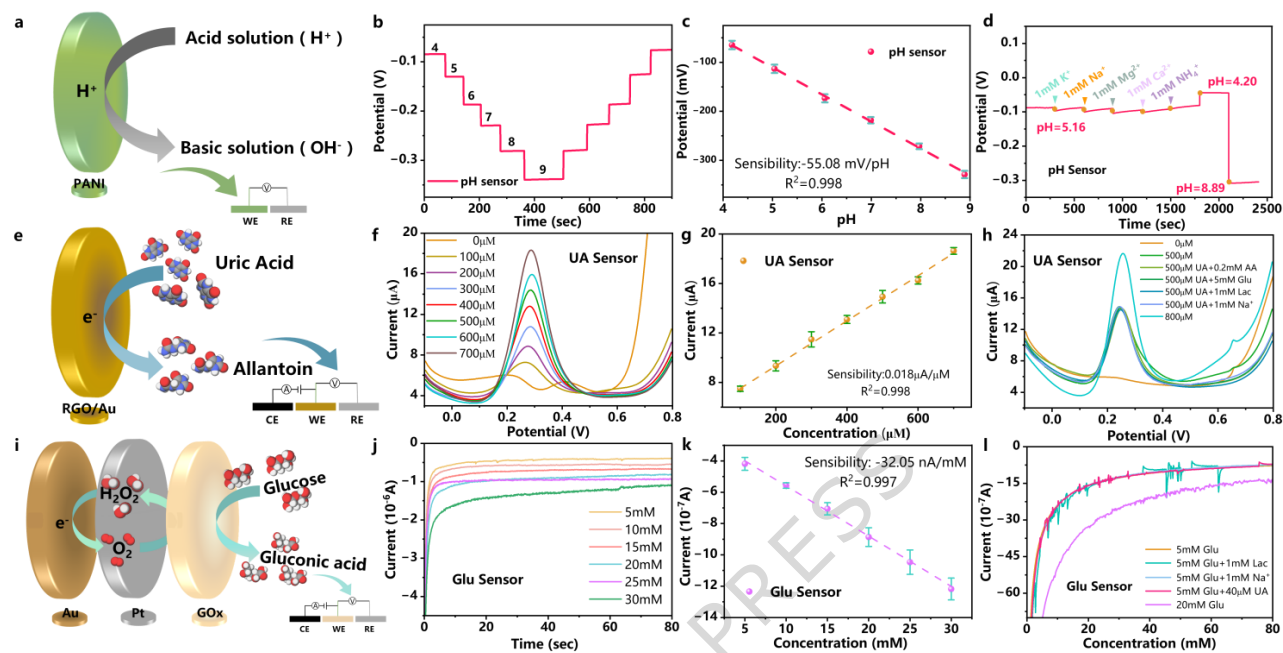


Figure 5.