Biomimetic Scaffold Using Graphene Quantum Dots-Hybrid Hydrogel for Diabetic Wound Healing

Siddhartha Pahari[a], Nikhita Pandian[b], Monalisa Mukherjee[b]*

[a]Department of Chemical Engineering & Applied Chemistry, University of Toronto, Canada.

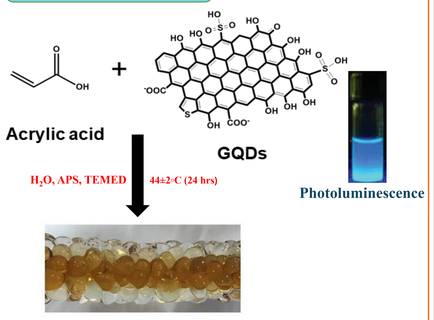
[b]Amity Institute of Click Chemistry Research and Studies, Noida, India.

*** Email: mmukherjee@amity.edu**

Abstract

- In this study we develop a pragmatic biomimetic scaffold that can heal diabetic wounds with diminutive inflammation, we investigated the creation of graphene quantum dot (GQD)-polyacrylic acid (PAA) hybrid hydrogel. We observe an appropriate percentage of GQD incorporation in PAA to demonstrate lower pro-inflammatory cytokines, interleukin (IL-6), and tumour necrosis factor (TNF-α) along with higher anti-inflammatory (IL-10) expressions in contrast to natural and standard controls.
- The histological examinations corresponding to the in-vitro and in-vivo toxicological analysis of GQD-PAA manifested as a non-toxic, biocompatible saviour of diabetic wounds. This hybrid hydrogel reports the quickest diabetic wound healing of 13 days. Additionally, the hybrid hydrogel also demonstrates salient antibacterial activity against E. coli.

Methodology



Synthesis of GQD-polyacrylic acid hybrid hydrogel.

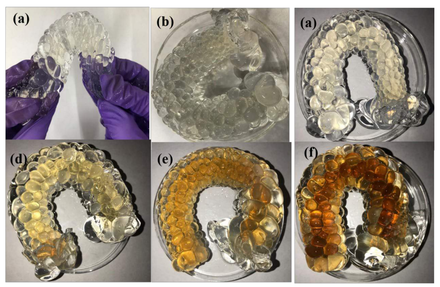
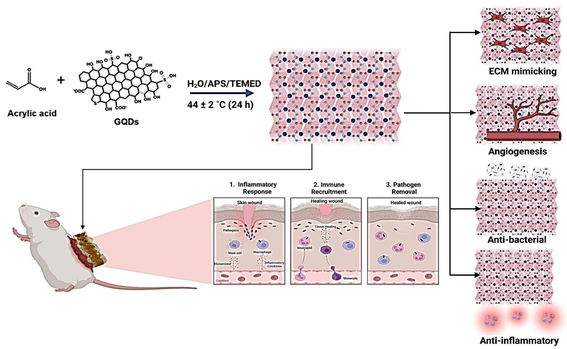


Figure1. Increment of GQD incorporation percentage into PAA hydrogel can be observed by means of deepening of brownish-yellow of GQDs from (b)-(f).
Optical image of (a) PAA, (b) 0.05% GQD-PAA, (c) 0.1% GQD-PAA, (d) 0.3% GQD-PAA, (e) 0.5% GQD-PAA, (f) 1% GQD-PAA hybrid hydrogel.



Results

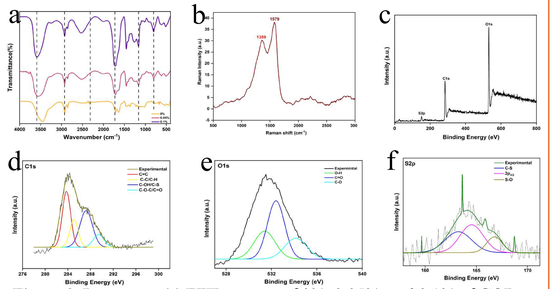


Figure 2. Represents (a) FTIR spectra of 0%, 0.05%, and 0.1% of GQD-PAA hybrid hydrogel, (b) Raman spectra of 0.1% GQD-PAA hydrogel, and XPS peak of 0.1% GQD-PAA hydrogel composite, (c) survey peak, (d) O1s peak, (e) C1s peak, (f) S2p peak.

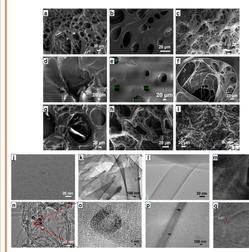


Figure 3. SEM micrographs of swollen GQD-PAA hydrogels: (a-c) cross-section after swelling in pH 1.2 and 7.2 respectively; (d) external surface of hydrogel after swelling in PBS (pH 7.4); (e-g) average pore size of PAA hydrogel and GQD-PAA respectively; (h-i) polymer wrinkles. TEM micrograph of GQD-PAA hydrogel: (j) showing distribution of GQD in hydrogel matrix. (k-l) stacking and rolling of polymer sheet. (m-n) tubular architecture, (o) enlarge tubular architecture. (p) impregnated GQD within nanotube. (q) SAED pattern corresponds to area in image (Inset: SAED pattern).

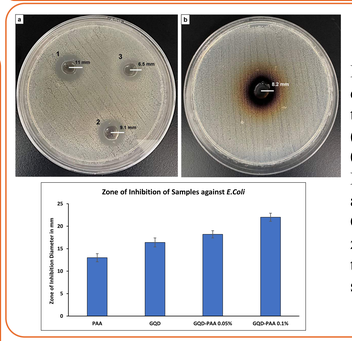


Figure 4. Agar well diffusion assay; (a) showing the bactericidal activity of (1) 0.1% GQD-PAA, (2) 0.05% GQD-PAA and (3) PAA hydrogel; (b) GQD against *E. coli;* (c) Quantification of bacterial zone of inhibition when treated with different samples. (n=3)

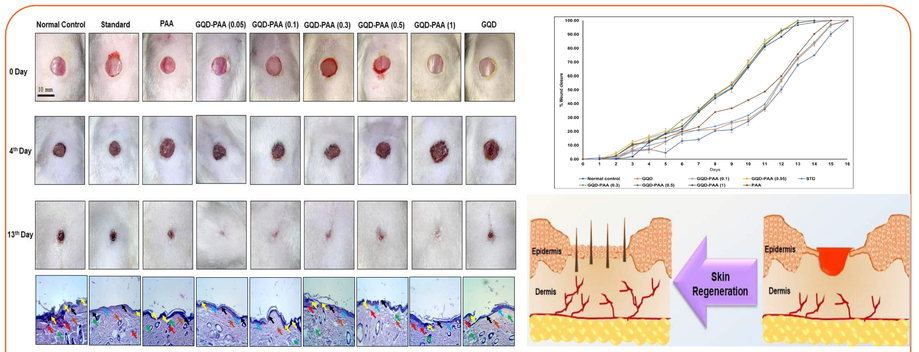


Figure 5. *In vivo* wound healing evaluation. Study showing control, standard, and hybrid hydrogel administered to treat diabetic wounds in Wistar rats on days 0, 4th, and 13th days. Black arrow: re-epithelialization, red arrow: leukocytes infiltration, yellow arrow: exudates deposition, green arrow: collagen deposition, brown arrow: angiogenesis and blue arrow: tissue granulation in H&E-stained skin tissues of wound area at magnification of 100X.

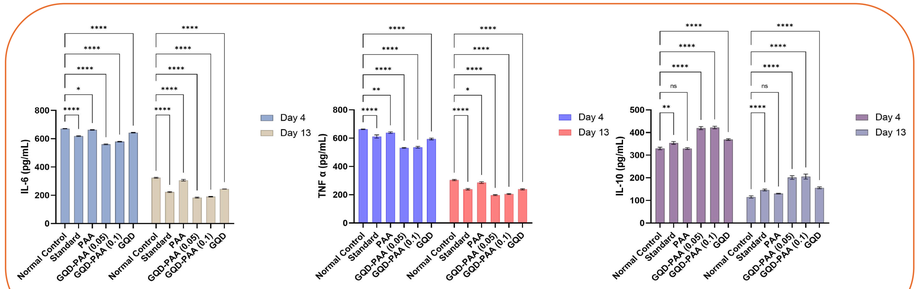


Figure 6. Quantification of (a) IL-6, (b) TNF-α, (c) IL-10 at days 4th and 13th post-wound closure.

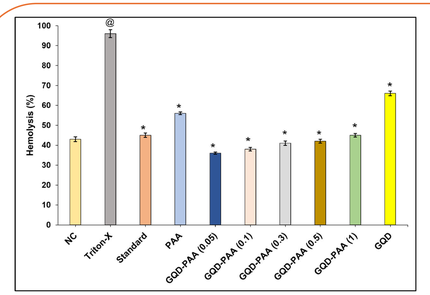


Figure 7. Graph represent the % haemolysis in different mixture of RBC and respective formulations.

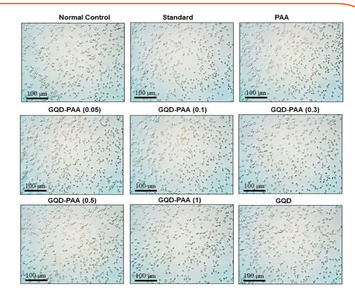
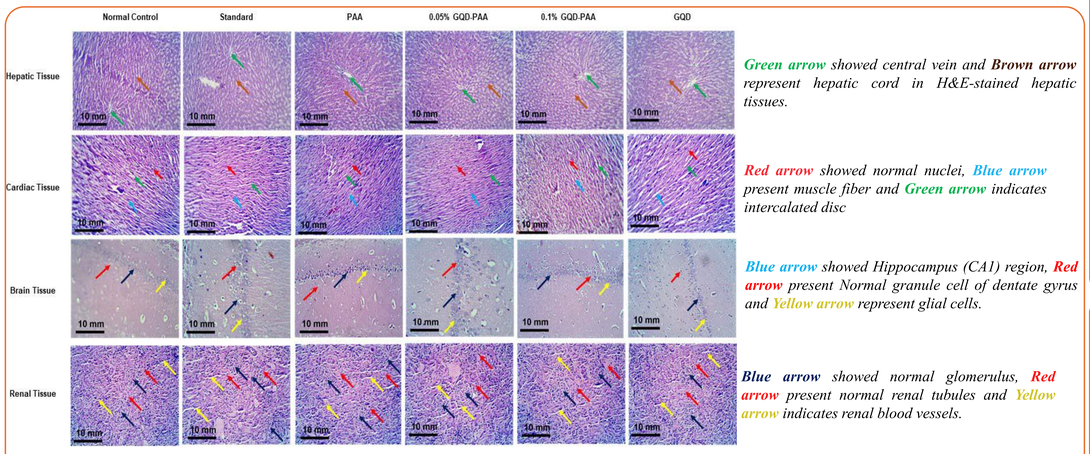


Figure. Optical micrographs of RBCs in the presence of normal control, standard and various formulation of GQD-PAA.



Green arrow showed central vein and Brown arrow represent hepatic cord in H&E-stained hepatic tissues.

Red arrow showed normal nuclei, Blue arrow present muscle fiber and Green arrow indicates intercalated disc

Blue arrow showed Hippocampus (CA1) region, Red arrow present Normal granule cell of dentate gyrus and Yellow arrow represent glial cells.

Blue arrow showed normal glomerulus, Red arrow present normal renal tubules and Yellow arrow indicates renal blood vessels.

Figure 8. Histological assessment of murine tissues treated with normal control, standard and various formulation of GQD-PAA.

Conclusion

- In this report, we administered various concentrations of GQD-PAA in diabetic Wistar albino rat models to examine its wound healing response. In contrast to natural control and standard betadine, the hybrid hydrogel reported excellent wound remediating activities, specifically we observed lower incorporation percentages of GQDs (0.05-0.1% GQD-PAA) to exhibit complete wound closure by the 13th day.
- From these results, we postulated the hydrophilicity in conjugation with the porosity of the hydrogel framework allows for the oxygenation and regulation of a moist milieu for the cells to migrate and thereby heal the wound in a scarless fashion. Along the same lines, the nano-dimension of the filler attributed to the cell signaling pathway necessary to induce initial inflammation as well as plausibly generate ROS to simultaneously destroy the bacterial infection consequences of the diabetic wound.
- Hybrid hydrogels demonstrate antibacterial, biocompatible, porosity, water-retainability, and wound fluid absorption properties. Synthetic PAA hydrogels outperform natural gels in structural integrity, making them a promising bandage.

Acknowledgment- Amity University, Noida, DBT & SERB