

Abstract

Diabetic wounds remain a major clinical challenge due to impaired angiogenesis, persistent inflammation, and reduced cellular proliferation under chronic hyperglycemic conditions. Conventional wound dressings often fail to effectively modulate the complex pathological microenvironment associated with diabetic wounds. In this study, we developed a γ -poly(glutamic acid) (γ -PGA)-based hybrid scaffold incorporating bioactive silica, strontium ions (Sr^{2+}), and fibroblast growth factor (FGF) to enhance wound healing. The γ -PGA matrix provided a hydrated and biocompatible environment, while silica and Sr^{2+} ions promoted angiogenesis and cellular activity. FGF further facilitated tissue regeneration by enhancing fibroblast proliferation and endothelial cell migration. The scaffold was fabricated and systematically characterized, followed by in vitro evaluation of cytocompatibility, cell migration, and angiogenic potential. Its therapeutic efficacy was further assessed using a streptozotocin-induced diabetic mouse model. The results demonstrated that the developed scaffold significantly improved tissue regeneration and accelerated wound healing under diabetic conditions, highlighting its potential as an effective biomaterial strategy for diabetic wound management.

Graphical Abstract

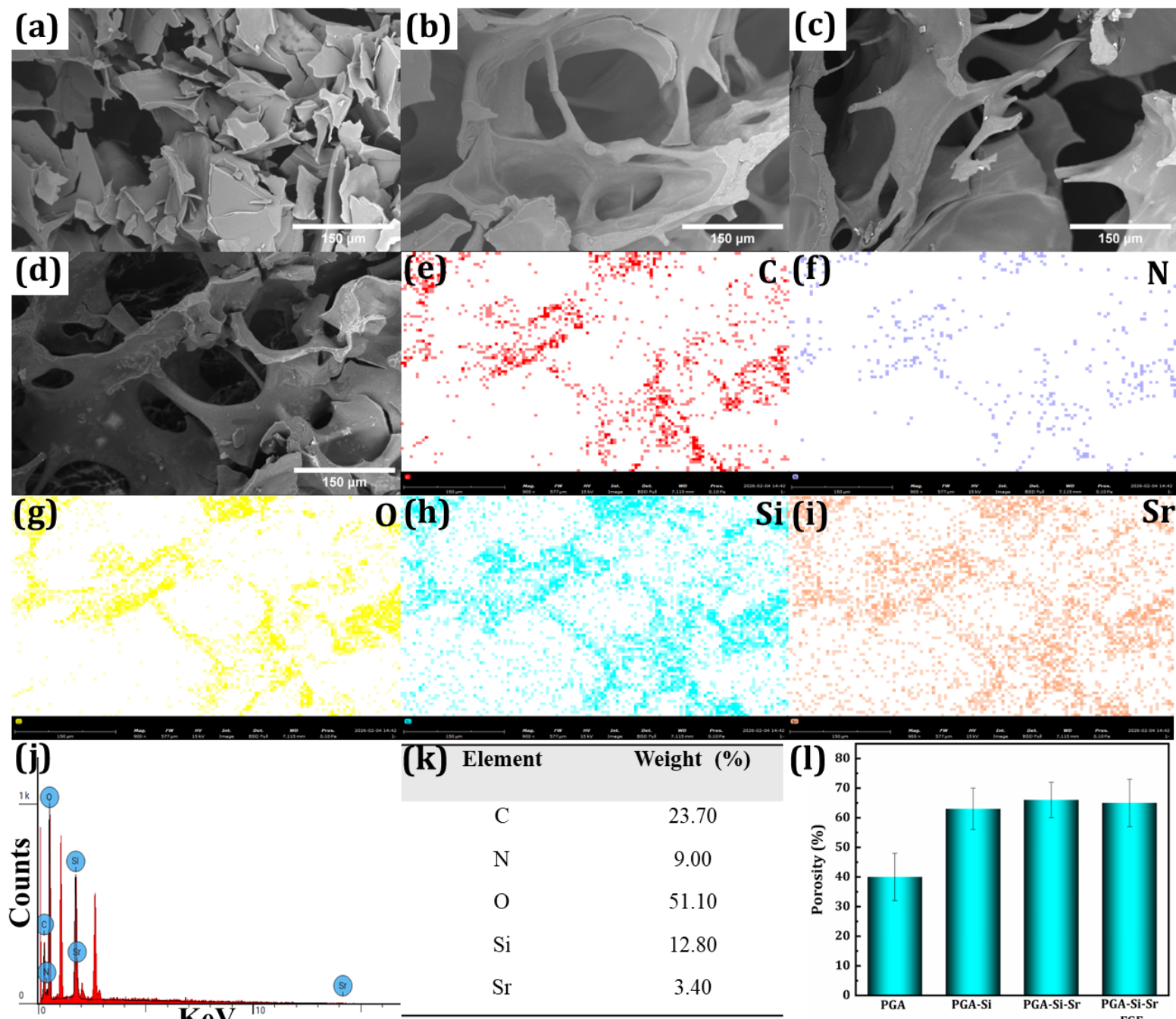
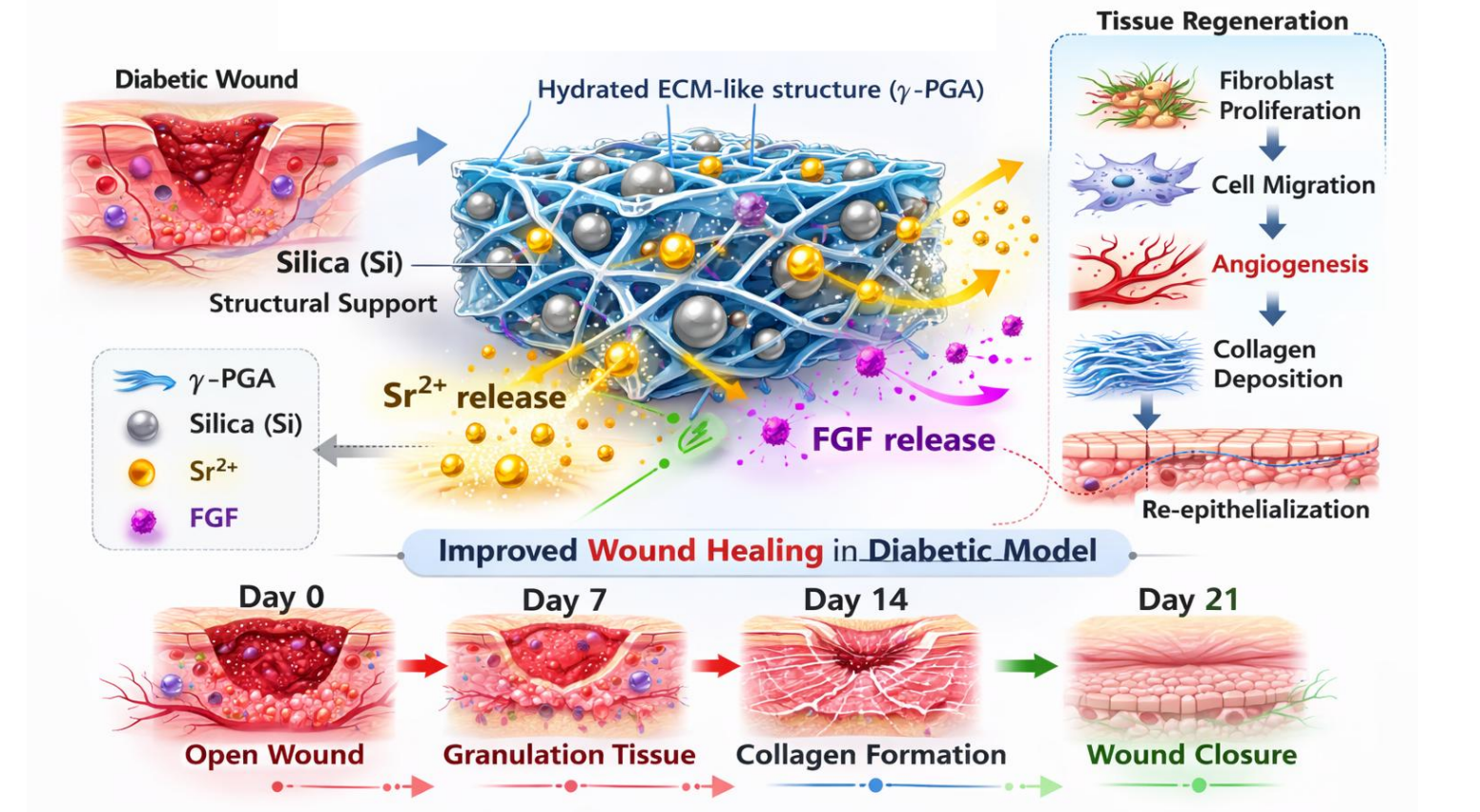


Figure 1. SEM images (a–d) showing porous morphology of γ -PGA-based scaffolds. Elemental mapping (e–i) and EDS analysis (j–k) confirm uniform distribution of Si and Sr. (l) Porosity increases with incorporation of Si, Sr, and FGF.

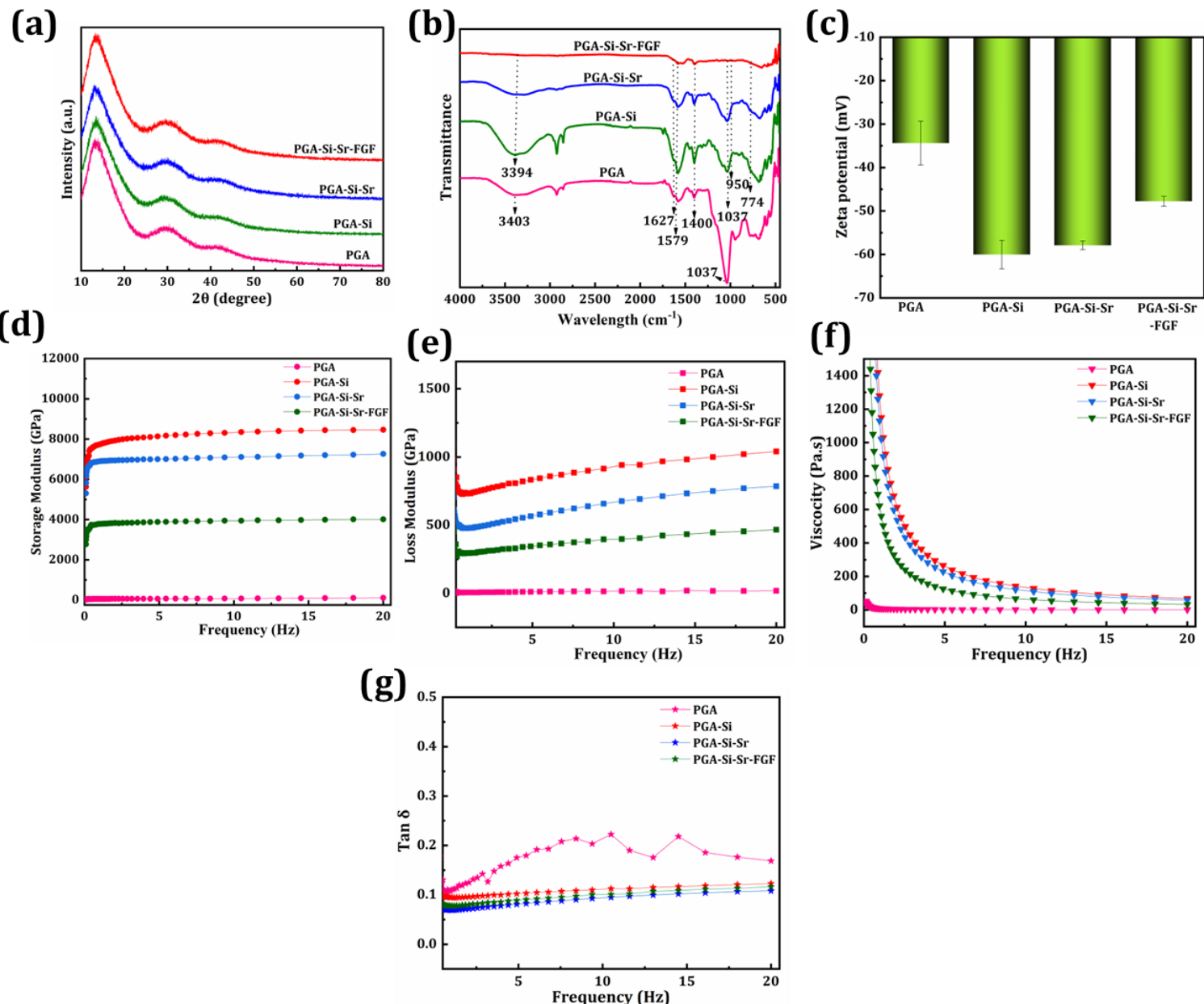


Figure 2. Physicochemical and rheological characterization of γ -PGA-based scaffolds. (a) XRD patterns, (b) FTIR spectra, and (c) zeta potential analysis. (d) Storage modulus, (e) loss modulus, (f) viscosity, and (g) $\tan \delta$ as a function of frequency.

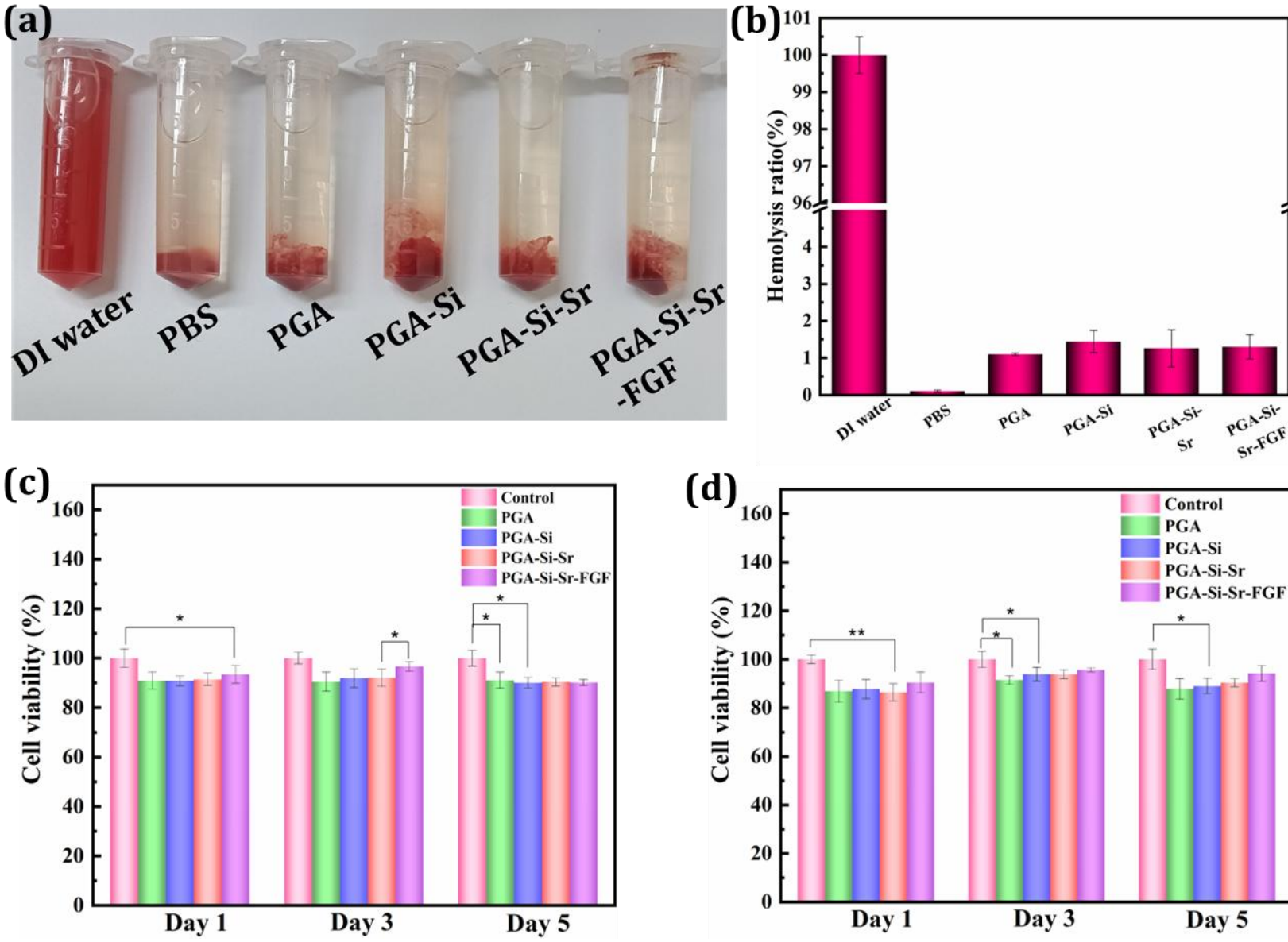


Figure 3. Biocompatibility evaluation of γ -PGA-based scaffolds. (a) Hemolysis assay images of different samples (DI water, PBS, PGA, PGA-Si, PGA-Si-Sr, and PGA-Si-Sr-FGF). (b) Quantitative hemolysis ratio. (c–d) Cell viability of treated cells on Day 1, Day 3, and Day 5.

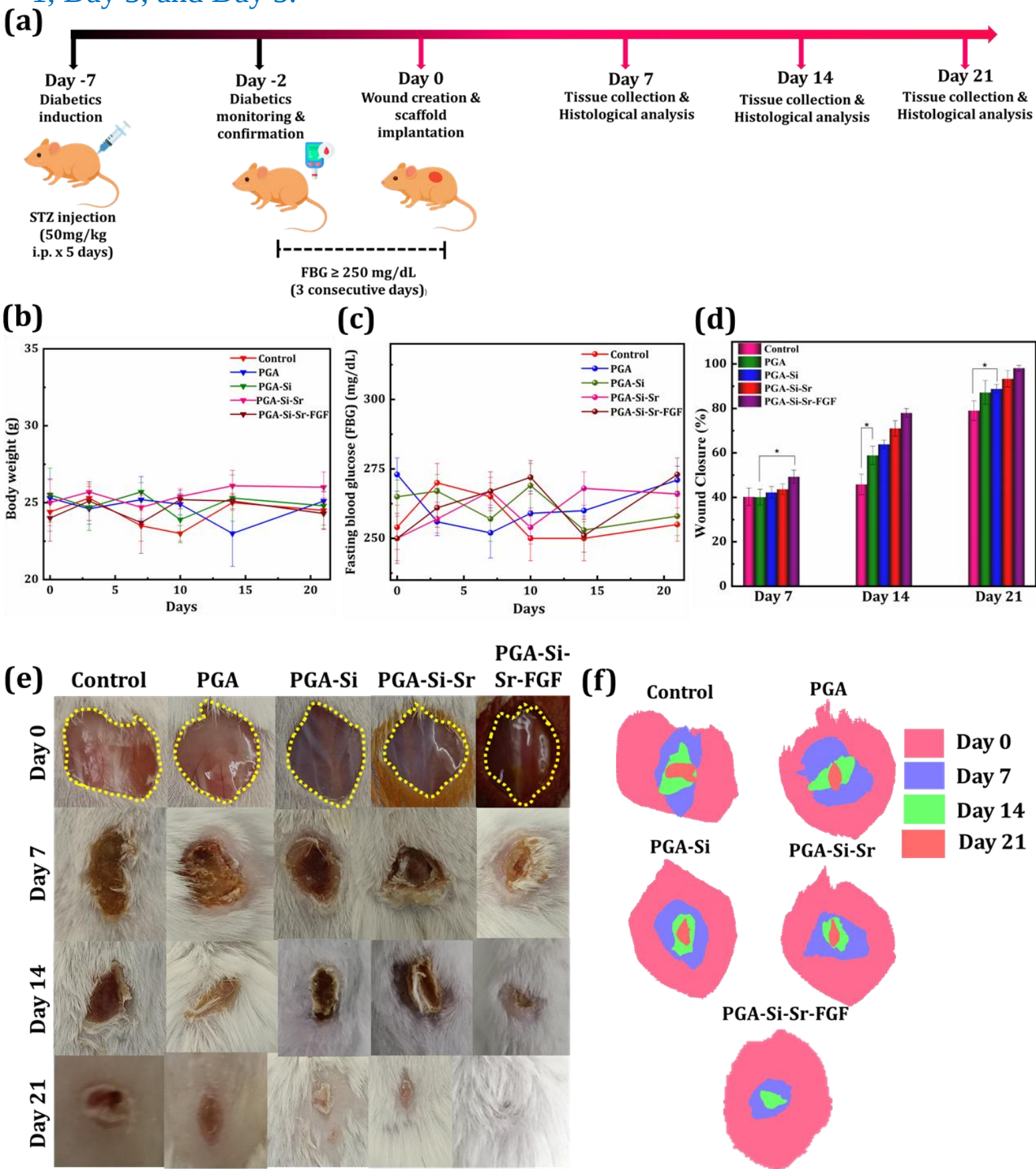


Figure 4. In vivo evaluation of diabetic wound healing. (a) Schematic of experimental timeline and treatment procedure. (b–c) Body weight and fasting blood glucose levels during the study. (d) Quantitative wound closure at Days 7, 14, and 21. (e) Representative images of wound healing progression. (f) Schematic analysis of wound area reduction, showing enhanced healing in the PGA-Si-Sr-FGF group.

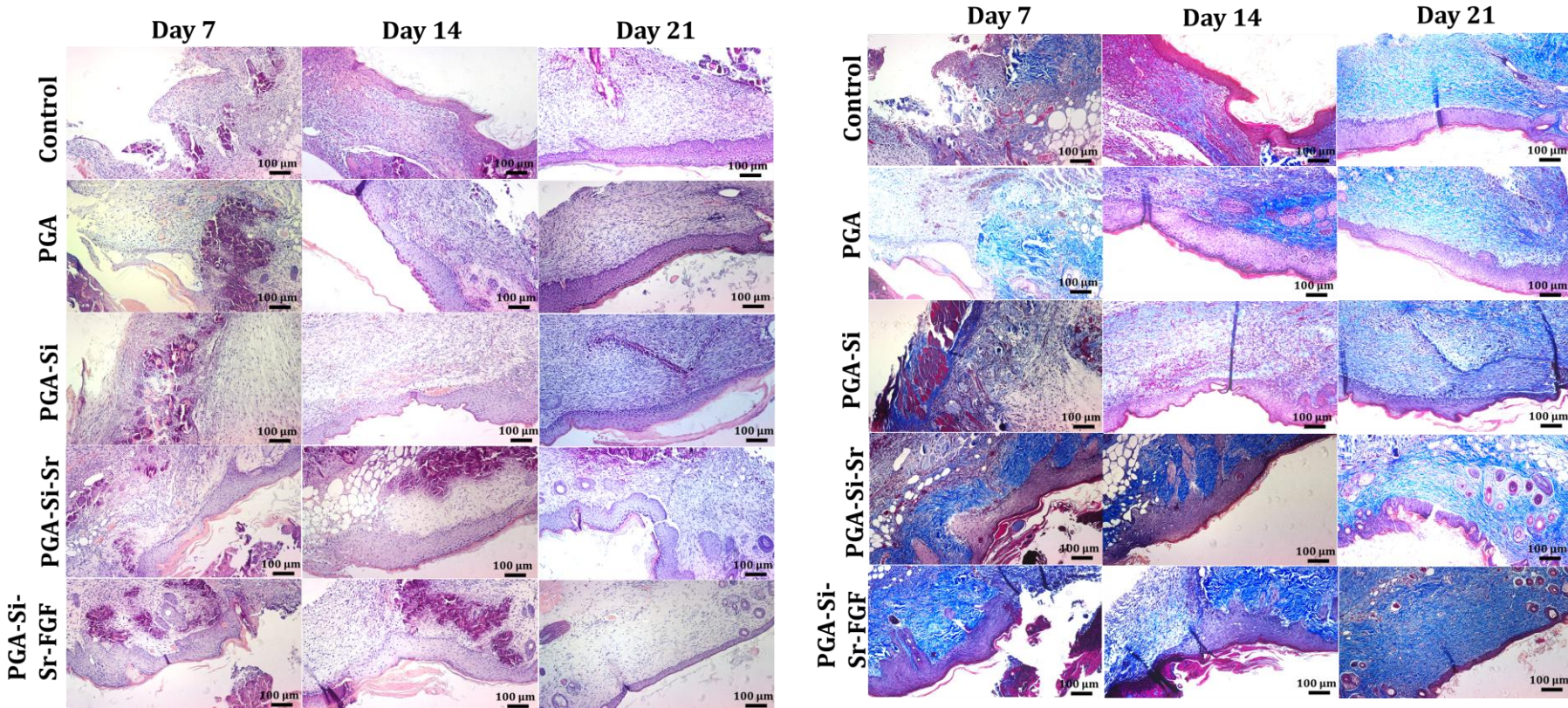


Figure 5. H&E-stained sections of Control, PGA, PGA-Si, PGA-Si-Sr, and PGA-Si-Sr-FGF groups, showing progressive re-epithelialization and tissue regeneration, with the PGA-Si-Sr-FGF group exhibiting the most advanced healing (scale bar: 100 μm).

Conclusion

The hybrid scaffold incorporating Si, Sr, and FGF significantly enhanced diabetic wound healing by promoting angiogenesis, cell proliferation, and tissue regeneration. Both in vitro and in vivo results demonstrated improved biocompatibility, mechanical properties, and accelerated wound closure, with the PGA-Si-Sr-FGF group showing the best performance. This multifunctional scaffold presents a promising strategy for effective diabetic wound treatment—PGA-based.