Porcine small intestinal submucosa (SIS) and graphene oxide/reduced graphene oxide scaffolds for potential application in electrostimulation therapy: preliminary formulation and characterization

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Abstract

The implementation of scaffolds or hydrogels, based on natural and biosynthetic extracellular matrix (ECM) or individual components of ECM, have shown to provide an adequate environment to enhance cellular migration, angiogenesis and regulation of wound healing processes. Additionally, electrostimulation therapies have gained attention in recent years due to their capability for simulating electric currents to direct cell migration, promote cell proliferation and increase oxygenated blood perfusion towards damaged tissues. In the present work, We propose innovative regenerative 3D scaffolds based on small intestinal submucosa (SIS) combined with graphene oxide (GO)/reduced graphene oxide (rGO) to improve their electrical conductivity such that they can be potentially applied in the healing of chronic wounds.

Results

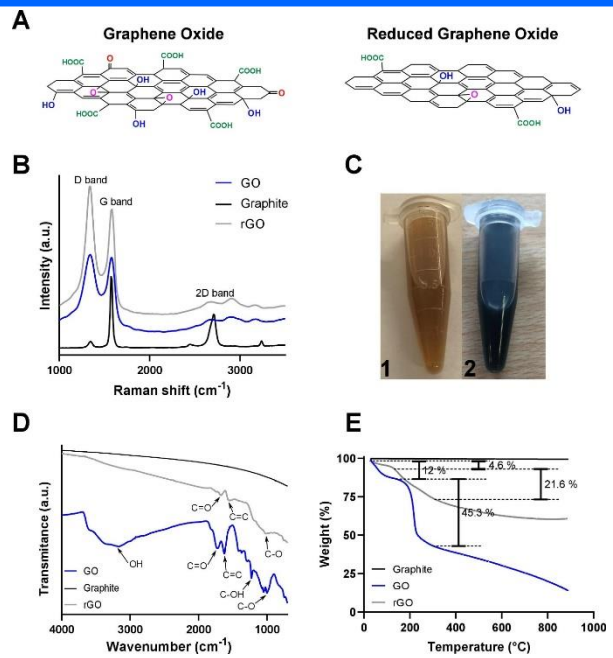

Figure 1. (A) Schematic of the chemical structure of GO and rGO. **(B)** Raman spectra (514 nm) of graphite, GO and rGO. **(C)** GO/ultra-pure ethanol solution **(1)** and rGO/ultra-pure ethanol solution **(2)**. **(D)** FTIR spectra of graphite, GO and rGO. **(E)** TGA thermograms for graphite, GO and rGO .

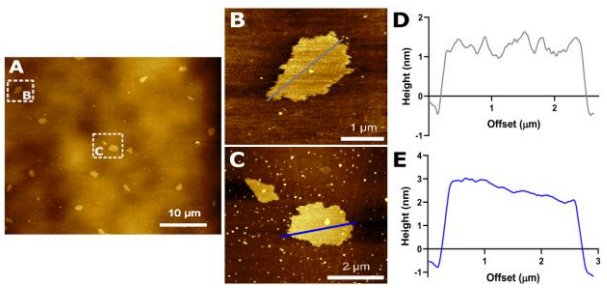

Figure 2. (A) AFM image of GO nanosheets. **(B)** and **(C)** correspond to enlarged areas of Figure 3(A). The height profile of GO nanosheets **(B)** and **(C)** is represented in **(D)** and **(E)** respectively.

Scaffolds

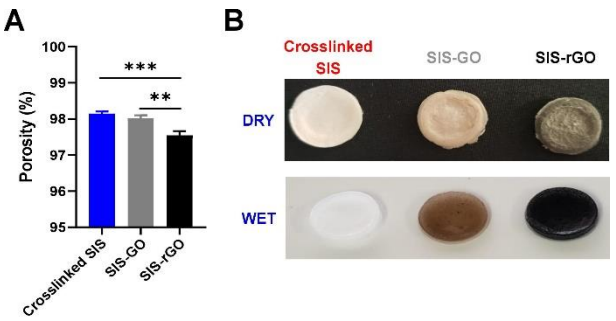

Figure 3. (A) Porosity of the scaffolds (liquid displacement method) .**(B)** Crosslinked SIS, SIS-GO and SIS-rGO scaffolds (before and after hydration).

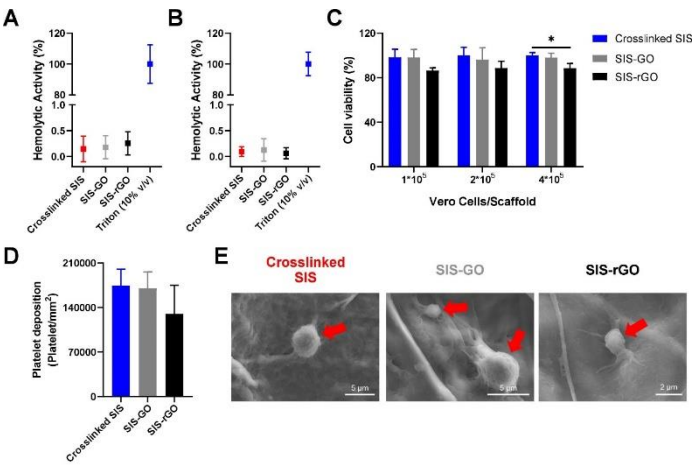

Figure 4. Hemolytic effect of the different scaffolds by extracts **(A)** and direct contact **(B)**. **(C)** Cell viability (Alamar blue assay) of the different scaffolds in Vero cells. Platelet activation (LDH assay) **(D)** and SEM images of platelet deposition **(E)**. Red arrows show activated platelets.

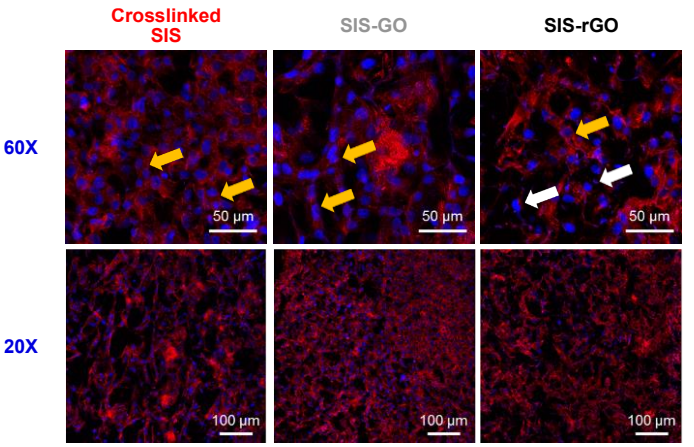

Figure 5. Confocal images of Vero cells morphology in the different scaffolds at 60X and 20X. Cell nuclei were stained with Hoechst 33342 (Blue) and cytoplasm with Alexa Fluor 594 Phalloidin (Red). Yellow arrows show cells with the correct elongated morphology (strongly adhered to the matrix) and white arrows show cells with abnormal round-shape morphology (not adhered to the matrix).

Conclusions

Innovative SIS-GO and SIS-rGO hybrid scaffolds were successfully developed in this study. Biological characterization of the scaffolds suggest that they are highly biocompatible, due to high hemocompatibility, low cytotoxicity (Vero cells) and no negative effects on human platelet aggregation. In addition, high porosity, high pore interconnection as well as their powerful cell attachment abilities are evidence of the enormous potential of the developed scaffolds for multiple applications in tissue engineering, tissue regeneration and chronic wound healing treatments. Future studies should be dedicated to testing the scaffolds within a relevant environment capable of mimicking the specific application of electrostimulation therapy in wound healing.