ELECTROSPUN COMPOSITE NANOFIBERS CONTAINING BIOCOMPATIBLE INORGANIC TUNGSTEN DISULFIDE NANOPARTICLES

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Objectives

Tungsten disulfide nanoparticles (WS_2) emerged as an excellent theranostics tool due to their exquisite optical properties and wide surface available for bioconjugation. However, their controlled delivery in vivo remains a challenge. Poly (lactic-co-glycolic acid) (PLGA) nanofibers are widely used as preferred carriers for the controlled release of drugs due to their biodegradability and their easy formation and preparation. A novel fluorescent nanofibrous material consisted of inorganic WS_2 nanoparticles and PLGA biopolymers was fabricated via a single-nozzle electrospinning method.

Preparation and morphological characterization

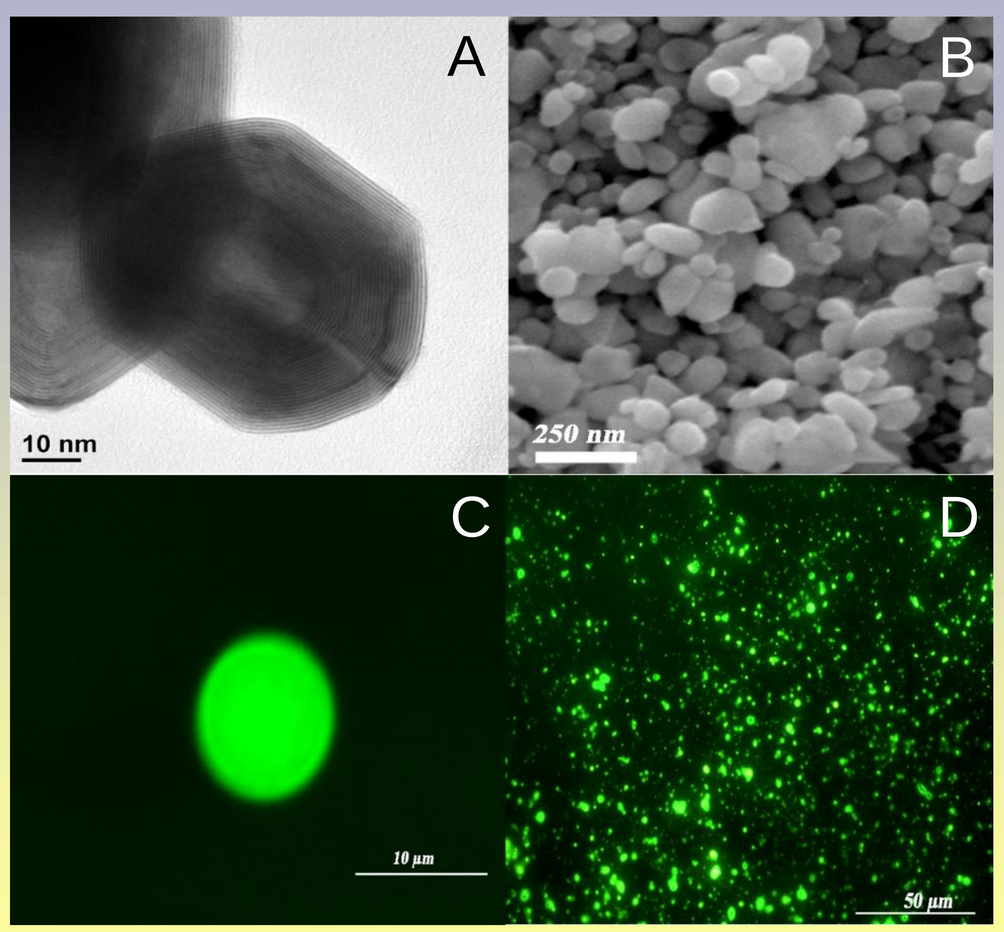

Fig. 1. A) Transmission electron microscopy (TEM) and **B)** Field emission scanning electron microscopy (FE-SEM) imaging were used to examine the morphology of the WS_2 nanoparticles. For labeling WS_2 nanoparticles, FITC-APTES was prepared by the addition of 3-aminopropyl triethoxysilane (APTES) to fluorescein isothiocyanate (FITC) in ethanol solution. **C)** and **D)** Fluorescence optical micrograph showing green fluorescence from FITC-APTES-labeled inorganic WS_2 nanoparticles.

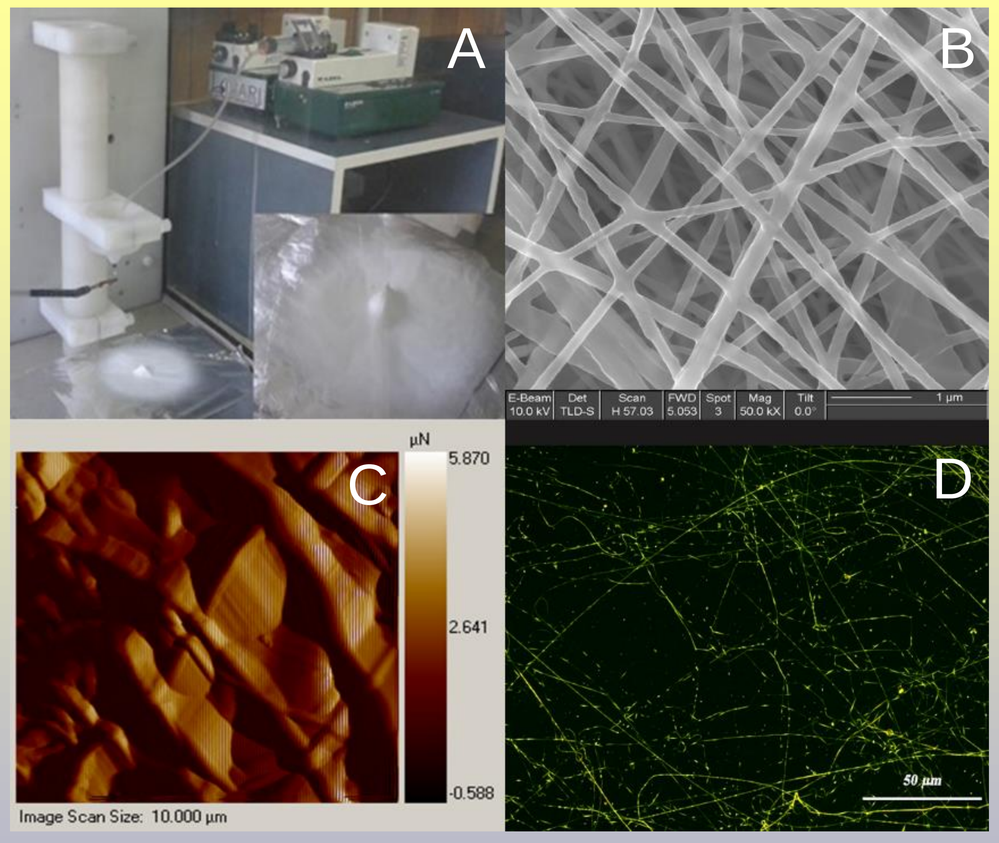

Fig. 2. A) The electrospinning system. **B)** FE-SEM photographs of blank PLGA nanofibers. **C)** Scanning probe microscopy (SPM) gradient image of the in-situ nanoindentation with a surface roughness of 195.5 nm. **D)** Fluorescence image of composite nanofibers containing FITC-APTES-labeled inorganic WS_2 nanoparticles (2 wt.%).

Results

PBMC were cultivated in the presence of different concentrations of WS_2 nanoparticles (12-100 µg/ml) for 48h, after which apoptosis and necrosis of cells was analyzed by Annexin V/Propidium iodide (PI) staining on flow cytometry. **A)** Representative dot plots of PBMC stained after the cultures is shown and **B)** the summarized data from 3 independent experiments is shown as mean % of Annexin V positive (Ann+) or PI+ cells ± SD. **C)** Internalization of WS_2 was analyzed after 24h cultures of MACS (Magenetic activated cell sorting)-purified peripheral blood monocytes and WS_2 nanoparticles at 50 µg/ml or 100 µg/ml. Representative images of cytospin preparation stained with May-Grunwald Giemsa are shown, demonstrating high internalization of WS_2 nanoparticles by monocytes. **D)** Proliferation of phytohemagglutinin (PHA), or CD3/CD28 beads - stimulated PBMCs, previously loaded with Cell-trace Far Red stain, and cultivated in the presence of different doses of WS_2 nanoparticles (3-100 µg/ml), was analyzed after 3 day cultures. Representative histograms of with non-proliferated (dark-green) and proliferated (light-green) PBMC with the indicated % of proliferated cells, proliferation index (PI) and division index (DI) are shown. **E)** The summarized data from 3 independent experiments are shown as mean % of proliferated PBMCs (± SD) stimulated with either PHA or CD3/CD28 beads, as indicated.

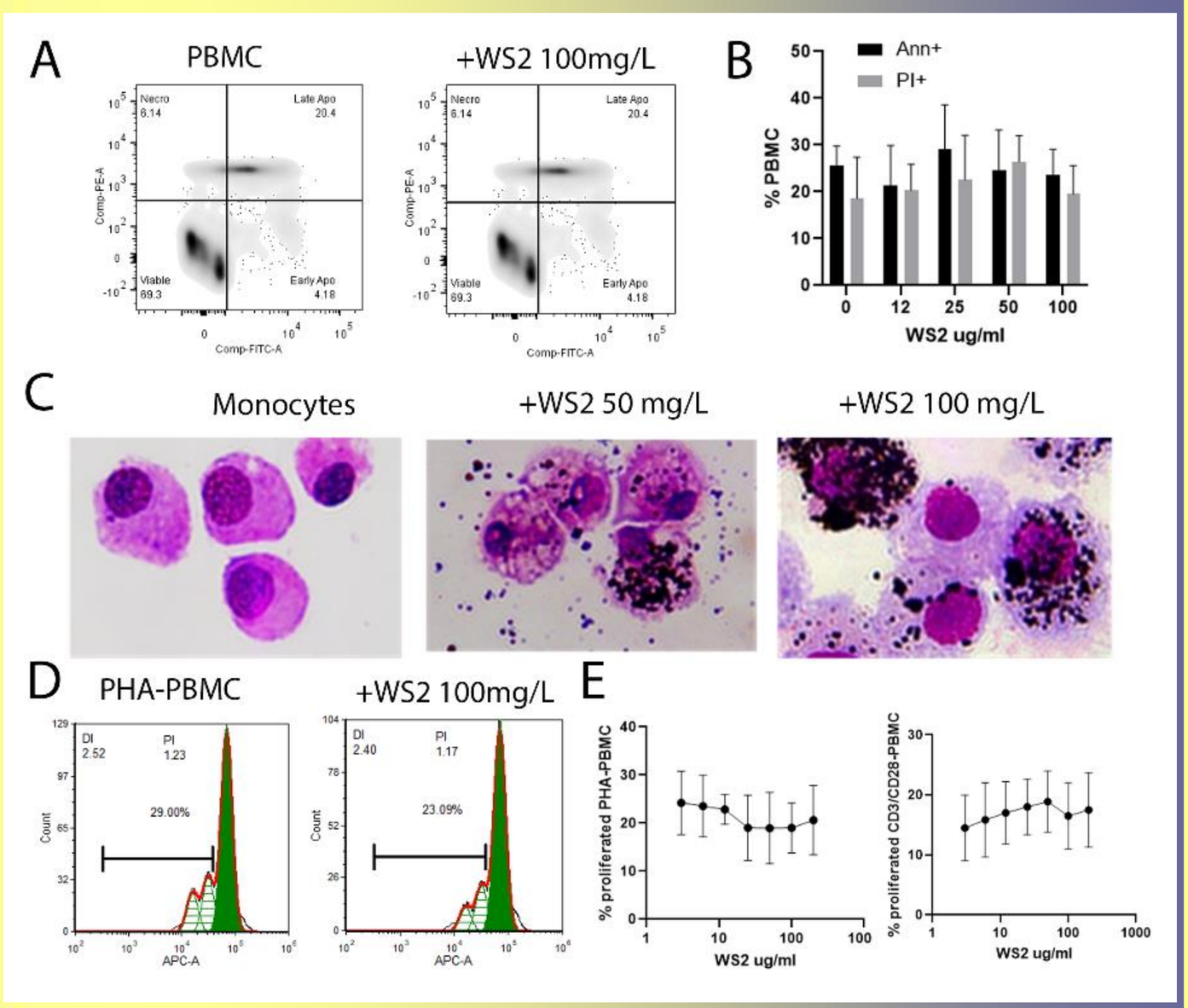

Fig. 3. Toxicity and modulatory potential of WS_2 nanoparticles in human peripheral blood mononuclear cells (PBMC)

Conclusions

In this study, the inorganic WS_2 nanoparticles demonstrated lack of cytotoxicity towards human peripheral blood mononuclear cells (PBMC) in vitro up to 100 µg/ml. Although these nanoparticles were easily internalized by monocytes, they did not modulate PHA-induced proliferation of PBMCs significantly. After loading of WS_2 with (FITC-APTES) as a model drug, they displayed similar cytotoxic profile in culture with PBMCs. Cumulatively, the electrospun composite nanofibers incorporated with biocompatible WS_2 inorganic nanoparticles represent new attractive theranostics platform, enabling a well-controlled delivery of bioactive molecules.

***Acknowledgments**: This work was supported by the project „Twinning to excel materials engineering for medical devices – ExcellMater"grant no. 952033, H2020-WIDESPREAD-2018-2020/H2020-WIDESPREAD-2020-5,2020-2023 and by the Science Fund of the Republic of Serbia, PROMIS, #6062673, Nano-MDSC-Thera*