Antioxidant albumin-based nanocomposites containing sulforaphane drug and superoxide dismutase plasmid

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Introduction

Albumin nanostructures are promising biocompatible, non-immunogenic and non-toxic platform for biomedical applications such as bioimaging and drug delivery. Sulforaphane (SF) can stimulate the expression of antioxidant genes via activation of a transcription factor, nuclear factor-erythroid-2–related factor 2 (Nrf2).

The goal: To synthesize albumin-based nanocomposites doped with sulforaphane and superoxide dismutase 1 gene and to stimulate endogenous antioxidant defense mechanisms in lung epithelial cells L-132 through combinatorial effect of SF and superoxide dismutase 1 gene (pSOD1 plasmid) delivered by HSA-PEI-SF-pSOD1 nanocomposites (NCs).

Synthesis of HSA-PEI-SF-pSOD1 NPs

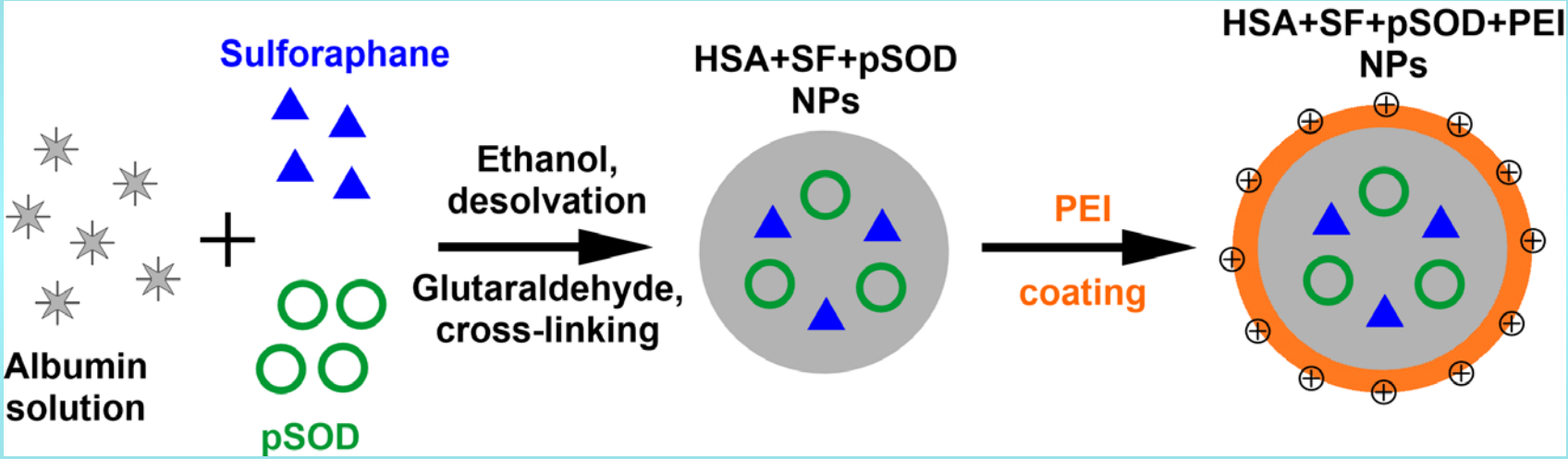


Figure 1. Schematic representation of the basic steps in the fabrication of composite HSA-PEI-SF-pSOD1 nanoparticles.

Characterization of nanoparticles

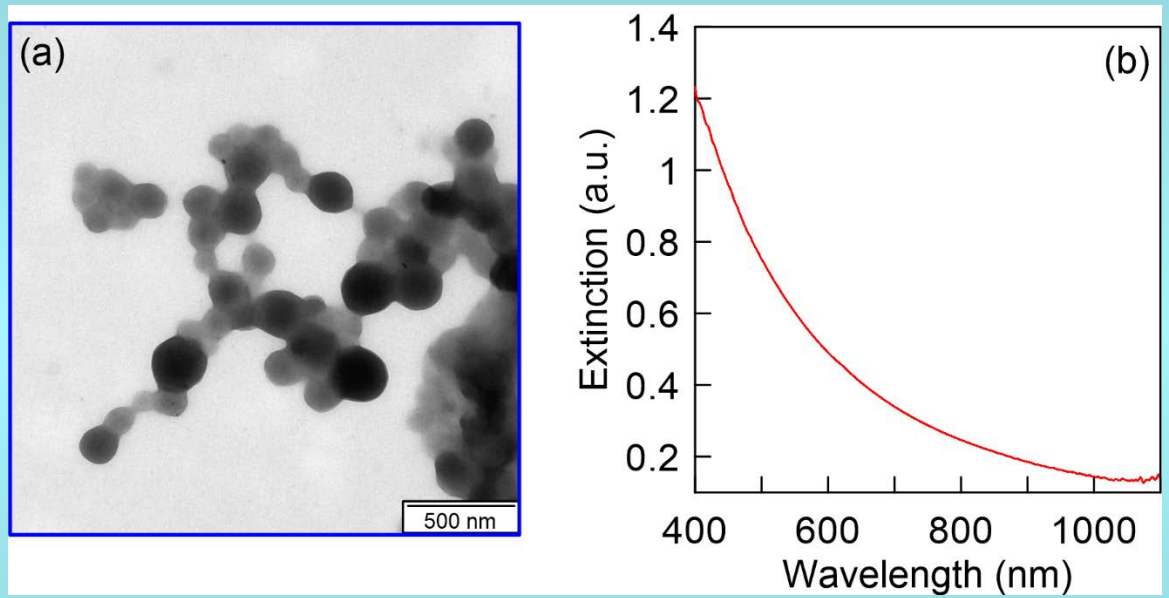


Figure 2. TEM image (a) and extinction spectrum (b) of synthesized albumin nanoparticles.

Sample	Zeta potential (mV)
HSA NPs	0.28
HSA+PEI NPs	59.4
HSA+SF+PEI NPs	59.2
HSA+pSOD1+ PEI NPs	52.0
HSA+SF+pSOD1 +PEI NPs	61.0

Table 1. Zeta potential of the synthesized nanoparticles.

Toxicity of nanocomposites

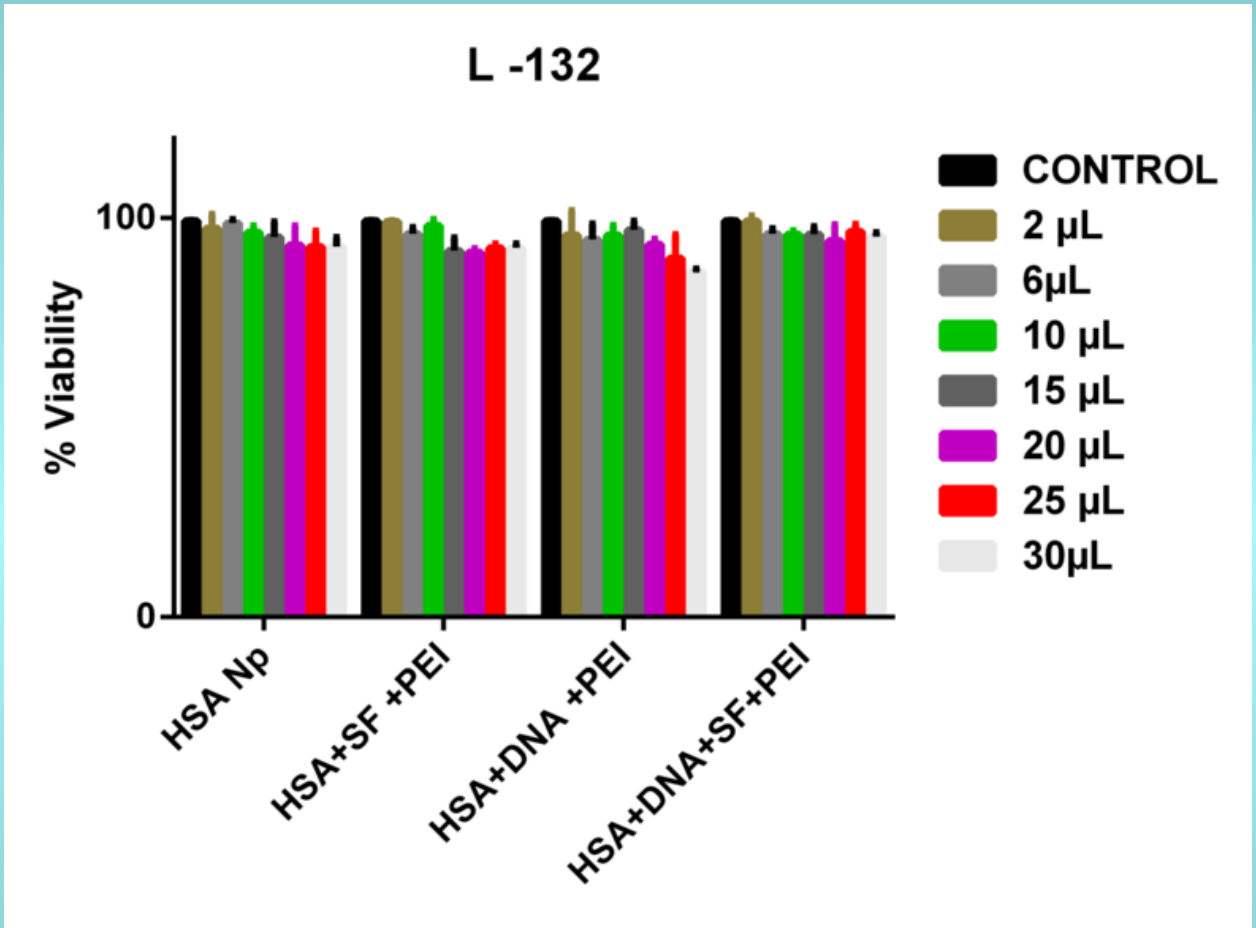


Figure 3. The effects of blank HSA NPs and loaded with Sulforaphane and pSOD-1 transgene on cell proliferation and viability of L-132 cells as determined by MTT assay. Concentration-dependent cytotoxic effects of nanoparticles were evaluated after 96 h incubation.

Antioxidant activity of nanocomposites

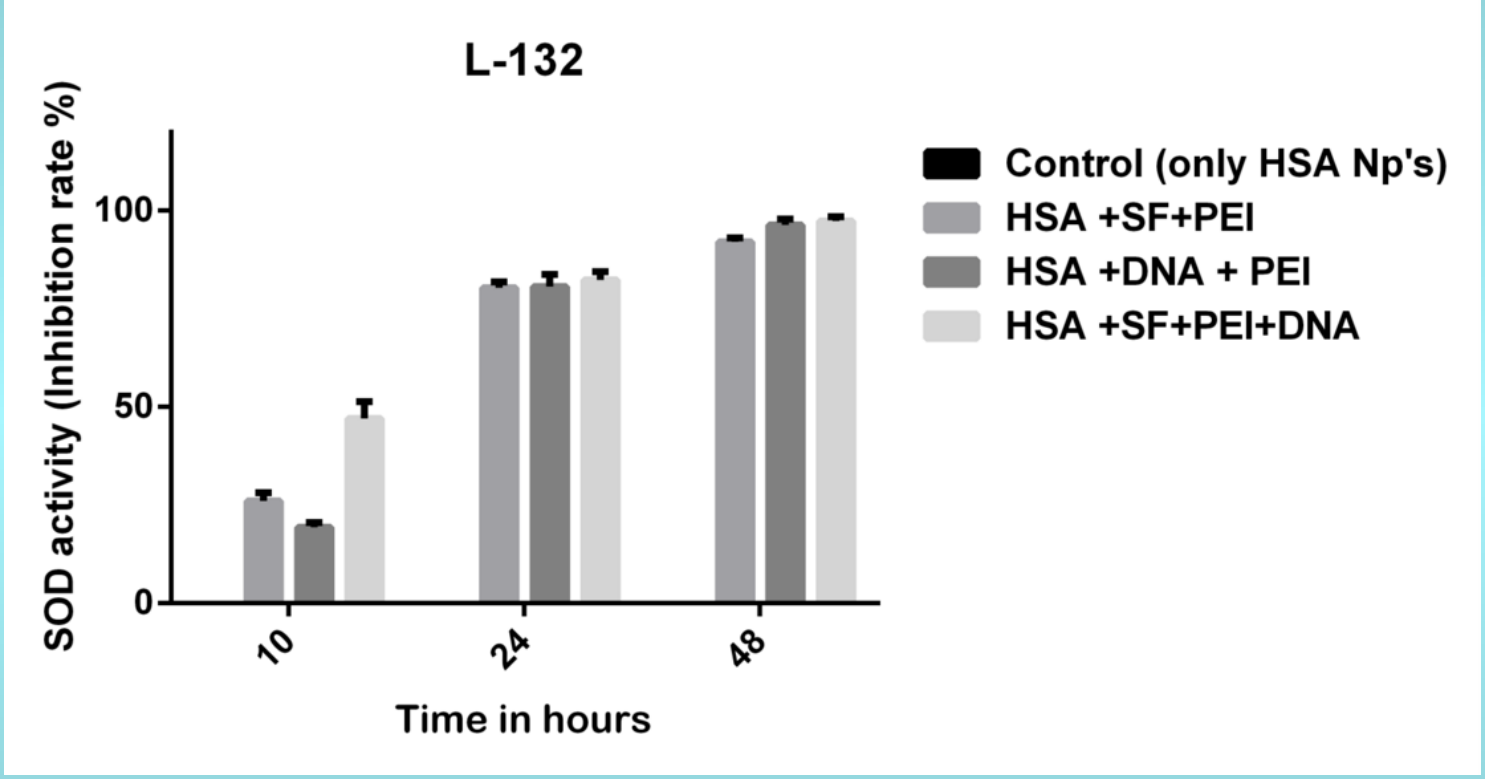
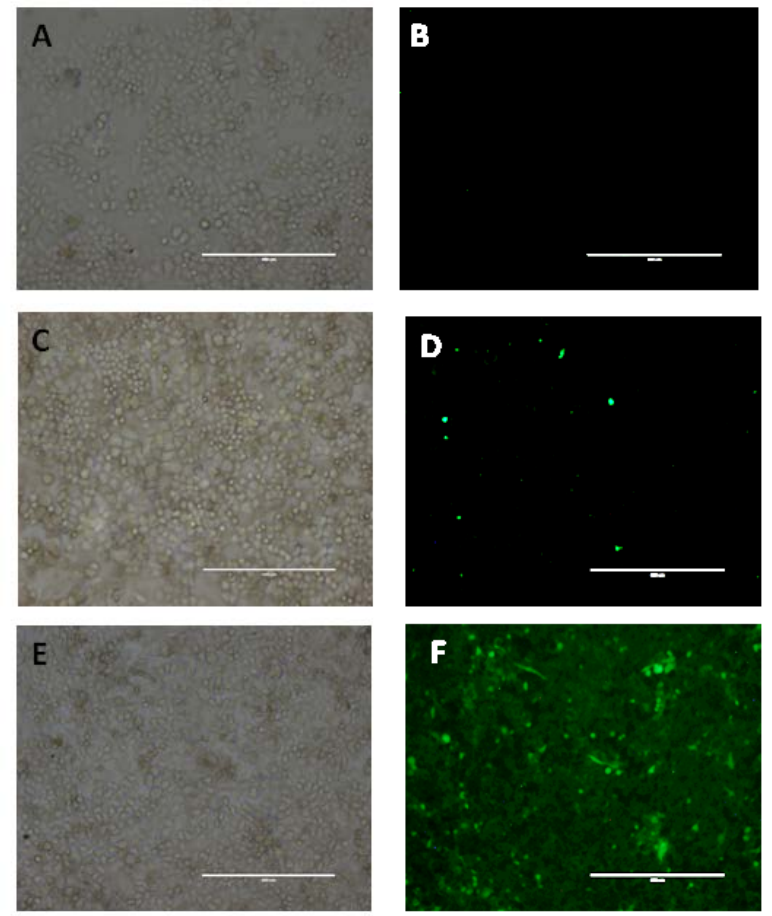


Figure 4. SOD activity (inhibition rate %) of the blank HSA Np's and loaded with Sulforaphane and pSOD-1 transgene showing the increase in SOD activity as a function of time.

Transfection efficiency



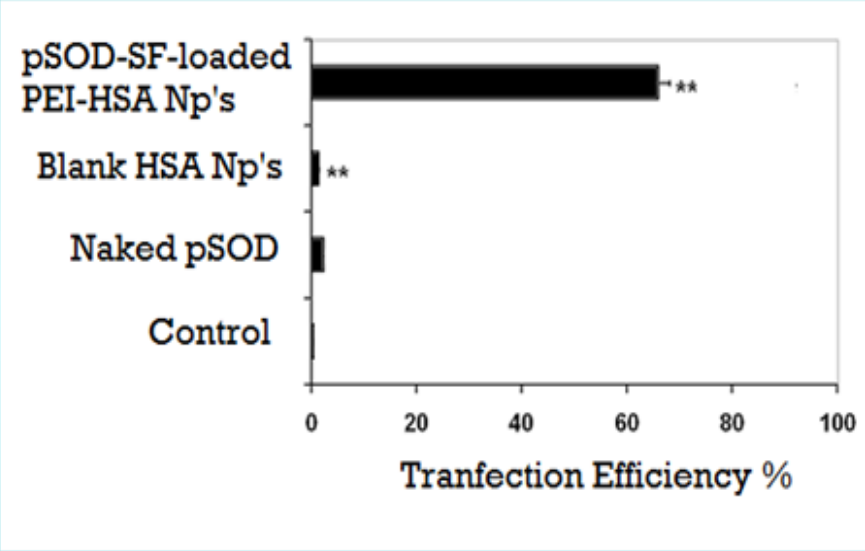


Figure 5. The expression of SOD1 tagged GFP transgene in L-132 cells after incubation with blank HSA NPs (A&B), 5000ng of pSOD1 plasmid (C&D) and HSA-PEI-SF-pSOD1 (E&F) following 6h incubation. Transfection was assessed after 48 h. The transfection efficiency is around 66% after incubation with HSA-PEI-SF-pSOD1 nanocomposites.

Scavenging of reactive oxygen species in L-132 cells

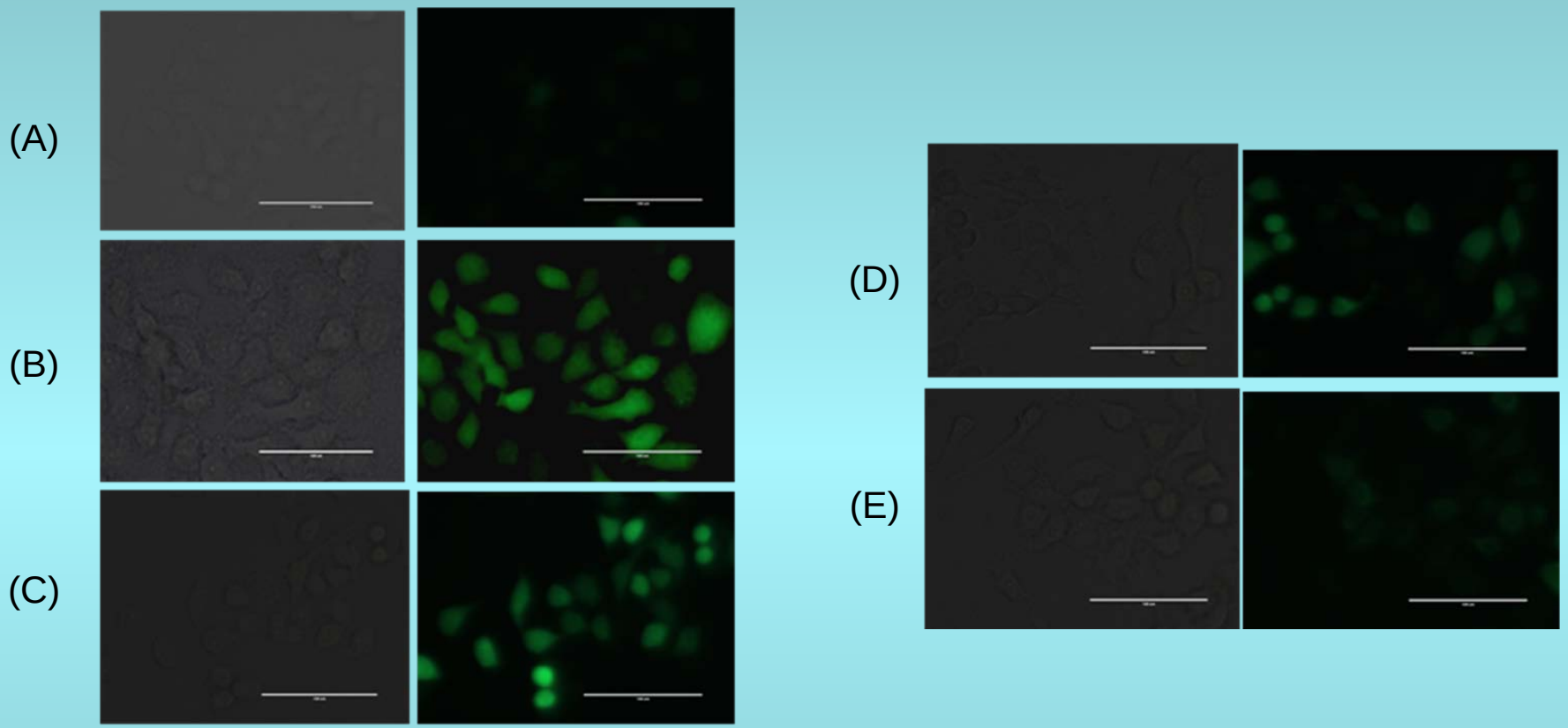


Figure 6. Fluorescence images of H_2O_2-treated L-132 cells after staining with DCFH-DA dye. (i) Untreated cells (A), H_2O_2 treated cells without HSA-PEI-pSOD1-SF preincubation (B) and H_2O_2-treated cells with a 12 (C), 24 (D) and 96 h (E) preincubation time with HSA-PEI-pSOD1-SF. All the scale bars represent 100 µm.

Conclusions

We have developed HSA-PEI-SF-pSOD1 nanocomposites by using the desolvation cross-linking method to fabricate PEI-stabilized HSA nanoparticles that have been further loaded with SF drug and pSOD1 plasmid. Antioxidant and cytoprotective effects of HSA-PEI-SF-pSOD1 nanoformulations have been examined *in vitro* against human lung epithelial cells (L-132). MTT assay has shown high biocompatibility of approx. > 95% up to 96 h, whereas the time-dependent SOD activity study has shown high antioxidant activity of nanocomposites. The expression of GFP tagged transgene SOD1 has been examined by a fluorescence microscope and revealed the transfection efficiency around 66% in L-132 transfected cells.

Thank you for attention.

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