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Polycaprolactone nanoparticle-Induced dose-dependent acute Nephrotic damage is ameliorated by customized conjugation of biocompatible and biodegradable polymer over polycaprolactone as observed in-vitro studies and in-vivo animal model

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Objectives: Dose dependent Acute nephrotic damage was evaluated in swiss albino mice for naïve polymeric nanoparticles and nanoparticles coated with biodegradable, biocompatible polymer. HEK-293 cell lines in-vitro studies established that polymer conjugation increases biocompatibility and minimizes toxicity of nanocarriers in specific doses (1-800 µg/mL). Various physiological, biochemical, histopathological nephrotic damage biomarkers and inflammatory parameters evaluated in Swiss Albino mice to observe Acute Kidney damage in response to intravenous administration of naïve-uncoated and coated nanocarriers.

Methods: Acute nephrotoxicity evaluation in mice was in compliance with OECD guidelines. Animals were divided into groups, (I): Normal Control animals. GROUPs (II), (III) and (IV) (A, B): mice receiving 4, 20 and 100 mg/kg single exposure of naïve uncoated and coated SPIONs in normal saline, i.v. Mice were observed for 14 days and sacrificed on 15th day. Blood and kidneys harvested at sacrifice time. Serum and other biomarkers like β2-microglobulin, Neutrophil Gelatinase-Associated Lipocalin, α1-microglobulin, Fatty Acid–Binding Protein, Retinol-Binding Protein, Cystatin-C, Interleukin-18, Microalbumin, Kidney Injury Molecule-1, Cysteine-Rich Protein, Serum creatinine, Urea, Blood-Urea Nitrogen, Serum Albumin, Serum Total proteins performed. H&E and mast-cell staining was performed to assess histopathological and inflammatory alterations in acute kidney damage, Tubular cell apoptosis and presence of apoptotic bodies by TUNEL and activated caspase -3 staining.

Results: Statistically significant changes were observed in serum and other biomarkers in naïve-uncoated nanoparticle treated animals in dose dependent manner as compared to normal control animals. These abnormalities were ameliorated and pathologies were normalized significantly in polymer grafted group. Severe kidney damage in terms of glomerular degeneration, severe cortical tubular necrosis, edema formation, severe inflammatory cell leukocyte (mainly monocyte) infiltration etc. in naïve uncoated NP treated animals as compared to the normal control animals.

Conclusions: Naïve polymeric nanoparticles are nephrotoxic due to extremely smaller size. Functionalization of these nanocarriers with biocompatible and biodegradable polymer ameliorates the acute nephrotic damage.