KSN 2019
Seoul, Korea · May 23 - 26

Abstract Type : Poster
Abstract Submission No. : PO-1017

Grafting of Biocompatible and Biodegradable Polymer Aminocellulose Ameliorates the In-vitro and In-vivo Dose Dependent Acute Oral Nephrotoxicity of Customised Trilayer Superparamagnetic Iron-Oxide Nanocarriers (SPIONs) formulated for Drug Delivery Purpose.

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Objectives: Acute Kidney Injury was assessed in dose dependent acute nephrotoxicity of Customised Superparamagnetic Iron-Oxide Nanocarriers (SPIONs). In-vitro HEK-293 cell lines studies confirmed that Aminocellulose grafting enhances biocompatibility and reduces toxicity of nanocarriers in specific doses (0.78-500 µg/mL). Therefore we studied various physiological, biochemical, and histopathological nephrotoxicity biomarkers and inflammation parameters in Swiss Albino Mice to observe the Acute Kidney Injury in response to the oral administration of naive uncoated and aminocellulose coated SPIONs.

Methods: Acute nephrotoxicity assessment in mice was in accordance with OECD guidelines. Animals were divided into groups, GROUP I: Normal Control mice. GROUP II, III and IV (A, B): mice receiving 50, 300 and 2000 mg/kg single exposure of naïve uncoated and coated SPIONs in normal saline, p.o. Mice were observed for 14 days and sacrificed on 15th day. Blood and kidneys were collected 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 SPIONs group in dose dependent manner as compared to normal control animals. These alterations were normalized and pathologies were ameliorated significantly in Aminocellulose 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 animals as compared to the normal control animals.

Conclusions: Naïve iron-oxide nanoparticles are nephrotoxic in their smaller size. Coating of these nanocarriers with biocompatible and biodegradable Aminocellulose ameliorates the Acute kidney injury.