

Glomerular Targeting Using Mesoscale Nanoparticles for Therapeutic Delivery

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Chronic kidney disease is frequently driven by proteinuric glomerular disorders, highlighting the need for targeted therapies. Polymeric mesoscale nanoparticles (MNPs) are highly kidney-selective carriers which demonstrate renal accumulation up to 26-fold greater than other organs. These particles, typically 300–500 nm in diameter, are biocompatible and capable of sustained therapeutic release over multiple days. Earlier investigations showed predominant localization of MNPs within tubular epithelial cells, though more recent evidence indicates enhanced uptake by podocytes during glomerular injury. Amiloride, a clinically approved diuretic that inhibits urokinase-type plasminogen activator (uPA), has been reported to reduce proteinuria and protect podocyte integrity. Based on these observations, this study explored the use of amiloride- MNPs as a targeted therapeutic strategy for glomerular disease.

Fluorescently labeled MNPs containing Cy5 dye were engineered alongside formulations encapsulating amiloride. Nanoparticles were analyzed for physicochemical characteristics including particle diameter, surface potential, and encapsulation efficiency. Experimental glomerular injury was established using lipopolysaccharide (LPS) administration in mice. Cy5-loaded nanoparticles were used to evaluate tissue distribution, while therapeutic formulations were tested in normal and diseased animals to assess treatment response. Proteinuria, renal functional markers, and fibrosis were measured as primary outcomes. After tissue collection, fluorescence imaging and histologic analyses, including immunofluorescence and immunohistochemistry, were performed to verify nanoparticle localization and biological effects. All statistical analyses amongst groups will be performed by ANOVA. Nanoparticle formulations incorporating fluorescent Cy5 dye, or amiloride were synthesized with diameters ranging from 300–450 nm and an average surface charge near –20 mV. Biodistribution studies demonstrated preferential renal accumulation of Cy5-MNPs in both healthy and injured kidneys, with markedly increased podocyte uptake in disease states. Therapeutic MNP formulations significantly improved disease outcomes in both animal models, reducing proteinuria and renal fibrosis while improving indicators of kidney function.

Targeted polymeric mesoscale nanoparticles represent a promising delivery platform for treating glomerular kidney disease. These nanoparticles exhibit strong kidney tropism and enhanced podocyte internalization during glomerular injury. Furthermore, delivery of therapeutic agents through MNPs produced measurable improvements in renal function and attenuated fibrotic progression, supporting their potential as a novel treatment approach for chronic kidney disease.