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Surface-Engineered PLGA Nanocapsules of crocetin nano-renal protective with improved biopharmaceutical attributes against Acute Kidney Injury via PI3K/Akt/Nrf2 singling pathway

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Objectives: In the current investigation, we fabricated the PLGA loaded nano-particles of naringenin and scrutinized the protective effect and possible underlying mechanism of crocetin against renal reperfusion/ischemia injury in anesthetised rats.

Methods: Nanoparticles were prepared by ultra-sonication technique and influential formulation parameters were systematically optimized by Box-Behnken design to obtain quality attributes in the desired range. Rats were divided into 4 groups to induce the renal reperfusion/ischemia injury in anesthetised rats and after 45 min the renal tissue was removed to estimate the renal ischemia/reperfusion injury. Renal injury was scrutinized via determined the blood urea nitrogen, creatinine clearance, potassium, uric acid, sodium and identified the morphological changes. Oxidative parameters including superoxide dismutase, catalase, reduced glutathione, thiobarbituric acid reactive species and myeloperoxidase, respectively. The renal expression phosphorylated-PKC, Nrf2, HO-1, Akt and inflammatory caspase-3 were also estimated, respectively.

Results: Extensive evaluation of naringenin PLGA nanoparticles (NG-PLGA-NPs) indicated average particle size of 205 nm with poly-dispersity index 0.22, zeta potential <22 mV, drug loading > 85% and sustained *in vitro* drug release with 94.2% release after 48 h. The renal I/R induced AKI was scrutinized via observed the significant alteration in the urine and plasma parameters BUN (45%), creatinine (68%), uric acid (56%), potassium (73%) and sodium (70%); oxidative stress such as SOD (69%), GSH (56%), TBRAS (72%), CAT (50%) and MPO (78%) along with the marked histopathology changes in renal tissue. The dose dependent treatment of crocetin reduced the acute tubular necrosis in the renal tissue histopathology. Dose dependent treatment of crocetin altered the Nrf2, p-Akt, pro-caspase-3, HO-1 and caspase-3, respectively.

Conclusions: We can be concluded that crocetin attenuates I/R renal injury rats via PI3K/Akt/Nrf2 Signaling Pathway.