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Surface engineered nanocapsules of Umbelliferone via PI3K/AKT/Nrf2 are potential candidate for Acute kidney alignments treatment

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Objectives: Acute renal insult (AKI) is taking an increase trend and becoming a common clinical burden in modern world with high morbidity and mortality rate. Renal reperfusion/ischemia injury a key factor in activation of AKI initiates the interrelated sequence within the renal tissue which culminates in renal damage and induction the death of renal cells. Not many but few researchers are of opinion that Nuclear Factor Erythroid 2 related factor may have some and important role in the expansion of oxidative stress, via increased the protein kinase C (PKC) pathway activation. In the current study, we make attempt to scrutinize the renal protective effect of surface engineered nano-formulation of Umbelliferone against renal ischemia/reperfusion (I/R).

Methods: Umbelliferone was developed via cost-effective doses system and tested for their potential to reduce transforming growth factor-β (TGF-β) signalling via docking. The rats were divided into 5 groups and left renal tissue was removed to investigate the renal I/R damage. The renal morphology and serum parameters were estimated, respectively. Renal expression of Nrf2, phosphorylated-PKC, AkT, HO-1 and caspase-3 were determined.

Results: The formulation of UF in its nano-form were smooth spherical with relatively narrow size distribution. Umbelliferone significantly down-regulation LPO (60%), creatinine (68%) and BUN (58%) content. I/R group rat showed the reduced expression of p-Akt (0.6%), Nrf2 (0.4%), HO-1 (0.5%), pro-caspase-3 (0.4%) and enhanced the renal expression of caspase-3 (2.4%), which was significantly altered by Umbelliferone p-Akt (1.4 and 1.1%), Nrf2 (0.6 and 0.9 %), HO-1 (0.8 and 0.9%), pro-caspase-3 (0.7 and 0.5%) and enhanced the renal expression of caspase-3 (1.4 and 1.1%) treatment at dose 25 and 50 mg/kg. The histopathology studied showed the less number of tubular necrosis, inflammatory blood vessel in Umbelliferone treated group.

Conclusions: Our study clearly showed that nano-formulation of umbelliferone attenuates the renal injury in I/R injury rats via PI3K/Akt/Nrf2 Signalling Pathway.