Anti-fibrotic and Anti-apoptotic effects of naringin on Cisplatin induced renal injury via Nrf2/PI3K/Akt signaling pathway

Prakash Bhatt¹, Vikas Kumar²
¹Department of Pharmaceutical Sciences, Jamia Hamdard, India
²Department of Pharmaceutical Sciences, Shuats, India

**Objectives:** Chronic Kidney disease faces the risk of its expansion from Acute Kidney injury (AKI) and it increases the risk of mortality and death via damage to renal tubular cells driven through oxidative stress and mitochondrial dysregulation. Every year around 5000 cases per million of AKI are reported and 295 requires dialysis during the AKI. About 10-15% risk death factor increase during the AKI, with resultant increase in 50% mortality rate. Although cisplatin is an anticancer drug that has protective action against malignant tumor, it is reported to induces nephrotoxicity. The purpose of current study is to scrutinize the anti-fibrotic and anti-apoptotic effects of naringin on cisplatin (CIS) induced renal injury via Nrf2/PI3K/Akt signaling pathway.

**Methods:** Swiss albino Wistar rats divided into different groups with CIS injection (4 and 10 days), respectively naringin is administered at end of the experimental study. Renal biochemical, antioxidant parameters were measured. The histopathological examination to identify the changes in renal tissue and apoptosis of the proximal tubular cells was performed. Western blot techniques were used for estimation of relationship between upregulation of Nrf2, phosphorytion of Akt and down-regulation of WNT/β-catenin and TGF-β, respectively.

**Results:** Naringin significantly (P<0.001) down-regulated the CRE (68%), BUN (75%); renal antioxidant parameters MDA (65%) and up-regulation of SOD (77%) and GSH (58%), respectively. The inflammatory mediators significantly (P<0.001) reduced the TNF-α (68%), IL-1β (53%) and IL-6 (40%). Moreover, the western blotting showed the significantly (P<0.001) suppressed the Nrf2 (47%), PI3K (43%), Akt (51%), Caspase-3 (35%), Caspase-9 (28%), cyclooxygenase-2 (48%), NF-kB (40%) and iNOS (38%), suggesting the inhibition of inflammation and apoptosis.

**Conclusions:** Overall, Naringin may possess beneficial effect in cisplatin induced AKI via suppression of Nrf2/PI3K/Akt pathway.