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Chemomodulatory effect of betanin against paracetamol and diclofenac induced neurotoxicity and endocrine disruption in rats

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Abstract

Paracetamol and diclofenac are two of the most popular analgesics and anti-inflammatory medications. Despite of their several therapeutic benefits, their over consumption led to subsequent cellular damage. Their cytotoxicity is attributed to reactive radical generation. Betanin has antioxidant and anti-inflammatory properties. The protective effects of betanin against paracetamol or diclofenac induced neurotoxicity or endocrine disruption has not been investigated before. Therefore, this study aims to explore the protective potential of betanin against paracetamol or diclofenac neurotoxicity and endocrine disruption in a rat model. In brain, paracetamol (400 mg/ kg) and diclofenac (10mg/kg) enhanced DNA fragmentation and lipid peroxidation level. A depletion of GSH content concomitant with a reduction in the activities of antioxidant enzymes (HOX-1, POX-1, CAT and SOD) were detected. Serotonin, nor-adrenaline and dopamine levels were markedly reduced after paracetamol and diclofenac challenge. In serum, a significant reduction of testosterone, TRH, TSH, T3 and T4 were associated with the enhanced oxidative damage. Cotreatment of rats with betanin (25mg/kg) by gavage for 28 consecutive days ameliorated most of the biochemical and histopathological changes induced by paracetamol or diclofenac. In conclusion, betanin exerted a potential chemomodulatory effect against paracetamol or diclofenac overconsumption induced neurotoxicity and endocrine disruption. PAR and DF administration in high dose and long-time induced liver and kidney injury, disrupted serum lipid profile, enhanced serum levels of inflammatory and oxidative stress markers, triggered DNA fragmentation and caused drastic changes in the histopathological pictures of the two organs. Bet supplementation succeeded to ameliorate most of the biochemical changes and protected DNA from damage as obtained from comet assay. Histological features in H&E taken to different groups also mirrors this findings. Treatment with betanin alleviated the paraquat-incurred acute kidney injury, evidenced by histological improvement, reduced serum and urine markers for kidney injury. Betanin antagonized the paraquat-induced inflammation, indicated by reduced expression of inducible nitric oxide synthase and cyclooxygenase, blunted activation of nuclear factor kappa B, and diminished lysosomal protease activities. Betanin also decreased oxidative stress elicited by paraquat. In conclusion, betanin may have a protective effect against paraquat-induced acute kidney damage. The mechanisms of the protection appear to be the inhibition of oxidative stress and inflammation. Betanin was successfully isolated from fruits of Opuntia elatior Mill (Cactaceae) and purified by column chromatography. The results showed that betanin attenuated diabetic kidney injury by significantly inhibiting proteinuria, blood glucose, serum creatinine and BUN levels and restored antioxidant enzyme activities in kidney tissue. Histological studies exhibited that betanin treatment reduced the glomerular surface area, glomerulosclerosis and tubulointerstitial fibrosis. Furthermore, betanin modulated mRNA and protein expression of TGF-β, type IV collagen, α-SMA and E-cadherin in kidney.

Conclusions: The results conclude that betanin can effectively suppress renal fibrosis in DN, and may slow down the progression to end-stage renal disease by regulating TGF-β signal pathway.

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