

## **The modulatory effect of *Moringa oleifera* leaf extract on endogenous antioxidant systems and inflammatory markers in acetaminophen induced nephrotoxic mice model**

### **ABSTRACT**

N-Acetyl-p-Aminophenol (APAP), also known as acetaminophen, is the most commonly used over-the counter analgesic and antipyretic medication. However, its overdose leads to both liver and kidney damage. APAP-induced toxicity is considered as one of the primary causes of acute liver failure; numerous scientific reports have focused majorly on APAP hepatotoxicity. Alternatively, not many works approach APAP nephrotoxicity focusing on both its mechanisms of action and therapeutic exploration. *Moringa oleifera* (MO) is pervasive in nature, is reported to possess a surplus amount of nutrients, and is enriched with several bioactive candidates including trace elements that act as curatives for various clinical conditions. In this study, we evaluated the nephro-protective potential of MO leaf extract against APAP nephrotoxicity in male Balb/c mice. A single-dose acute oral toxicity design was implemented in this study. Group 2, 3, 4 and 5 received a toxic dose of APAP (400 mg/kg of bw, i.p) and after an hour, these groups were administered with saline (10 mL/kg), silymarin-positive control (100 mg/kg of bw, i.p), MO leaf extract (100 mg/kg of bw, i.p), and MO leaf extract (200 mg/kg bw, i.p) respectively. Group 1 was administered saline (10 mL/kg) during both the sessions. APAP-treated mice exhibited a significant elevation of serum creatinine, blood urea nitrogen, sodium, potassium and chloride levels. A remarkable depletion of antioxidant enzymes such as SOD, CAT and GSH-Px with elevated MDA levels has been observed in APAP treated kidney tissues. They also exhibited a significant rise in pro-inflammatory cytokines (TNF- $\alpha$ , IL-1 $\beta$ , IL-6) and decreased anti-inflammatory (IL-10) cytokine level in the kidney tissues. Disorganized glomerulus and dilated tubules with inflammatory cell infiltration were clearly observed in the histology of APAP treated mice kidneys. All these pathological changes were reversed in a dose-dependent manner after MO leaf extract treatment. Therefore, MO leaf extract has demonstrated some therapeutic effectiveness against APAP-induced nephrotoxicity through enhancement of the endogenous antioxidant system and a modulatory effect on specific inflammatory cytokines in kidney tissues.

**Keyword:** Acetaminophen nephrotoxicity; Antioxidant enzymes; Inflammatory cytokines; Kidney histology; *Moringa oleifera*; Serum biochemical markers