

## ABSTRACT

**Background:** In general, cytotoxic agents are known to cause devastating side effects in various organs and their functions which includes changes in histological features, alterations in biochemical parameters and blood counts. Hence the present study was aimed to observe the histopathological changes due to subacute toxicity with anticancer chemotherapeutic agent namely methotrexate in various organs of rats and the possible ameliorative effect of an antioxidant, quercetin.

**Materials and Methods:** Forty male rats were divided into 5 different groups with each group consisting of 8 rats. The Group 1 was a control and they were treated with 0.5ml of carboxy methyl cellulose. The Group 2, 3, 4 and 5 animals were treated with Methotrexate 0.125 mg/kg; Methotrexate 0.250mg/kg; Methotrexate (0.125mg/kg) + Quercetin (500mg/kg); and Methotrexate (0.250mg/kg) + Quercetin (500mg/kg), respectively. All drugs were administered orally through oral gavage once daily for 14 days. At the end of the study, blood samples were collected from all the animals in each group. The animals were then sacrificed and few organs were collected for histopathological analysis.

**Results:** All the rats exposed to two different doses of methotrexate (Group 2 and 3) produced significant increase in levels of AST, ALT, ALP and Total Protein along with renal markers such as urea, creatinine levels. In groups treated with quercetin along with methotrexate showed significant improvement on liver and renal enzyme parameters. Haemoglobin and blood sugar levels were reduced in Group 2 and 3 and these levels showed slight improvement in Group 4 and 5. Dose dependent histopathological changes and protective effect of quercetin were observed and main target organs affected were lungs, liver and kidneys.

**Conclusion:** It can be concluded from this study that exposure to methotrexate produced minimal changes at 0.125mg/kg body weight and significant changes at 0.250mg/kg body weight and possible ameliorative effect of quercetin observed in lung, liver and kidney. The findings observed are of significant importance due to its hepatotoxic, nephrotoxic and lung toxicity characters.

**Keywords:** Antioxidants, Quercetin, Cytotoxic, Methotrexate, Histopathology.