Methotrexate (MTX), a folate antagonist used for the treatment of cancer and inflammation, causes potential side effects like hepatotoxicity and in previous studies, it has been shown that oxidative damage is the causative reason for the MTX toxicity. Vitamin C (Vit C) is a well-known antioxidant and it has been used in various studies for this property. Thereby Vit C could be an alternative prophylactic agent against MTX-induced hepatotoxicity.

A total of thirty-six male Wistar rats weighting 200–250 gr were equally divided into the six groups as follows: Controls (saline i.p. for 5 days), MTX (20 mg/kg, i.p., single dose), Vit C (250 mg/kg Vit C, orally, 1 day), Vit C (250 mg/kg Vit C, orally, 3 days), MTX + Vit C group (250 mg/kg Vit C orally 1 hour prior to 20 mg/kg single dose MTX i.p.), MTX + Vit C group (250 mg/kg Vit C orally 1 hour prior to 20 mg/kg single dose MTX i.p. and continued for 2 days). At the end of the study, liver tissues were evaluated. Histopathological and the biochemical analysis for malondialdehyde (MDA), superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx) were performed.

In hepatic tissues, MDA levels were increased and SOD, CAT and GPx levels were decreased by MTX. All parameters but except CAT levels, were significantly restored after the administration of Vit C for three days (Table 1). Similar to the biochemical findings, by the use of MTX, the evidences of oxidative damage were seen in liver tissues by histopathologic examination (Fig 2). Compare to the control group (Fig 1), the findings of oxidative damage were not seen in any MTX plus Vit C treatment groups (Fig 3 & Fig 4). The use of MTX is often limited because of the drug-induced severe hepatotoxicity. Despite the exact mechanism of MTX-induced hepatotoxicity is not well-understood, recent studies have indicated the oxidative damage as the causative factor. This study was aim to find out whether Vit C, a potent antioxidant could restorate the MTX-induced oxidative damage in the rat liver. As a result of this study, Vit C at various doses can ameliorate the toxic effect of MTX on the rat liver tissues.