## عنوان مقاله:

Transferrin Receptor-dependent Iron Uptake Is Responsible for Cisplatin-induced renal toxicity: Role of Deferiprone

## محل انتشار:

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## خلاصه مقاله:

Cisplatin is one of the widely used antitumor agents with major clinical side effect, nephrotoxicity. The role of iron in free radical-dependent tissue injury has been shown in several studies, however, the exact underlying mechanism that link iron, ROS, and apoptosis are still not well known. In the present study, we examined the role of transferrin receptor as a gatekeeper for iron uptake and the effect of iron chelator deferiprone on the nephrotoxicity and anti-proliferative effect of cisplatin.Thirty male Wistar rats were used. They were randomly divided into six groups. Group I as a control group received physiological saline by gavage; animals in group II received a single intraperitoneally injection of cisplatin (7 mg/kg Maylan); a 10 days of deferiprone pretreatment in different concentrations (50, 100 and 200 mg/kg) was applied to the animals in groups III, IV, V and VI with a single IP injection of cisplatin in group III, IV and V on 5th day. At the end, blood and tissue sample were collected for biochemical and molecular analysis.Administration of iron chelator deferiprone in rats provided remarkable functional and significant histological-proven protection in group IV. Similarly, the decreased SOD and aconitase enzymes and increased MDA and TfR levels in the kidney of animals treated with cisplatin were significantly (P <0.05) improved with deferiprone pretreatment at 100 mg/kg. Exposure to deferiprone also dramatically inhibited cisplatin-induced apoptosis, as measured by caspase-3, Mcl-1 and survivin levels.In overall, the results obtained supported a critical role for iron in oxidative stress signaling of cisplatin-induced nephrotoxicity and transferrin receptor, a carrier protein for transferrin, may serve as an important source of iron. Based on these finding deferiprone pretreatment may play a role in preventing cisplatin-induced nephropathy in cancer patient in future.

## کلمات کلیدی:

Cisplatin, Nephrotoxicity, Iron, Deferiprone, Transferrin, HIF-1α