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Title: Immunohistochemical Tracing of Ferroptosis in Tamoxifen-related Testicular Toxicity in Mature Rats

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Use of tamoxifen (TMX) as a cornerstone in breast cancer therapy has become challenging regarding its adverse effects. The objective of this study was immunohistochemical (IHC) tracing of ferroptosis in TMX-related testicular toxicity in mature rats. Eighteen mature male *Wistar* rats were assigned into three equal groups including untreated control, sham (0.10 mL olive oil; orally (PO), daily for 10 days) and TMX₈₀₀ (800 $\mu\text{g k}^{-1}$ TMX; PO, daily for 10 days). All animals were euthanized after 35 days, and TfR1 and 4-HNE levels in testicular tissue were analyzed through IHC analyses. Oral administration of TMX resulted in a marked increase in TfR1 and 4-HNE levels in seminiferous tubules of mature rats' testicular tissue compared to the control and sham groups. As a result, the findings of this study provide IHC evidence for the role of ferroptosis in the TMX-evoked reproductive toxicity in a male rat model.

Keywords: Ferroptosis, Immunohistochemistry, Rat, Tamoxifen, Testis