Hepatotoxicity In the Context of Mitochondrial Dysfunction Is Associated with Triptolide

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ABSTRACT

Background: *Tripterygium wilfordii* Hook f., a traditional Chinese medicine, is available in China as *Tripterygium wilfordii* glycoside tablets. Triptolide, an active constituent of *Tripterygium wilfordii* Hook f., has multiple therapeutic effects along with various organ toxicities i.e. immunotoxicity, cardiotoxicity, nephrotoxicity and hepatotoxicity.

Objective: We tried to find out the mitochondrial injury caused by triptolide induced hepatotoxicity.

Methods: HepG2 cells and wistar rats were used for *in vitro* and *in vivo* studies respectively.

Results: Working on its hepatotoxicity, we observed that it has decreased the cell viability, ATP production, mitochondrial membrane potential and caused mitochondrial fragmentation in HepG2 cell line. This mitochondrial fragmentation is associated with an imbalance in mitochondrial dynamics i.e. an increase in mitochondrial fission and a decrease in mitochondrial fusion. Triptolide increased the mRNA expression of Drp1 fission protein and decreased the mRNA expression of Mfn1 fusion protein. mRNA levels of other mitochondrial fusion proteins, Mfn2 and Opa1, were not changed. PCR results also showed that mitochondrial fission protein Fis1 level was also not changed. For *in vivo* studies wistar rats were used. H&E staining showed the hepatotoxicity in triptolide treated group. Transmission electron micrographs indicated that triptolide distorted the cristae structure in rat liver tissues. This distortion of cristae structure is associated with an increase in Drp1 mRNA level as observed in PCR results.

Conclusion: Taken together, these results depicted that triptolide-induced hepatotoxicity is associated with disruption in mitochondrial dynamics.