Paracetamol: overdose-induced oxidative stress toxicity, metabolism, and protective effects of various compounds *in vivo and in vitro*

Xu Wang, Qinghua Wu, Aimei Liu, Arturo Anadón, José-Luis Rodríguez Department of Toxicology and Pharmacology, Faculty of Veterinary Medicine, Universidad Complutense de Madrid, Madrid, Spain;
View further author information
, María-Rosa Martínez-Larrañaga, show all
Pages 395-437 | Received 24 Mar 2017, Accepted 05 Jul 2017, Accepted author version posted online: 02 Aug 2017, Published online: 16 Aug 2017

Paracetamol (APAP) is one of the most widely used and popular over-the-counter analgesic and antipyretic drugs in the world when used at therapeutic doses. APAP overdose can cause severe liver injury, liver necrosis and kidney damage in human beings and animals. Many studies indicate that oxidative stress is involved in the various toxicities associated with APAP, and various antioxidants were evaluated to investigate their protective roles against APAP-induced liver and kidney toxicities. To date, almost no review has addressed the APAP toxicity in relation to oxidative stress. This review updates the research conducted over the past decades into the production of reactive oxygen species (ROS), reactive nitrogen species (RNS), and oxidative stress as a result of APAP treatments, and ultimately their correlation with the toxicity and metabolism of APAP. The metabolism of APAP involves various CYP450 enzymes, through which oxidative stress might occur, and such metabolic factors are reviewed within. The therapeutics of a variety of compounds against APAP-induced organ damage based on their anti-oxidative effects is also discussed, in order to further understand the role of oxidative stress in APAP-induced toxicity. This review will throw new light on the critical roles of oxidative stress in APAP-induced toxicity, as well as on the contradictions and blind spots that still exist in the understanding of APAP toxicity, the cellular effects in terms of organ injury and cell signaling pathways, and finally strategies to help remedy such against oxidative damage.