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# Quantum chemical computations provide insight into liver toxicity

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Balasubramanian and Basak have recently reported quantum chemical computations that enhance our understanding of mechanisms for the causes of liver toxicity.

Hepatocellular carcinoma is one of the most common forms of cancer, and the primary cause has been attributed to liver fibrosis by chemical toxins, which is followed by liver cirrhosis. By employing high-level quantum chemical computations, the researchers have unraveled the underlying mechanism of hepatocellular toxicity as metabolic electron attachment to certain environmental toxins.

Fifty-five halocarbons were tested in silico using high-level quantum computations. They have established that the primary step of toxic action is electron attachment to halocarbons in metabolic pathways by binding to an electron donating enzyme in hepatocytes. It was shown that the transferred electron from the hepatocyte enzyme CYP2E1 to the halocarbon causes bond elongation resulting in auto-detachment as evidenced from potential energy surfaces. This leads to the C-X bond dissociation causing the production of highly reactive free radicals which extract a proton from the liver's lipid membrane in order to reach a more stable state. Consequently, prolonged exposure causes damage to the liver membrane resulting in liver toxicity.

As shown by experimental studies, this could lead to hepatocellular carcinoma depending on the hydrogen extraction propensity of the free radical and vertical electron affinity of the neutral halocarbon. By

systematic computational studies on 55 hydrocarbons Balasubramanian and Basak have ranked the toxicity of halocarbons on the basis of the electron affinity and proton-extraction propensity from the lipid membrane of the liver. Experimental studies on CCl4 induced liver cirrhosis by Fuji et al. have provided further confirmation to computational studies on CCl4. The halocarbon alters the permeability of the plasma membranes, lysosome, and mitochondria.

Consequently, quantum chemical computations provide clear and compelling evidence for the cause of hepatotoxicity of halocarbons.

**More information:** Krishnan Balasubramanian et al, Metabolic Electron Attachment as a Primary Mechanism For Toxicity Potentials of Halocarbons, *Current Computer Aided-Drug Design* (2016). DOI: 10.2174/1573409912666160120151627

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