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Toxicity of carbon tetrachloride, free radicals and role of antioxidants

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Abstract

Several chemicals, including environmental toxicants and clinically useful drugs, cause severe cellular damage to different organs of our body through metabolic activation to highly reactive substances such as free radicals. Carbon tetrachloride is an organic compound of which chemical formula is CCl_4 . CCl_4 is strong toxic in the kidney, testicle, brain, heart, lung, other tissues, and particularly in the liver. CCl_4 is a powerful hepatotoxic, nephrotoxic and prooxidant agent which is widely used to induce hepatotoxicity in experimental animals and to create hepatocellular carcinoma, hepatic fibrosis/cirrhosis and liver injury, chemical hepatitis model, renal failure model, and nephrotoxicity model in recent years. **The damage-causing mechanism of CCl_4 in tissues can be explained as oxidative damage caused by lipid peroxidation which starts after the conversion of CCl_4 to free radicals of highly toxic trichloromethyl radicals ($\cdot\text{CCl}_3$) and trichloromethyl peroxy radical ($\cdot\text{CCl}_3\text{O}_2$) via cytochrome P450 enzyme. Complete disruption of lipids (i.e., peroxidation) is the hallmark of oxidative damage.** Free radicals are structures that contain one or more unpaired electrons in atomic or molecular orbitals. These toxic free radicals induce a chain reaction and lipid peroxidation in membrane-like structures rich in phospholipids, such as mitochondria and endoplasmic reticulum. **CCl_4 -induced lipid peroxidation is the cause of oxidative stress, mitochondrial stress, endoplasmic reticulum stress. Free radicals trigger many biological processes, such as apoptosis, necrosis, ferroptosis and autophagy.** Recent researches state that the way to reduce or eliminate these CCl_4 -induced negative effects is the antioxidants originated from natural sources. For normal physiological function, there must be a balance between free radicals and antioxidants. If this balance is in favor of free radicals, various pathological conditions occur. **Free radicals play a role in various pathological conditions including Pulmonary disease, ischemia / reperfusion rheumatological diseases, autoimmune disorders, cardiovascular diseases, cancer, kidney diseases, hypertension, eye diseases, neurological disorders, diabetes and aging.** Free radicals are antagonized by antioxidants and quenched. Antioxidants do not only remove free radicals, but they also have anti-inflammatory, anti-allergic, antithrombotic, antiviral, and anti-carcinogenic activities. Antioxidants contain high phenol compounds and antioxidants have relatively low side effects compared to synthetic drugs. The antioxidants investigated in CCl_4 toxicity are usually antioxidants from plants and are promising because of their rich resources and low side effects. Data were investigated using PubMed, EBSCO, Embase, Web of Science, DOAJ, Scopus and Google Scholar, Carbon tetrachloride, carbon tetrachloride-induced toxicity, oxidative stress, and free radical keywords. This study aims to enlighten the damage-causing mechanism created by free radicals which are produced by CCl_4 on tissues/cells and to discuss the role of antioxidants in the prevention of tissue/cell damage. In the future, Antioxidants can be used as a therapeutic strategy to strengthen effective treatment against substances with high toxicity such as CCl_4 and increase the antioxidant capacity of cells.