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Tert-Butyl hydroperoxide: An Overview

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Abbreviations: DNA, Deoxyribonucleic acid; GSH, glutathione; GSSG, glutathione disulfide; NADH, Nicotinamide adenine dinucleotide.

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Abstract

Cancers and aging may results from oxidative stress exposed to the cells. This hypothesis can be tested in laboratories by introducing oxidative stress into a biology model. It is convenient to induce oxidative stress by adding a chemical compound to introduce radicals in a biology model. Hydroperoxide can produce radicals and subsequently induce oxidative stress in a biology model. *Tert*-Butyl hydroperoxide is commonly used on this purpose. After metabolic activation, it produces several types of radicals and they damage different compartment of a cell. Lipid peroxidation is one of the toxicity that discussed here. Under the existence of metals, t*ert*-Butyl hydroperoxide can produce alkoxyl radical which initiate lipid peroxidation. Another type of radicals it produced is a methyl radical. A methyl radical attacks DNA and produces DNA damage.

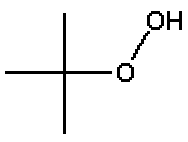
Introduction

Oxidative stress in mammal cells may contribute to cancer and aging [1-5]. The sources of oxidative stress can vary from leakage of electrons form mitochondria, nutrition deprivation, lipid, protein oxidation, environmental stress, chemical stress, photosensitization, mutation and radiation. Chemical stress can be introduced in a biology system by adding a stable hydroperoxide which produces radicals. Hydrogen peroxide and *tert*-Butyl hydroperoxide are commonly used in the research of free radicals in biology.

Tert-butyl hydroperoxide is a short-chain organic hydroperoxide. It contains a tertiary butyl group and a hydridodioxygen(•) group. After metabolic activation, it produces free radicals which can oxidize organelles nearby and lead to oxidative stress. This oxidative stress has been implicated in the etiology of cancer, aging and some diseases [1-5].

Physical properties

Tert-Butyl hydroperoxide is colorless liquid with pungent odor. Its density is 0.94 g/mL at 25°C. The prefix, "*tert*" refers to the tertiary organic structure; 3 methyl groups are bound to the carbon atom that has the hydridodioxygen ($HO_2^{\bullet}$) group on it. Its molecular formula is $(CH_3)_3COOH$, the chemical structure is depicted below and the molecular weight is 90.12 [6].



In industry, it is used as an oxidizing agent, a bleaching agent and an initiator of polymerization. It is a strong free radical source and decomposes rapidly, causing fire and explosion.

Reactions

A. alkoxyl radicals formation

Under the existence of metals, *tert*-Butyl hydroperoxide can be reduced to produce an alkoxyl radical, $(CH_3)_3CO^{\bullet}$

$$(CH_3)_3COOH + M^{n+} \rightarrow (CH_3)_3CO^{\bullet} + OH^- + M^{n+1} \quad \text{(reaction 1)}$$

This alkoxyl radical then initiates the classic lipid peroxidation [7] and produces alkyl radical, $L^{\bullet}$.

$$L\text{-}H + (CH_3)_3CO^{\bullet} \rightarrow L^{\bullet} + (CH_3)_3COH \quad \text{(reaction 2)}$$

The alkyl radical, $L^{\bullet}$ then reacts with oxygen and produce an alkylperoxyl radical. And an alkylperoxyl radical reacts with another LH and produce a new alkyl radical, $L^{\bullet}$.

$$L^{\bullet} + O_2 \rightarrow LOO^{\bullet} \quad \text{(reaction 3)}$$

$$LOO^{\bullet} + LH \rightarrow LOOH + L^{\bullet} \quad \text{(reaction 4)}$$

Under the existence of oxygen, reactions 3 and 4 will recycle, recruit new lipid molecules and propagate lipid peroxidation. In addition, LOOH can be reduced by metals and produce alkoxyl radical, $LO^{\bullet}$, which also propagates the lipid peroxidation.

$$LOOH + M^{n+} \rightarrow LO^{\bullet} + OH^{-} + M^{n+1} \quad \text{(reaction 5)}$$

$$LO^{\bullet} + LOOH \rightarrow LOH + LOO^{\bullet} \quad \text{(reaction 6)}$$

$$LO^{\bullet} + LH \rightarrow LOH + L^{\bullet} \quad \text{(reaction 7)}$$

$$LO^{\bullet} \rightarrow OL^{\bullet} \quad \text{(reaction 8)}$$

$$OL^{\bullet} + O_2 \rightarrow OLOO^{\bullet} \quad \text{(reaction 9)}$$

B. methyl radicals formation

In addition to the alkoxyl radical, $(CH_3)_3CO^{\bullet}$, methyl radical was identified as one of the radicals that produced by *tert*-Butyl hydroperoxide. It is proved by using the completely ^{13}C-labeled *tert*-Butyl hydroperoxide and EPR signal by Sonia[8]. Sonia also demonstrated that the methyl radical produced by *tert*-Butyl hydroperoxide attacks DNA and produces 8-methylguanine.

C. antioxidants degrade hydroperoxide

Tert-Butyl hydroperoxide can be degraded to alcohol by glutathione peroxidase system [9].

$$(CH_3)_3COOH + 2GSH \rightarrow (CH_3)_3COH + H_2O + GSSG \quad \text{(reaction 10)}$$

Biological effects

The toxicity of *tert*-Butyl hydroperoxide has been reported in lipid peroxidation [10], GSH depletion [9], DNA damage [11], NADH and elevating Ca^{2+}[12] and damaging mitochondria [13]. The above findings suggest that the toxicity that *tert*-Butyl hydroperoxide brings is very distinct and the radicals produced by *tert*-Butyl hydroperoxide may present in very distinct compartments of a cell.

Summary

Tert-Butyl hydroperoxide is used to study free radicals in biology. It produces several types of radicals after metabolic activation. These different radicals showed distinct toxicity in a cell.

Under the existence of metals, *tert*-Butyl hydroperoxide can be reduced to alkoxyl radicals. Alkoxyl radicals can initiate the lipid peroxidation and produce alkyl radicals. The alkyl radicals can react with oxygen and produce alkylperoxyl radicals. Alkylperoxyl radicals react with other LH and produce new alkyl radicals. This recycle process will propagate the lipid peroxidation.

Methyl radicals were another type of radicals that produced by *tert*-Butyl hydroperoxide. They attack DNA and produce DNA damage.

GSH can degrade *tert*-Butyl hydroperoxide into alcohol. It is reasonable that *tert*-Butyl hydroperoxide can consume GSH and decrease the steady state GSH/GSSG ratio.

Even though *tert*-Butyl hydroperoxide have been study for decades, the detail mechanisms about how it produces radicals or how it is metabolized remain unclear.

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