Why antioxidant therapies have failed in clinical trials

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Abstract

In spite of considerable research, and many clinical trials involving thousands of patients, there is a conspicuous lack of antioxidant therapies available. In this paper we present results for the interaction and neutralization of a free radical species. We adopt two modeling techniques, one based upon Gillespies Stochastic Simulation Algorithm and one based upon a discrete Markov chain. An advantage of these models is that they incorporate the number of molecules present per unit volume, and with the Markov chain model, the relative dimensions of these molecules. By means of these models we question the basis of antioxidant therapies based on trapping or scavenging of reactive species. We demonstrate the extraordinary capacity of the enzymatic antioxidant defenses relative to non-enzymatic defenses. We conclude that, if the concentration of an non-enzymatic antioxidant is too low there is little chance of collision and interaction with a free radical species. Furthermore, if the rate of reaction between the free radical and the non-enzymatic antioxidant is below a necessary threshold then the effect of an antioxidant will be dwarfed by the free radical defense systems naturally present. As such we suggest that failure of most antioxidant therapies in clinical trials is to be expected.

Keywords: Antioxidant, Free Radical, ROS, Gillespie, Markov Model

1. Introduction

The free radical theory of ageing, Harman (2016), put forward the hypothesis that free radicals, usually reactive oxygen species generated as a by product of respiration are a causal factor in the process of ageing. This is based on the supposition that free radicals are highly reactive and are a cause of continual and cumulative damage to cellular protein, lipid, and DNA (the soma). This damage, unless repaired, will lead to a progressive