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Review

A review on antioxidants, prooxidants and related controversy: Natural and synthetic compounds, screening and analysis methodologies and future perspectives

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ABSTRACT

Many studies have been conducted with regard to free radicals, oxidative stress and antioxidant activity of food, giving antioxidants a prominent beneficial role, but, recently many authors have questioned their importance, whilst trying to understand the mechanisms behind oxidative stress. Many scientists defend that regardless of the quantity of ingested antioxidants, the absorption is very limited, and that in some cases prooxidants are beneficial to human health. The detection of antioxidant activity as well as specific antioxidant compounds can be carried out with a large number of different assays, all of them with advantages and disadvantages. The controversy around antioxidant *in vivo* benefits has become intense in the past few decades and the present review tries to shed some light on research on antioxidants (natural and synthetic) and prooxidants, showing the potential benefits and adverse effects of these opposing events, as well as their mechanisms of action and detection methodologies. It also identifies the limitations of antioxidants and provides a perspective on the likely future trends in this field.

Contents

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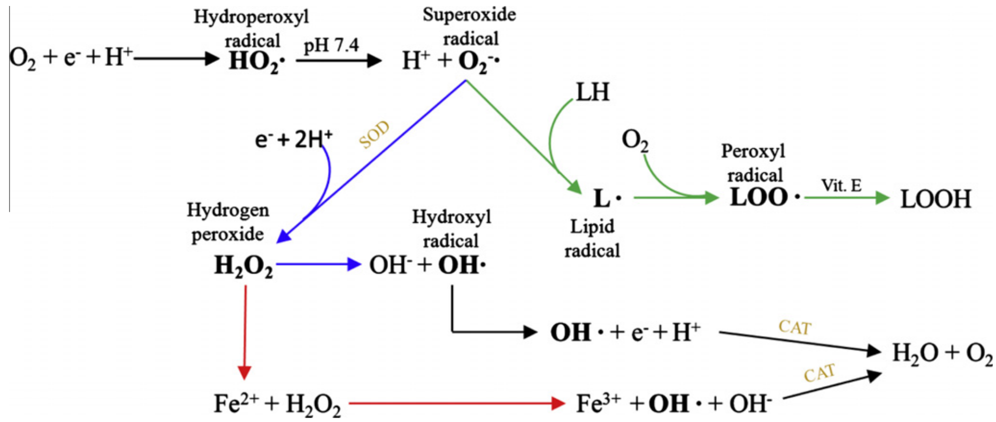

Fig. 1. Overview of the reactions leading to the formation of ROS. Green arrows represent lipid peroxidation. Blue arrows represent the Haber–Weiss reactions and the red arrows represent the Fenton reactions. The bold letters represent radicals or molecules with the same behavior (H_2O_2). SOD refers to the enzyme superoxide dismutase and CAT refers to the enzyme catalase. Adapted from Ferreira et al. (2009) and Flora (2009). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

1. Introduction

1.1. From free radicals to oxidative stress

Biochemical reactions that take place in the cells and organelles of our bodies are the driving force that sustains life. The laws of nature dictate that one goes from childhood, to adulthood and finally enters a frail condition that leads to death. Due to the low number of births and increasing life expectancy, in the near future, worldwide population will be composed in a considerable number of elderly. This stage in life is characterized by many cardiovascular, brain and immune system diseases that will translate into high social costs (Rahman, 2007). It is therefore important to control the proliferation of these chronic diseases in order to reduce the suffering of the elderly and to contain these social costs. Free radicals, antioxidants and co-factors are the three main areas that supposedly can contribute to the delay of the aging process (Rahman, 2007). The understanding of these events in the human body can help prevent or reduce the incidence of these and other diseases, thus contributing to a better quality of life.

1.1.1. Free radicals and oxidative stress mechanisms

Free radicals are atoms, molecules or ions with unpaired electrons that are highly unstable and active towards chemical reactions with other molecules. They derive from three elements: oxygen, nitrogen and sulfur, thus creating reactive oxygen species (ROS), reactive nitrogen species (RNS) and reactive sulfur species (RSS). ROS include free radicals like the superoxide anion ($O_2^{-\cdot}$), hydroperoxyl radical ($HO_2^{\cdot}$), hydroxyl radical ($^{\cdot}OH$), nitric oxide (NO), and other species like hydrogen peroxide (H_2O_2), singlet oxygen ($^1O_2$), hypochlorous acid (HOCl) and peroxynitrite ($ONOO^-$). RNS derive from NO by reacting with $O_2^{-\cdot}$, and forming $ONOO^-$. RSS are easily formed by the reaction of ROS with thiols (Lü et al., 2010). Regarding ROS, the reactions leading to the production of reactive species are displayed in Fig. 1. The hydroperoxyl radical ($HO_2^{\cdot}$) disassociates at pH 7 to form the superoxide anion ($O_2^{-\cdot}$). This anion is extremely reactive and can interact with a number of molecules to generate ROS either directly or through enzyme or metal-catalyzed processes. Superoxide ion can also be detoxified to hydrogen peroxide through a dismutation reaction with the enzyme superoxide dismutase (SOD) (through the Haber–Weiss

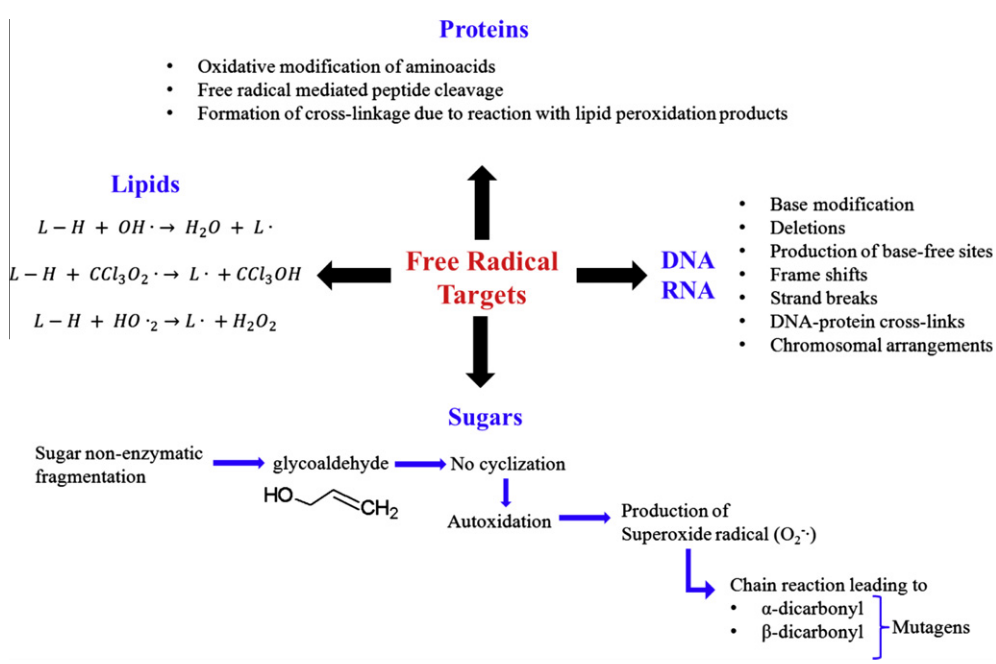

Fig. 2. Targets of free radicals. Adapted from Dizdaroglu et al. (2002), Valko et al. (2004), Benov and Beema (2003), Halliwell and Chirico (1993) and Lobo et al. (2010).