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# Free Radicals And The Scavenging Capacity Of Vitamin C (Ascorbic Acid)

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***Abstract***
*A significant contributor to human pathologies is cellular deterioration, particularly in cancer, where malignant cells exhibit elevated synthesis of compounds containing O—O single bonds. This deterioration is largely attributed to the excessive generation of free radicals during metabolic processes, frequently exacerbated by exposure to ionizing radiation. The resulting free radical overload induces a cascade of cellular damage, encompassing lipid peroxidation, DNA lesions potentially leading to genetic alterations, protein oxidation with consequent loss of enzyme activity, and ultimately, potential cell death. While organisms possess inherent antioxidant defense mechanisms, including glutathione, vitamin E, and ascorbic acid (AA), diminished antioxidant reserves increase susceptibility to oxidative damage and free radical-mediated cellular transformation. Dietary intake rich in antioxidants, found in foods such as legumes, vegetables, and fresh fruits, along with vitamin supplementation, can offer protection against free radical-induced damage. Ascorbic acid (vitamin C), a potent naturally occurring antioxidant, effectively neutralizes free radicals and mitigates oxidative processes.*
***Keywords***: *Free radicals; Scavenger; Ascorbic acid*

## 1. Free radicals

Free radicals are atomic, molecular, or ionic species characterized by one or more unpaired valence electrons or an open electronic shell, effectively representing intermediate entities with one or more "dangling" covalent bonds existing independently [1]. These unpaired electrons confer high reactivity, enabling them to readily interact with other substances, including themselves, and even initiate chain reactions due to their mobility and pronounced reactivity. Typically, molecules possess paired bonding electrons and lone electron pairs, also known as non-bonding or unshared electron pairs. Each bonding or non-bonding electron pair comprises two electrons with opposite spin orientations (+1/2 and -1/2) within an orbital, as dictated by the Pauli exclusion principle. The majority of molecules contain an even number of electrons, and the covalent chemical bonds holding atoms together within the molecule generally consist of electron pairs shared between the atoms through bonding. Most free radicals originate from the homolytic cleavage of conventional electron-pair bonds; each cleavage event generates two distinct species, each bearing a single, unpaired electron derived from the broken bond. The presence of these unpaired electrons renders free radicals highly reactive. They may combine with each other or with single atoms also possessing unpaired electrons to form conventional molecules where all electrons are paired; alternatively, they can react with intact molecules (e.g., within living organisms), abstracting molecular fragments to complete their own electron pairing and generating new free radicals in the process [2, 3].Free radicals play a crucial role in a variety of chemical processes, including radical addition, substitution, elimination, and chain reactions. In biological systems, free radicals are generated as a normal byproduct of cellular metabolism and other physiological processes. These reactive species can also be formed through synthesis involving highly dilute or rare reagents, reactions conducted at extremely low temperatures, or the cleavage of chemical bonds in larger molecules. The decomposition of molecules into free radicals can be induced when the parent molecule acquires sufficient energy, for instance, through thermal treatment, exposure to ionizing radiation, electrolysis, and certain chemical reactions [4]. Ionizing radiation encompasses both particulate radiation (neutrons and charged particles) and electromagnetic radiation (photons) originating from the decay of unstable atomic nuclei or the de-excitation of atoms and their nuclei within nuclear reactors, particle accelerators, and similar devices. Upon interaction with matter, these radiations transfer a portion or all of their energy, leading to the

ionization of the material and the subsequent formation of free radicals and ions. Notably, one of the most significant free radicals generated through this process, particularly when irradiating aqueous media, is the hydroxyl radical (OH•) [5].

In the context of biomedical applications, the Linear Energy Transfer (LET) describes the energy transferred from ionizing radiation to the traversed material [5].

$$LET = \frac{\Delta E}{\Delta x}$$

The energy transferred (ΔE) by an incident particle or photon per unit path length (Δx) defines the Linear Energy Transfer (LET). Measured in J/m or keV/μm, LET is directly related to the linear ionization density of the radiation. This implies that even with identical initial energies, different types of radiation will have distinct LET values owing to variations in their ionization efficiency. This is exemplified by the higher LET of alpha particles compared to beta particles and gamma photons. The LET also varies along the particle's track, with a higher LET observed at the track's end due to the reduced particle velocity and increased interaction cross-section, resulting in enhanced ionization [5].The mechanism of free radical formation and their subsequent impact are strongly dependent on the Linear Energy Transfer (LET) of the radiation [6]. High-LET radiation, exemplified by alpha particles and electron beams, tends to cause direct ionization and excitation of solute molecules, resulting in localized clusters of free radicals. In contrast, low-LET radiation, such as gamma and X-rays, predominantly interacts with water, initiating the radiolysis of water and producing diffusible free radicals, such as hydroxyl radicals (OH•) and hydrogen atoms (H•). These reactive species, both ions and free radicals, engage in a cascade of chemical reactions that can trigger physical, chemical, and biological damage. The effects of ionizing radiation on living systems can be categorized as direct or indirect [7]. Direct action involves the direct interaction of radiation with critical biomolecules like DNA, enzymes, lipids, and vitamins. Indirect action, mediated by the radiolysis of water, generates reactive oxygen species (ROS) and other free radicals that can diffuse and damage biomolecules, leading to disruptions in biological function, mutations, and ultimately, cell death or organismal demise. [8, 9].

**2. Free radical scavenging mechanisms of polyphenols**

Polyphenols are naturally occurring plant-derived compounds recognized for their potent antioxidant capacities. These compounds contribute to the protection of the organism against a range of diseases associated with free radical damage. Structurally, they are characterized by the presence of aromatic rings (benzene rings) bearing one or more hydroxyl (OH) groups directly attached to the ring. [10]. Variations in the number and relative positions of these hydroxyl groups within the molecular structure influence their physicochemical properties and biological activities [11, 12].

*2.1 The Mechanism of Hydrogen Atom Transfer (HAT)*

The antioxidant ArOH exerts its protective effect by scavenging free radicals (e.g., peroxyl ROO•) through a hydrogen atom transfer mechanism, where a hydrogen atom from the OH group of ArOH is donated to the ROO• radical [13].

$$ROO\bullet + ArOH \rightarrow ROOH + ArO\bullet \quad (2)$$

The phenoxyl radical (ArO•) formed in this process may undergo further reactions, such as hydrogen atom abstraction to form quinones or reactions with other radical species, including other phenoxyl radicals, propagating a chain reaction. The Hydrogen Atom Transfer (HAT) mechanism involves the cleavage of the O-H bond within the polyphenol structure. This reaction, occurring at each hydroxyl (OH) group of the polyphenol (ArOH), is governed by the bond dissociation enthalpy (BDE) of the O-H bond and the reaction enthalpy of reaction 2. The BDE value is a measure of the O-H bond's thermodynamic strength within the polyphenol [14]. A lower BDE signifies a greater propensity for O-H bond scission and subsequent hydrogen atom donation to the free radical, thus significantly influencing the antioxidant activity.

*2.2 The Single Electron Transfer-Proton Transfer (SET-PT) Mechanism*

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This mechanism involves two distinct steps. The first step comprises the transfer of a single electron from the polyphenol to the free radical, followed by a second step involving proton transfer [15].

$$ROO\bullet + ArOH \rightarrow ROO^- + ArOH^+\bullet \rightarrow ROOH + ArO\bullet \quad (3)$$

The SET-PT mechanism is governed by the electron transfer capacity, characterized by the Ionization Energy (IE). In the second step, heterolytic O-H bond cleavage occurs, characterized by the Proton Dissociation Enthalpy (PDE), which is highly exothermic for phenolic compounds [16, 17]. Furthermore, the solvent also influences the reaction enthalpy of the first step. Therefore, solvent effects should be considered to obtain an accurate representation of the polyphenol's oxidation characteristics [18].

*2.3 The Sequential Proton Loss Electron Transfer (SPLET) Mechanism*

The Sequential Proton Loss Electron Transfer (SPLET) mechanism involves an initial deprotonation step, followed by electron transfer [19-21]. This process is characterized by two thermodynamic quantities: Proton Affinity (PA) and Electron Transfer Enthalpy (ETE). The SPLET mechanism is pH-dependent.

$$\begin{aligned} ArOH &\rightarrow ArO^- + H^+ \\ ArO^- + ROO\bullet &\rightarrow RO_2^- + ArO\bullet \\ RO_2^- + H^+ &\rightarrow ROOH \end{aligned} \quad (4)$$

**3. The antioxidant activity of ascorbic acid**

Ascorbic acid (AA) exists in nature in three prevalent forms: ascorbic acid, its oxidized form dehydroascorbic acid, and the bound derivative ascorbigen [22]. Its aqueous nature allows it to function in both intracellular and extracellular environments, where it scavenges free radicals, reactive oxygen species, and singlet oxygen through electron donation, effectively suppressing lipid peroxidation [23]. Furthermore, AA protects DNA integrity against free radical-mediated damage and mutagen-induced lesions, thus preventing adverse genetic changes and protecting lymphocytes from chromosomal aberrations. AA also exhibits a regenerative effect on vitamin E, thereby indirectly bolstering antioxidant defenses. Synergistic interactions between AA and other antioxidants, such as vitamin E, vitamin A, and selenium, further amplify their combined antioxidant efficacy.The antioxidant capacity of ascorbic acid (AA) can be elucidated by its chemical structure. AA possesses four hydrogen bond donor sites and six hydrogen bond acceptor sites [24]. Functioning as a free radical scavenger, AA can inhibit free radical chain initiation reactions and disrupt free radical chain propagation reactions [24]. AA also protects biomolecules from free radicals, such as hydroxyl radicals (OH•), by donating an electron to these radicals for stabilization before they can reach and attack biomolecules. The OH• radical abstracts an electron or a hydrogen atom (H) from AA to form a more stable water molecule, and in this process, AA is converted into ascorbate radicals (•Asc-) (Figure 2). These newly formed ascorbate radicals exhibit weak reactivity, are innocuous to the surrounding environment, and are readily neutralized by other reactions [24].

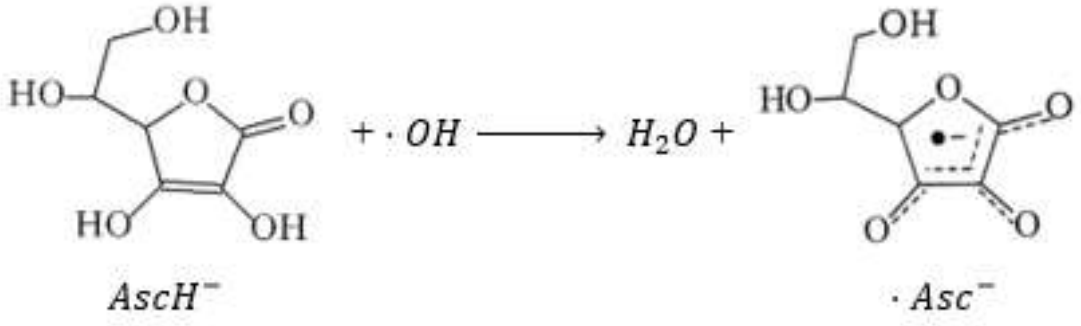


Fig1. The Reaction of AA with Hydroxyl Radicals

**4. CONCLUSIONS**

This study highlights the significant role of free radicals in mediating cellular damage and contributing to the pathogenesis of diseases, particularly cancer. Ascorbic acid (vitamin C), a potent naturally occurring antioxidant, demonstrates a clear capacity to neutralize free radicals and mitigate oxidative processes. These findings support the importance of adequate vitamin C intake through diet and/or supplementation as a crucial component of a comprehensive approach to combating oxidative stress and promoting overall health. Future investigations should focus on exploring the optimal dosage and delivery methods of ascorbic acid to maximize its therapeutic potential in preventing and treating free radical-related pathologies.

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