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Chemistry Related to Biology and Medicine

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ABSTRACT

Reviewing several facets of Fenton Chemistry's involvement in biology and medicine. There is growing indication that a number of Fenton and Fenton-like reactions can result in the formation of both the OH radical and ferryl $[Fe(IV)=O]^{2+}$. There are a few examples of hydroxyl radical generation that is unrelated to metals. The wood-decaying fungus that causes white rot and brown rot serve as examples of extracellular Fenton reactions. Numerous studies have been published in this area ever since Fenton chemistry and biomedicine were initially linked. Understanding and advancing this topic would be aided by a thorough exposition of the principles of Fenton chemistry and a synopsis of its representative applications in cancer therapy. The current state of Fenton chemistry is then examined, and a few pertinent illustrative instances are provided. Additionally, the current methods for further improving the efficacy of chemotherapy dynamic therapy under the direction of Fenton chemistry are highlighted. The combination of biomedicine and Fenton chemistry or a larger range of catalytic chemistry techniques is given with future possibilities being especially significant. Recently developed reactive oxygen species (ROS) engineered nano catalytic medicines in cancer therapy based on the Fenton reaction, defined as chemical dynamic therapy (CDT), have been extensively studied and made rapid progress. However, the complexity and heterogeneity of tumors reduce the Fenton reaction's ability to oxidize molecules effectively. To increase the effectiveness of CDT and conventional therapeutic approaches, numerous modified tactics, including the Fenton-like reaction and other reactions, are being investigated. This study highlights current developments in the development and use of Fenton nanocatalysts that use the Fenton or modified Fenton reaction for CDT. Also highlighted is the catechol-driven Fenton reaction's natural and useful use.

Keywords: Reactive O_2 Species; Redox Cycling; Oxidative Stress; Free Radicals; Carcinogenesis; Fenton Reaction and Chemo Dynamic Therapy

INTRODUCTION

All aerobic cells produce free radicals and other reactive O_2 and N_2 species, which remain recognized to take part in an extensive range of biological and metabolic processes. In addition to free radicals like superoxide radical anion ($O^{\bullet-}$), carbon-dioxide radical anion ($CO_3^{\bullet-}$), hydroperoxyl radical ($HOO^{\bullet}$), hydroxyl radical ($HO^{\bullet}$), peroxyl radical ($ROO^{\bullet}$), and alkoxyl radical ($RO^{\bullet}$), the ROS designation also includes non-radicals like hydrogen peroxide (H_2O_2), singlet oxygen ($^1O_2$), hypochlorous acid (HOCl), and ozone (O_3). Since H_2O_2 is a significant ROS in living organism, maintaining the aforementioned equilibrium can take a variety of physiological and pathological effects. Additionally, H_2O_2 can undergo a Fenton or Fenton-like reaction to yield reactive $HO^{\bullet}$ radicals or the intermediary $[Fe(IV)=O]^{2+}$ (Carter et al., 2022).

H_2O_2, and other ROS oxidants have been linked to elderly, as well as serious human illnesses like cancer, heart disease, Alzheimer's, and other associated neurological diseases. Alternatively, new data suggest that H_2O_2 has a physiological function in cellular signal transduction as a second messenger. The production of ROS may result from exposure to several noxious hazard elements, including more or less xenobiotics, infectious agents, contaminants, Ultra violet light, cigarette smoke, and radiation (Halliwell and Gutteridge, 2015). On the other hand, ROS are constantly produced in minor amounts during usual cellular practices, along with RNS like nitrogen monoxide ($^{\bullet}NO$) and nitrogen dioxide ($^{\bullet}NO_2$), as well as non-radicals like peroxynitrite anion ($ONOO^-$), peroxy-nitrous acid (ONOOH), nitrosoperoxycarbonate anion ($ONOOCOO^-$), nitronium cation ($^+NO_2$), and dinitrogen trioxide (N_2O_3) Endogenously generated ROS and RNS play a vital role in a multiplicity of biological processes, making them vital to life. The significant role Fenton chemistry plays in physiological and pathological processes in living organisms is a highly important fact. The first chemical mechanisms used by Nature to generate ROS are likely the Fenton and Fenton-like reactions. This method results in the making of the most sensitive species, such as hydroxyl radicals (Daniel et al., 2006; Yeung et al., 2019; Valko et al., 2006).

PROGRESS OF FENTON CHEMISTRY

Knowledge of key factors affecting Fenton/efficiency is about the Fenton-like reaction has received a great deal of attention from researchers Optimize the Fenton chemistry. In this section, for the systematic development of Fenton chemistry, Details including morphological adjustments and facets Synthesis of Fenton/Fenton-like catalysts, monatomic Fenton/ Construction of Fenton-like catalysts, double reaction centers Fenton/Fenton-like catalysts that use electrons to improve Fenton/Fenton-like efficiency, in situ generation of H_2O_2 Fenton/Fenton-like reaction and during introduction a physical field for support (Tang et al, 2021).

THE BASIC INFFORMATION ABOUT FENTON CHEMISTRY

H. J. H. Fenton demonstrated that the arrangement $Fe(II)\text{-}H_2O_2$ displays severe oxidation effects to various organic acids in his seminal study titled "Oxidation of tartaric acid in presence of iron" more than 110 years past (Prousek, 2007). Later, it turns out that this mixture, recognized as the Fenton reagent, is a commanding oxidizer for a range of organic substrates (Koppenol, 2022). The presence of the hydroxyl radical ($HO^{\bullet}$) in the Fenton reaction has been hypothesized forty years later. The coordinated ferrous ion (LFe^{2+}), which is oxidized by H_2O_2 to produce LFe^{3+}, $HO^{\bullet}$ radical, and HO^- ions (Fenton reaction, Ia reaction), or an oxoiron (2+)

complex, is now preferred as an inner-sphere electron-transfer mechanism (Ib reaction) (Deguillaume et al, 2005).

$$H_2O_2 + LFe^{2+} \longrightarrow LFe^{3+} + HO^{\bullet} + OH^- \quad \text{(Ia)}$$

$$LFe{=}O^{2+} + H_2O \quad \text{(Ib)}$$

It is believed that during the anaerobic stage of life on Earth, iron became firmly entrenched as a bio-essential element. Enzymes involved in electron-transfer reactions primarily include it. Additionally, iron has harmful effects. The breathing thing takings excessive care to store iron in secure complicated arrangements as a result. Similar to other transition metals, the Fenton reaction may be the cause of iron toxicity. The availability of a functioning metal redox-cycling mechanism is a crucial component for Fenton chemistry action in Nature because quantity of iron in biological systems is frequently relatively low (Gozzo, 2001). In biological systems, the superoxide radical anion ($O^{\bullet -}$) serves as a reducing agent. A crucial metabolic process that leads to numerous biological responses is the reduction of $Fe(II)$ to Fe (II). As the result, the superoxide-driven Fenton reaction is a crucial biological event (Pryshchepa et al., 2022).

$$LF^{3+} + O^{\bullet -} \longrightarrow LFe^{2+} + O_2 \quad \text{(II)}$$

$$H_2O_2 + LFe^{2+} \longrightarrow LFe^{3+} + HO^{\bullet} + OH^- \quad \text{(Ia)}$$

Now, the iron is coordinated with the accessible biological ligand by LFe^{3+} or LFe^{2+} (Gutteridge and Bannister, 1986). Coordinated $Fe(III)$ is condensed by superoxide to $Fe(II)$ in the initial step, that is required for subsequent Fenton reaction. Iron reactivity in the Fenton reaction and, consequently, ultimate oxidative harm to biological systems, are governed by iron coordination (Bloot et al., 2021). The hydroxyl radical, also known as ferryl, is the reactive byproduct of the Fenton reaction, as was already mentioned. Therefore, the chemistry of these responsive intermediates is primary focus of Fenton chemistry. Ferrell or hydroxyl radicals' significant reactivity is effectively demonstrated interactions with biological substrates in their atmosphere. According to the ($HO^{\bullet}$) radical's responses can remain divided into the following categories (Engelmann et al., 2003):

i) Reactions happening with perception of H_2.

$$R\text{-}H + HO^{\bullet} \longrightarrow HO^- + ArH^{\bullet +} \quad \text{(III)}$$

ii) addition reactions

$$ArH + HO^{\bullet} \longrightarrow HO\text{-}ArH^{\bullet} \quad \text{(IVa)}$$

$$R_2C{=}{=}{=}CR_2 + HO^{\bullet} \longrightarrow HO\text{-}C(R)_2\text{-}C(R^{\bullet})_2 \quad \text{(IVb)}$$

iii) oxidation reactions

$$ArH + HO^{\bullet} \longrightarrow HO^- + ArH^{\bullet +} \quad \text{(Va)}$$

$$M^{n+} + HO^{\bullet} \longrightarrow HO^- + M^{(n+1)+} \quad \text{(Vb)}$$

Both inorganic and organic chemicals have been used to study the ferryl ion reactivity (Engelmann et al, 2003; Loegager et al., 1992). The actions of the hydroxyl radical, or H-abstraction, are extremely similar to the

reactions of organic molecules in terms of their reaction processes. What is ferryl's nature and function within the biological system? The unswerving $HO^{\bullet}$ radical production from H_2O_2+Fe_2^{+} appears to be the utmost widely recognized arrangements, particularly at low pH, in spite of the lengthy history of the ferryl ion intermediary being projected in the Fenton reaction. Even so, the ferrell charged atom intermediate is frequently planned in procedure of Fe_2^{+} multiplexes with H_2O_2 , in the response of H_2O_2 within the existence of biological substrates, and in porphyrin complexes (Cui et al., 2022; Dong et al., 2020; Barbusiński, 2009; Prousek, 2007; Yin et al., 2018). The two-e^{-} oxidized heme (compound I), which is typically a ferrous - porphyrin radical cation $[Por^{\bullet+}\ Fe(IV)=O]$, is produced by peroxidases and catalases when they counter with H_2O_2 ($\sim 10^7 M^{-1}\ s^{-1}$) and is then reduced by the substrate to form the peroxidase compound II, $Pro\ Fe(IV)=O$. Horseradish peroxidase (HRP) was used to identify the porphyrin iron hydrogen peroxide, also known as $Pro\ Fe(III)\text{-}OOH$ or compound O (Yin et al., 2018; Chen et al., 2022). For instance, myoglobin (Mb) incubation with H_2O_2 results in the slow $\sim 10^2\ M^{-1}\ s^{-1}$ conversion of the Fe^{3+} heme to a ferryl heme [$Pro\ Fe(IV)=O$], which is comparable to compound II in HRP. Contrarily, peroxidases and catalases easily form compound I from H_2O_2 ($\sim 10^7\ M^{-1}\ s^{-1}$) (Yin et al., 2018).

The main oxidizing intermediates in enzymatic processes are compound I species. H_2O_2's second oxidizing equivalent, $[Por^{\bullet+}\ Fe(IV)=O]$, is connected to the porphyrin cation radical. The hydrogen abstraction/oxygen reflection apparatus has been put forth for cytochrome P450 substrate oxidation (Chen et al., 2022).

$$Fe{=}O + H\text{-}C \longrightarrow \{Fe...O...H...C\} \longrightarrow Fe + HO\text{-}C \qquad (VI)$$

There has been using of the modified Fenton system (Fe^{2+}-H_2O_2-CH_3CN). The procedures of H_2O_2 reactions with catalases and peroxidases appears to be more widely accepted than that of reactions with ferrous and ferric salts. In the initial stage, both enzymes produce compound I. (VII reaction) (Chen et al., 2022).

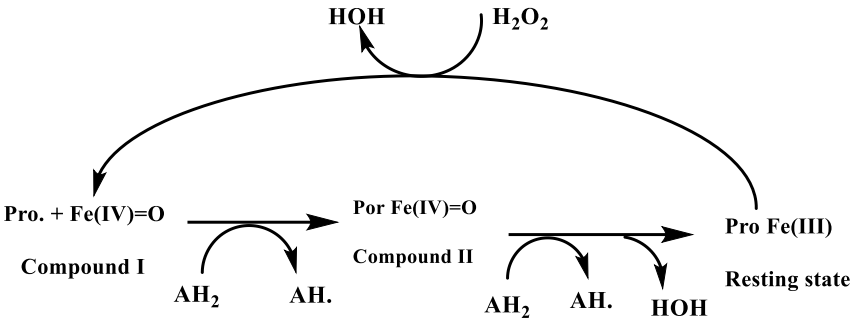
$$Peroxidase/Catalase + H_2O_2 \longrightarrow Compound\ I + H_2O \qquad (VII)$$

Catalases undergo a further reaction with H_2O_2 after forming chemicals.

$$Compound\ I + H_2O_2 \longrightarrow Catalase + O_2 + H_2O \qquad (XIII)$$

The water association in the peroxidase active site was used to explain this reactivity discrepancy. Water prevents H_2O_2 from gaining access. Compound II and the porphyrin radical cation are where compound I is reduced by organic substrates for peroxidases. In contrast to catalases, which rapidly release water from the active site, water is kept in the active site to allow H_2O_2 to prolix into the active site in the heme pocket (Jones, 2001).

For instance, HRP, a plant peroxidase with heme as a prosthetic group, uses H_2O_2 to catalyze the oxidation of a range of substrates. It has been determined that the process shown in Scheme 1 where chemicals 1 and 2 stand in for the ferryl intermediates and AH_2, the HRP substrate is how enzymatic reactions in an aqueous buffer often develop (Neelwarne and Rudrappa, 2013).



Scheme 1. Composite I is returned to its ferric latent state also through two successive one-electron transfer procedures from the peroxidase substrate or through two-electron oxidation events linked to the transfer of oxygen to the substrate (for example, R-S-R R-SO-R). As a two-oxidation corresponding overhead the inactive ferrous state, compound I participates in the catalytic turnover of HRP with H_2O_2 (Dunford, 2002). Biology places a high value on the involvement of ferryl intermediates in enzymatic Fenton-like reactions (Carter et al., 2022; Halliwell and Gutteridge, 2015), and the procedure of the response between heme-containing peroxidase and catalase enzymes with H_2O_2 is thus fully understood (Dunford, 2002).

MORPHOLOGY AND FACET REGULATION FENTON/FENTON-LIKE CATALYSTS

High physical and chemical properties of materials Based on morphology and facets for different Surface atom arrangement and coordination greatly affects Fenton/Fenton-like efficiency reaction. This section presents our current progress Fenton/Fenton-like morphology and facet regulation Catalysts and their mechanisms are discussed in detail (Tang et al, 2021).

The structure of a material determines its properties. The same atoms on different exposed facets have different chemical substances .A property that greatly affects catalytic activity (Jung et al, 2009; Hollingsworth, 2022). For example, Zhang's group Hematite Fenton catalyst system containing H_2O_2 and ascorbateion, the exposed face shows comparatively higher activity due to different amounts of iron cations contained in facet and facets (Xing et al, 2018). These are triple under adjusted (Fe_{3uc}) and 5-fold under coordinated (Fe_{5uc}), respectively. Fe_{5uc} sites show more steric hindrance Effect of reaction of H_2O_2 and acerbate on surfaces. The Fe3uc site has a higher affinity for ascorbate, Better catalysis of the face (Tang et al, 2021).

CLASSIFICATION AND PROPETIES OF FENTON REACTION IN CHEMO DYNAMIC THERAPY (CDT)

The unique properties of TME (H_2O_2 over expression and weak acidity) are able to induce the Fenton reaction in the presence of a Fenton catalyst. This specific Fenton reaction within tumor tissue only produces locally abundant toxic OH to induce pathological effects, resulting in tumor-specific therapeutic efficacy without significant side effects on normal tissues. Make it possible. The rapid development of the intratumoral Fenton reaction in cancer therapy is spurring the emergence of versatile therapeutic modalities (Meng et al., 2020).

FENTON TESPONSE IN CDT

The Fenton reaction and its cousins have been discovered for over 100 years, and this catalytic reaction has been extensively studied in versatile applications such as water purification. It is believed that OH produced by the Fenton reaction can convert organic pollutants into harmless substances (carbon dioxide, water, etc.) Cancer cells are usually composed mostly of organic matter, which triggers the Fenton reaction, which can destroy natural bio-molecules (DNA, proteins, lipids, etc.) and kill cancer cells. Fortunately, relatively high levels of H_2O_2 within tumor cells provide sufficient reactants for the Fenton reaction (Meng et al., 2020).

However, most Fe species in the human body are bound to some specific proteins. Few available free iron ions can be used to induce apoptosis or ferroptosis in the Fenton reaction (Liu et al, 2019). Therefore, various nanomedicine with ROS modulating properties have been designed for biomedical applications. Mainly, Fe-based Fenton nanocatalysts such as Fe_3O_4 and α-Fe_2O_3 can release iron ions. Iron ions can be tuned to convert endogenous H_2O_2 into highly toxic OH through the catalytic Fenton reaction, which fights cancer and interferes with cancer cells by reducing oxidative stress (Fan et al, 2019; Dixon and Stockwell, 2014). Inaddition, OH has a very short half-life (10-9 seconds), so that it damages only surrounding DNA, proteins, or lipids in situ and not distant areas (Zhao et al, 2019). Therefore, it is suitable to deliver Fe-based Fenton nanocatalysts to cancer cells to trigger intracellular Fenton reaction for cancer therapy with high therapeutic efficiency and low side effects (Meng et al, 2020).

BIOCHEMISTRY AND MEDICINE USING FENTON CHEMISTRY

Metal ions play numerous structural and functional roles in nature. Metal ions play a critical role as biological catalysts in electron-movement process as well as the activation and movement of small molecules like dioxygen. The assembly of the metallic, including the shapes of the multipart and the type of ligands connected to the metallic, and the situation of the metal composite are the two main determinants of the behavior of metal ions in biological structures (Halliwell and Gutteridge, 2015; Daniel et al., 2006; Yeung et al., 2019).

Iron is a crucial component of several proteins involved in the metabolism or transport of oxygen. Additionally, it needs to be stored, moved through the figure, and prepared available for the creation of iron proteins. Iron's capacity for redox cycling is a crucial component of how it works. Approximately 4.5 g of iron makes up a typical adult male human. Ferritin and hemosiderin are two important proteins that hold the iron in cells. It is primarily found in enzymes involved in electron transport in bacteria. For instance, Escherichia coli has about 10^6 ions of iron in per cell. The availability of numerous redox states is a second noteworthy characteristic of metallic ions with regard to their capacity to conduct biological oxidations. The oxidation states of iron that are physiologically significant are typically +2 and +3 (Dunford, 2002).

The availability to produce various ROS is linked to the process by which oxygen exhibits its toxicity, despite the fact that oxygen is necessary for living things. The one-electron reduction of molecular oxygen occurs step by step and is best described as below:

$$O_2 \longrightarrow O_2^{\bullet -} \longrightarrow H_2O_2 \longrightarrow HO^{\bullet} + H_2O \qquad (IX)$$

Water is end product of the lessening of oxygen. Few highly sensitive ROS, such as hydroxyl radicals, have the potential to harm a variety of biological target molecules, including DNA, proteins, and lipids. For these reactions, Fenton chemistry is crucial due to the bio-molecules it strongly reacts with.

The hydroxyl radical is arguably the ROS that can harm biological systems the most (Nordberg and Arnér, 2001; Pryor, 2006; Toyokuni, 2020).

REACTIVE N_2 AND O_2 SPECIES AND THEIR REACTIONS

All aerobic organisms produce and break down ROS and RNS, which result in oxidative stress, a pathogenic condition that impairs normal cellular activity. ROS are increasingly being shown to be used by cells in a variety of physiologically important ways, with intercellular waving and redox parameter. Since its discovery as a signaling molecule, nitric oxide (•NO) has gained widespread recognition as a controller of transcript cause activity and another factors that affect gene countenance. Similar intracellular effects are produced by H_2O_2, hypochlorous

acid ($HOCl$), and superoxide radical anion (Pryor, 2006). On the other hand, it has been demonstrated that ROS are linked to a wide range of adverse events, including radiation, inflammation, carcinogenesis, and reperfusion wound. The very rampant transition-metal ion in human bodies, iron, could function a catalyst to increase ROS production under pathological circumstances. Carcinogenesis is linked to iron excess. Additionally, a novel notion known as "genomic regions sensitive to the Fenton reaction" was developed as a result of the possibility that the Fenton reaction could result in oxidative harm at a certain region of the genome in vivo (Willson, 1977). The primary ROS created is superoxide radical anion, which function with some other molecules to produce secondary ROS, primarily by enzyme- or metal-catalyzed reactions, such as the hydroxyl radical (Fenton reaction). Through a process involving superoxide dismutase, superoxide is depleted (SOD).

$$2O_2^{\bullet -} + 2H^+ + SOD \longrightarrow H_2O_2 \longrightarrow O_2 \qquad (X)$$

SOD Enzymes four remits of extent faster this response within living arrangement. SOD Enzymes cooperate with H_2O_2 oxidizing enzymes like catalases and glutathione peroxidases in biological systems (Toyokuni, 2020). The majority of switching metals have complex redox and coordination chemistry that is intimately connected to production of numerous unrestricted radicals. Fenton chemistry is a key component of the main methods by which transition-metal ions activate oxygen. As a result, the redox form of the cell is kept strictly in physio-logical bounds. Superoxide releases Fe^{2+} ions from biological components that store iron when under stress. The Fenton reaction, which creates reactive hydroxyl radicals, can involve the released Fe^{2+} ions (Willson, 1977).

$$M^{n+} + H_2O_2 \longrightarrow M^{(n+1)+} + HO^{\bullet} + HO^- \qquad (XI)$$

$$M^{(n+1)+} + O_2^{\bullet -} \longrightarrow M^{n+} + O_2 \qquad (XII)$$

HYDROXYL (OH) FREE RADICALS AND METAL-UNBIASED PRODUCTION

A frequent species in cellular metabolism is $X^{\bullet -}$, a single-electron lessening intermediary of several radical anions. Superoxide radical anions (O^{o-}), semiquinone radical anions (Q^{o-}), and various one-electron reduced 2^{o-} xenobiotics , such as RNO_2 radical anions, are the major forms of these chemicals in connection to ROS generation (Carter et al., 2022; Halliwell and Gutteridge, 2015; Daniel et al., 2006; Yeung et al., 2019). Typically, the radical anion intermediate $A^{\bullet -}$ is generated when neutral molecule A receives one electron. In living systems, electron-transfer reactions are crucial metabolic processes. The electron adduct $A^{\bullet -}$ will initially form in a system containing the distinct solutes A, B, C, and D, each one of that reacts with e^-s at speeds close to dispersal control and which are exist in concentrations like $[A]>>[B]>>[C]>>[D]$. Nevertheless, following electron-transfer procedures could take place (Winterbourn, 1981):

$$A^{\bullet -} \longrightarrow B^{\bullet -} \longrightarrow C^{\bullet -} \longrightarrow D^{\bullet -} \qquad (XIII)$$

This illustration accurately depicts the actual condition in living biosystems. Stable radical anions can typically serve as an electron source for various biological electron-transfer processes. However, some of these radical anions quickly transform into free radicals and anions (e.g., halogenated xenobiotics). As a result, after undergoing a one-electron reduction, either quinone (Q) or oxygen (O_2) produce the fairly steady semi Quinone radical anion ($Q^{\bullet -}$) or superoxide radical anion ($Q^{\bullet -}$), correspondingly. On the other hand, when HCl_4 is reduced by one

electron, it produces $HCl_4^{\bullet -}$ radical anion, that instantly divide into the $\dot{C}Cl_3$ radical and Cl^- ion. Contingent on their like-mindedness for electrons, certain radical anions including $O^{\bullet -}$, semiquinone ($Q^{\bullet -}$), and $RNO^{\bullet -}$ can participate in the redox-cycling of transition metals or redox-decompose HOX molecules (HOOH, HOCl, HOONO, HOSCN, ROOH, etc.) by single-electron transferal to contribute to Fenton chemistry (XIV–XV reactions) (Saran et al., 1999).

$$O_2^{\bullet -} + HOX \longrightarrow O_2 + HO^{\bullet} + X^- \qquad (XIV)$$

$$Q^{\bullet -} + HOX \longrightarrow Q^{+} + HO^{\bullet} + X^- \qquad (XV)$$

$$RNO_2^{\bullet -} + HOX \longrightarrow RNO_2 + H\dot{O} + X^- \qquad (XVI)$$

Where X^- is an ion of HO, Cl, NO, or SCN. The examples provided make it abundantly evident that dissociative electron transfer frequently consequences in the creation of radical anions within biological systems. The generation of hydroxyl radicals is crucial from the perspective of Fenton chemistry. A very significant metal-independent source of the hydroxyl radical within phagocytosis, in addition to the Fenton-like reaction (17 reaction), is the interaction of superoxide with HOCl (XIII reaction) (Valko et al., 2006; Saran et al., 1999).

$$Fe^{2+} + HOCl \longrightarrow Fe^{3+} + HO^{\bullet} + Cl^- \qquad (XVII)$$

$$O_2^{\bullet -} + HOCl \longrightarrow O_2 + HO^{\bullet} + Cl^- \qquad (XVIII)$$

A significant amount of $HO^{\bullet}$ radicals will be produced by reaction 27 ($k_{27}=10^7\ M^{-1}\ S^{-1}$), which is crucial for the formation of ROS during phagocytosis. Since Adriamycin exhibits this behavior, its reduction by xanthine oxidase in the presence of nitrogen offers a practical technique to continuously produce semi Quinone ($Q^{\bullet}$). Additionally, hydroxyl radicals were produced when Adriamycin was combined with xanthine oxidase and xanthine under N_2 in the presence of H_2O_2 (Williamson and Davison, 2020).

$$Q^{\bullet -} + H_2O_2 \longrightarrow Q + HO^{\bullet} + HO^- \qquad (XIX)$$

This reaction doesn't require $O^{\bullet -}$ or a metal catalyst. The properties of this reaction suggest that it might play a significant role in the way that Adriamycin exerts its anticancer effects (Williamson and Davison, 2020). Adriamycin semi Quinone and H_2O_2 appear to react quickly, with the primary result being the hydroxyl radical. Ubiquinol, or reduced coenzyme Q, exhibits a similar pattern of behavior (Zhu et al., 2002). In the investigation of lipid peroxidation, the ubisemiquinone intermediary was discovered as a first reaction byproduct of ubiquinol. Hydroxyl radicals were produced as a result of semiquinone and H_2O_2 simultaneously forming (S reaction). It was discovered that ubisemiquinone interacts with together cumol (CumOOH) and lipid (LOOH) hydroperoxides in addition to inorganic peroxides like H_2O_2. Alkoxyl radicals, which are potent catalysts for lipid peroxidation, were reaction products of the reductive homolytic cleavage (Koppenol, 2022).

$$CumOOH/LOOH + Q^{\bullet -} \longrightarrow CumO / LO^{\bullet} + Q + HO^- \qquad (XX)$$

Semi Quinones ($Q^{\cdot-}$) have been discovered to interact with several substances existing during oxidative strain (O_2, H_2O_2, LOOH, HOX), showing that $Q^{\cdot-}$ may start a range of prooxidative processes. The second example illustrates the metal-independent hydroxyl radical generation from H_2O_2 and tetrachloro-1, 4-benzoquinone (TCBQ), a cancer-causing byproduct of the commonly used wood preservative penta-chlorophenol (Koppenol, 2022). This work employed electron spin resonance (ESR) trapping. It's interesting to note that 2, 5-Dichloro and 2-Chloro-1, 4-Benzoquinone were more effective at generating hydroxyl radicals than TCBQ . In contrast, H_2O_2 1, 4-benzoquinone, a non-halogenated Quinone, and the methyl-substituted Quinones 2,6-dimethyl and tetra-methyl-1, 4-benzoquinone did not produce any hydroxyl radicals (Haugland et al., 1990). The result that hydroxyl radical is formed by TCBQ and H_2O_2 from side to side a metal-independent process is well supported by a comparison investigation using ferrous ions and H_2O_2, the traditional Fenton system. The fact that the addition of H_2O_2, which was accompanied by the production of hydroxyl radicals, significantly reduced the $TCSQ^{\cdot-}$ ESR signal is another crucial indicator of such a process. These findings imply that H_2O_2 is directly reacted with by the $TCSQ^{\cdot-}$ semi Quinone radical anion, reducing it to a hydroxyl radical. It has already been suggested that a metal-independent Fenton reaction can theoretically occur when a Quinone/semi Quinone pair has a lessening potential of between -330 and +460 (Metosh-Dickey et al., 1998). These processes can be carried out thermodynamically and not needing metal ions for catalysis. The Quinone/semi Quinone pair for 2-chloro, 2,5-dichloro, and TCBQ , where the lessening capacities are, respectively, -100, +60, and +250 mV, may very well be examples of this. Contrarily, the 2, 6-dimethyl- and tetramethyl-1, 4-benzoquinone reduction potentials of -430 and -600 mV, correspondingly, is outside of this range, and hydroxyl radical production hasn't been noticed either (Williamson or Davison, 2020). It has fascinating biological ramifications because chlorinated quinines could react with H_2O_2 to form hydroxyl radicals in a metal-independent manner. For instance, many commonly used chlorinated aromatic compounds, including the well-known priority environmental pollutants 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) and 2,4-dichlorophenoxyacetic acid (2,4-D), can be metabolized in vivo to chlorinated Quinone's , that will have poisonous effects through the generation of hydroxyl radicals (Okado-Matsumoto and Fridovich, 2000).

Xenobiotic are broken down by a variety of enzymes and by a number of different mechanisms. Enzymes could make a xenobiotic radical anion through one-electron transfer, which can start a chain reaction that can produce further radicals that can damage cells. This is an instance of the enzyme glucose oxidase, which has the ability to catalyze the single-electron lessening of numerous kinds of xenobiotic, including 1, 4-naphthoquinone (1,4NQ) and 4-nitropyridine-N-oxide (4NPO), leading to the production of radical anion products (Okado-Matsumoto and Fridovich, 2000). The enzyme glucose oxidase couples oxygen reduction to glucose oxidation, producing H_2O_2 without any observable one-electron reduced intermediates (e.g., superoxide). Both $1,4NQ^{\cdot-}$ and $4NPO^{\cdot-}$ radical anions are identified by ESR when 4NPO and 1,4NQ where gestated collected at an equimolar concentration in the existence of glucose oxidase and glucose. The spectrum of the $4NPO^{\cdot-}$ is heavily dominated by the signal of $1,4NQ^{\cdot-}$. After being added, the ferric ion was converted to the ferrous ion and participated in the Fenton reaction, which produced a hydroxyl radical from H_2O_2. However, the likelihood of hydroxyl radical generation by the

interaction of $Q^{\bullet-}$ or $RNO^{\bullet-}$ radical anions with H_2O_2 cannot be firmly dismissed [Saran et al., 1999; Benov and Beema, 2003).

$$1,4NQ^{\bullet-} + H_2O_2 \longrightarrow 1,4NQ + HO^{\bullet} + HO^- \qquad (XXI)$$

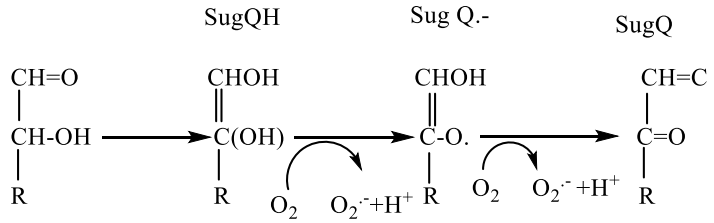
$$4NPO^{\bullet-} + H_2O_2 \longrightarrow 4NPO + HO^{\bullet} + HO^- \qquad (XXII)$$

Following is a description of how any appropriate radical anion $X^{\bullet-}$ participates in this kind of metal-free Fenton-like reaction (XXIII reaction).

$$X^{\bullet-} + H_2O_2 \longrightarrow X + HO^{\bullet} + HO^- \qquad (XXIII)$$

For a better knowledge of the mutagenic and carcinogenic characteristics of several significant pollutants for the environment, more research is required to describe the metal-independent hydroxyl radical generation.

Sometimes, a surprising issue with the carcinogenic potential of short-chain sugars is other illustration of how Fenton chemistry works in life. It is true that the short-chain reducing sugars can cause mutagenesis. The fundamental mechanisms of their activity involve the generation of ($HO^{\bullet}$) radicals by metal-independent or -dependent Fenton-like processes. When non enzymatic glycosylation first begins, short-chain sugars including glycol aldehyde, glyceraldehyde, and dihydroxyacetone are formed. Such molecules tau-isomerize to enediols because the cyclization process cannot block the carbonyl groups on their carbon atoms (SugQH). One way in which their air oxidation produces the superoxide is in the final generation of H_2O_2 (Benov and Beema, 2003; Jay et al., 2006). On the other hand, enediols produce a semi Quinone-like intermediate ($SugQ^{\bullet-}$) after transferring one electron to oxygen, and a,-dicarbonyl (SugQ) after transferring a second electron (2 Scheme).



Scheme 2

$$2O_2^{\bullet-} + 2H^+ \longrightarrow 2HOO^{\bullet} + H_2O_2 + O_2 \qquad (XXIV)$$

Superoxide, which yields oxygen, can cause the one-electron oxidation slowly, while H_2O_2, which yields superoxide, can cause it more quickly (XXIV reaction). DNA can sustain damage from short-chain carbohydrates. Their oxygen-dependent mutagenesis impact is prevented by SOD. This shows that $O^{\bullet-}$ is essential for the mutagenicity generated by short-chain sugars. There are now two techniques to produce hydroxyl radicals: I by metal-free hydroxyl radical synthesis (XXV reaction) (Jay et al., 2006).

$$SigQ^{\bullet-} + H_2O_2 \longrightarrow SugQ \longrightarrow HO^{\bullet} + HO^- \qquad (XXV)$$

Either I by superoxide, which releases $Fe(II)$ from the [$4Fe\text{-}4S$] clusters, or (ii) by the Fenton reaction. We do know that oxidative stress brought on by diabetes mellitus might speed up the development of atherosclerosis (Hammel et al., 2002).

CONCLUSION

Due to the comparable chemistry of the ($HO^{\cdot}$) radical and ferryl involvement in Fenton chemistry, differentiation between them is not as significant in biology. More significant, however, is our understanding of the role that Fenton chemistry plays in biological systems, particularly in pathological processes like carcinogenesis, neurological disorders, atherosclerosis, etc. Knowing the kind of Fenton reaction that takes place in the specific biological system is also crucial. As one of the emerging cancer treatment modalities, CDT is characterized by high therapeutic efficiency in inhibiting cancer growth and negligible side effects on healthy cells/tissues. Although CDT and CDT-based combination therapies represent an active research frontier, some of the above-mentioned unresolved issues should be exploited in the coming years. Through joint efforts of chemists, materials scientists and biologists, nanocatalytic medicine with specific tumor targeting and on-demand anti-tumor efficacy will soon reach clinical application. Finally, it may be argued that while the Fenton reaction has been crucial to biology for the duration that life has existed on Earth, its significance for diseases associated with contemporary civilization is relatively recent.

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