ScieniQ Publishers

Advance Medical and Clinical Research

Research Article

Prediction, validation, and learning for mitochondrial-damaged tumor cells

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Received: 10 January 2026
Accepted: 17 January 2026
Published: 09 Februay 2026

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Abstract
Through Molecular Modeling using software Spartan, we learned about cell engine. i.e., mitochondria. the following: (1) Chemical energy hydrated superoxide anion radical $[O_2^{-*}(H_2O)_2]$ is generated in mitochondrial endoplasmic reticulum lipid bilayer, (2) This chemical energy $[[O2-^*(H_2O)_2]]$ generates a capacitive current in the mitochondrial membrane. (3) Capacitive current between mitochondrial membranes generates microwave and radio frequency energy. (4) Microwave and radio frequency energy which are identical with infrared (IR) and far infrared (FIR) energy, i.e., thermal energy, which promotes thermal metabolic reactions in cells. (5) When the chemical energy $[O2^{-*}(H_2O)2]$is overproduced, and undergoes intra molecular disproportionation reaction, hydrated hydroxyl radical $[HO^*(H_2O)_2]$, the main cause of cell aging,(Cellular Theory) is generated in the bilayer mitochondrial membranes, causing major changes in the molecular membrane structure, leading to cellular enlargement. It is also verified that iodine therapy for cancer is due to the excellent antioxidant effect of iodide ion. Assumed the cause of cancer is cellular aging, cells with active mitochondrial reticulum activated by iodide ion are immune cells, and cells with enlarged, and degraded mitochondrial reticulum are tumor cells.

Keywords: **Circulating tumor cell,** Germ Theory vs. Cellular Theory mitochondrial reticulum, iodine therapy, superoxide anion radical, hydroxyl radical

Introduction
American physician Michael B. Schachter explains that iodine deficiency is the cause of all diseases and that Lugol consisting of iodine [I2] and potassium iodide [KI]I , plays a role in cancer prevention and treatment [1].We focused on the research report of Taro Shirakawa, a former professor at Kyoto University's School of Medicine who has reported on iodine therapy for cancer on social media.He has identified enlarged tumor cells in cancer patients as circulated tumor cells (CTRs) [2].We propose that the molecular and chemical phenomena occurring within cells related to cancer treatment can be explained by the involvement of both superoxide anion radicals $[O_2^{-*}]$ and hydroxyl radicals $[HO^*]$ generated in the mitochondrial endoplasmic reticulum, the cellular engine, and that the electron transfer process are governed by their electronic energy structure. We report that tumor cells are senescent cells whose cellular engine mitochondria, their membrane structure, has been destroyed by hydrated hydroxyl radicals. Furthermore, we report that hydrated iodide ions repair aged mitochondrial endoplasmic reticulum as an anti-aging medicine.

Method
Molecular modeling (DFT/MM/Spartan) based on density functional theory was performed using Spartan, a quantum chemistry calculation software developed by Wavefunctions Inc [3]. Density functional theory (DFT), which takes into account the electron density interactions of the frontier electron orbitals inherent in atoms and molecules, determines the stable equilibrium 3D structure (geometry) of hydrated molecular species and quantitatively examines and evaluates UV/Vis/IR/FIR spectra that reflect the energy structure of the 3D association.The 3D equilibrium structure of the association of hydrated superoxide anion radical$[O_2^{-*}(H2O)_2]$ generated from triplet oxygen and D-glucose in the mitochondrial endoplasmic reticulum, hydrated hydroxyl radical $[HO^*(H_2O)_2]$generated from $[O_2^{-*}(H_2O)_2]$, and the lipid bilayer membrane that constitutes the mitochondrial endoplasmic reticulum with $[HO^*(H_2O)_2]$ can be studied.

Results and discussion
Chemical energy in the cellular engine, mitochondria; generation of stabilized superoxide anion radical $[O_2^{-*}(H_2O)_2]$ and its extremely high electron energy potential
Using DFT/MM/Spartan, we verified the association equilibrium 3D conformation of hydrated triplet oxygen $[^3O_2(H_2O)_2]$ and hydrated D-glucose [D-glucose(H_2O)]: [D-glucose(H_2O)@$[^3O_2(H_2O)_2]$], which generates the superoxide anion radical $[O2^{-*}(H_2O)_2]$ by intramolecular electron transfer (Figure 1). The formation of $[[O_2^{-*}(H_2O)_2]$ has a large heat of formation of -55.7 kcal/mol, indicating that $[O_2^{-*}(H_2O)_2]$ is stable (Figure 1). We were surprised to learn that the electron potential of the highest occupied molecular orbital (HOMO) of the hydrated superoxide anion radical $[O_2^{-*}(H_2O)_2]$molecular-modeled by DFT/MM/Spartan is extremely high at +0.97 eV.

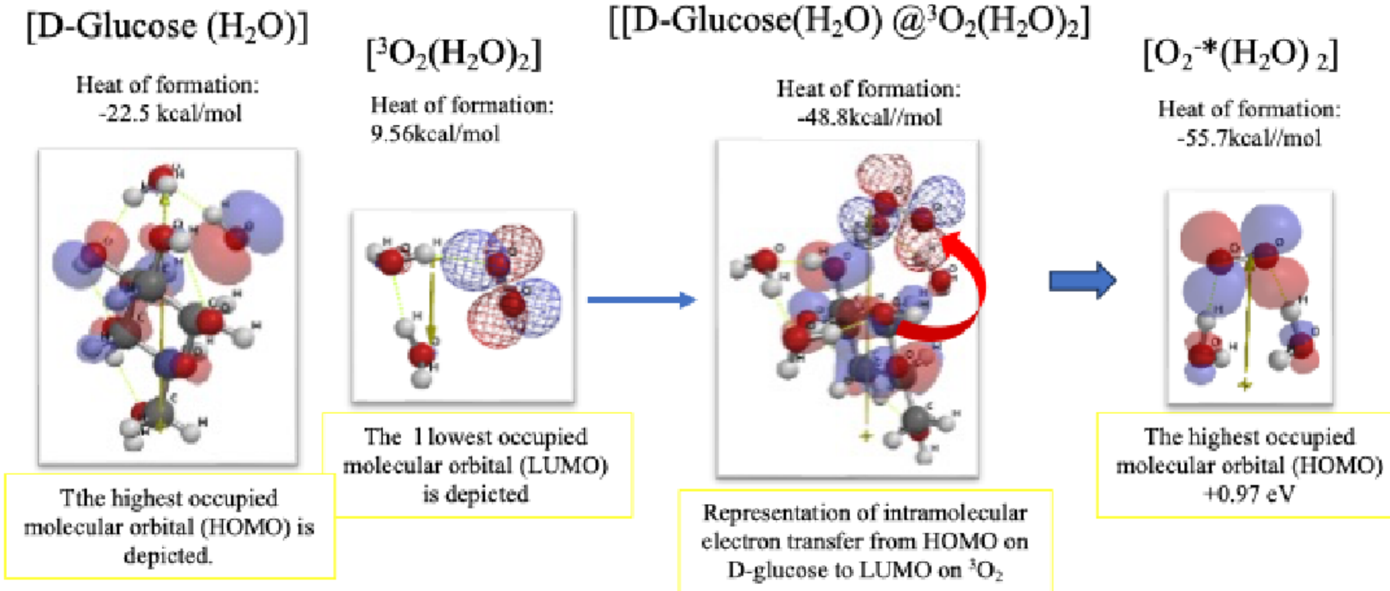


Figure 1. DFT/MM/Spartan-verified aggregation of hydrated triplet oxygen [$^3O_2(H_2O)_2$] and hydrated D-glucose [D-glucose (H_2O)]: Verification of exothermic generation of superoxide anion radical [O_2-*$(H_2O)_2$] via thermal intra-aggregate electron transfer in [D-glucose(H_2O)@[$^3O_2(H_2O)_2$]

The energy produced in the cellular engine mitochondria is not ATP but microwaves and radio waves

When chemical energy [$O_2^{-*}(H_2O)_2$] is generated in the mitochondrial endoplasmic reticulum (ER), it generates a high potential of +0.97 eV on the ER membrane. This results in the formation of an electric double layer in the ER membrane, which acts as a charge source for capacitive current. When a time change occurs in the ER's electric double layer electrode, the charge changes over time, resulting in the flow of capacitive current (AC) [3]. This generates AC across the lipid bilayer of the ER, generating microwave/radio frequency (MW/RF) energy. MW/RF energy is the same as far-infrared (IR) and far-infrared (FIR) energy. IR and FIR energy from the mitochondrial ER lipid bilayer can be understood as generating hot spots within the cells, which thermally drive metabolic reactions (Figure 2).

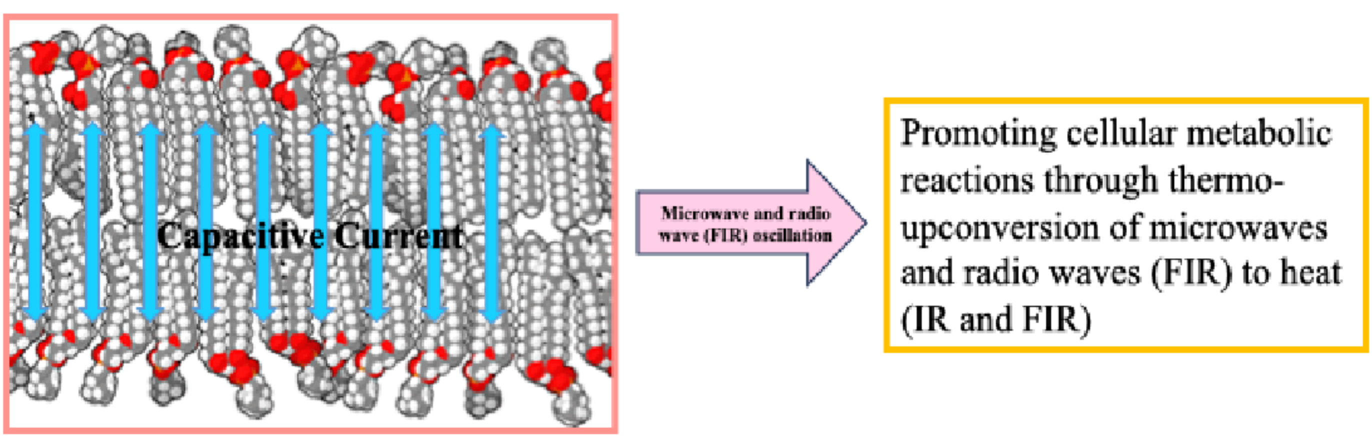


Figure 2. Heat (IR) generation process (thermo-upconversion) associated by microwave and radio wave and Radio wave to capacitive current generation (blue line) from superoxide anion radicals [O_2^-*$(H_2O)_2$] (Red circle) adsorbed on mitochondrial membrane bilayers.

This is the same mechanism as the thermo-upconversion mechanism in which microwave energy generated in a microwave oven creates hot spots in an aqueous solution, rapidly heating it [5].

Recently, it has beenmentioned in review articles that mitochondrial endoplasmic reticulum (ER) organization generates heat [6]. Furthermore, in biological and medical research, it is common knowledge that the energy source from mitochondria is ATP, and there are also reports that ATP is converted into heat. Figure 3 shows the energy structures of ATP, and ADP with $[O_2^{-*}(H_2O)_2]$.The potentials of the highest occupied molecular orbitals (HOMOs) of ATP and ADP are respective -5.77 eV and -5.72 V, which are much lower, than that of $[O_2^{-*}(H_2O)_2]$, so they will not produce capacitive current.

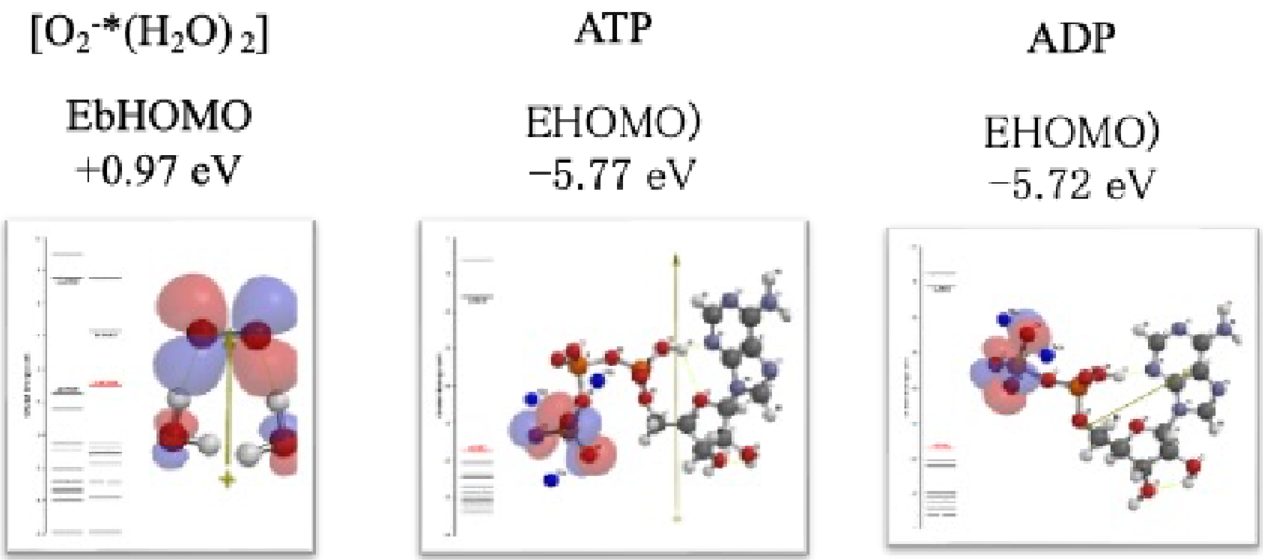


Figure 3. Highest occupied molecular orbital (HOMO) energy structures of $[O_2\text{-}^*(H_2O)_2]$, ATP and ADP

The root cause of aging will be as due to generation of hydroxyl radicals (HO*)in cells[7]

As people age, their physical activity decreases. We hypothesized that hydrated superoxide anion radicals $[O_2^{-*}(H_2O)_2]$ generated in the mitochondrial endoplasmic reticulum accumulate in mitochondria. Using DFT/MM/Spartan, we determined the equilibrium conformation of[$O_2^{-*}(H_2O)_2$]. We confirmed that the superoxide anion radical $[O_2^{-*}]$ undergoes a hydrogen abstraction reaction from the hydratirng water molecule $[H_2O]$, converting the water molecule into a hydrated hydroxyl radical [HO*], which thenalso gives rise to hydrated hydrogen peroxide $[HOOH(H_2O)_2]$ (Figure 4).

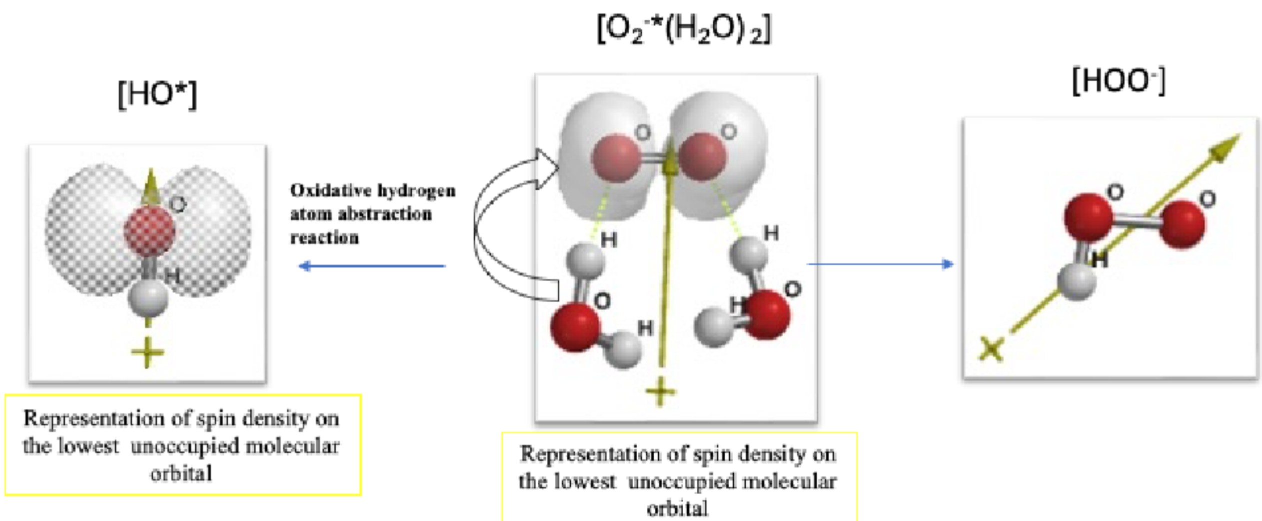


Figure 4. The process of generating [HO*] and $[HOO^-]$ by the oxidative intramolecular reaction at the spi ndensity site of the hydrated superoxide anion radical $[O_2\text{-}^*(H_2O)_2]$.

Furthermore, when the hydrated hydrogen peroxide [$HOOH(H_2O)_2$] is reduced by [$O_2^{-*}(H_2O)_2$], it gives [$HOOH(H_2O)_2$]$^{-*}$], and we learned that if [$O_2^{-*}(H_2O)_2$] will not be cousumed, the formation of [$HO^*(H_2O)_2$ will be enavitable in cells(Figure. 5).

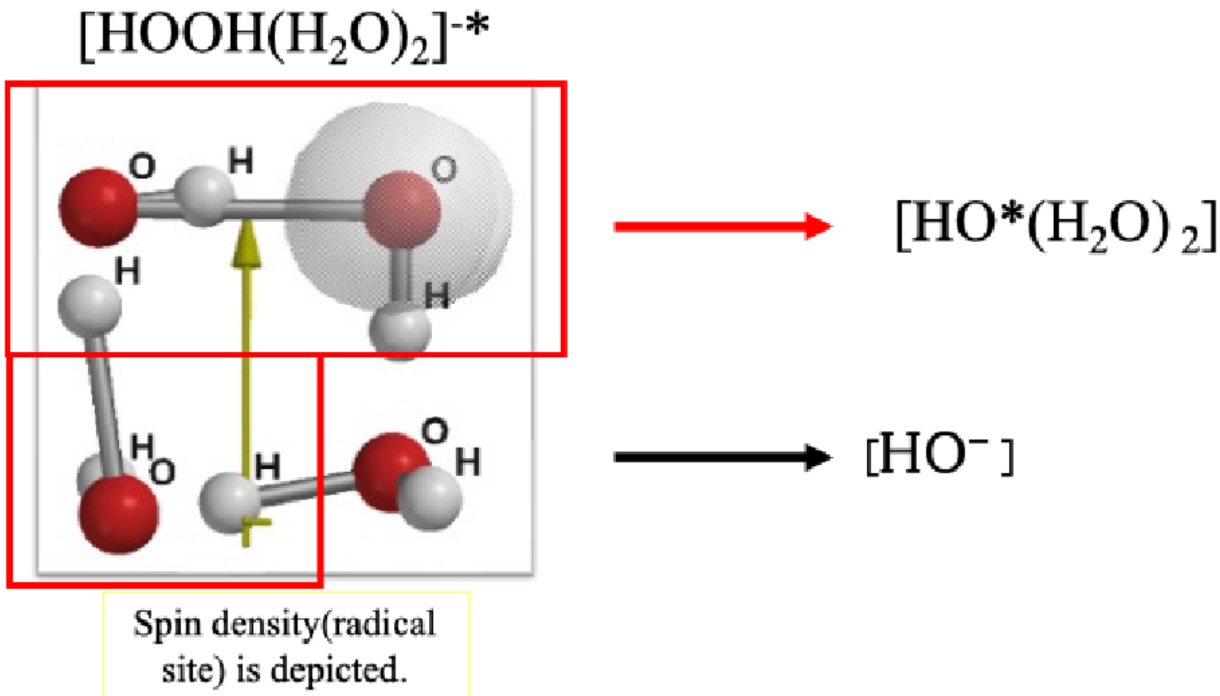


Figure 5. Hydrated hydrogen peroxide undergoes one-electron reduction to form [$HOOH(H_2O)_2$]$^{-*}$, which intramolecularly result in giving hydrated hydroxyl radical [$HO^*(H_2O)_2$].

Disease is caused by cellular aging. and then microorganisms lurking in aging cells cause disease [7]. The cell theory is a theory of disease origin proposed by Antoine Besham. We learned through social media that Pasteur, who believed that bacteria were the cause of disease, also agreed with the cell theory in his later years. Furthermore, we now predicted that cellular aging is due to the aging of mitochondria, the engine of cells, and that mitochondrial aging is due to the strong oxidizing power (EbLUMO=-3.61 eV) of the hydrated hydroxyl radical [$HO^*(H_2O)_2$](Figure 6).

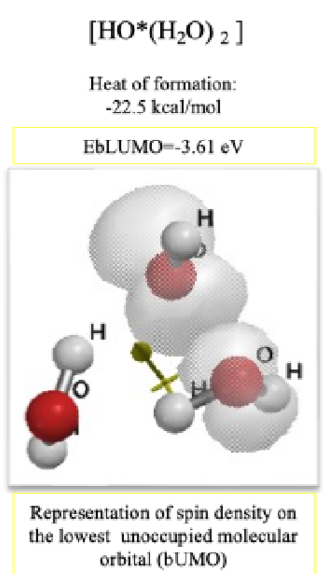


Figure 6: Equilibrium geometry and energy structure of hydrated hydroxyl radical [$HO^*(H_2O)_2$

The structural destructive oxidation reaction of the mitochondrial endoplasmic reticulum lipid bilayer membrane by association with hydrated hydroxyl radical [HO*](H_2O)₂].

Hydrated hydroxyl radicals [HO*(HO)₂] associate with mitochondrial lipid bilayers via carboxylic acid groups. For the complex of a hydroxyl radical [HO*(HO)₂] with a lauric acid trimer [n-C_{11}COOH]₃], a model of the mitochondrial endoplasmic reticulum membrane, we attempted to analyze the single-point energy (SPE) structure [SPE[n-C_{11}COOH)₃@ HO*](H₂O)₂] and its stable equilibrium structure (EQG[n-C_{11}COOH)₃@ HO*(H₂O)₂] using DFT/MM/Spartan. The initially formed aggregate [SPE[n-C_{11}COOH)₃@HO*(H₂O)₂] does not undergo significant structural changes. However, surprisingly, we found that the equilibrium geometry (EQG[n-C_{11}COOH)₃@HO*H₂O)]undergoes significant structural changes (Figure 7).

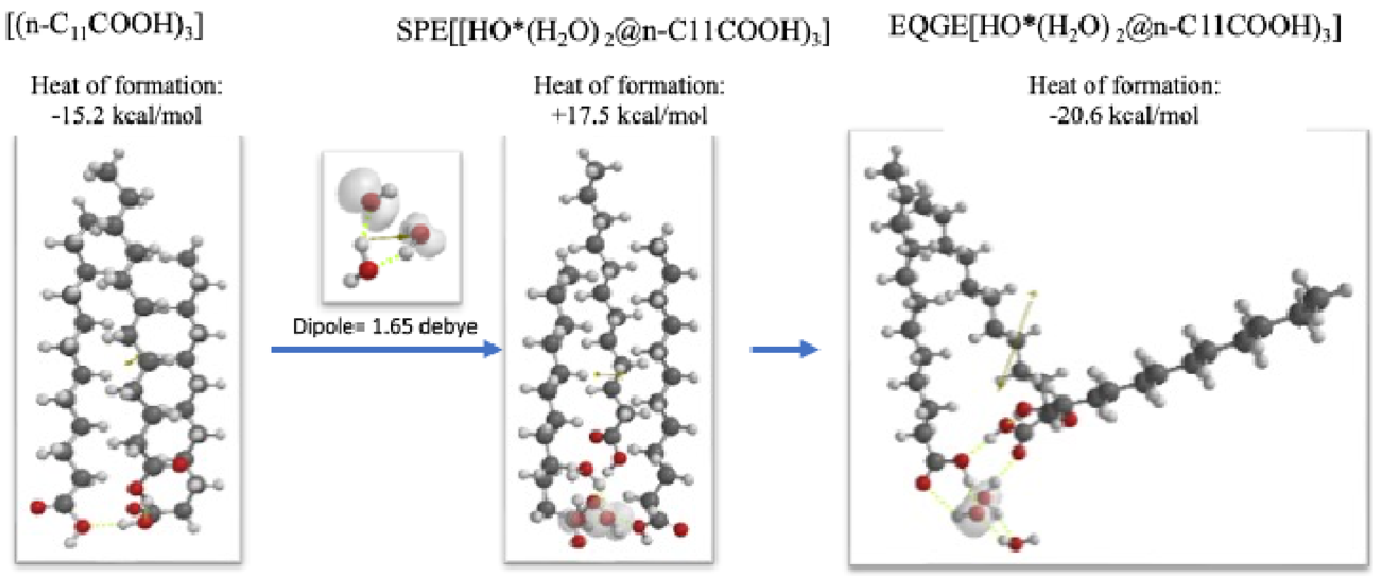


Figure 7. Structure of the complex between the mitochondrial lipid bilayer model molecule lauric acid trimer [n-C_{11}COOH)$_3$] and the hydrated hydroxyl radical [HO*(H_2O) $_2$]; [A] Single-point energy equilibrium structure SPE [HO*(H_2O) $_2$@n-C_{11}COOH) $_3$]; [B] Equilibrated three-dimensional structure EQG [HO*(H_2O) $_2$@n-C_{11}COOH) $_3$]

Furthermore, we found that this association reaction is an exothermic oxidation reaction (heat of formation = -20.6 kcal/mol). This equilibrium geometry was confirmed to result from the strong interaction of the hydrogen atoms near the terminal carboxyl groups of the fatty acids with the hydroxyl radical [HO*(H₂O)₂], disrupting the molecular arrangement that maintains the membrane structure, resulting in the destructive expansion of the mitochondrial body membrane.

When changes occur in the lipid bilayer structure of the mitochondrial endoplasmic reticulum, capacitive current generation decreases, inhibiting the smooth generation of heat energy from mitochondria. Assuming that an average cell is composed of 1,000 mitochondrial endoplasmic reticulum [6], destruction of the mitochondrial membrane structure by hydroxyl radicals leads to cell enlargement. Cell enlargement is a state of cellular aging, and the 6 μm-sized cancer cells (circulating tumor cells) collected from Taro Shirakawa's cancer patient are also senescent cells with enlarged mitochondria due to damaged mitochondria.

The pharmacological effect of iodine in cancer treatment reported by Schachter and Shirakawa is its excellent antioxidant effect against hydroxyl radicals as iodide ions [I-] in cells.

Iodine molecules [I2] react with water to form iodide ions and hypoiodite ions, forming a colorless, transparent solution. Lugol's solution and Polydone solution containing iodine also gradually decompose into water, turning from brown to colorless. This cpalor change can be verified by a series of UV/Vis spectra and the heat of formation of the equikibrium geometry of hydrated iodine [I_2(H_2O)] molecula-modeled using DFT/MM/Spartan. The following chemical formulas show the exothermic reaction process in which iodine hydrate [I_2(H_2O)₂] undergoes intramolecular disproportionation to form intermediates [I- I+ (H_2O)₂], [HI@IOH @H_2O], and then [HI(H_2O)₂] and [IOH(H_2O)₂], resulting in a brown to colorless solution.

[I_2(H_2O)₂] (heat of formation: -8.25 kcal/mol brown) (Figure 8) → [I- I+ (H_2O)₂)] → [HI@IOH @H_2O] (heat of formation: -17.6 kcal/mol colorless) (Figure 9) → [HI(H_2O)₂] (heat of formation: -18.3 kcal/mol colorless) + [IOH(H_2O)₂] (heat of formation: -20.3 kcal/mol colorless).

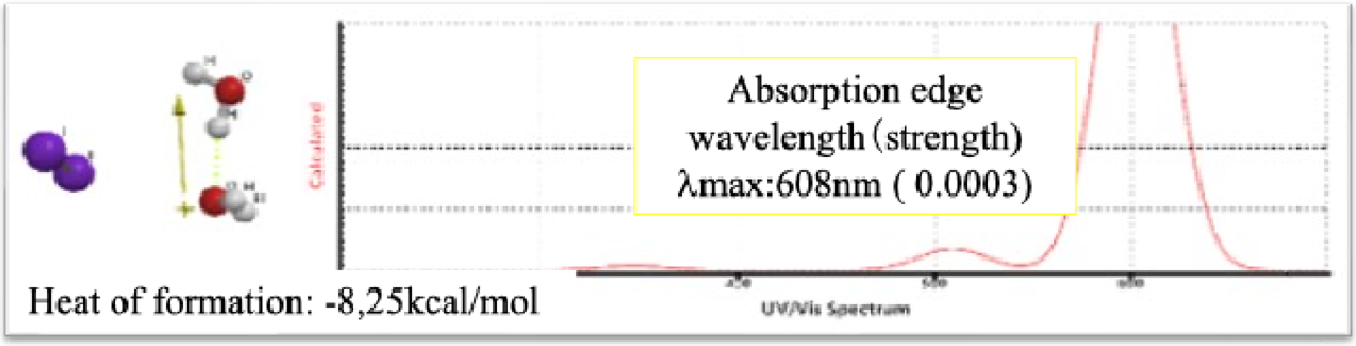


Figure 8. Equilibrium geometry of hydrated iodine [$I_2(H_2O)_2$]: Heat of formation and UV/Vis spectrum

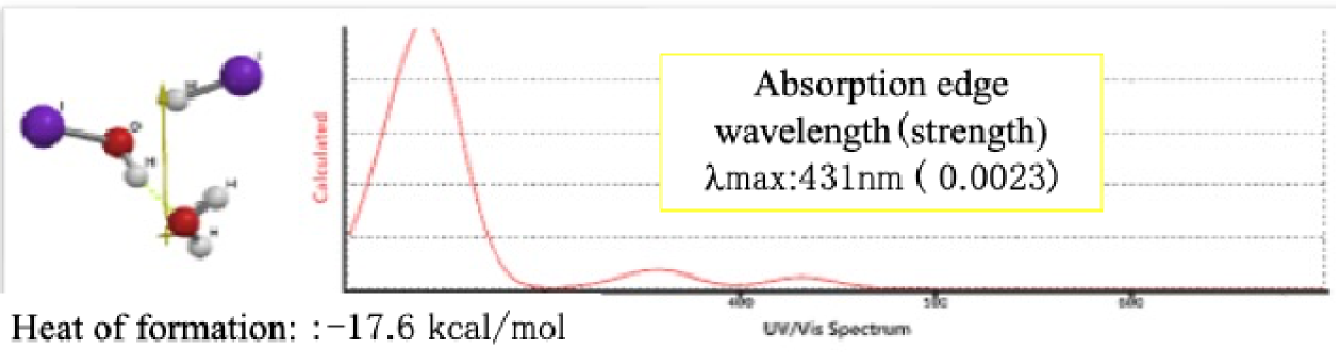


Figure 9. Equilibrium geometry of HI @ IOH@H2O predicted to form slowly from hydrated iodine [$I_2(H_2O)_2$]: Heat of formation and UV/Vis spectrum

Potassium iodide [KI], hydrogen iodide [HI], and hydrated hypoiodous acid [IO] react exothermically with hydrated hydroxyl radicals [$HO^*(HO)_2$] to give the aggregates [$KI@HO^*(HO)_2$] and [$HI@HO^*(H_2O)_2$ [$IOH@HO^*(H_2O)_2$], respectively. By examining the spin density (radical site) on the hydroxyl radical in each equilibrium conformation, we found that the spin density (radical density) localized on the oxygen atom in the vicinity of the hydroxyl radical, which verifies its oxidizing power as a radical, is delocalized on the iodine atom in [$KI@HO^*(H_2O)_2$] and [$HI@HO^*(HO)_2$ [$IOH@HO^*(H_2O)_2$]. This proves that [KI], [HI], and [IOH] are extremely effective antioxidants that react with hydroxyl radicals to weaken their oxidative power to abstract hydrogen atoms (Figure 10).

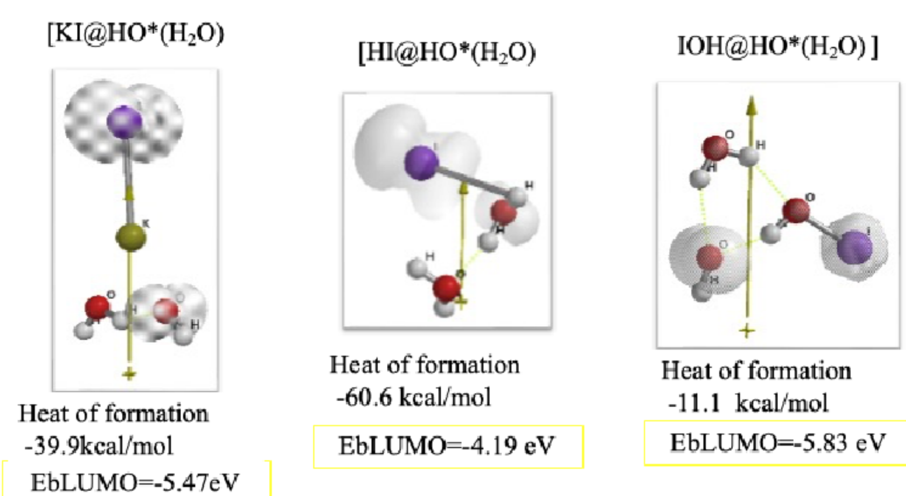
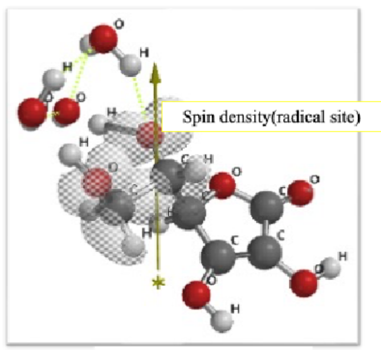


Figure 10. Distribution of radical (spin density) sites in [$KI@HO^*(H_2O)$], [$HI@HO^*(H_2O)_2$, $IOH@HO^*(H_2O)$]

Linus Carl Pauling, the father of modern chemistry, advocated taking vitamin C as a health regimen, and the common knowledge that "taking vitamin C will cure a cold" became widespread. Using DFT/MM/Spartan, we now can verify that vitamin C (ascorbic acid) also reacts exothermically with hydrated hydroxyl radicals [[HO*$(H_2O)_2$] to give the equilibrium 3D structure [ascorbic acid @HO*$(H_2O)_2$] (Figure 11).

[ascorbic acid @HO*@$(H_2O)_2$]



Heat of formation
-55.3 kcal/mol

Figure 11. Equilibrium geometry of vitamin C (ascorbic acid) associated with hydrated hydroxyl radical [ascorbic acid @HO*@$(H_2O)_2$]: Spin density (radical site) and heat of formation.

It was verified that in vitamin C (ascorbic acid) aggregates [ascorbic acid @HO*@$(H_2O)_2$], the spin density (radical site) near the hydroxyl radical is delocalized to the central oxygen molecule of ascorbic acid, resulting in the loss of hydrogen abstraction oxidizing power at the radical site. In other words, this vitamin C contributes to maintaining mitochondrial activity as an antioxidant molecule.

Conclusions

Cancer cells exhibit enlarged shapes due to the aging of the cellular engine mitochondria. The function as engine can be rationalized as due to the generation of microwave and radio frequency energy, i.e., thermal energy. The hydroxyl radical-caused mitochondria damaged cell nevermaintainers healthy metabolic reactions in cells.The production of hydroxyl radicals comes from aging due to lack of exercise. Antioxidants against hydroxyl radicals act as activators of mitochondrial function.

Iodine therapy for cancer relies on the antioxidant power of iodide ions within cells. Iodide ions eliminate the oxidative power of hydroxyl radicals and maintain cellular metabolic reactions by generating heat energy in the mitochondrial endoplasmic reticulum. Maintaining mitochondrial activity is essential for preventing all kinds of diseases and maintaining good health.

Lastly,we would like to add that our research based on DFT/MM/Spartan has been honored by Scholar GPS as a 2025 Highly Ranked Scholar [7, 8].

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Cite this article: Shozo Yanagida*, Noriyuki Murakami, Juro Nakagawa. (2026) Prediction, validation, and learning for mitochondrial-damaged tumor cells. Advance Medical & Clinical Research. 7 (1): 255-261.