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IN SILICO DEMONSTRATION OF ANTI-AGING WITH THE USE OF RESVERATROL ASSOCIATED WITH NITROGEN BASES APPLYING QUANTUM CHEMISTRY

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ABSTRACT

Resveratrol (RVT) is a well-known polyphenolic compound in several plants, including grape seeds, peanuts, and other food sources such as wine. RVT is quite famous for its association with various health benefits such as anti-obesity, neuro-protective cardioprotective, anti-tumor, anti-diabetic, antioxidant, anti-aging effects, and glucose metabolism. Hyperchem software was used as a quantum chemistry simulator. The fundamental basis of quantum calculations was the Electron Transfer Coefficient (ETC) theory. As a result of these calculations, it is observed that the RVT is located at the bottom of the well. This location leads us to infer that RVT is a long-acting substance; due to this location, the biological organism cannot quickly eliminate this substance. Another finding shows us that this molecule presents a quantum superposition of HOMO and LUMO. This quantum property infers that the RVT forms spheres or micelles naturally. RVT is an excellent antioxidant for nitrogenous bases (BN).

KEYWORDS: Resveratrol, Anti-aging, Quantum Chemistry, Nitrogen Bases, Anti-inflammatory.

INTRODUCTION

Resveratrol

Resveratrol (RVT) is a well-known polyphenolic compound in several plants, including grape seeds, peanuts, and other food sources such as wine. RVT is famous for its association with various health benefits such as anti-obesity, neuroprotective cardioprotective, anti-tumor, anti-diabetic, antioxidant, anti-aging effects, and glucose metabolism. Notably, RVT has been reported to have promising therapeutic properties in various types of cancer, neurodegeneration, and atherosclerosis. These therapeutic properties are regulated by several synergistic pathways that control oxidative stress, cell death, and inflammation, providing reassurance about its potential benefits.[1]

RVT was first isolated from the roots of white hellebore (Veratrum grandiflorum O. Loes) in 1940.[7] RVT modulates mitochondrial function, redo biology, and dynamics in both in vitro and in vivo experimental models. RVT attenuates mitochondrial deterioration induced by unavoidable stressors.[4]

Chemistry of resveratrol

RVT belongs to the polyphenol family and is extracted from many natural plants. This molecule is susceptible to degradation and can undergo chemical changes during food processing. Therefore, researchers have paid more attention to various aspects of RVT, including anti-aging, antioxidant, and anti-cancer activity.[5]

Aging

Aging decreases cellular biological functions and increases the risk of age-related diseases such as cancer, type 2 diabetes mellitus, cardiovascular diseases, and neurological disorders. These pathologies are commonly classified as age-related diseases affecting life expectancy and health. Aging is a complex and sophisticated biological process that involves damage to biochemical macromolecules, including DNA, proteins, and cellular organelles such as mitochondria. Aging causes multiple alterations in biological processes, including energy metabolism and nutrient sensing. These two alterations reduce cell proliferation and cause cellular senescence.[7]

Hallmarks of aging are genomic instability, telomere attrition, epigenetic changes, loss of proteostasis, dysregulated nutrient sensing, mitochondrial dysfunction, cellular senescence, stem cell exhaustion, and altered intercellular communication. These are considered general

aging factors and phenotypes that occur during normal aging. Experimental deterioration of these factors accelerates aging, while attenuation delays it.[8]

Relationship of RVT with aging

RVT is a significant compound in preventing and treating aging and age-related diseases. Researchers have highlighted its crucial role in the treatment of aging, emphasizing its ability to suppress oxidative stress, inhibit the inflammatory response, improve mitochondrial function, and modulate apoptosis. This information enlightens the audience about the potential of RVT in aging research.[8]

Among polyphenolic phytochemicals, some scientists believe that RVT reduces the adverse effects of the aging process through its multiple biological activities. RVT increases the lifespan of several model organisms by regulating oxidative stress, energy metabolism, nutrient sensing, and epigenetics. This compound activates sirtuin one and increases life expectancy.[9]

RVT is a critical player in the battle against aging. By regulating nutrient sensing (NAD+ sensing) and mitochondrial function and controlling cellular senescence, cancer cell proliferation, apoptosis, and inflammation, RVT effectively slows down the aging process. Numerous studies have confirmed its conventional results in phytochemical research, providing molecular markers of age-related diseases, such as antioxidant activity. Reassure the audience about the potential benefits of RVT.[9]

RVT associated with diseases

Amidst numerous studies that highlight the benefits of RVT on the cardiovascular system, diseases such as diabetes, and longevity, there is a prevailing sense of promise. While some authors caution against equating in vitro and in vivo studies, the consensus is that RVT, due to its high tolerance, is a promising compound for preventing various diseases, including diabetes and its complications. The only hurdle is its low bioavailability and solubility.[3]

RVT crosses the blood-brain barrier and exerts its antioxidant effect by improving the metabolic functions of antioxidant enzymes. The RVT participates in Sirtuin (SIRT1)-mediated lifespan extension activity. RVT has reduced glial activation and helped increase hippocampal neurogenesis.[10] RVT shows significant antibacterial effects against foodborne pathogens (Listeria et al. aureus and E. coli) by inhibiting an electron transport chain (ETC)

and F0F1-ATPase. RVT decreases cellular energy production, which leads to the spread of pathogens.[1]

MATERIAL AND METHODS

Computational quantum chemistry, specifically the Hyperchem software, was used in addition to other simulators. The most crucial methodology was the calculation of the ETC. This methodology consists of calculating the HOMO and LUMO of both RVT and the human NB. The electrostatic potential is also calculated, and the absolute difference value of the HOMO-LUMO results in the bandgap. The difference in the absolute value of the negative and positive electrostatic potential is equal to the potential difference. Then, the HOMO-LUMO difference is divided by the electrostatic potential difference. In this way, the electron transfer coefficient is obtained.

Table 1: Quantum equations.

Bg = |HOMO-LUMO|	*Equation 1*
EP = |-E-(+E)|	*Equation 2*
ETC = Bg/EP	*Equation 3*
Where: *HOMO = Highest occupied molecular orbital.* *LUMO = Lowest energy unoccupied orbital.* *EP = Electrostatic Potential.*	*-E = Negative electron density.* *+E = Positive electron density.* *Bg = Prohibited Band. Band gap.* *ETC = Electron transfer coefficient.*

Nuclear magnetic resonance simulation was used to obtain the first moment of attraction between molecules. The second moment of the molecular interaction was obtained by drawing HOMO and LUMO.

Figure 1 shows the positions of the quartiles of the ETC values in the quantum well. The ETCs of the molecular interactions located at the bottom of the well have greater chemical affinity. In contrast, the molecular interactions located as supernatants in the quantum well have the weakest affinity. The oxidative molecular interactions are on the right side, and the reducing or antioxidant ones are on the left.[17-21]

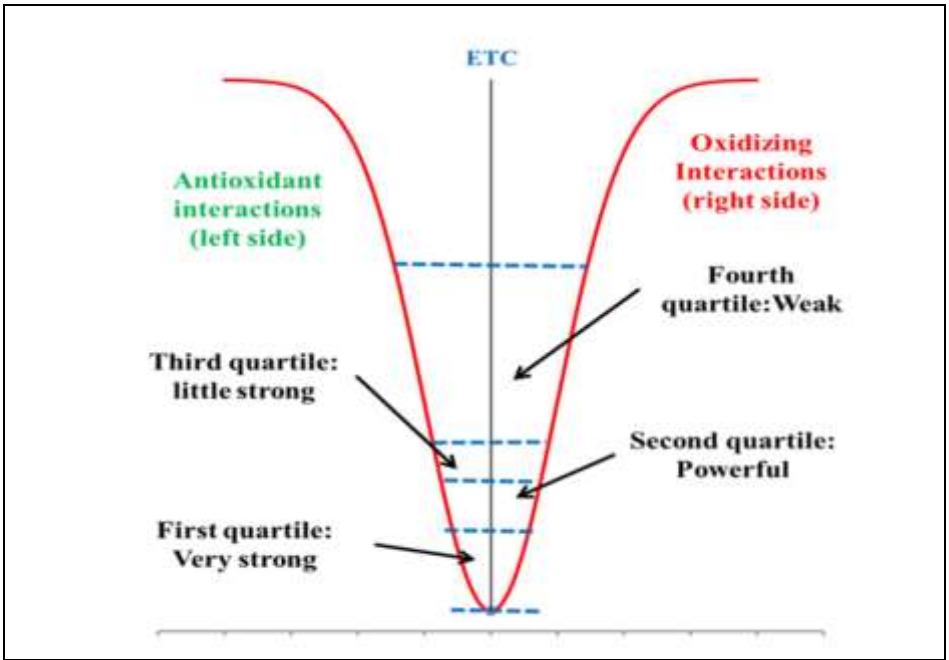


Fig. 1: Quantum well. Interpretation of interactions in the four statistical quadrants.

RESULTS AND DISCUSSION

Classic characterization

Figures 2 and 3 show the results of the simulated characterization of Nuclear Magnetic Resonance H^1 and C^{13} and their scientific names according to the RVT's UIPAC.

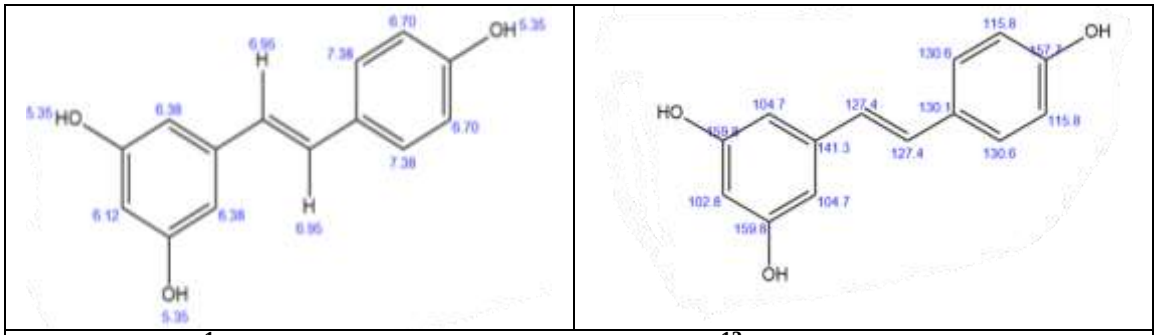


Fig. 2: Left H^1 nuclear magnetic resonance; right C^{13} nuclear magnetic resonance.

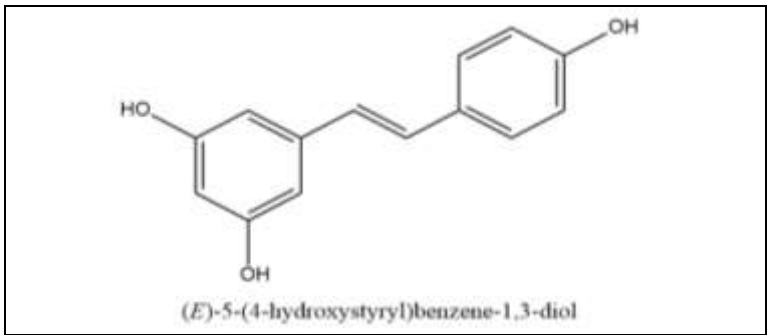


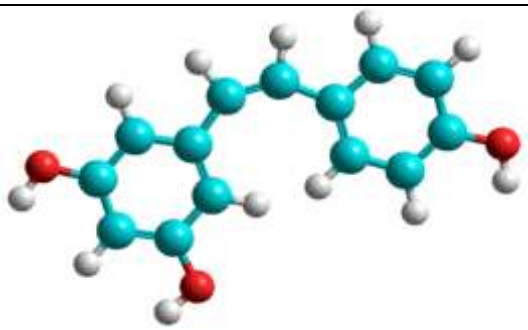
Fig. 3: Scientific name of RVT according to IUPAC.

The most unprotected protons are located at a value of 7.38 ppm, while the most unprotected carbons are located at a value of 159.8 ppm.

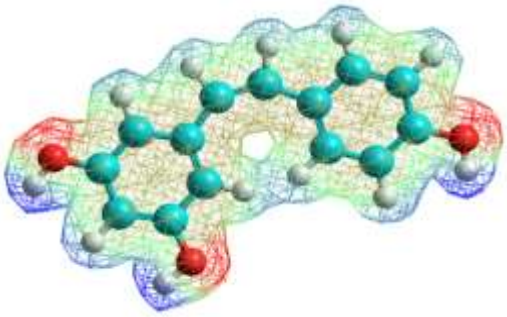
These atoms with these values are the most unstable in the face of a nucleophilic attack.

Quantum characterization

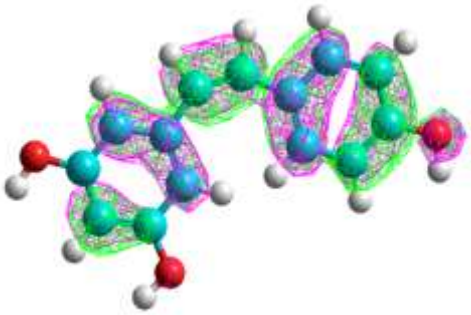
Figure 4 represents the RVT molecule characterized by the different quantum concepts. This molecule presents a quantum superposition of HOMO and LUMO. This quantum property infers that it has spheres or micelles.



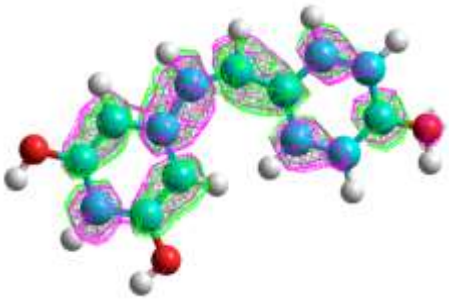
A. RVT. Hyperchem



B. RVT. Potencial Electrostático, -E = -0.005 eV/a°; +E = 0.194 eV/a°.



C. RVT. HOMO. -8.507854 eV



D. RVTT. LUMO. -0.6543006 eV

Fig. 4: Quantum characterization. A) Cyan = C; White = H; Red = O; B) Electrostatic Potential; C) HOMO; D) LUMO.

In Table 2, the ETCs are ordered according to the quantum well. The RVT is located at the bottom of the well. This location suggests that RVT is a long-acting substance that cannot be eliminated quickly by the body.

Table 2: ETC of pure substances AAs and RVT.

N	Reducing agent	Oxidizing agent	HOMO	LUMO	BG	E-	E+	EP	ETC
21	Val	Val	-9.914	0.931	10.845	-0.131	0.109	0.240	45.188
20	Ala	Ala	-9.879	0.749	10.628	-0.124	0.132	0.256	41.515
19	Leu	Leu	-9.645	0.922	10.567	-0.126	0.130	0.256	41.279
18	Phe	Phe	-9.553	0.283	9.836	-0.126	0.127	0.253	38.879

17	Gly	Gly	-9.902	0.902	10.804	-0.137	0.159	0.296	36.500
16	Ser	Ser	-10.156	0.565	10.721	-0.108	0.198	0.306	35.037
15	Cys	Cys	-9.639	-0.236	9.403	-0.129	0.140	0.269	34.956
14	Glu	Glu	-10.374	0.438	10.812	-0.111	0.201	0.312	34.655
13	Ile	Ile	-9.872	0.972	10.844	-0.128	0.188	0.316	34.316
12	Thr	Thr	-9.896	0.832	10.728	-0.123	0.191	0.314	34.167
11	Gln	Gln	-10.023	0.755	10.778	-0.124	0.192	0.316	34.108
10	Asp	Asp	-10.370	0.420	10.790	-0.118	0.204	0.322	33.509
9	Asn	Asn	-9.929	0.644	10.573	-0.125	0.193	0.318	33.249
8	Lys	Lys	-9.521	0.943	10.463	-0.127	0.195	0.322	32.495
7	Pro	Pro	-9.447	0.792	10.238	-0.128	0.191	0.319	32.095
6	Trp	Trp	-8.299	0.133	8.431	-0.112	0.155	0.267	31.577
5	Tyr	Tyr	-9.056	0.293	9.349	-0.123	0.193	0.316	29.584
4	His	His	-9.307	0.503	9.811	-0.169	0.171	0.340	28.855
3	Met	Met	-9.062	0.145	9.207	-0.134	0.192	0.326	28.243
2	RVT	RVT	-8.508	-0.654	7.854	-0.085	0.194	0.279	28.149
1	Arg	Arg	-9.176	0.558	9.734	-0.165	0.199	0.364	26.742

In Figure 5, the scheme on the left represents the antioxidant interaction of RVT with nitrogenous bases. The center diagram represents the oxidative interaction of RVT with BN, and the diagram on the right represents the interactions of the BN combined in DNA and RNA. The Y axis indicates the ETC of each interaction. The diagram on the left looks a little lower than the one on the right. This observation leads us to predict that RVT is a better antioxidant than an oxidant of nitrogenous bases.

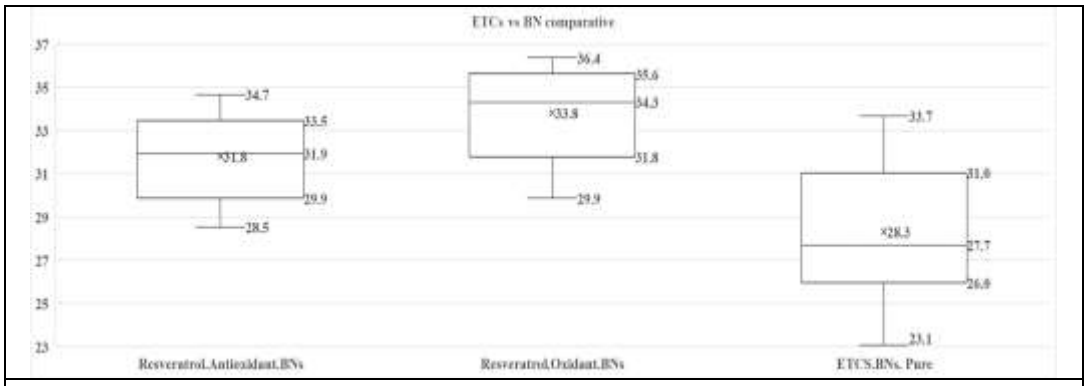


Figure 5: Whisker diagrams of the CTEs of quantum-chemical interactions.

CONCLUSIONS

Aim

Demonstrate the use of RVT in aging associated with BN through quantum chemistry.

Thesis

The diagram (Fig. 5) shows the quantum chemical interactions. This diagram leads us to predict that RVT is a better antioxidant than an oxidant of BN.

Corollary

In an unexpected turn, we discovered that RVT is located at the bottom of the well. This surprising finding leads us to infer that RVT is a long-acting substance, making it resistant to easy elimination by the biological organism.

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Conflict of interests

There is no conflict of interest between our universities.

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